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6000

HIGHLY SENSITIVE TARGETS FOR DIAGNOSIS AND SPECIATION OF HUMAN LEISHMANIASIS

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Leishmaniasis, caused by various species of the *Leishmania* parasite, remains a significant public health concern in many parts of the world. Accurate and efficient diagnostic methods are crucial for timely intervention and management. The limitations of current diagnostic approaches necessitated the exploration of novel targets and tools. Through bioinformatic analysis of highly repeated elements in satellite regions of all Leishmania spp. genomes followed by PCR validation, CL3 and CL179 were identified as novel qPCR targets that were predicted to amplify all known Leishmania spp. Pathogenic to humans. The limits of detection for CL3 and CL179 qPCRs were consistently below 150 fg of gDNA - equivalent to fewer than ~5 copies of the haploid genome across all available Leishmania species known to infect humans (*L. aethiopica, L. amazonensis, L. braziliensis, L. chagasi, L. donovani, L. guyanensis, L. infantum, L. major, L. mexicana, L. panamensis* and *L. tropica*). The CL3 and CL179 qPCRs each reliably detected a single infected macrophage, using in vitro infected murine macrophages. Both CL3 and CL179 demonstrated high specificity, showing no cross-reactivity with other related parasitic intracellular protists. When tested with DNA extracted from skin biopsies from patients confirmed positive for leishmania infection by 18S qPCR (n=8), both CL3 and CL179 exhibited 100% sensitivity. Swabs and/or microbiopsies from a subset of these patients were also qPCR positive. Subsequently, we adapted the CL179 qPCR for use in recombinase polymerase amplification (RPA). The RPA amplicons were analyzed by Nanopore™ sequencing, resulting in the identification of species-specific SNPs and indels that enabled accurate parasite speciation in patients confirmed to have leishmaniasis (n=6). Our methodology provides an ultrasensitive one step approach to the rapid diagnosis and subsequent speciation of all known human Leishmania species.

6001

THE ROLE OF LIPIDS AS POTENTIAL BIOMARKERS OF DISEASE PROGRESSION AND THERAPEUTIC RESPONSE IN PATIENTS WITH CHRONIC *TRYPANOSOMA CRUZI* INFECTION

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Chagas disease, caused by the parasite *Trypanosoma cruzi*, is a zoonosis that affects more than 7 million people, mostly in Latin America, and represents an increasingly serious public health concern in the United States, Western Europe, Australia and Japan. Gaps in the understanding of the disease pathogenesis prevent the development of novel tools for diagnosis, prognosis and evaluation of treatment response, making the study of practical outcomes in clinical trials challenging; and hindering the approval of new therapies. The infection is known to disrupt several host metabolic pathways, and lipid metabolism is considered essential for parasite survival, providing an opportunity for the identification of biomarkers. The metabolomic and lipidomic profile of a cohort of eight symptomatic and 20 asymptomatic patients with *T cruzi* infection and a group of 15 uninfected controls was studied using liquid chromatography/mass spectrometry. All infected participants were tested for detectable parasitaemia using qPCR before and after receiving treatment. Differences between all groups were analyzed using a covariate-adjusted multiple linear regression, and changes before and after receiving treatment with benznidazole were evaluated using paired t-tests. Significance values were adjusted for multiple comparisons using the Benjamini-Hochberg's method. We studied the abundance of over 2,600 metabolites, identifying two phosphatidylethanolamines and one saturated fatty acid able to discriminate between symptomatic and asymptomatic participants. Additionally, three closely-related and possibly parasite-derived sphingolipids showed significant reductions in their abundance following treatment with benznidazole, reaching levels similar to those observed in uninfected controls, and among patients with no evidence of treatment failure. Pending further validation, these molecules represent potentially useful biomarkers to monitor cardiovascular damage and therapeutic response in patients with chronic *T. cruzi* infection.

6002

DEVELOPMENT OF A CRISPR-LAMP BASED BIOSENSOR WITH A LATERAL FLOW READOUT FOR THE DETECTION OF CUTANEOUS LEISHMANIASIS

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Cutaneous Leishmaniasis (CL) constitutes a significant public health challenge, particularly in resource-limited regions where it is endemic and where the lack of rapid and accurate diagnostic tools often leads to delayed treatment and increased morbidity. Conventional diagnostic methods for these NTDs are often time-consuming, expensive, and require specialized equipment, which limits their utility in remote areas. Therefore, there is an urgent need to develop an efficient, cost-effective, and user-friendly diagnostic tool for the early detection of CL. This study was aimed at the development of a Crispr-Lamp based diagnostic platform with a lateral flow readout for the detection of CL. A Loop-mediated isothermal amplification (LAMP) assay with primers targeting the unique CL conserved A2 gene were developed and optimized. The limit of detection and sensitivity were evaluated using 108 PCR PCR confirmed clinical samples (88 positives and 22 negative samples). A CRISPR-Cas12a system assay for molecular detection of Leishmania spp targeting the small subunit ribosomal ribonucleic acid (SSU rRNA) was then developed. The limit of detection and sensitivity were also evaluated using the 108 clinical samples. The two assays were then integrated with visual detection by lateral flow test strip. The limit of detection for both the Lamp test and the Crispr-cas test as well as the combined platform was found to be $1.0x10^3$ parasites/ml. The LAMP test had a sensitivity of 81.4% (70/86) and a specificity of 100% (22/22) whilst the Crispr Cas 12 assay had a sensitivity of 86.0% (74/86) and a specificity of 100% (22/22). Combined, the Crispr Lamp assay had a sensitivity of 98.8% (85/86) and a specificity of 100% (22/22). We show the development of a Crispr-Lamp platform with high sensitivity and specificity for the detection of cutaneous Leishmaniasis. With an integration of a heating platform, this could be adapted for use in remote endemic communities for the detection of CL.

6003

DEVELOPMENT AND CLINICAL VALIDATION OF LEISHID, A LAMP-BASED SPECIES-SPECIFIC *LEISHMANIA* DETECTION TOOL FOR THE MOLECULAR DIAGNOSIS OF LEISHMANIASES

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Point-of-care (PoC) molecular differential diagnostic tests for the detection and identification of *Leishmania* species are urgently needed, influencing effective treatment and avoiding misdiagnosis of leishmaniases, a neglected tropical disease threatening 1 billion people living at risk of infection. Recent reports reveal the presence of dermotropic-associated species, causing visceral leishmaniasis (VL) and vice-versa. Thus, a test able to concomitantly identify the *Leishmania* species is important to better understand the epidemiology and physiopathology of leishmaniases. In this regard, we developed the LeishID, a LAMP-based molecular tool able to detect small quantities of parasite DNA and differentiate among *L. amazonensis*, *L. infantum*, and *L. braziliensis*, the main species occurring in Brazil. The probes were designed based on a *Leishmania* pangenome approach, where species-specific DNA sequences were filtered from the accessory genome. The loop-mediated isothermal DNA amplification (LAMP) reaction result is detected by the naked eye using a pH-sensitive colorimetric sensor. Depending on the target, positive reactions can be detected as soon as 15 min at 65 ºC. The LAMP test was able to detect as low as 1 pg of extracted Leishmania DNA for all tested species. Species-specific sets of primers were able to detect the species they were designed for without cross-reactivity among them, neither on mammalian DNA. Clinical validation using spleen biopsies of dogs with VL, samples derived from skin lesions of cutaneous leishmaniasis from human patients, and Phlebotominae sandflies, revealed sensitivity varying from 93-98% and specificity of 90-100%. To meet PoC requirements, we selected a boiling/spin DNA extraction method able to amplify L. infantum DNA derived from skin biopsies. Additionally, we are developing a CRISPR/Cas-based PoC diagnostic tool for one-pot reaction with high sensitivity and specificity for *Leishmania* DNA detection. In this sense, LeishID is a PoC-compatible solution for rapid, accurate, and sensitive detection tool to differentiate Leishmania species in clinically relevant concentrations.

6004

NEW STRATEGY FOR THE OPTIMIZATION OF TAQMAN QPCR FOR *ENTAMOEBA HISTOLYTICA* BY DROPLET DIGITAL PCR

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Taqman-probed quantitative PCR (Taq-qPCR) is considered as high diagnostic value for amebiasis. However, there are variations in methodology among institutions. Furthermore, the absence of a clear cutoff value for cycle threshold (Ct) leads to numerous low-titer positives, complicating result interpretation. Here, we developed a new strategy evaluating amplification efficacy of primer-probe set of Taq-qPCR using droplet digital PCR (ddPCR). Twenty one primer-probe sets, which targeting small subunit ribosomal RNA gene region (X64142), were designed according to the previous reports. Amplification efficacy of primer-probe set was evaluated by absolute positive droplets (APD) counts and average amplitude of APDs in ddPCR. Firstly, we compared the amplification efficacy using laboratory strain of *Entamoeba histolytica* (HM1:IMSS strain) and ddPCR with low annealing temperature (AT) (59℃). Amplification efficacy is the same extent by different primer-probe sets at high PCR cycles (35-50 cycles). However, it was clearly differentiated by lower cycles (minimum 25 cycles), in which seven primer-probe sets showed high amplification efficacy. Among them, only two primer-probe sets maintained amplification efficiency on the higher AT (62℃). Thereafter, the correlation curve between APD counts (ddPCR by 50 cycles) and Ct value (Taq-qPCR) were made by the titration of HM1:IMSS templates, which determined cut-off Ct value as 35 cycles in Taq-qPCR. Thereafter, we performed ddPCR (50 cycles) and Taq-qPCR using clinical samples. Interestingly, in some cases, we found that unexpectedly higher number of APD counts with low average amplitude of APDs from the sample with high Ct value (>35 cycles by Taqman qPCR), which indicating that higher Ct value than cutoff was caused by the non-specific amplification in the templates extracted from fecal samples. The causative agent producing non-specific amplification is currently under investigation. Droplet digital PCR (ddPCR) visually and quantitatively evaluates and optimizes primer-probe sets for Taq-qPCR, ensuring accurate *E. histolytica* detection and highlighting false-positive risks.

6005

CHARACTERIZATION OF THE LEISHMANIN SKIN TEST ANTIGEN AS A BIOMARKER OF VACCINE EFFICACY AND DISEASE SURVEILLANCE

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Leishmaniasis is a neglected tropical disease transmitted through sand fly vectors carrying protozoan parasites from the genus *Leishmania*. Currently, there is no vaccine available for human use to prevent the spread of leishmaniasis. The leishmanin skin test (LST) has been used for almost a century in endemic countries to determine the exposure status and immunity of the local population. Lack of availability of a well-characterized *Leishmania* antigen manufactured under Current Good Manufacturing Practice (cGMP) conditions has hindered its use as a diagnostic and surveillance tool in the field. Therefore, the development of an effective, shelf-stable *Leishmania* antigen for the LST is needed for its use in endemic countries where consistent cold chains might not be available. Our lab has established a well-characterized leishmanin soluble antigen from *Leishmania donovani* (Indian strain) and produced it under Good Laboratory Practice (GLP) conditions. Using both a mouse model of cutaneous leishmaniasis and a hamster model of visceral leishmaniasis, the GLP-LST antigen induces a delayed-type hypersensitivity (DTH) response following both Leishmanization and vaccination with a live-attenuated vaccine comprised of a *Leishmania major* strain lacking the *Centrin* gene. As *Leishmania* vaccines are being developed, LST could also be used as a surrogate of vaccine immunogenicity. Characterization of leishmanin antigens using high-dimensional flow cytometry analysis of the cell populations isolated from the DTH sites in murine models showed an enrichment of CD69+ and CD4+ skin resident memory T cells. Additionally, the presence of activated macrophages and Langerhans cells at the DTH site was detected, consistent with previous studies. These studies provide evidence for the large-scale production of a well-characterized cGMP-LST antigen that can be used in future vaccine clinical trials as a marker for immunity and in

active surveillance studies of endemic and emerging areas of *Leishmania* infection. *"My contributions are an informal communication and represent my own best judgement. These comments do not bind or obligate FDA."*

6006

VISCERAL LEISHMANIASIS DIAGNOSIS WITH DIGITAL MICROSCOPY AND EDGE-AI MODELS

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Visceral leishmaniasis (VL) remains a significant public health concern, with an estimated 30,000 new cases/year and the highest burden in rural settings in eastern Africa and Brazil. Tissue aspirate (mainly spleen and bone marrow) remains a cornerstone in the VL diagnostic algorithm and is the reference method to assess parasitological cure. Therefore, continuous quality assurance for both sample preparation and microscopist expertise is essential to ensure an accurate diagnosis.We developed an innovative digital microscopy solution enhanced with edge-based artificial intelligence (AI), integrated within a mobile app for real-time detection and quantification of Leishmania amastigotes. This consists of two modules: a smartphone-based app able to transform conventional microscopes into digital ones, and TeleSpot, a web-based platform for remote collaborative image analysis. This system was deployed in the Leishmaniasis Research Treatment Center, Gondar, Ethiopia following an implementation research approach and conducting a technology usability and acceptability evaluation with the participation of 5 laboratory staff after training. The solution allows evaluation of the quality of the smear and its staining, as well as the score (from 0 to 6+) that determines the parasite load. Six independent samples were digitised with 13 different smartphones. For AI model development, experts annotated 85 images, resulting in 1060 labels. Using a Yolo v8 algorithm, a precision of 85.9% and a recall of 79.3% were retrieved.This project represents a significant advancement in the standardization and automation of VL diagnosis, facilitating remote quality control in resource-limited settings and allowing for a potential improvement in the accuracy of microscopic diagnosis.

6007

DYNAMICS OF DENGUE VIRUS-REACTIVE B CELLS IN PEDIATRIC CASES FROM A HOSPITAL STUDY IN NICARAGUA

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Dengue virus serotypes 1-4 (DENV 1-4) cause an estimated 100 million febrile infections annually in the tropics. DENV-reactive memory B cells are important for protective immunity in the subsequent infection as they can differentiate to secrete antibodies (Abs). Yet, their dynamics and persistence are not well understood. To enumerate DENV-reactive B cells, we developed a novel and sensitive approach that does not depend on B cell stimulation. We fluorescently labelled whole mature virions of DENV1, DENV2, and DENV3 with Alexa Fluor (AF)-488 and AF647, yielding 6 single-fluor antigens that retain key neutralizing epitopes only present on the quaternary structure of the virus. A cocktail of antigens was applied to peripheral mononuclear cells (PBMCs) from Nicaraguan pediatric hospitalized cases of dengue. DENV-reactive B cells were defined as positive for both fluorescent antigens: $CD3^-/CD14^-/CD16^-/CD19^+$/DENV-$AF488^+$/DENV-$AF647^+$. We detected counts of DENV-reactive live B cells from early convalescent PBMCs across primary (1°) and secondary (2°) infections of DENV1-3 at frequencies 2-11-fold higher than a naïve sample. To analyze the dynamics of DENV-specific B cell populations over time, we selected a set of 6 longitudinal PBMCs collected at acute phase, early convalescence (days 14-28), and 3-, 6-, 12-, and 18-months post-infection in 1° DENV1 and 2° DENV1 cases. In preliminary results, we found DENV-reactive B cells at 18 months, with peak levels between 6-12 months. DENV-reactive activated memory B cells (MBCs; $IgD^-/CD20^+/CD21^-/CD27^+$) were highest in acute 2° DENV1. Interestingly, DENV-reactive atypical MBCs ($IgD^-/CD20^+/CD21^-/CD27^-$) were higher 6-18 months post-2° than the same time post-1° DENV1. Our ongoing analyses support that: 1) levels of DENV-reactive B cells may increase with each exposure; 2) activated MBCs participate in the acute 2° immune response; 3) levels of atypical DENV-reactive B cells increase post-2° infection; and 4) peak DENV-reactive B cells are found at 6-12 months post-infection and persist up to 18 months. Our approach will enable a better understanding of protective B cell immunity against DENV.

6008

ORDER MATTERS: DENV2-ZIKV AND ZIKV-DENV2 SEQUENTIAL INFECTIONS DIFFERENTIALLY MODULATE THE MAGNITUDE AND BREADTH OF HOMOTYPIC AND DENV CROSS-REACTIVE ANTIBODY RESPONSES

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Dengue (DENV) and Zika (ZIKV) viruses, closely related flaviviruses, present significant public health and vaccine development challenges due to their complex immune interactions. Based on our prospective pediatric cohort study in Nicaragua, we have shown an increased risk of symptomatic DENV infection following a DENV-ZIKV but not a ZIKV-DENV infection sequence. Here, we further investigate how the order of DENV/ZIKV infections influences antibody (Ab) responses. Using samples from participants with DENV2-ZIKV (n=28) and ZIKV-DENV2 (n=12) infection sequences collected post-first (1°) and post-second infection, we analyzed the neutralizing Ab (nAb) potency and Ab binding profiles to DENV1-4 and ZIKV antigens. We found that the order of ZIKV/DENV2 infections impacts homotypic (DENV2, ZIKV) responses in a non-reciprocal way. Higher ZIKV nAb titers were generated after DENV2-ZIKV compared to after 1° ZIKV infection, suggesting that prior DENV2 exposure increases the magnitude of the ZIKV nAb response; in contrast, comparable nAb titers to DENV2 were measured after 1° DENV2 and ZIKV-DENV2 infection, showing no impact of prior ZIKV infection. Moreover, the sequence of infection significantly affected homotypic and heterotypic DENV Ab responses both in terms of magnitude of binding and neutralization. The DENV2-ZIKV sequence showed consistently lower Ab responses to DENV1, 2, 3, 4 and ZIKV compared to the ZIKV-DENV2 sequence, suggesting that a second ZIKV infection may limit the development of DENV-induced Ab responses. Further, the order of infection affected the breadth of the Ab repertoire; NS1 Abs from the ZIKV-DENV2 group were highly cross-reactive to DENV1, 2, 3, and ZIKV, unlike those from the DENV2-ZIKV group, which predominantly cross-reacted to only DENV1 and 2. Overall, these results demonstrate that the order of DENV2/ZIKV infections strongly modulates the magnitude and breadth of Ab responses, with a second ZIKV infection dampening the DENV Ab response. This has significant implications for vaccine development strategies, underscoring the importance of considering prior flavivirus exposure history.

6009

MECHANISTIC MODELING OF HOST-VIRAL INTERACTIONS TO ELUCIDATE IMMUNE MECHANISMS UNDERPINNING DISPARATE RESPONSES TO DENGUE VIRUS INFECTION BY PRIOR EXPOSURE HISTORY

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The immunological mechanisms underpinning disease pathogenesis and protection against dengue, especially the dysregulated host response in secondary dengue virus (DENV) infection, remain only partially understood. We have developed a mechanistic mathematical model that explicitly considers interactions between DENV target cells, including monocytes, dendritic cells, and macrophages, as well as virus, NK cells, neutrophils, CD4 T cells, CD8 T cells, B cells, antibodies, and a milieu of cytokines to model innate responses and how they modulate adaptive responses. First, we have modeled both intrinsic and extrinsic antibody-dependent enhancement using a sub-model of the interaction between the virus, target and infected cells, and IFN-beta and IL-10 assuming the rate of viral production is proportional to IL-10 and inhibited by IFN-beta. Under this assumption, our model simulations showed rapid viral clearance and target cells returning to homeostasis, indicating effective viral resolution. However, lack of IFN production led to increased viremia and infection of all the target cells. Assuming increased viral infectivity and production, we observed delayed viral clearance, infected cells persistence, and high IFN and IL-10 concentrations beyond day 30, suggesting an inflammatory disease phenotype. Our ongoing work involves fitting the sub-model and full model to data from the literature as well as our unique Phase 1 trial (NCT05691530) to safely measure how distinct immune histories impact host response to a live-attenuated DENV3 monovalent vaccine. The clinical trial has so far enrolled 20 of 45 healthy adult participants with no (naive, n=15), one (non-DENV3 heterotypic, n=15), or more than one (polytypic, n=15) previous natural DENV infection(s). We are measuring at serial timepoints; immune cell populations, cytokine profiles, DENV-specific plasmablasts, viral load, and antibody titers. Our full model will be calibrated to these data to elucidate how recall responses perturb *de novo* responses in secondary infection, identifying immune mechanisms driving severe dengue pathology, and potential therapeutic targets.

6010

IMMUNOLOGICAL FEATURES ASSOCIATED WITH SEVERE DENGUE IN CHILDREN AND YOUNG ADULTS WITH OBESITY AND NORMAL WEIGHT

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Dengue virus infections are spreading globally. Host immune responses are believed to drive dengue pathogenesis, through mechanisms which remain poorly understood. Obesity is emerging as a risk factor for severe dengue (SD). The reasons for this remain unknown but may involve chronic low-grade inflammation leading to ineffective anti-viral immunity. In this study we test the hypothesis that SD associates with dysfunctional T/NK-cell responses, and that these defects are exacerbated in overweight/obese (OB) individuals, thus underpinning their increased susceptibility to SD. We analysed the phenotypical/functional features of $CD4^+$, $CD8^+$-T and NK-cells using multiparametric flow cytometry in peripheral blood mononuclear cells (PBMCs) of Vietnamese OB dengue patients aged 10-30 years, with each OB patient matched by age, sex and illness phase to one of normal weight. PBMCs from a total of 124 patients (94 non-SD, 30 SD) were analysed at admission (days of illness: 2-5) and 3 days later. Our data shows altered $CD4^+$/$CD8^+$-T and NK-cell responses in SD compared to non-SD. Dengue-specific and total $CD4^+$-T and $CD8^+$-T-cells of SD patients displayed features of T-cell exhaustion with high expression of PD-1 and other inhibitory receptors (e.g, TIGIT, LAG-3, TIM-3), and decreased granzyme B levels. These features were exacerbated in OB patients compared to their normal weight counterparts. *Ex vivo*-blockade of PD(L)-1 with anti-PD(L)-1 antibodies enhanced the cytotoxic potential of DENV-specific $CD8^+$-T-cells in some patients, suggesting their function can be restored. SD patients also displayed NK-cell dysfunction, whereby NK-cells expressed inhibitory receptors (LILRB1, NKG2A, PD-1, PDL-1, TIGIT and LAG-3) and decreased cytotoxicity. Importantly, T and NK-cell inhibitory receptor expression associated strongly with markers of dengue severity and endothelial dysfunction (e.g., plasma leak, ferritin, Angiopoietin-2, syndecan-1, VCAM-1). Our data suggests that $CD8^+$-T and NK-cell dysfunction leading to poor clearance of dengue-infected cells may underlie SD, and potentially contribute to the increased risk of OB individuals to SD.

6011

NEW INSIGHTS INTO AN OLD VACCINE: HETEROLOGOUS FLAVIVIRUS INFECTION ENHANCES THE POTENCY AND BREADTH OF 17D-ELICITED NEUTRALIZING ANTIBODIES AGAINST A PANEL OF WILD-TYPE YELLOW FEVER VIRUSES

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Mosquito-borne yellow fever virus (YFV) remains a pathogen of public health concern, with recent outbreaks of yellow fever in South America and Africa. While the live-attenuated YFV vaccine, 17D, elicits neutralizing antibodies (NAbs) in >99% of vaccinees by 28 days post vaccination, and immunity from a single dose of 17D is touted as “lifelong,” the durability of 17D-elicited NAbs differs between populations, and the need for booster doses remains controversial. A major limitation of most NAb studies of 17D-elicited immunity is the almost exclusive reliance on 17D as the test virus in serologic studies, and the breadth of human serum NAbs against antigenically diverse wild-type (WT) YFVs implicated in human disease remains largely uncharacterized. Here we address two knowledge gaps: (1) the potency and breadth of 17D-mediated NAbs against WT viruses from all 7 genotypes, and (2) the effect of heterologous flavivirus

immunity on potency and breadth of NAbs in humans. Using non-endemic 17D-vaccinee sera ≤10 years post vaccination, from participants with diverse heterologous flavivirus immunity (n=55), and a unique panel of 14 YFV strains isolated from 10 countries between 1927 and 2018, we performed focus reduction neutralization tests (FRNT). Here we show (1) a 5- to 35-fold reduction in potency of NAbs against WT viruses compared to 17D, with a strong correlation between FRNT50 and amino acid similarity to 17D; (2) poor neutralization of South America genotype I (SA-I) strains, where up to 56% of vaccinees (28/50) were seronegative (FRNT50 <1:10); and (3) significantly increased potency of NAbs against SA-I strains amongst vaccinees with heterologous flavivirus immunity exhibiting 94% seropositivity (15/16), compared to just 25% seropositivity in vaccinees without heterologous immunity (6/24). We hypothesize that a glycosylation site, N67, shared exclusively between SA-I strains and all four serotypes of dengue viruses, confers the greater breadth of neutralization observed in heterologously infected 17D vaccinees. These findings have the potential to significantly impact future YFV vaccine design and deployment strategies.

6012

PROTECTIVE VACCINATION OF NONHUMAN PRIMATES AGAINST AEROSOL EXPOSURE TO MARBURG VIRUS USING A VESICULAR STOMATITIS VIRUS-VECTORED VACCINE: IMPLICATIONS FOR MUCOSAL VACCINE STRATEGIES AND UNPREDICTABLE FILOVIRUS TRANSMISSION

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Recent increases in outbreaks caused by filoviruses, including Marburg virus (MARV) pose a serious global health threat due to a lack of countermeasures shown to be effective in people. Zoonotic spillover of MARV likely from Rousettus bat virus reservoirs followed by human-to-human transmission through contact with infected body fluids, has been associated with outbreaks. However, lethal infection by aerosol exposure, an unnatural route, has been demonstrated in preclinical models, which further establishes MARV as a substantial bioweapon threat. We have previously shown that a single intramuscular (IM) injection with a clinical-ready replication-competent recombinant vesicular stomatitis virus vaccine vector encoding the MARV glycoprotein GP (rVSVΔG-MARV-GP) was highly efficacious in protecting cynomolgus macaques exposed to MARV-Angola by systemic infection. Here, we demonstrate that either IM or mucosal intranasal (IN) rVSVΔG-MARV-GP vaccination regimens can elicit immunity that protects cynomolgus macaques following MARV-Angola aerosol exposure. We found that all rVSVΔG-MARV-GP vaccinated macaques developed potent systemic immunity as measured by anti-MARV GP binding titers and viral neutralization responses, regardless of the route of vaccine delivery and that the humoral responses appeared to be predictive of MARV aerosol protection. Moreover, macaques vaccinated by the IN route displayed superior protection against MARV aerosol exposure as indicated by improved control of MARV viremia, decreased clinical pathologies and increased survival. Together, these results support that rVSV-based vaccines have broad utility as effective countermeasures against natural and unpredictable pathogen exposures. Moreover, this work highlights that rVSV-based vaccines can be safely deployed within the mucosal environments and can provide significant benefits for protection against respiratory pathogen exposure.

6013

FIRST, DO NO HARM: FIELD EVALUATION OF AN INDEPENDENT RIFT VALLEY FEVER VACCINATION CAMPAIGN AND THE IMPACT ON PREGNANT LIVESTOCK IN A SEMI-PASTORAL AREA IN KENYA

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Rift Valley fever (RVF) is a devastating zoonotic and livestock disease causing abortion and death of young animals. There are currently no human vaccine options and, therefore, livestock vaccination is key tool to protect public health and livelihoods. The effectiveness of RVF livestock vaccination is complicated by the population covered and reaction time following early warnings. This study was initiated following an independent vaccine event in Loitokitok sub-county, southern Kenya. We sampled vaccinated animals and had a unique opportunity to understand the impact of the live-attenuated Smithburn vaccine on pregnancy in a field setting. Vaccinated pregnant dams were prioritized for sampling. We sampled 150 animals including 123 females (76 sheep, 47 goats) and 23 males (6 sheep, 17 goats) across two large herds in Imbirikani and Risa villages, with 41 and 47 days between vaccination and sampling. Over this time, farmers reported 23 sheep abortions and nine goat abortions and at sampling, we counted 289 sheep and 79 goats in total. Despite these abortions, anti-RVFV IgG antibodies were detected only in 43.3% (65/150) of adult animals, and we found no evidence of a statistical association with the animals' village, sex, species, or age. We sampled 108 dams and matched them to 74 offspring. Seroprevalence was higher in the aborted dams present for sampling (75%, 6/8) compared to all adults ($p=0.08$). Abortions occurred between 18-32 (median: 24.5) days post-vaccination, and dams vaccinated earlier in gestation were more likely to abort ($p=0.001$). Offspring had low seroprevalence (21.6%, 16/74) and seropositivity was associated with having a seropositive mother ($p=0.05$). Abortions following the vaccination event is concerning given the low seroprevalence. This study design does not support causation, yet the Smithburn vaccine's association with abortion suggests an improved strategy including safe vaccines for pregnant animals is needed as abortions contribute to farmers' loss of livelihood. In addition, models to assess efficacy before programme delivery can mitigate vaccine hesitancy in vulnerable livestock owning populations.

6014

USING A ONE HEALTH APPROACH IN INVESTIGATING A CRIMEAN-CONGO HEMORRHAGIC FEVER OUTBREAK IN LYANTONDE DISTRICT, UGANDA 2024.

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In January 2024, a cluster of deaths in Buyanja village, Lyantonde district, Uganda, initially suspected to be anthrax, prompted investigation and identification of Crimean-Congo Hemorrhagic Fever (CCHF) cases. This

study describes the outbreak investigation, including case findings, public health actions, and control measures. Initially, there was an outbreak of Anthrax in the district neighboring Lyantonde. The first two cases were suspected to be anthrax and were sent to the Uganda Virus Research Institute (UVRI) for Anthrax testing. The samples tested negative for anthrax, prompting a request for them to be tested for other Viral Hemorrhagic Fevers. Both samples were tested by RT-PCR and were positive for Crimean-Congo Hemorrhagic Fever (CCHF) and were negative for Ebola, Marburg, and Rift Valley Fever viruses. Following confirmation of these two cases, the Rapid Response Team conducted an investigation involving both veterinary and human medicine following a one health approach to ascertain the risk factors for these cases and sampled more humans and livestock, which were tested by both PCR and ELISA. We sensitized community leaders on CCHF causes, advised on control measures, and collected GPS coordinates for mapping purposes. Following the confirmation of two initial CCHF cases in Lyantonde, three additional cases were confirmed, totaling five cases. The outbreak was linked to close contact with infected body fluids, primarily from slaughtering animals. Investigations revealed that all cases were males involved in animal-related occupations, such as butchering and livestock care. Public health actions included community sensitization, supply of health education materials, and extensive sampling of animals and humans for testing. This outbreak highlights the importance of early detection, prompt public health response, and community engagement in controlling zoonotic diseases like CCHF. Efforts to enhance surveillance, improve laboratory capacity, and educate at-risk populations are crucial for preventing future outbreaks.

6015

AN EPIZOOTIC OF DEER TICK VIRUS ON MARTHA'S VINEYARD DUE TO AMPLIFICATION OF A SINGLE VIRAL GENOTYPE

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Deer tick virus (DTV), or lineage II Powassan virus, is the cause of a rare encephalitis with a high case fatality rate. During longitudinal studies of the ecology and epidemiology of tick-transmitted pathogens on Martha's Vineyard, Massachusetts, we detected a >5-fold increase in DTV prevalence in 2021,4.5% of 2194 host-seeking nymphs tested, up from 0.8% in 2020 and 0.5% in 2019. We used molecular epidemiologic methods to generate hypotheses for the biological basis for this increase. Transmission on the island was highly focal; most of the 72 sites sampled did not yield infected ticks. From the 14 sites with infected ticks, 99 were determined to be positive by RT-qPCR screening and confirmed by sequencing. Prevalence estimates at these sites ranged from 1% to 65.3%, with 75% of positives derived from only 4 sites. Whole virome sequencing determined that there were 3 distinct genotypes on the island. Genotype 2 was found primarily on Chappaquiddick, which is connected to the main island by a narrow beach. Types 1 and 3 were identified across the main island with some sites yielding both. Type 1 was responsible for 78% of the infected ticks, most of which were from the few hot foci. We tested the hypothesis that foci were due to horizontal transmission from a single reservoir species with individuals serving as super-spreaders. We identified the host upon which the infected ticks had fed as larvae using our previously described bloodmeal analysis assay. None of these sites yielded a single bloodmeal source from their infected ticks, indicating that a super-spreader host was not likely to be responsible for the great prevalence of infections. Almost half of the infected ticks (47%) had fed on shrews, 7% on mice, 5% on birds, 5% on deer and 35% did not yield bloodmeal results. It is possible that ticks acquired infection by inheritance (transovarial transmission); sequencing of whole tick mitochondrial genomes to determine whether the infected ticks could derive from the same egg batch is ongoing. It may be that the 2021 DTV epizootic on Martha's Vineyard was caused by the amplification of a single viral genotype maintained by transovarial transmission.

6016

GENOMIC SURVEILLANCE OF TICK AND MOSQUITO POOLS FROM GEORGIA (SOUTH CAUCASUS), SCREENED FOR VIRUSES ASSOCIATED WITH ACUTE FEBRILE ILLNESSES

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Genomic surveillance of arthropod-borne viral diseases is an important aspect of infectious disease surveillance that allows for monitoring of viral activity in vectors. Understanding the amount of viral activity in a region assists in predicting the likelihood or risk of human infection in an area, which in turn informs disease prevention strategies for force health protection. Here, we present findings from sequencing of 100 pools of ticks and mosquitoes screened for viruses associated with acute febrile illnesses (AFI) which were collected in the country of Georgia from May to October 2022 after an outbreak of human cases of Crimean-Congo hemorrhagic fever virus. RNA was extracted from tick and mosquito pools prior to shotgun sequencing. A total of 7,570 million reads were processed through in-house pipelines MetaDetector and VirusSeeker 2.0, an enhanced version of the public VirusSeeker pipeline. Viral sequences present in the results of both pipelines were investigated further. AFI-associated viruses were found in approximately 18% of the sample pools. The emerging pathogens Jingmen tick virus (JMTV) and Haseki tick virus (HTV) were the most frequently identified AFI-associated viruses. Both these viruses were previously identified in patients suffering from febrile illnesses following tick bites. JMTV is a segmented virus belonging to the *Flaviviridae* family and was identified in our study in pools of *Rhipicephalus bursa* ticks. Complete JMTV genomes were assembled from two tick samples allowing for phylogenetic analysis that revealed the nearest sequenced neighbor for both strains is a JMTV from Turkey. Similarly, HTV belongs to the *Flaviviridae* family and was seen in pools of both *Dermacentor reticulatus* and *Haemaphysalis punctata* ticks. We were able to extract partially complete coverage of the HTV polyprotein from pooled samples resulting in a phylogenetic analysis that showed clustering with HTV strains from Russia. This study expands our knowledge of AFI-associated viral pathogens in the region and provides further understanding of the range of these emerging pathogens and the vectors from which humans may be exposed to them.

6017

THE BAT BUSHMEAT TRADE AS AN INTERFACE FOR FILOVIRUS AND HENIPAVIRUS SPILLOVER IN THE REPUBLIC OF CONGO

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Outbreaks of Ebola virus and the potential for emergence of henipaviruses in sub-Saharan Africa underscores the need to identify when and where

these viruses spillover into human populations. Molecular evidence of Ghana virus (GhV) and antibodies to Ebola virus (EBOV) have been detected in African straw-colored fruit bats (*Eidolon helvum*), the most commonly hunted bat in sub-Saharan Africa. Therefore, hunters of this bat species may be at risk for henipavirus and ebolavirus spillover. A cross-sectional surveillance study of 164 bat hunters and 420 *E. helvum* bats in the Republic of Congo was conducted. Serum from hunters and bats was collected and tested by an envelope glycoprotein-based multiplex microsphere immunoassay for IgG against ten filoviruses and seven paramyxoviruses. We detected henipavirus seropositivity in 18.3% (7.1 - 29.5%) of bats sampled, including 11.3% (5 – 17.6%) GhV seropositivity, 5.2% (1.9 – 8.6%) Nipah virus (NiV) seropositivity, and 6.3 (1.2 – 11.4%) Mòjiāng virus (MojV) seropositivity. There was also evidence of filovirus seropositivity in 25.4% (4.3 - 46.4%) of bats sampled, including 15.1% (0.7 – 29.5%) Ebola virus (EBOV) seropositivity and 21.3% (3.6 – 39.1%) Bundibugyo (BDBV) seropositivity. Additionally, we detected henipavirus seropositivity in 17% (4.3 – 29.9%) of bushmeat hunters sampled, including 15.6% (4.3 – 29.8%) MojV seropositivity. We also detected 23% (17.7 – 29.8%) filovirus seropositivity, including 12.8% (6.7 – 18.9) EBOV seropositivity and 11.6% (3.7 – 19.5%) BDBV seropositivity. Here, we report the first estimates of filovirus and henipavirus serological prevalence in African straw-colored fruit bats and bushmeat hunters in the Republic of Congo. Overall, henipavirus and EBOV seroprevalence in this species of bat has been reported in other countries in sub-Saharan Africa but estimates of seroprevalence of GhV and other antigenically distinct henipaviruses in bats is limited. Additionally, our detection of MojV-like henipavirus infections humans suggests exposure to novel henipaviruses that are distantly related to the prototypic species.

6018

NEXT-GENERATION SEQUENCING SURVEY OF ACUTE FEBRILE ILLNESS IN SENEGAL (2020-2022)

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Acute febrile illnesses (AFI) in developing tropical and sub-tropical nations are challenging to diagnose due to the numerous causes and non-specific symptoms. The proliferation of rapid diagnostic testing and successful control campaigns against malaria have revealed that non-Plasmodial pathogens still contribute significantly to AFI burden. Thus, a more complete understanding of local trends and potential causes is important for selecting the correct treatment course, which in turn will reduce morbidity and mortality. Next-generation sequencing (NGS) in a laboratory setting can be used to identify known and novel pathogens in individuals with AFI. In this study, plasma was collected from 228 febrile patients tested negative for malaria at clinics across Senegal from 2020-2022. Total nucleic acids were extracted and converted to metagenomic NGS libraries. To identify viral pathogens, especially those present at low concentration, an aliquot of each library was processed with a viral enrichment panel and sequenced. Corresponding metagenomic libraries were also sequenced to identify non-viral pathogens. Sequencing reads for pathogens with a possible link to febrile illness were identified in 51/228 specimens, including (but not limited to): *Borrelia crocidurae* (N=7), West Nile virus (N=3), *Rickettsia felis* (N=2), *Bartonella quintana* (N=1), human herpesvirus 8 (N=1), and Saffold virus (N=1). Reads corresponding to *Plasmodium falciparum* were detected in 19 specimens, though their presence in the cohort was likely due to user error of rapid diagnostic testing or incorrect specimen segregation at the clinics. Mosquito-borne pathogens were typically detected just after the conclusion of the rainy season, while tick-borne pathogens were mostly detected before the rainy season. The three West Nile virus strains were phylogenetically characterized and shown to be related to both European and North American clades. Surveys such as this will increase the understanding of the potential causes of non-malarial AFI, which may help inform diagnostic and treatment options for clinicians who provide care to patients in Senegal.

6019

INVESTIGATION OF YELLOW FEVER VIRUS, VECTOR AND HOST NETWORK IN THE METROPOLITAN REGION OF MINAS GERAIS, BRAZIL IN 2023, INDICATES THE CONTINUED CIRCULATION OF YELLOW FEVER VIRUS

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In 2016-18, Southeast Brazil experienced a huge yellow fever outbreak, notably in Minas Gerais state, the epicenter of the outbreak. Since then, yellow fever virus (YFV) has been detected in non-human primates (NHP) in the state, including the Metropolitan region of Belo Horizonte (BH). To investigate the virus-host-vector network that could sustain YFV maintenance and transmission, we have been performing NHP and mosquito surveillance in six urban parks of BH, since mid 2023. So far, a total of 2,548 mosquitoes have been collected in six urbans parks of BH. 45.64% of individuals have already been identified to genus level as *Aedes, Haemagogus, Sabethes, Culex, Limatus, Uranotaenia, and Psorophora.* Sera from 63 free-living black-tufted marmoset (*Callithrix penicillata)* captured or rescued in 2023, tested negative for YFV, ZIKV, CHIKV by RTqPCR, indicating that none of the animals were actively infected by these arboviruses. Additionally, 36 sera have been screened via plaque reduction neutralization test (PRNT) against YFV showing 20 positives (PRNT 50% at 1:20 dilution). These samples were from *C. penicillata (*3 infant (0-5 months of age), 6 young (6-17 months of age) and 11 adult (more than 18 months of age), sampled in the Metropolitan region of BH (n=19), and southwest Minas Gerais (n=1). Four out of 20 PRNT positive sera also tested positive for IgM anti-YFV (3 adults, 1 young). These four *Callithrix i*ndividuals were collected in urban areas from the Metropolitan region of BH, in 2023. Although it is known that IgM can persist after orthoflavirus infection, these NHP were sampled in 2023, more than 4 years since the end of yellow fever outbreaks in 2018, Minas Gerais. The detection of neutralizing and IgM against YFV in NHP (including young and adults sampled in 2023) reinforces the circulation of YFV in urban areas of Minas Gerais. Urbans parks in BH present the host-vector network: NHPs and sylvatic mosquitoes (*Haemagogus and Sabethes),* that could contribute to the maintenance and transmission of YFV. Continued surveillance and studies are vital to public health in Southern Brazil due to ongoing YFV circulation.

6020

DYNAMICS AND REGULATION OF SEXUAL COMMITMENT IN *PLASMODIUM FALCIPARUM*

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Human-to-human malaria transmission via mosquitoes requires the production of sexual stage parasites, known as gametocytes. In vitro, during each asexual cycle this important developmental transition takes place during schizogony in a sub population of blood stage parasites. We generated a series of transgenic reporter lines to assess the dynamics of sexual commitment from RBC invasion through schizogony to the next generation of parasites. The results reveal that translation of *gametocyte development 1* gene (*gdv1*) tagged with nanoluciferase is first detected

26-27 hpi and TdTomato-tagged GDV1 is visible before the first nuclear division (30-32 hpi) just prior to the initial detection of AP2 transcription factor, *ap2-g,* RNA (31-32 hpi). The initial increase in *ap2-g* transcription plateaus until 37-38 hpi before continuing to increase through schizogony. The marked increase in *ap2-g* transcript after 37-38 hpi fits well with the first detection of mScarlet-tagged AP2-G at 39-40 hpi and is consistent with AP2-G transcriptional autoregulation. Two hours later (41-42 hpi) the cells already positive for mScarlet AP2-G also begin to express mNeonGreen-tagged MSRP1. This dual AP2-G/MSRP1 positive schizont population continues to increase through schizogony indicating that it is only the mature schizont population that can be used to determine the sexual conversion rate. The regulatory roles of GDV1 and AP2-G were then investigated using GDV1 inducible lines containing nanoluciferase-tagged active or inactive *ap2-g* and demonstrated that the initial increase in *ap2-g* transcription requires GDV1 and is AP2-G independent, whereas the further increase after 38 hpi requires active AP2-G. Together the findings define the time course of sexual commitment through schizogony and the distinct roles of GDV1 and AP2-G. The transgenic reporter lines developed are also powerful tools to study the initial signaling events underlying sexual commitment and screen molecules with transmission-blocking potential. Disclaimer: The opinions expressed are those of the authors, not the affiliated Institutions.

6021

SPECIALIZED SPOROZOITE-TYPE RIBOSOMES IN *PLASMODIUM YOELII* DRIVE INITIAL RAPID ASEXUAL BLOOD STAGE GROWTH AND SEXUAL DEVELOPMENT

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Eukaryotes use ribosome specialization to promote specific translational outcomes in distinct cell types and stages of development. Specialization is often derived from rRNA sequence heterogeneity within the expansion segments (ESs) that emanate from the conserved core, as well as differential ribosome protein (RP) paralog expression and incorporation. However, it has been challenging to study individual ribosome types genetically because most eukaryotes encode hundreds of tandem copies of rRNA genes. Therefore, we have overcome this challenge by studying the rodent-infectious malaria parasite *Plasmodium yoelii*, a eukaryote with only four 18S/5.8S/28S rRNA genes on Chromosomes 5, 6, 7, and 12. These four rRNAs have different temporal expression patterns that enable their characterization as "Asexual" A-type rRNAs (Chr 7 and 12, with nearly identical sequences) and "Sporozoite" S-type (Chr 5 and 6) rRNAs that vary in sequence from the A-type and each other primarily at ESs. Previous genetic studies have only identified that S-type rRNAs impact oocyst growth and sporozoite development in mosquitoes. However, our phenotypic characterization of parasites lacking either or both S-type rRNA genes surprisingly revealed two biologically and statistically significant defects during the blood stage, when S-type rRNAs are only weakly expressed. Deletion of the Chr 5 rDNA locus led to the disruption of the initial rapid wave of asexual blood stage growth. In contrast, deletion of the Chr 6 rDNA locus decreased the production of mature male gametocytes at this same point. Moreover, the Chr 6 deletion phenotype dominated when both loci were deleted, thus restoring the initial wave of asexual growth. Based on these data and follow-on studies focused on identifying the contributing components of these rRNAs, we propose a model in which S-type ribosomes provide specialized functions, with one S-type ribosome (Chr 5) driving asexual blood stage growth and acting to dampen the promotion of gametocytogenesis by the other (Chr 6).

6022

IDENTIFICATION OF NOVEL ANTI-GAMETOCYTE TRANSMISSION BLOCKING VACCINE TARGETS

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Inhibiting transmission of *Plasmodium* is a central strategy in malaria eradication, and the biological process of gamete fusion during fertilisation is a proven target for this approach. The lack of knowledge of the mechanisms underlying fertilisation have been a hindrance in the development of transmission blocking interventions. Here we describe a protein disulphide isomerase essential for malarial transmission (*PDI Trans* PBANKA 0820300) to the mosquito. We show that *PDI Trans* activity is male specific, surface expressed, essential for fertilisation and transmission, and exhibits disulphide isomerase function which is up regulated post gamete activation. We demonstrate that *PDI Trans* is a viable anti malarial drug and vaccine target blocking malarial transmission with the use of repurposed the PDI inhibitors and anti *PDI Trans* peptide antibodies. These results reveal that protein disulphide isomerase function is essential for malarial transmission and emphasise the potential of anti PDI agents to act as an anti malarial, facilitating the development of novel transmission blocking interventions.

6023

LOSS OF FUNCTION OF THE *PLASMODIUM FALCIPARUM* PROLINE TRANSPORTER *PF*APIAT2 MEDIATES HALOFUGINONE RESISTANCE BUT RESULTS IN OOCYST DEVELOPMENTAL DYSFUNCTION

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Resistance to halofuginone (HFG), a potent antimalarial targeting the cytoplasmic proline-tRNA synthase of the human malaria parasite *Plasmodium falciparum*, can be mediated through loss-of-function (LOF) mutations in the Apicomplexan Amino acid Transporter 2 gene (*pfapiat2)*. During the asexual stage, *Pf*ApiAT2-LOF results in accumulation of cytoplasmic proline which competes with HFG for target site binding. Previous work in the *Plasmodium berghei/Anopheles stephensi* mouse malaria system pointed to an essential role of *Pb*ApiAT2 in oocysts, but there is nothing known of its role in the transmission stages of *P. falciparum*. To understand the role of *Pf*ApiAT2 during mosquito stages, we generated HFG-resistant parasites in the transmissible NF54 line. These *Pf*ApiAT2-HFGR parasites were 10-fold more resistant than the parental line to HFG. Sequencing of the *pfapiat2* locus revealed two independent non-synonymous mutations (G449R and R345I) in these lines. Both lines were fed to female *Anopheles gambiae* mosquitoes, and we observed no defect in early stages of parasite development in the mosquito midgut but saw strongly reduced growth during the oocyst stage. Preliminary analysis showed that *Pf*ApiAT2-HFGR oocysts were five-fold smaller than wild-type oocysts on day 7 and could not complete proper development to sporozoites by day 14 and day 21. To determine localization of *Pf*ApiAT2 in the mosquito stages, we generated an NF54 *Pf*ApiAT2-HA line. Pilot immunofluorescence assay microscopy suggests that *Pf*ApiAT2 localizes at peripheral membranes of developing oocysts, colocalizing with *Pf*s25, a known plasma membrane marker. We are further validating the essentiality of *Pf*ApiAT2 in oocyst development through genetic knockouts. Our data

suggests a crucial role of *Pf*ApiAT2 during oocyst development, and we are characterizing proline transport activity of *Pf*ApiAT2 through heterologous expression in a *Xenopus laevis* oocyte system.

6024

PARTIAL CLEARANCE OF PRE-ESTABLISHED *PLASMODIUM FALCIPARUM* INFECTION IN MOSQUITOES BY MIMICKING A BLOODMEAL ON TREATED PATIENTS WITH ARTEMETHER+LUMEFANTRINE + ATOVAQUONE-PROGUANIL

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In addition to curative treatment against the pathogenic asexual stage of the malaria parasite, targeting the transmissible sexual stage is essential to impede the spread of drug resistance. The present study relies on a clinical trial testing the benefits of combining Atovaquone Proguanil (AP) with Artemether-lumefantrine (AL) in the treatment of uncomplicated malaria. AP has been shown to prevent transmission post-treatment by affecting parasite development in mosquito vectors in mice models. Atovaquone exhibits further properties by persisting in the blood of treated patients for days, possibly hindering parasite development during ookinete to oocyst and oocyst to sporozoite transition. We aim to assess the parasite clearance properties of plasma from AL *versus* AL+AP treated patients in mosquitoes with pre-established *Plasmodium falciparum* infection. Eight time points (Day 0 to 28) plasma from 17 patients treated with either AL+placebo or AL+AP was collected for mosquito feeding. Infectious blood meal was provided to laboratory reared female *Anopheles* mosquitoes and infected mosquitoes were exposed to a second blood meal containing the plasma from treated patients. A total of 9,259 mosquitoes were dissected, 4,850 at 7 and 4,409 at 14 days post-infection (dpi). Infection rate and intensity in the control groups range from 20% to 89.19% and 8.75 to 71.96 respectively at 7 dpi. Our preliminary analysis demonstrates that in *P. falciparum* infected mosquitoes, a blood meal with plasma from AL+AP treated patients significantly inhibits parasite development with a reduction in the prevalence of infected mosquitoes and infection intensity and slower sporogonic development, whereas plasma from patients treated with AL alone had no effect. The AL+AP effect however decreases after 5 days post-treatment. Further analysis including correlation with drug dosage, mosquito survival and quantification of sporozoites in the salivary glands is ongoing. These results highlight a benefit of triple ACT containing AP as when treated patients are bitten by infected mosquitoes, they may be partially “cured” of the infection and therefore reduce transmission.

6025

UNRAVELING THE JOURNEY OF *PLASMODIUM FALCIPARUM* PARASITES INSIDE THEIR MOSQUITO VECTOR AT THE SINGLE CELL RESOLUTION

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Plasmodium parasites, often incorrectly referred to as obligate intracellular parasites, replicate exclusively within host cells in humans. Their cycle within the *Anopheles* mosquito vector, however, takes a markedly different path. Following the mosquito’s ingestion of an infected blood meal, newly formed zygotes evolve into ookinetes that traverse the midgut epithelium and transform into oocysts underneath the basal lamina. This extracellular replicative stage develops over more than a week, maturing into thousands of sporozoites—the form able to infect humans. The processes mediating ookinete traversal and oocyst growth remain largely unknown. We employed single cell RNA sequencing of both parasite and mosquito cells across four critical timepoints for parasite survival and growth to generate a new parasite single cell atlas spanning from invading ookinetes to segmenting oocysts. We found an unexpected preferential invasion route followed by ookinetes during epithelial cell traversal, which is currently being validated by genetic and microscopy means. Moreover, we detected and validated processes that are essential for oocyst growth and sporozoite segmentation, identifying previously unknown players and mechanisms. Our study enhances our understanding of the host-pathogen dynamics during the mosquito development phase and opens avenues for the identification of novel targets for mosquito-specific, transmission-blocking strategies.

6026

DEFINING TRANSCRIPTIONAL SIGNATURES OF *PLASMODIUM FALCIPARUM* HEMATOPOIETIC INFECTION AT THE SINGLE CELL LEVEL

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During blood stage malaria infection, most parasites undergo asexual reproduction, exponentially increasing the parasite load and leading to clinical manifestations of the disease. However, a small subset of asexually replicating blood-stage parasites differentiate to become transmission-competent gametocytes in a process known as sexual stage conversion. Recent work has established that the hematopoietic niche of the bone marrow is an essential site for gametocyte development, in addition to being an under-appreciated reservoir of asexual parasites. Whether the bone marrow microenvironment specifically promotes commitment to the sexual development trajectory in addition to serving as the major site for gametocyte maturation is not known. Several factors have been implicated as potential mediators of sexual commitment within the bone marrow, including a local depletion of the host phospholipid lysophosphatidylcholine (LysoPC), levels of which have been shown to regulate stage conversion in *P. falciparum in vitro*, as well as an enrichment of immature red blood cells (reticulocytes), which have been shown to promote gametocytogenesis in *P. berghei*. Nonetheless, the mechanisms whereby these and other features of the bone marrow microenvironment might contribute to parasite development and differentiation remain poorly understood. Here, we apply single-cell RNA sequencing to study *P. falciparum* development within the hematopoietic niche using complementary *in vitro* and *ex vivo* approaches. For our *in vitro* studies, we compare parasites cultured in primary human bone marrow cells to parasites cultured in peripheral blood cells, focusing on pathways relating to sexual commitment. For our *in vitro* studies, we

compare orthopaedic samples from naturally infected donors in Malawi to donor-matched peripheral blood samples. Results suggest that a combination of host cell intrinsic and extrinsic factors contribute to parasite development and differentiation within the hematopoietic niche and provide insight into mechanisms whereby parasites can regulate the balance within-host growth and between-host transmission.

6027

ENHANCING MALARIA DATA QUALITY IN BENIN: IMPACT OF MONTHLY DATA VALIDATION AND DEATH DATA AUDIT

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In Benin, malaria incidence and mortality rates stagnated from 2020 to 2022 despite increased prevention efforts. Concerns about the accuracy of rapid diagnostic test (RDT) results reporting, overall data quality, and a need for strengthened governance and leadership at regional and district levels led to guidance and procedural revisions. In 2023, the Benin malaria control program introduced new guidelines for malaria data validation meetings and death audits. Data review meetings went from quarterly at regional levels to monthly at district levels and emphasized data accuracy, investigating discrepancies, and peer-to-peer cross-checking of patient registers including RDT cassette verification. Benin found a decline in malaria incidence from 221 per 1,000 population in 2022 to 168 in 2023, with regional reductions ranging from 1% to 38%. In 2023, as compared with 2022, suspected malaria cases remained at 4.0M and patients tested by RDT increased by 3% from 3.4M to 3.5M while confirmed cases decreased from 2.7M to 2.1M (-21%), and ACT prescriptions from 2.2M to 1.6M (-24%), and RDT test positivity decreased by 25% from 66% to 51%. Reductions in confirmed cases appear to be related to improved oversight in RDT result reporting. Death audits led to reductions in seven of the 10 hospitals reporting 66% of malaria-related deaths, driving reductions in malaria mortality from 25.4 to 24.2 per 100,000 inhabitants. Like many malaria-endemic countries, malaria in Benin is often seen as a syndrome that can lead to reporting non-malaria fevers as malaria. Increased focus on quality assured RDT result reporting and malaria death definition and verification led to more accurate estimates of malaria cases and deaths and ACT consumption. This allows for improved impact and trend monitoring, and targeting of limited resources

6028

INTEGRATED COMMUNITY CASE MANAGEMENT (ICCM) COMMUNITY HEALTH WORKERS AND THEIR IMPACT ON SEVERE MALARIA AND MALARIA MORTALITY IN LUAPULA PROVINCE, ZAMBIA'S HIGHEST MALARIA BURDEN PROVINCE, 2016-2023

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Luapula Province has Zambia's highest malaria burden at 63.3% parasite prevalence in children under age 5. Since deployment of integrated community case management (iCCM) in 2018, 2,115 community health workers (CHWs) have been trained and deployed in 9 of the 12 districts using a ratio of 1 CHW per 500 population. iCCM provides accessible testing and treatment of uncomplicated malaria and pre-referral treatment of severe malaria for children ages 2 months to 6 years. Over an 8-year period from 2016 to 2023, an analysis was conducted on health management information systems and malaria rapid reporting data. Negative binomial regression models were developed for 4 outcomes to assess the impact of iCCM in the 9 identified districts. ITNs, IRS, rainfall, temperature, and vegetation covariates were included in the models to reduce potential confounding over the years. From 2016 to 2023, there were 99,449 severe malaria admissions and 2,553 malaria deaths for all ages. On average, in 2023, CHWs detected 40.3% of total confirmed malaria cases in Luapula, compared to 0% in 2016. CHW activity declined in 2020-2021 coinciding with the COVID-19 pandemic, which disrupted health systems and affected commodity supply, and recovered in 2022-2023 with improved commodity availability. The analysis showed that each 10% increase in the proportion of cases detected by CHWs was associated with a 7% decrease in severe malaria in all ages, an 8% decrease in severe malaria for all children under age 5, a 9% decrease in deaths in all ages, and a 9% decrease in deaths in all children under age 5. More cases detected in the community means quicker access to care and fewer cases progressing to severe disease. The National Malaria Elimination Program can use these data to advocate for continued scale-up of iCCM in high malaria burden areas.

6029

ANTENATAL CARE SURVEILLANCE FOR MONITORING PREVALENCE AND COVERAGE OF INSECTICIDE-TREATED NETS - A MULTI-COUNTRY ANALYSIS

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Estimates of malaria prevalence and intervention coverage in Africa are primarily based on nationally representative household (HH) surveys. However, their expense and infrequency limit their utility for operational action by malaria programs. We assessed whether data collected during the first antenatal care (ANC1) visit, consisting of data on malaria prevalence using rapid diagnostic tests and ownership of insecticide-treated nets (ITNs), could provide relevant data to guide decision-makers. Malaria prevalence among ANC1 attendees in select areas of six countries (Benin, Burkina Faso, Mozambique, Nigeria, Tanzania, and Zambia) were compared to prevalence data among children under five (u5) from cross-sectional HH surveys in the same areas. To examine the relationship between prevalence among ANC1 attendees and u5 prevalence we fitted a linear trend to the log-odds ratio of the risk of testing positive. The predictive performance of the model was assessed by leave-one-out cross-validation (LOOCV). District-level ANC1 prevalence and u5 prevalence have a linear relationship (Pearson correlation coefficient, r = 0.80, 95% confidence interval, CI = 0.66-0.88, $p < 0.001$) and ANC1 prevalence is predictive of prevalence among u5s (LOOCV mean absolute error = 6.2%). To understand whether data on ITN ownership collected at ANC1 are representative of that collected in HH surveys, we assessed the district-level proportion of household ownership in five countries (Benin, Burkina Faso, Mozambique, Nigeria, and Zambia). ITN ownership at the level of one ITN per HH as assessed by ANC1 questionnaires was strongly correlated with ITN ownership at the level of one ITN per HH in HH questionnaires (r = 0.80, 95% CI = 0.63-0.90, $p < 0.001$). There was moderate correlation in ITN

ownership at the level of one ITN per two persons (r = 0.64, 95% CI = 0.38-0.81, p < 0.001). Estimates of malaria prevalence and ITN coverage derived from ANC1 attendees correlate with estimates derived from HH surveys and may be useful in monitoring malaria prevalence and prevention efforts.

6030

MALARIA SURVEILLANCE TO PREVENT THE RE-ESTABLISHMENT OF MALARIA IN MOBILITY DYNAMIC SETTING OF RAMREE TOWNSHIP IN MYANMAR

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The President's Malaria Initiative Eliminate Malaria (PMI-EM) Activity in Myanmar provides technical and operational assistance to implement case-based and community-based surveillance in malaria-elimination townships. The receptivity and vulnerability assessments were conducted from May to July 2023 using qualitative methods, applying participatory mapping, focus group discussions, and reviewing the program data to prevent malaria re-establishment in Ramree Township. Regarding receptivity of 228 villages, 11 at the forest fringes were high, 193 along paddy fields/coastal areas were moderate, and the remaining 24 in urban plains were low. Regarding vulnerability, 11 villages were high, and 122 were moderate based on the influx of migrants and visits to forested worksites related to logging, tobacco plantation, fishing, and oil exploration. The indigenous transmission was interrupted in 2021 after five malaria cases were detected in one village in 2020. Five malaria cases were detected but maintained zero active focus in 2022. In 2023, 17 cases were detected and classified as 11 imported (65%), two relapses (12%), and three indigenous/one introduced (23%). Integrated Community Malaria Volunteers (ICMVs) were deployed in 162 villages (71%), and the remaining 66 villages (29%) were covered by facility-based surveillance of basic health staff. In 2023, 11,212 RDTs were performed for the township population 96,957, and the township's annual blood examination rate (ABER) was 11.6%. Community surveillance through ICMVs contributed to 67% of RDTs performed, 71% of cases detected, and 100% case-based surveillance in 2023. Only two cases were detected in an area with high receptivity, and no cases were detected in areas with high vulnerability in 2023. After the coup in February 2021, there was a resurgence of malaria nationally, and there was an increase of 240% in malaria cases from 5 in 2020 to 17 in 2023 in Ramree. It was unpredictable where the cases would be caught. To prevent the re-establishment of malaria in dynamic and conflict-affected mobility areas like Ramree, community surveillance through ICMVs should be sustained.

6031

DATA INTEGRATION FOR DECISION-MAKING: A MALARIA DATA DASHBOARD THAT MERGES ROUTINE SURVEILLANCE AND GENOMIC RESEARCH DATA WITH MODELED OUTPUTS FOR PROGRAMMATIC ACTION IN SENEGAL

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The National Malaria Control Program (NMCP) in Senegal has been working in collaboration with research groups in Senegal and around the world to leverage genomic surveillance and modeled data for operational decision-making. To bring together the NMCP epidemiological data with novel molecular and modeled data, a data dashboard was conceived from a research consortium led by Le Centre International de recherche et de formation en Génomique Appliquée et de Surveillance Sanitaire (CIGASS; Dakar, SN) with direction from the NMCP. Software development and design was led by the Institute for Disease Modeling (IDM; Bill & Melinda Gates Foundation, Seattle, USA). NMCP routine surveillance data were used by the Malaria Atlas Project (MAP; Perth, AU and Dar es Salaam, TZ) to generate a Senegal-specific geospatial model of malaria incidence that accounts for data challenges such reporting completeness and access to care. Molecular surveillance data, including molecular markers for drug resistance and parasite population relatedness statistics, were generated by CIGASS in partnership with the Harvard T.H. Chan School of Public Health and The Broad Institute (Boston, USA). With the permission and partnership of the NMCP, all data were added to the digital dashboard platform. The resulting dashboard allows the NMCP routine data to be compared side by side with modeled outputs from MAP. These could each be overlaid with genomic summary statistics. Maps and time series plots allow data comparisons to be made across both space and time. The ability to visualize changes in parasite populations and drug resistance markers over space and time, referenced to programmatic data, is an important step towards making novel molecular surveillance data operationally relevant. The Senegal data dashboard highlights the potential breadth of data that NMCPs can add to their toolkits, and also the quality of outputs made possible through research and programmatic collaboration.

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FORECASTING GLOBAL NEED AND DEMAND FOR CRITICAL MALARIA COMMODITIES TO ANTICIPATE POTENTIAL MARKET DISRUPTIONS

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Challenges for malaria elimination such as increasing populations, emerging treatment and insecticide resistance, the spread of HRP2 gene deletions and global budgetary constraints are driving the need to be more selective with how malaria commodities are chosen and distributed. The Malaria Commodities Forecasting Project produces comprehensive forecasts to generate consensus views on market trends, highlight gaps in demand for essential commodities and identify supply risks. We use statistical modeling to predict future trends in commodity needs from historical data, dynamic modeling to explore the impact of future interventions, and scenario analysis of the impact of factors such as policy, pricing, and global budgets. In 2023 the project published its second long-term forecast of global need and demand for insecticide-treated nets (ITNs), insecticides for indoor residual spraying (IRS), rapid diagnostic tests (RDTs), and antimalarial treatments. Under the baseline scenario, global ITN demand is expected to grow from 227 million in 2023 to 309 million ITNs in 2032, with an estimated 46% of this demand being for newer (dual active ingredient) ITNs. The global public sector demand for ACTs is also projected to increase, from 365 million in 2026 to 394 million treatments in 2032. We identify high levels of incorrect treatment in sub-Saharan Africa, with a predicted 438 million antimalarials used to treat non-malarial fevers in 2032. The need for non-HRP2 RDTs could rise to 56% of the African market by 2032 according to modelled HRP2 deletion spread. Demand for SP+AQ, used for seasonal malaria chemoprevention, is expected to increase from 225 million in 2026 to 249 million treatments in 2032, far below the projected need. These forecasts play a crucial role in identifying areas with insufficient funding and coverage, predicting commodity demand under various scenarios and uptake of new tools to fight malaria. Publicly accessible and updated annually, they provide

policymakers, donors, manufacturers and the broader global malaria community with a platform to anticipate market risks and disruptions in the ongoing efforts to fight malaria.

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TEMPORAL TRANSCRIPTOMICS UNRAVEL MOLECULAR SIGNATURES OF SEVERE COVID-19

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Hospitalized COVID-19 patients often experience severe symptoms, with some progressing to respiratory failure necessitating prolonged ICU care. To better understand the underlying molecular characteristics of severe COVID-19 pathogenesis, transcriptomics by next-generation sequencing was performed on a matched subset (n=36) of temporally (Days 0,1, 2, 3, and 6 following enrollment) collected RNA from peripheral blood of COVID-19 patients with severe disease (n=21), defined as admission to the ICU and/or death, or those who did not require ICU support (non-severe, n=15). Differential gene expression analysis between severe and non-severe patients revealed 3690, 2605, 4289, 3879, and 3454 differentially expressed genes (DEGs, $P<0.05$) at D0, D1, D2, D3, and D6 respectively. Enrichment analysis using Metacore™ revealed significant enhancement of the COVID-19: Immune Dysregulation (FDR=4.54e-7), COVID-19 Associated Coagulopathy (FDR=9.20e-2), and COVID-19: SARS-CoV-2 Entry into Target Cells (FDR=8.22e-2) pathways. MHC class I, MHC class II, and CD4 were downregulated, while GLUT1, PKM2, and GATA were upregulated across all time points in the Immune Dysregulation pathway, indicating impaired antigen presentation, reduction in functional CD4 T cells and altered metabolic state. In addition, the upregulation of P2Y1, CD147, P-selectin, von Willebrand factor, and GP-IB alpha genes were identified in the COVID-19 Associated Coagulopathy pathway, suggesting platelet activation, adhesion, and inflammation dysregulation, which could contribute to COVID-19 severity. Syndecan-4 and CD147 were also upregulated across time in the COVID-19: SARS-CoV-2 Entry into Target Cells pathway. CD147 upregulation may enhance viral entry into host cells, while Syndecan-4 may contribute to the dysregulation of endothelial cells. Collectively, these findings underscore the complex interplay between immune dysregulation, coagulopathy, and viral pathogenesis in severe COVID-19 cases in a diverse population of patients, offering insights for potential therapeutic interventions.

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EVALUATING THE BURDEN OF RESPIRATORY TRACT INFECTIONS IN DECEASED IN KARACHI, PAKISTAN: A POST-PANDEMIC MORTALITY SURVEILLANCE ANALYSIS

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Respiratory tract infections (RTIs) are of critical concern in the wake of the COVID-19 pandemic, necessitating extensive examination of their impact on mortality rates. We assessed the prevalence of COVID-19 and other RTIs among deceased individuals within peri-urban areas in Karachi, Pakistan in the post-pandemic period. We also aimed to assess the efficacy of nasal swabs stored in dry tubes (dry nasal swabs) compared to standard nasal swabs stored in transfer medium (wet nasal swabs) for RT-PCR COVID-19 detection. Samples from the recently deceased were collected between September 2022 and October 2023 using both wet and dry swabs. 350 samples underwent PCR testing for common respiratory pathogens and genomic sequencing for variant identification. 6% (21/350) of cases tested positive for COVID-19 on either wet or dry swabs. 57% of positive cases occurred in those aged 60 or higher. A majority of COVID-19 positive deaths (47.6%) occurred at home. Seasonality revealed spikes in positive cases in October (5/20) and June (5/33). 22F omicron was the most prevalent strain. 19 COVID-19 positive cases had co-infection with another organism with *K. pneumonia* found in 62% of these cases. Among all cases, *K. pneumonia* and *S. aureus* were the two most common organisms detected. *K. pneumonia* had a slightly higher prevalence in home deaths (43%) and *S.* aureus (42%) in hospital deaths. *K. pneumonia complex* was most common in children under five years with *S. aureus* most common in all other age groups. Dry nasal swabs detected more positive COVID-19 cases (19/21) than standard wet swabs (16/21) and had a negative predictive value of 99.3% compared to 98.5% in wet swabs. In the post-pandemic period, there remains a higher-than-expected prevalence of COVID-19 in our target population. Dry nasal swabs storage showed slightly better efficacy than standard transfer media storage for collecting/preserving COVID-19 genetic material for RT-PCR testing. Furthermore, variations in respiratory pathogen predominance showcases age-specific mortality trends and the pivotal role of healthcare setting, urging targeted interventions and improved end-of-life care.

6035

BIOMARKERS FOR PROGNOSTIC PREDICTION OF CHILDHOOD CLINICAL PNEUMONIA IN SUB-SAHARAN AFRICA

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Pneumonia is a leading cause of pediatric hospitalization and mortality. Prompt diagnosis and prognosis in patients with clinical pneumonia would optimize prioritization of patient care, particularly in resource limited settings. Current studies have highlighted procalcitonin and C-Reactive Protein as markers to prognosticate disease in patients with pneumonia or sepsis, but these markers have only moderate accuracy (80% sensitivity, 50% specificity). An improved signature of markers is needed to increase accurate classification of clinical pneumonia prognosis. We studied 140 patients in 2 hospitals in rural Gambia, aged 2-59 months who sought care for symptoms of clinical pneumonia and followed-up for five days during admission, at discharge, and 30 days after admission with a phone call. Poor-moderate prognosis (n=82) was defined as either readmission, over 3 days of hospitalization, diminished feeding ability, or death. Good prognosis (n=58) was defined as discharged well, had a hospital duration under 3 days, and did not re-seek care. 45 inflammatory proteins were quantified in plasma at admission through Luminex immunoassay. We sought a combination of these proteins (biomarker signatures) that allowed for distinction between children with poor-moderate vs. good prognosis through classification trees. 12 proteins showed statistically significantly ($P < 0.05$) differences between children with poor-moderate prognoses and good prognoses: IL18, SCF, IL1R2, TNFR2, YKL40, Resistin, TIMP1, IL6, IL8, SCF, sIL2R, and PAI. A biomarker signature of TIMP1, TNFa, IL1R2, sIL6R, and PARC had high (91%) sensitivity and moderate (60%) specificity to discriminate between those with good and moderate/prognosis. Markers in this signature could be incorporated in a future a point-of-care test to identify children with clinical pneumonia and poor-moderate prognosis to support decisions about care.

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THE EFFECT OF AZITHROMYCIN ON *STREPTOCOCCUS PNEUMONIAE* CARRIAGE AMONG KENYAN CHILDREN DISCHARGED FROM THE HOSPITAL

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More than 2.8 million deaths occur each year among children under five years in sub-Saharan Africa, primarily due to preventable infectious conditions, most commonly pneumonia. Azithromycin reduces child mortality in some settings and may work through reductions in the nasopharyngeal carriage of *Streptococcus pneumoniae*. Data are lacking on the impact of such interventions on *S. pneumoniae* carriage over time. We analyzed data from a double-blind, randomized placebo-controlled trial which followed 1,400 hospitalized Kenyan children to evaluate the impact of a 5-day course of azithromycin prescribed at discharge on mortality and re-hospitalization (published elsewhere) and carriage of *S. pneumoniae* at 3- and 6-months post-discharge. Randomization to azithromycin or placebo arm (1:1) was stratified by enrollment site (Kisii or Homa Bay counties in western Kenya). We calculated prevalence ratios (PRs) for *S. pneumoniae* carriage in the two arms at 3- and 6-months post-discharge using generalized estimating equations (GEE) with a Poisson link and exchangeable correlation structure, adjusting for enrollment site. We assessed effect modification by *S. pneumoniae* status at discharge using the likelihood ratio test. Overall prevalence of *S. pneumoniae* was 24% at hospital discharge and increased to 67% at 3- and 6-months post-discharge. Prevalence was similar between azithromycin and placebo arms at month 3 (65.8% versus 67.2%, PR 0.98, 95% CI 0.70-1.27) and month 6 (66.7% versus 66.5%, PR 1.00, 95% CI 0.68-1.32). Results were similar after adjustment for factors that were slightly imbalanced following randomization: baseline *S. pneumoniae,* breastfeeding, and household crowding. There was no evidence for statistical interaction between the intervention and baseline carriage of *S. pneumoniae*. Any effect of azithromycin treatment on the prevalence of *S. pneumoniae* carriage was not seen 3- or 6-months post-discharge. Future work will examine the intervention's impact on resistance to azithromycin and other antimicrobial agents among *S. pneumoniae* isolates.

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COMPARISON OF ANTIBIOTIC RESISTANCE PATTERNS OF *STREPTOCOCCUS PNEUMONIAE* IN CASES OF INVASIVE PNEUMOCOCCAL DISEASE AND PAIRED NASOPHARYNGEAL COLONIZATION ISOLATES

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The successful treatment of pneumococcal disease significantly depends on the right choice and use of antibiotics. This study assessed whether nasopharyngeal isolates of *Streptococcus. pneumoniae* from hospitalized children in rural Gambia could be used to predict the prevalence of antimicrobial resistance (AMR) of strains that cause invasive pneumococcal diseases (IPD). Population-based surveillance for pneumonia, septicaemia, and meningitis was conducted among children under 5 years in a rural area of The Gambia under demographic surveillance from September 2019 to December 2023. Nasopharyngeal swabs (NPS), blood cultures, cerebrospinal fluid (CSF) and lung aspirates were collected from eligible children. Conventional microbiological culture was used to identify and isolate *S. pneumoniae*. Antibiotic susceptibility testing was performed using the Kirby-Bauer disc diffusion method. We used descriptive statistics to determine and compare the proportions of AMR in patients with IPD in whom the homologous *S. pneumoniae* was detected in NPS. Of the 49 IPD cases detected with homologous NPS collected, *S. pneumoniae* was isolated in 45 (91.8%) NPS cultures. Of the paired IPD and NPS homologous *S. pneumoniae* samples, 19 (42.2%) of oxacillin, 0 (0%) of chloramphenicol, 23 (51.1%) of tetracycline, 42 (93.3%) of trimethoprim-sulfamethoxazole, 40 (88.9%) of vancomycin and 0 (0%) of ceftriaxone showed resistance in NPS samples. 23 (51.1%) of oxacillin, 2 (4.4%) of chloramphenicol, 26 (57.8%) of tetracycline, 45 (100%) of trimethoprim-sulfamethoxazole, 5 (11.1%) of vancomycin and 0 (0%) of ceftriaxone demonstrated resistance in invasive samples. The proportions of AMR of *S. pneumoniae* isolates from invasive samples and NPS were comparable. These findings demonstrate that nasopharyngeal isolates of *S. pneumoniae* from children with suspected pneumonia may be considered as a tool to monitor for AMR in a defined setting. Using NPS, a relatively non-invasive procedure as a tool for AMR surveillance programs in developing countries will enable a rational and effective use of antibiotics in the clinical management of IPD including pneumonia.

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HIGH RESIDUAL NASOPHARYNGEAL CARRIAGE OF VACCINE SEROTYPE PNEUMOCOCCI AFTER 12 YEARS OF INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINE IN THE GAMBIA

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The introduction of Pneumococcal Conjugate Vaccines (PCVs) into routine immunization programs has led to a substantial decrease in the incidence of Invasive Pneumococcal Diseases attributable to vaccine type (VT) serotypes globally. The impact of PCVs is measured through a reduction in disease or nasopharyngeal (NP) carriage of VT serotypes. Despite the long-term use of PCVs in most African countries, VT carriage persists, in contrast to similar post-PCV introduction time points in high-income countries. The residual VT carriage in Sub-Saharan Africa is of concern as it has the potential to sustain pneumococcal transmission and a persisting disease burden. We conducted population-based cross-sectional surveys of NP carriage before the introduction of PCV13 in 2009, and after in 2015, 2017, and 2022. Nasopharyngeal swabs were taken from selected household members of all ages in the Basse and Fuladu West HDSS, transported, stored, and cultured. *Streptococcus pneumoniae* isolation and serotyping were performed using standardized methods according to WHO guidelines. The prevalence of PCV13 VT pneumococcal carriage among all ages was 19%, 12%, 13%, and 8.5% in 2009 (n=2,988), 2015 (n=3,162), 2017 (n=2,709), and 2022 (n=3,822) respectively. The prevalence of VT carriage decreased from 46% in those aged 2-59 months in 2009 to 15%, 17%, and 10% in 2015, 2017 and 2022 respectively. In those aged <60 days, VT carriage prevalence fell from 27% in 2009 to 10%, 13%, and 11% respectively in 2015, 2017, and 2022. The prevalence of VT serotypes in 2009, 2015, 2017, and 2022 was 17%, 14%, 15%, and 9% among those 5-17 years, and 5%, 6%, 6%, and 2% among adults ≥18 years. In 2022, serotypes 3, 19F, 14, 23F, and 6A were the most abundant VT serotypes. Dry season, younger age group, and having a runny nose in the preceding two weeks were associated with VT carriage. Twelve years after the introduction of PCV13 in the Gambia, substantial direct effects on VT carriage have been

observed in children with limited indirect effects in adults. While additional VT reductions were observed in 2022 in those 5-17 years old, the effect in those aged <60 days appears to have plateaued in 2015.

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EVALUATION OF THE USABILITY, ACCEPTABILITY, AND FEASIBILITY OF TWO DEVICES FOR THE DELIVERY OF INTRANASAL VACCINES IN LOW-AND-MIDDLE INCOME COUNTRIES

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The COVID-19 pandemic highlighted the need for rapid and equitable global access to vaccines, including methods to enhance vaccine acceptability, uptake, and supply chain. An intranasal vaccine with an optimized delivery system has potential to expand global access and transform the vaccine delivery landscape for COVID-19 and other respiratory diseases. Intranasal vaccines could offer advantages for health workers and clients over intramuscular injections by eliminating the need for sharps disposal, decreasing risk of contamination and injuries, and reducing discomfort associated with needles. Intranasal vaccines can potentially induce local immunity in the nasal passages and upper airways, which could prevent infection at the virus entry site, directly reduce transmission, and enable a stronger immune response. PATH evaluated the usability and feasibility of two intranasal delivery devices from a provider and program perspective through simulated use by target users in Kenya, Nepal, and the U.S., and through interviews with country and global stakeholders. The devices tested were the Mucosal Atomization Device and the ZEOx1 Orion Delivery System. Simulated use participants described the devices as easy to use and successfully delivered a mock vaccination with minimal difficulties, although use errors and deviations were observed. Participants described several advantages of intranasal delivery. Having a needle-free option was the most important advantage since it is painless, eliminates sharps waste, and may be more acceptable for some clients, although a few concerns were raised around suitability for young children. Factors influencing acceptability of the individual devices included the number of steps for use, perceived comfort of the nasal tip, training required, and waste management, with community sensitization being an important component. In conclusion, this study highlights the potential of intranasal vaccine delivery devices for use in global vaccination efforts against infectious diseases and the importance of intranasal product profile characteristics in supporting usability and acceptability.

6040

THE LIVED EXPERIENCES OF UGANDAN COMMUNITY HEALTH WORKERS ENGAGED IN PREVENTION OF VERTICAL TRANSMISSION OF HIV AND A CAPACITY-BUILDING INTERVENTION

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An estimated 220,000 new HIV infections are averted annually with coordinated efforts toward the elimination of vertical transmission (EVT). This study explored the lived experiences of community health workers (CHW) engaged in EVT of HIV and to assess the impact of a capacity-building intervention. The study consisted of: (1) a qualitative assessment of lived experiences of CHWs; (2) a capacity-building intervention tailored to identified needs; and (3) assessment of the intervention using pre- and post-intervention questionnaires. Focus group discussions (FGD) and semi-structured key informant interviews (KII) were conducted. Interactive CHW training sessions for HIV/EVT were held in one rural and one semi-urban setting in Uganda, based on training materials developed by the WHO and USAID. We used standardized pre- and post-intervention questionnaires to assess comprehensive knowledge and accepting attitudes toward HIV. Qualitative exploration of the lived experience of 152 CHWs in ten FGDs and four KIIs revealed several themes: (1) CHWs as bridges between health system and community; (2) CHW assets (tacit knowledge and shared social networks); (3) CHW challenges (stigma, secrecy, and ethical quandaries); (4) favorable community reception; and (5) need for continuing education and reinforcement of skills. In response to identified needs, a capacity-building intervention was designed and implemented with 143 CHWs participating in 10 sessions. The proportion of participants with comprehensive knowledge of HIV increased from 45% to 61% (p=0.006) and the proportion endorsing accepting attitudes increased from 63% to 76% (p=0.013). In summary, CHWs are valuable players in global EVT efforts. Ongoing training is needed to support community-level initiatives.

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FACTORS CONTRIBUTING TO LOW LINKAGE TO HIV TREATMENT IN GHANA, 2023

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Successful linkage of persons living with HIV ensures prevention of new infections, prolong survival, and improved quality of life. Despite the importance of early linkage of HIV cases to care, Ghana recorded suboptimal linkage rate of 53% and 59% for 2020 and 2021 respectively and attained 78-81-68 of UNAIDS target in 2022. We analyzed issues resulting in low linkage to care in Ghana. A cross-sectional design with a mixed method approach employed. Sixteen health facilities were selected with multi-stage sampling across three geographical zones. Data on HIV testing, evidence of profiling of clients (i.e., probing of patients whether they are re-testing for HIV) assessing HIV testing services, confirmation of tests, linkage to care, and ART initiation and retention in care were reviewed from July 2022 to June 2023 in each facility. We observed the linkage process while key informant interview and FGDs were conducted among service providers. Ten clients per facility diagnosed with HIV within six months were interviewed. We used proportions to estimate patients profiled, confirmatory tests, linkage to care and retention. Of the 47,493 persons tested over the period, HIV positivity was 5.2% (2472). Of those testing positive, only 70% (1732/2472) were actual newly positive with the rest being those re-testing. About 44% (1082/2472) of those testing positive for HIV were not profiled. Confirmatory tests for HIV were limited in 63% (10/16) facilities while 80% (13/16) facilities did not have linkage registers. Of the 1732 new cases, 80% (1379/1732) were successfully referred to ART care and 62.4% (1081/1732) were linked and initiated on ART and 37.6% (651/1732) were not linked and initiated on ART because of sub-optimal referral system, non-use of triplicate referral forms and non-use of linkage registers. Inadequate profiling of patients, reporting of re-testing patients as new HIV positives and, sub-optimal referral system and non-use of the linkage registers accounted for low linkage to care. Intensive orientation and monitoring of healthcare workers to adherence to linkage to ART care implementation activities is key for improving linkage rates.

6042

ASSESSING THE RISK OF ADVERSE PREGNANCY OUTCOME AMONG HIV-POSITIVE AND HIV-NEGATIVE PREGNANT WOMEN: ANALYSIS FROM A COHORT OF WOMEN PARTICIPATING IN TWO INDIVIDUALLY RANDOMIZED CONTROLLED TRIALS IN WESTERN KENYA

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The intersection of maternal human immune deficiency virus (HIV) infection and pregnancy outcomes has been a subject of critical importance in the realm of maternal and child health. Numerous studies have shown that maternal HIV infection is associated with adverse pregnancy outcomes. However, this has been contradicted with the introduction of antiretroviral therapy (ART) for the prevention of mother-to-child HIV transmission (PMTCT). The Improving Pregnancy Outcome (IMPROVE) trials have provided a comprehensive platform to investigate the intricate relationship between maternal HIV status and the risk of adverse pregnancy outcomes among pregnant women. HIV-negative data was extracted from IMPROVE 1, a randomized, double-blind, three-arm trial conducted in regions with elevated sulfadoxine-pyrimethamine resistance in Kenya. Data for HIV-positive women were extracted from IMPROVE 2, a randomized, double-blind, two-arm, placebo-controlled trial focused on monthly IPTp with dihydroartemisinin-piperaquine for malaria in HIV-infected participants on daily cotrimoxazole eligible for (or on) daily tenofovir-lamivudine-dolutegravir (TLD) and with an undetectable viral load. Women with viable singleton pregnancies between 16-28 weeks gestation were enrolled. A total of 1224 HIV-negative and 701 HIV-positive pregnant women were recruited. Multivariable logistic regression was employed to identify associations between maternal HIV status and adverse pregnancy outcomes. The median age at enrolment was 25 years, with an interquartile range (IQR) of 21 to 30 years. HIV- positive women had increased odds of experiencing adverse pregnancy outcomes (AOR = 1.39, 95% CI: 1.04, 1.85), miscarriage (AOR=1.83, 95% CI: 1.06, 2.77) and stillbirth (AOR =1.80, 95% CI: 1.16–3.09) whereas Cohabiting women exhibited nearly a two-fold increase in the odds of adverse pregnancy outcomes (AOR = 1.75, 95% CI: 1.08, 2.82). Despite the study recruiting HIV-positive women on effective ART and with undetectable viral loads, adverse pregnancy outcomes remained higher among this group as compared with HIV negative counterparts.

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AFRICAN BRAIN POWERED GAMES APPS AVAILABLE ON COMPUTER TABLETS CAN BE USED TO DYNAMICALLY ASSESS BRAIN/BEHAVIOR INTEGRITY AND NEUROCOGNITIVE PERFORMANCE IN UGANDAN AND MALAWIAN SCHOOL-AGE CHILDREN AFFECTED BY HIV

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Brain Powered Games (BPG) is an app with 10 games designed to improve attention, working memory and learning, visual-spatial analysis, and problem solving. In Phase II we developed Village Builder (VB) to engage school-age children in a prosocial game using reasoning and planning skills to garner the resources needed to build a simulated village community. The goal was to evaluate the use of both BPG and VB as dynamic measures of brain/behavior integrity and neurocognitive function in school-age Ugandan and Malawian children (HIV, HEU, HUU cohorts). 60 HIV, 120 HEU, and 120 HUU boys and girls (MU-JHU Kampala Uganda; MCM-JH Blantyre Malawi) were randomized to either 12 one-hour training sessions of BPG over 2 months (Phase I), or "wait-listed" to 12 sessions of VB in Phase II. Performance on BPG or VB before and following the training period was then compared to performance on our "gold standard" neuropsychological battery of the Kaufman Battery for Children (KABC-II), Tests of Variables of Attention (TOVA), CogState computerized cognitive ability test, and the Achenbach Child Behavior Checklist (CBCL; completed by caregiver). Ugandan and Malawian children randomized to 12 BPG sessions in Phase I had significantly higher post-training performance on all principal outcomes of our gold-standard neuropsychological tests, when compared to "wait-listed" children. These included the KABC-II Mental Processing Index (MPI), Nonverbal Index (NVI), TOVA attention errors, TOVA impulsivity errors, CogState attention and maze learning, and CBCL internalizing symptoms (emotional problems). Similar Findings were obtained for children receiving VB in Phase II of the study. Although neuropsychological performance of HIV and HEU children was below that of the reference group (HUU) on both game achievement and gold standard assessment outcomes, all three group significantly benefitted from the game app training. Improvements in performance on the game apps were significantly related to improvements on neuropsychological tests for all three cohorts of study children. We also report on adaptation of these apps to the cloud for community-based scalability.

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ONE AND TWO DOSE TYPHOID CONJUGATE VACCINE SAFETY AND IMMUNOGENICITY IN HIV-EXPOSED UNINFECTED AND HIV-UNEXPOSED UNINFECTED MALAWIAN CHILDREN

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Vaccine safety and immunogenicity data in HIV-exposed uninfected (HEU) children are important for decision-making in HIV and typhoid co-endemic countries. In an open-label study, we recruited Malawian HEU and HIV unexposed uninfected (HUU) infants aged 9-11 months. For HEU participants, HIV exposure was determined by documented maternal history of HIV. For HUU participants, a negative maternal HIV rapid test was obtained. HIV status for all participants was confirmed by non-detectable infant HIV viral load at enrollment. HEU participants were randomized to receive: Vi-tetanus toxoid conjugate vaccine (Vi-TT) at 9 months (HEU9), 15 months (HEU15), or 9 and 15 months (HEU9+15). HUU participants received Vi-TT at 9 and 15 months. Safety outcomes included solicited and unsolicited adverse events (AE) within 7 and 28 days of vaccination, respectively. Serum was collected before and 28 days after vaccination to measure anti-Vi immunoglobulin G (IgG) antibodies by enzyme-linked immunosorbent assay (ELISA). Seroconversion was defined as ≥4-fold rise in antibody titers from day 0. Enrollment occurred from 2 December 2019 and was paused on 25 March 2020 due to the COVID-19 pandemic and resumed from 1 March - 27 August 2021. A total of 166 participants were vaccinated; 50 HEU9, 43 HEU15, 48 HEU9+15, and 25 HUU. Solicited AEs were mostly mild, and occurrence did not differ significantly in HEU and HUU participants, or one- and two-dose groups. At day 28 post-9 months vaccination, HEU (HEU9 and HEU9+15), and HUU participants had similar significant geometric mean titers (GMT) increases from day 0, reaching 3111.8 ELISA Units (EU)/mL (95% CI 2301.1- 4208.1) and 3493.7 EU/mL (95% CI 2729.4-4471.9), respectively. At 28 days post-15 months vaccination, GMT ranged from 2572.0 EU/mL (95% CI 1844.6-3586.2) to 4117.6 EU/mL (95% CI 2362.8-7175.8) and were similar in the first dose HEU15 group and second dose HEU9+15 and HUU groups. All participants seroconverted by the final study visit. Our findings of comparable safety and immunogenicity of Vi-TT in HUU and HEU children support country introductions with single-dose Vi-TT in HIV-endemic countries.

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THE CLINICO-EPIDEMIOLOGICAL EXPERIENCE OF AN MPOX OUTBREAK AT A LARGE HEALTHCARE SYSTEM IN LOUISIANA, USA.

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Mpox, a viral zoonosis of the Orthopoxvirus genus, garnered attention in May 2022 when cases emerged in non-endemic countries, including the United States. The outbreak quickly spread, with Louisiana reporting its first case in July 2022. This study analyzed Mpox cases seen across the Ochsner health system, which comprises 46 hospitals and several clinics in Louisiana and southern Mississippi. The goal of this study was to use the results as lessons learned to improve outbreak response and optimize care. Patient data from January 1, 2022, to February 28, 2023, across all Ochsner facilities was analyzed. One hundred and forty-two confirmed and suspected cases of Mpox were identified in the electronic medical record. Of these 142 cases, 77 tested positive for Mpox (confirmed) while 65 had inconclusive test results (suspected). 90.9% of confirmed cases were male, and 68.8% were black. Most patients were aged between 18 and 49 (93.6%) and Medicaid was the predominant insurance type (42.9%). At the time of testing for Mpox, 69% of patients were tested for sexually transmitted infections (STI), including syphilis, chlamydia, and gonorrhea. Of those tested for STIs, 14.1% were infected with one or more STIs. Of the 77 confirmed cases, 45.5% were living with HIV. Of those living with HIV with available CD4 measurements, 25% had a CD4 count below 200. It took an average of 5.8 days for inconclusive results and 4.8 days for positive results to return, leading to delays in diagnosis and decision-making. Patients with severe immune compromise (including HIV patients with a CD4 count <200 and HIV patients not on treatment) met the criteria for tecovirimat. Of those living with HIV who met the criteria, 41.7% received tecovirimat. The results of this study serve as a valuable foundation for enhancing clinical management strategies in future outbreak responses, potentially leading to enhanced patient outcomes.

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PERFORMANCE EVALUATION OF FIVE POINT-OF-CARE TESTS FOR MPOX DETECTION

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The global outbreak of mpox in 2022 spurred the rapid availability of commercial diagnostics for this disease. However, given the limited data on test performance, particularly for tests suitable for use in decentralized settings and those that detect multiple monkeypox virus (MPXV) clades, we conducted a diagnostic accuracy study in 2 countries to determine the clinical performance of 5 point-of-care tests (3 antigen-based rapid tests [AgRDTs] and 2 point-of-care [POC] molecular tests) compared to PCR for the detection of MPXV. Individuals >=2 years of age suspected to have mpox were enrolled prospectively in the Democratic Republic of the Congo (DRC) and retrospectively in the United Kingdom (UK) in 2023. Paired lesion and oropharyngeal (OP) samples were collected at time of enrolment. All samples were tested with both PCR reference test and all 5 index tests. A total of 105 individuals (DRC: n=68, UK: n=37) were enrolled, providing 79 lesion swabs (DRC: n=68, UK: n=11) and 82 OP swabs (DRC: n=68, UK: n=14). Overall MPX positivity in the combined cohort was 37% (N=29; DRC: 28% [19/68], UK: 91% [10/11]). Clinical sensitivity on lesion samples was highest among the two POC molecular tests (SN: 76-79%) compared to the AgRDTs (SN: 7-10%), while clinical specificity was high among all tests (SP: 85-100%). Clinical performance trends were similar when analyzed by country, although POC molecular tests had higher point sensitivity in the UK (SN: 100%) compared to DRC (SN: 63-68%). Clinical performance of POC tests on OP samples was comparable to lesion samples. Based on this, POC molecular tests on lesion samples can be used for screening, while the utility of AgRDTs for screening is unclear. In addition, OP swabs may be an alternative sample type for diagnosis.

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BURDEN OF CHAGAS DISEASE RELATED TO CARDIOMYOPATHY IN THE UNITED STATES

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Chagas disease (CD) presents a growing concern in the United States (US). It stems largely from chronic Chagas cardiomyopathy, which causes progressive heart failure, arrhythmias, and sudden death. This condition not only has health impacts (morbidity and premature mortality) but also carries significant economic burden. Furthermore, the under-diagnosis of CD in the US limits effective monitoring and care. Our study assesses the health and economic burden of Chagas cardiomyopathy caused by adult inpatient population in the US from a health system perspective. We used the 2019 Healthcare Cost & Utilization Project National Inpatient Sample (HCUP-NIS) database to assess the economic and health impacts of Chagas cardiomyopathy, using six concurrent conditions. We evaluated treatment costs and health effects in the form of Disability Adjusted Life Years (DALYs) based on survival rates and life expectancy data. Prevalence rates were estimated using age-specific data and population data from publicly available sources. We calculated the number of individuals developing cardiomyopathy within age groups based on infection prevalence. Costs were computed by age group for those with and without CD. We included survival rates from various sources and disability weights from the Global Burden of Disease Study (GBD). We modified our results to account for multimorbidity and performed a one-way sensitivity analysis to account for uncertainty. The economic burden of Chagas cardiomyopathy in the US in 2019 was estimated to be $7.14 billion as a total, yielding 1.65 million total DALYs, or 376.42 DALYs per 100,000 population. After considering multimorbidity, the burden was $5.34 billion, yielding 1.25 million DALYs or 291.6 DALYs per 100,000 population. Our study highlights the significant health and economic burden of Chagas cardiomyopathy in the US. Comparison with the 2019 GBD reveals that the burden of Chagas cardiomyopathy ranks above Tuberculosis and HIV/AIDS in total DALYs in the US. These findings stress the importance of implementing effective early diagnosis strategies to prevent unnecessary adverse health and economic consequences.

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WHAT IS THE EFFECT OF DEFORESTATION OF THE ATLANTIC FOREST ON THE OCCURRENCE OF *PANSTRONGYLUS TIBIAMACULATUS* IN URBAN AREAS?

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In Salvador, Bahia, Brazil, we have observed a systematic reduction of the Atlantic Forest, as well as an increase in the records of triatomines. Our hypothesis is that the landscape influences the occurrence of *Panstrongylus*

tibiamaculatus in houses in Salvador. Our objective was to investigate the effect of disturbances in the natural landscape of the Atlantic Forest on the occurrence and spatial distribution of *P. tibiamaculatus* in neighborhoods of Salvador. Triatomines were recorded between 2007 and 2019 in Salvador by the Center for Zoonosis Control. We evaluated the influence of forest cover, deforestation, urban infrastructure, and population on the occurrence and spatial distribution of *P. tibiamaculatus*, the main species recorded. We obtained data from the deforestation module of MapBiomas. We analyzed the association between variables using bivariate and multivariate zero-inflated generalized linear models with negative binomial distribution (glmmTMB). Multivariate models were evaluated by the Akaike Information Criterion (AIC). We obtained 1511 records of *P. tibiamaculatus* between 2007 and 2019. We observed a clustered spatial distribution of triatomines, mainly in neighborhoods with higher deforestation rates, such as the Patamares neighborhood (78.97%, n=1199). The models indicated that deforestation is the most important factor in explaining the number of triatomine records per neighborhood in Salvador. Bivariate models indicated that deforested area, forest cover, and urban structure showed a positive and significant association ($p < 0.05$) with the occurrence of triatomines. Multivariate models indicated that the model with the best performance (lower AIC) was composed of deforested area and forest cover. We observed that deforestation of Atlantic Forest areas is the main effect influencing the spatial distribution of *P. tibiamaculatus* in neighborhoods of Salvador. We recommend strengthening triatomine surveillance in the most affected neighborhoods, and environmental management of palm trees and other natural refuges of triatomines in Atlantic Forest remnants

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SYSTEMIC CLINICAL PARAMETERS AND INFECTIVITY IN CANINE LEISHMANIOSIS

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Visceral leishmaniasis (VL), caused by the zoonotic intracellular protozoal parasite *Leishmania infantum*, is a significant public health concern for humans and domestic dogs, the primary reservoir. In areas where sand fly transmission occurs, public health interventions often focus on dogs, especially sick dogs, as a source of human infections, with a belief that the sicker the dog the more likely they are to transmit parasites. However, rates of canine leishmaniosis and human leishmaniasis have not significantly improved when public health interventions remove sick dogs from the population. Additionally, xenodiagnoses studies investigating infectivity and clinical disease, based on the LeishVet scoring guidelines, found that dogs with mild to moderate disease scores were the most infective to sand flies. This study aimed to evaluate, using RNAscope, dermal and systemic factors that predict infectiousness of *L. infantum*. The number and distribution of dermal parasitized phagocytes (amastin+/CD14+) in dogs at different LeishVet stages (a clinical scoring system from 1-4 commonly used in the field) was evaluated against systemic clinicopathology of the two predominant clinical values that assess renal failure and anemia (creatinine and hematocrit). In a subset of dogs used for xenodiagnoses, dermal parasitized phagocytes were also evaluated against infectivity to sand flies. Individuals with the lowest score, had significantly fewer parasitized phagocytes than individuals with scores 2-4, which did not significantly differ from each other. Additionally, parasitized phagocyte counts significantly increased as hematocrit decreased. There was an inverse correlation between hematocrit and infectivity. In contrast, no significant changes were associated with increasing creatinine despite these being characterized as the sickest animals with the highest LeishVet scores. Future work will articulate how and why infectivity correlates with low hematocrit. These initial findings suggest that disease presentation, not severity, influences infectivity and should be considered in VL-focused public health interventions.

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EPIDEMIOLOGY OF VISCERAL LEISHMANIASIS AND OTHER PARASITIC INFECTIONS IN REFUGEE CAMPS OF ETHIOPIA

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While national guidelines exist for controlling Visceral Leishmaniasis (VL) and other parasitic infections in Ethiopia, data on their prevalence among refugees remains scarce. The aim of this study is to describe the prevalence of VL and co-occurrence of other parasitic infections among refugees in Gambella and Benishangul-Gumuz Regions. A community-based cross-sectional study was conducted at four refugee camps located in Gambella and Benishangul Gumuz Regions of Ethiopia during May to August 2023. Sociodemographic, clinical, behavioral, housing, and environmental characteristics were collected. Blood and Stool specimens were obtained and underwent testing. Data were analyzed using SPSS 25. Finally, a binary logistic regression analysis was fit to identify risk factors to VL infection at p-value <0.05. Of 2702 participants, 2670 were willing to participate in the study. Based on Direct Agglutination test (DAT) and/or rK39 test, the overall prevalence of VL was 6.3%, with higher rates observed in refugees from the Sudan (7.4%) refugees residing in Benishangul Gumuz region (9.3%) and Tsore camp (11.3%). Among refugees with VL, the prevalence of VL co-infection with Malaria, Schistosoma mansoni, Ascaris lumbricoides, Trichuris Trichuria and Hookworm were 7.8%, 10.2%, 6.6%, 3.4% and 1.2%, respectively. In multivariable analysis, Age (<15 years) AOR 0.496, 95% CI: 0.264 -0.932; residing in the Gambella refugee camp AOR 3.860, 95% CI: 2.173 - 6.644; household size (&ge5) AOR 1.48, 95% CI: 1.022 - 2.149; no previous contact history of VL AOR 0.022, 95% CI: 0.007- 0.065; close proximity of termite hills to the home AOR 2.729, 95% CI: 1.770-4.210 and presence of stagnant water near to house AOR 2.11, 95% CI:1.405-3.183 were factors associated with VL infection. This study found high VL prevalence among refugee populations in Ethiopia. These findings suggest that screening for multiple parasites should be considered for refugee population. Finally, alongside early diagnosis and treatment, public health efforts should prioritize environmental interventions like drainage and termite control to combat VL in displaced populations.

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SPECIFIC PATHOGEN TESTING FOR OPPORTUNISTIC INFECTIONS IN PERSONS WITH HIV IN PERU AND BOLIVIA

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Neurological opportunistic infections are a significant cause of morbidity and mortality in people living with HIV (PLWH). Over the last five years, we enrolled 162 PLWH with new-onset neurological symptoms and 422 PLWH controls (52% hospitalized non-neurological, 48% ambulatory) in

Santa Cruz, Bolivia, Iquitos, and Lima, Peru. Specific pathogen testing was completed for *Toxoplasma gondii, Trypanosoma cruzi,* and *Cryptococcus spp*. Site-specific testing was completed for *Mycobacterium tuberculosis* and *Histoplasma* spp. *T. gondii* seroprevalence was 76% across all sites, with Iquitos having the highest at 97% and Lima having the lowest at 60%. Seroprevalence of *T. gondii* did not vary substantially between cases and controls. This study identified 19 cases of neurological toxoplasmosis across all three sites using qPCR in cerebral spinal fluid (CSF). All toxoplasmosis cases, except for 1, were in the neurological case group. Seroprevalence of *T. cruzi* was measured in Iquitos (1%) and Santa Cruz (21%). 26 cases of Chagas disease were identified using qPCR in blood or CSF, 25 from Santa Cruz and 1 in Iquitos; 24 specimens were positive in the blood specimen alone, while 2 were positive in both blood and CSF, concerning for CNS Chagas disease. Nine of the Chagas cases were in the neurological group, while 16 were in the control group. We identified 55 cases of Cryptococcus using Immy's CrAg lateral flow assay. 38 cases were in the neurological group and 17 were in the control group. Tuberculosis testing via microscopic-observation drug-susceptibility (MODS) occurred in Lima where 2 cases were identified and Santa Cruz where 15 cases were identified; all positive results were sputum, and no cultured CSF was found to be positive. There are 4 positive TB cases in the neurological group and 13 in the negative group. Histoplasmosis testing was only completed in Lima, where four cases were identified in urine; 1 in the neurological group and 3 controls. This limited pathogen testing allowed for the identification of a potential disease etiology for 44% of the neurological patients, 19% of hospitalized controls, and 4% of ambulatory controls.

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COHORT ESTIMATION ANALYSIS OF CUTANEOUS AND MUCOCUTANEOUS LEISHMANIASIS, 1990-2021

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Leishmaniasis is a vector-borne parasitic disease caused by species of the genus Leishmania and transmitted via female phlebotomine sandflies. Several factors are important to consider in estimating the disease including geographic location, species and dissemination of treatment. We aim to describe method updates to the cohort estimation process for calculating prevalence of cutaneous and mucocutaneous leishmaniasis (CL) for the Global Burden of Disease Study (GBD), from 1990 to 2021. We used estimates of CL from GBD 2021 and preliminary results from GBD 2023 to describe the impact of the results. We first updated incidence data to include reported cases of zero. To estimate incidence, we ran a Spatiotemporal Gaussian Process Regression (ST-GPR). The regression stage of ST-GPR was updated to a negative binomial, as opposed to linear, to improve the fit of the model. Assumptions around duration, percent experiencing chronic sequelae, and healthcare access were combined with incidence to estimate prevalence. Previously, prevalence estimates were calculated by running a cohort model from 1990 using GBD age bins. The updated model began in 1890 and ran with single-year age bins to accumulate chronic cases across ages from year to year. To estimate burden, we calculated disability-adjusted life years (DALYs), calculated as the sum of years lived with disability. Percent change and counts were estimated at 1-year intervals spanning 1990 to 2021. Globally, model updates resulted in prevalence and DALY increases of 42.1% (95% UI 38.0-47.7) and 50.2% (95% UI 34.4-71.2), respectively, in 2021. Total DALYs increased from 393,000 to 591,000. Afghanistan, Brazil and Syrian Arab Republic were estimated to have the highest prevalence estimates in 2021 across both analyses. The updated model showed decreases in prevalence and DALYs in 55 of 93 endemic countries. The significant differences between models describes a need for including lower data points and continuing to update methods for estimating CL. These estimates can be utilized as a resource for policymakers to develop control and treatment programs targeted to reduce the impact of CL burden.

6053

LOW RISK FOR LOCALLY ACQUIRED CHAGAS DISEASE IN CALIFORNIA: A REVIEW OF HUMAN CASES AND TRIATOMINE SUBMISSIONS, 2013-2023

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Chagas disease in humans is caused by infection with *Trypanosoma cruzi* parasites that are transmitted by triatomine bugs via infected feces. Most infections are acquired in rural parts of Mexico and Central and South America, though triatomines and *T. cruzi* are also endemic to the southern United States. Chagas disease is considered non-endemic in the United States. Most identified US patients with Chagas disease report travel history to Latin America, yet the presence of both the vector and causative agent in California has prompted questions about the risk of locally acquired infections. We summarize 226 triatomine bug submissions and 50 human case reports to the California Department of Public Health between 2013 and 2023. Of the 226 triatomines tested, 63 (28%) were positive for *T. cruzi* via multi-target PCR. We use a draft surveillance case definition and five criteria to evaluate evidence of *T. cruzi* infection and local transmission, respectively. Forty-three (86%) patients had evidence of infection and were classified as cases. We found limited overlap in the spatial and temporal distribution of triatomine collections and human cases. Country of birth, travel history outside the United States, and absence of triatomine detections in the county of residence ruled out local transmission for 26 (60%) cases. Local transmission could not be ruled out for the remaining 17 (40%) cases, though missing demographic information prevented full assessment of local transmission criteria for these cases. This is consistent with the documented behavior of triatomine bugs in California, which, in contrast to anthropophilic species in Latin America, typically defecate away from the bite site, reducing the risk of transmission. Results suggest low risk for locally acquired Chagas disease in California, though more complete collection of demographic data in human case reporting would improve our understanding.

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EFGH CATCHMENT AREA, DHAKA, SECONDARY *SHIGELLA* TRANSMISSION AND PREDISPOSING FACTORS FOR DEVELOPING SHIGELLOSIS AMONG HOUSEHOLD CONTACTS IN THE BANGLADESH

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Shigellosis, caused by *Shigella* spp., is a major global health concern, leading to millions of deaths annually, and under 5 children are more vulnerable. Previous studies showed the susceptibility of infection among household (HH) contacts of index cases. The purpose of the study was to illustrate the secondary transmission among HH contacts of *Shigella*-positive patients. Information on index cases was captured from EFGH study carried out in Bangladesh. The *Shigella*-positive patient was defined as an index case and the HH contacts who permanently resided in the same HH or were present for at least 7 days of the last 14 days, were enrolled in this study. Stool specimens and other information were collected from the HH contacts within 7 days of index cases enrollment. Microbiological culture and quantitative PCR were carried out to detect *Shigella* within HH contact. Descriptive statistics, bivariate, and multiple logistic regression models were used to evaluate the association of the secondary transmission of *Shigella* infection with different factors. A total of 235 HH contacts of the index cases (n=78) were enrolled. We found 23 culture-confirmed *Shigella* among HH contacts, which represented ~10% secondary transmission. The quantitative PCR revealed 79% (n=73/92)

Shigella infection. No significant association was found with secondary *Shigella* transmission and other predicted risk factors. However, in multiple regression analysis, individuals with secondary-level education had a 4-fold higher risk of secondary *Shigella* transmission compared to those with higher levels of education. Additionally, individuals who did not use soap after defecation had a 7-fold higher risk of secondary *Shigella* transmission compared to soap users.Evidence generated from this study on secondary *Shigella* transmission and household-level risk factors will help to plan strategies to reduce risk of transmission in the communities.

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GENETIC FACTORS CONTRIBUTING TO DISEASE IN *SHIGELLA*

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Shigella spp. are the leading bacterial cause of moderate-to-severe childhood diarrhoea in lower- and middle- income (LMICs) and the causative agent of shigellosis. Increasing antimicrobial resistance (AMR) and a lack of widely available licenced vaccine means *Shigella* is now classed by WHO as an AMR priority pathogen. Understanding pathogen-specific factors responsible for the manifestation of clinical disease is critical to inform future treatment and management strategies. To identify key genetic determinants associated with clinical disease we performed bacterial Genome Wide Association Studies (GWAS) on > 1000 *S. flexneri* and *sonnei* isolates from South Asia and sub-Saharan Africa collected during the Global Enteric Multicentre Study (GEMS), using case-control and severity score data. Our findings indicate that specific genotypes of *S. sonnei* and *S. flexneri* are more significantly associated with disease and clinical severity than others. Through bGWAS we identified multiple SNPs (*n*= 206) and accessory genes (*n*= 171) significantly associated with disease. Some accessory genome elements showed an epidemiological interaction with genotype, which subsequent laboratory investigation revealed was associated with an unstable virulence plasmid in *S. flexneri* Phylogroup 1 and variation in a transporter protein was shown to be associated with increased clinical severity in *S. sonnei.* These genetic factors might act as predictors of severe disease or be developed as novel therapeutic targets, and demonstrate the potential of bGWAS and functional microbiology to provide insight into genetic contributors of disease to support diagnostics, vaccine and drug development.

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ANTIBODY-MEDIATED PROTECTION AGAINST SHIGELLOSIS

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Shigella is the second leading cause of diarrheal disease-related death in young children in low and middle income countries. Efforts to develop an effective *Shigella* vaccine have been hindered by the limited understanding of immunological correlates of protection against shigellosis. To address this gap, we developed and applied a systems approach to analyze antibody-mediated responses to *Shigella* across individuals living in Shigella endemic and non-endemic regions. Using this approach we interrogate antibody specificities, isotypes, Fc-receptor binding and antibody-mediated phagocytic-cell activation to construct high-resolution antibody profiles. First, we analyzed serum samples collected from individuals experimentally challenged with *Shigella* and found that functional IgG against *Shigella* virulence factor IpaB bind to Fc-receptors and activate neutrophils and monocytes to elicit protective phagocytosis. More recently, we analyzed *Shigella*-specific antibody responses over time in the context of endemic resistance or breakthrough infections in a *Shigella* high burden location. Here, we unraveled a novel functional role for oligo-polysaccharide-specific FcaR binding IgA, found in resistant individuals, that activates bactericidal neutrophil functions including phagocytosis, degranulation and reactive oxygen species production. Finally, we analyzed serum samples of adults and kids hospitalized with shigellosis, to elucidate age dependent differences in antibody mediated protection against severe shigellosis. Overall, our findings suggest that *Shigella*-specific antibodies protect individuals by binding to Fc receptors on the surface of phagocytic cells and leveraging bactericidal activities of phagocytes. These findings will assist in the development and evaluation of vaccines against *Shigella* and other enteric pathogens.

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DEVELOPMENT OF A SEROEPIDEMIOLOGY TOOL FOR *SHIGELLA*

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Shigella is the leading cause of diarrheal mortality worldwide, with children under the age of five in low-and-middle-income countries (LMICs) bearing the highest burden of disease. A robust pipeline of *Shigella* vaccines are in clinical development, however, our understanding of the Shigella burden in LMICs remains limited due to the lack of accurate rapid diagnostic tests. Such data are essential to inform vaccine introduction and evaluation of impact. A cost-effective, seroepidemiology tool for Shigella can potentially overcome these challenges. We have previously developed a seroepidemiology tool for enteric fever based on leveraging antibody decay kinetics of anti-HlyE post-infection to estimate seroincidence in cross-sectional serosurveys. To apply this model to Shigella, we used a multiplex bead-based assay to measure semi-quantitative IgG and IgA levels to IpaB and the O-specific polysaccharide of the four most prevalent Shigella serotypes (*Shigella sonnei* and *Shigella flexneri* (Sf) 2a, Sf 3a, and Sf 6) in blood samples. We modeled the longitudinal antibody kinetics in Bangladeshi cases with culture or PCR-confirmed Shigella infections and evaluated the antibody distributions across endemic communities in Asia and Africa. We found that all antigens could discriminate convalescent Shigella cases and healthy controls with Areas Under the Curve of 0.98-1.00. IgA responses to all antigens peaked by day 7, while IgG peaked by day 7 to 30, varying according to age. Responses were highest to the homologous OSP of the infecting serotype, with the highest cross-reactivity seen between Sf 2a and Sf 3a, which are structurally similar. Children under the age of 5 years exhibited lower peak antibody responses and faster antibody decay compared to older children and adults. Additionally, we observed varied reactivity to these antigens across endemic communities with differences by age. These data highlight the potential utility of this assay to estimate Shigella seroincidence in communities where culture- or PCR-based serosurveillance is limited or unavailable.

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PROTECTION CONFERRED BY A SINGLE DOSE OF TYPHOID CONJUGATE VACCINE AMONG BANGLADESHI CHILDREN AFTER FIVE YEARS OF VACCINATION: ANALYSIS OF A CLUSTER RANDOMIZED CONTROLLED TRIAL

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Typhoid fever in low- and middle-income countries continues to be a serious public health concern. Large randomised controlled trials of typhoid conjugate vaccine (TCV) demonstrated high efficacy among children aged 9 months to 15 years after two years of receiving single dose of TCV. A cluster randomised controlled trial was conducted in Dhaka, Bangladesh, between 2018 and 2021. To generate data on medium-term protection, follow-up of the trial population was extended until August 2023 to evaluate the immunogenicity and protection of the vaccine 4-5 years after immunization. Japanese encephalitis (JE) vaccine was the control vaccine. Children who received JE vaccine were invited to receive TCV in 2021. Primary endpoint of the follow-up was to compare incidence of typhoid fever between children who received TCV in 2018/2019 and those in 2021 to evaluate the decline of vaccine efficacy (VE). An immunogenicity study was conducted on 1500 children. Previous TCV recipients (vaccinated in 2018/19) demonstrated higher risk of typhoid than recent recipients (vaccinated in 2021); the adjusted incidence rate ratio of 3.10 (95%CI: 1.39-6.95) indicated a decline in protection with a single-dose TCV after 4-5 years. The estimated VE after 4-5 years of follow-up was 50% (95%CI: -13-78). Using test-negative design (TND) analysis, the estimate of decline of VE was confirmed. Compared to non-vaccinees, VE was 84% (95%CI: 74-90) and 57% (95%CI: 39-70) in recent and previous TCV vaccinees, respectively. Over the study period, anti-Vi-IgG responses declined. Children who received vaccinations before the age of two showed the highest rate of decline. Negative correlation between age and decay of antibodies was also seen in subgroup analysis of VE, where the youngest age group (<7 years at fever visits) exhibited the fastest waning, with VE dropping to 31% (95%CI: -19-60) at 4-5 years post-vaccination. Children who received vaccine at a younger age showed the highest decline in immune responses and protection. To maintain protection against typhoid fever, a booster dose of TCV for children vaccinated under the age of two years could be recommended.

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SAFETY AND IMMUNOGENICITY OF A BIVALENT VACCINE AGAINST SALMONELLA TYPHI AND SALMONELLA PARATYPHI A: INTERIM DATA FROM A PHASE 1 RANDOMIZED CONTROLLED OBSERVER-BLIND, TRIAL AMONG HEALTHY ADULTS IN EUROPE

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Enteric fever remains a major cause of disability and death. In 2019, there were 13 million cases of enteric fever globally, 28% of these being caused by Salmonella Paratyphi A. There is a trend of increased incidence of S. Paratyphi A in parts of Asia, estimated as ~35% of cases in India and Nepal and >60% of enteric fever in China, with a similar trend of antimicrobial resistance. GVGH is developing a novel Typhoid and Paratyphoid A conjugate vaccine (bivalent Vi-CRM197+O:2-CRM197), for the prevention of both typhoid and paratyphoid A enteric fever in infants and older age groups. We present here the interim results from a first-time-in-human study aimed to evaluate the safety and immunogenicity of this candidate vaccine. Overall, 96 healthy adult participants were randomised 2:1 to receive 2 injections at 0 and 6 months, with the investigational product or comparator vaccines. There was a dose-escalation approach with 2 different doses (Low and Full, containing 5 µg Vi/ 5 µg O:2 and 25 µg Vi/ 25µg O:2, respectively), formulated with or without Alum. Interim analysis was performed 28 days after the first dose administration. Results showed no safety signals or concerns from the analysis of data collected up to 28 days after the first dose administration. Majority of Adverse Events (AEs) reported were of mild to moderate severity. No Serious AEs were reported. Both dose levels (with or without Alum) induced a robust immune response: 100% of the participants in the Low or Full Dose without Alum groups, 88.9% and 95.7% of participants in the Low and Full dose with Alum groups respectively, achieved Anti-Vi Ag IgG ≥4.3 µg/ml. 100% of the participants in the Low or Full Dose without Alum groups, 81.8% and 83.3% of the participants in the Low or Full Dose with Alum groups respectively, achieved at least 4-fold increase in Anti-O:2 IgG levels, with functionality against S. Paratyphi A confirmed using Serum Bactericidal Activity (SBA) assay. Based on these interim results, the clinical development with the Full dose without Alum formulation is progressing to phase 2 study in target population. Post dose-2 data are expected in Q3 2024.

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EFFECT OF BIANNUAL AZITHROMYCIN MASS DRUG ADMINISTRATION ON ENTERIC FEVER TRANSMISSION INTENSITY IN NIGER

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Enteric fever, a systemic bacterial infection caused by *Salmonella enterica serovars* Typhi and Paratyphi, remains a significant health concern in many low- and middle-income countries, where it is primarily managed with antimicrobials. Historically, assessing the enteric fever burden has been challenging in regions lacking blood culture surveillance. New methods coupling specific serologic markers with modeled antibody decay trajectories from blood-culture-confirmed enteric fever patients now allow accurate estimation of the force of infection from cross-sectional serosurveys. This secondary analysis aimed to assess enteric fever incidence within a population devoid of blood culture surveillance and evaluate the impact of biannual azithromycin mass drug administration on exposure. The MORDOR study, a cluster-randomized, placebo-controlled trial, allocated 30 communities in rural Dosso, Niger, to receive biannual azithromycin or placebo. All children 1-59 months weighing >3.8kg were eligible for treatment. Annually, a random sample of 40 children from each community provided capillary blood samples collected on filter paper. Samples from the 2015 and 2020 surveys were tested for IgA and IgG antibodies against Hemolysin E using ELISAs. Seroincidence rates were estimated by maximizing the likelihood of the cross-sectional antibody response data based on age-specific antibody kinetics using the Serocalculator package in R. Samples from 1455 children were available for analysis, 449 from baseline and 1006 from year 5 after 10 rounds of treatment. The median age was 2.9 years (IQR 1.7-3.9). The force of infection increased from 1.35 (95% CI 1.2 - 1.5) per person-years in 2015 to 2.8 (95% CI 2.5 - 2.1) and 3.0 (95%CI 2.7-3.3) in the intervention and control groups, respectively, by 2020. These results demonstrate a substantial and increasing burden of enteric fever among young children in rural Niger, with biannual azithromycin showing no discernible impact on transmission intensity. Interventions including introduction of typhoid conjugate vaccine are urgently needed to reduce the burden of enteric fever in this population.

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MACHINE LEARNING CAN REVEAL GENOMIC SIGNALS ASSOCIATED WITH ANTIGENIC DISTANCE IN DENGUE VIRUSES

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Dengue virus (DENV), a mosquito-borne flavivirus with four distinct serotypes (DENV1-4), affect between 100-400 million people each year. Given that dengue virus spreads through infected mosquitoes (Aedes aegypti or Ae. albopictus) prevalent in tropical and sub-tropical areas, nearly half of the world population faces the threat of contracting DENV. A previously published antigenic cartography map encompassing 348 Thailand dengue viruses over two decades discovered oscillating patterns in DENV antigenicity. One notable oscillating pattern corresponding with the magnitude of DENV epidemics in Thailand. However, the genetic processes underlying antigenic shifts remain undiscovered. Expanding on this previous work, we used random forest machine learning models to explore mutational space of DENV and the distances from the antigenic cartography to determine the genes and specific mutations associated with to the variance in antigenic distance First, we compared the prediction power of different genetic distance models and found that position-wise nucleotide pairs performed best. Next, we found that genetic signals in NS5, NS3, and E proteins were best able to predict antigenic distance. Finally, we used these findings to model epidemic outbreak prediction. To increase prediction power, we also tested our models using deep learning architecture. Our research identifies the signals in the DENV genome corresponding to antigenic changes, which cannot be identified through traditional statistical methods, such as linear regression. While this research focuses on DENV, our methodology exhibits versatility for application to other viruses for which the antigenic cartography maps are present. The utilization and ongoing development of this model alongside with other machine learning techniques are poised to empower researchers in anticipating the shifts in antigenicity through analyzing viral genomes. This proactive stance will facilitate preparedness for potential outbreaks impacting global populations and foster the strategic development of vaccines to combat various diseases.

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GENOMIC EPIDEMIOLOGY OF ARBOVIRUSES REVEALS NEW VIRUS INTRODUCTIONS AND SIMULTANEOUS VIRUS CIRCULATION DURING DENGUE AND CHIKUNGUNYA OUTBREAKS IN BRAZIL

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Viral genomic surveillance is crucial for epidemic response and public health preparedness, as well as for providing insights into virus transmission patterns and dynamics. Between 2019 and 2024, we conducted an active arbovirus investigation on 8,000 samples from patients with acute febrile illness from a dengue hyperendemic municipality in Sao Paulo, Brazil, identifying 1,650 positive samples. Full-genome deep sequencing and phylogenetic analyses of approximately 1,000 samples confirmed the prevalence of DENV-2 genotype III from 2019 to 2020. In 2021, we observed a serotype replacement, with DENV2-III (Asian-American) replaced by DENV-1 genotype V, which remains the prevalent serotype to date. However, at the beginning of 2024, we detected circulation of DENV-2 genotype II (Cosmopolitan) and demonstrated an increase in the number of cases caused by this serotype. Furthermore, we characterized autochthonous cases of DENV-3 genotype III in 2024, emphasizing the resurgence of DENV-3 after 15 years of absence. The molecular surveillance of CHIKV revealed the region's most significant CHIKV outbreak, with increased virus detection since December 2023. Phylogenetic analysis classified all the genomes as ECSA lineage, closely related to strains from the Northeast and Southeast of Brazil. We have also analyzed the circulating viruses during these years correlating it with epidemiological and clinical data. We demonstrated that differential diagnosis for DENV serotypes and other arboviruses is essential to understand the epidemiological landscapes in areas with simultaneous circulation of viruses with similar clinical profiles. Our results stress the importance of sustainable active arbovirus surveillance to detect new introductions and ensure rapid deployment of control strategies to mitigate outbreaks in regions with high epidemic potential.

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SEROLOGICAL AND GENETIC CHARACTERIZATION OF THE DENGUE VIRUS SEROTYPE 3 (DENV-3) INFECTING CHILDREN'S POPULATIONS DURING A DENGUE OUTBREAK IN MERIDA, MEXICO

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The dengue virus (DENV, *Flaviviridae* family), one of the most important mosquito-borne viruses that causes significant morbidity and mortality every year around the word. While DENV exists as four antigenically distinct serotypes (1 to 4), these serotypes are genetically clearly distinct "genotypes" which demonstrate varying pathogenicity and infectivity. DENV strains currently circulating in Mexico are not well studied at either serological or molecular level. Here, we performed a serological and molecular characterization of DENV strains from a dengue outbreak that affected children living in the city of Merida, Yucatan in 2023. Briefly, during an active surveillance phase (July and December 2023), 163 out of 536 (30.4%) clinically suspected febrile cases for arbovirus infection were identified as DENV-RNA positive by RT-qPCR. Of these, 30% (49/163) underwent full DENV genome sequencing using a combination of metagenomic library preparation and reference-based assembly. Preliminary molecular analyses identified all sequences as DENV 3 genotype III and were closely related to samples from the U.S, Cuba, and Brazil collected in 2023. Phylogenetic analysis revealed three distinct clades that differed by up to 3% at the nucleotide level and clustered independently on a maximum likelihood tree, suggesting that the outbreak was not due to a single new introduction. Additionally, screening of neutralizing antibody responses (NT_{50}) using a set of these DENV (PCR+) samples identified a higher prevalence of neutralizing antibodies mainly against DENV-1 and -2 and ZIKV but not DENV-3 (NT_{50} titer<1:20-100) suggesting that flavivirus cross-reactive immunity might not be equally protective against all four DENV serotypes. As DENV disease outcome is determined by complex interactions between immunopathologic, viral, and human genetic factors, understanding the genetic and serological variations elicit during DENV infections in endemic areas have important implications for the emerging of future outbreaks as well as the evaluation of dengue vaccines, and vector control trials.

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GENOMIC SURVEILLANCE OF DENGUE VIRUS FROM AN ACUTE FEBRILE ILLNESS STUDY IN EL SALVADOR, 2022-2023

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Recent dengue virus (DENV) epidemics in Central and South America highlight the need for improved surveillance, particularly regarding viral genomic surveillance. El Salvador is a Central American country where data regarding which DENV serotypes are circulating are sparse, and circulating DENV genotypes are largely unknown. To address the current gap in knowledge and to supplement El Salvador Ministry of Health's surveillance, DENV surveillance was conducted as part of an acute febrile illness study. Samples from acutely febrile patients were collected from two study sites located in the Santa Ana department of El Salvador from 2022-2023. Whole blood samples were screened for DENV using a quadraplex real-time PCR assay to define the serotype. A total of 134 samples tested positive for DENV in our study and included all four serotypes, with the majority positive for DENV-4 (70.9%), followed by DENV-1 (22.4%), DENV-3 (5.2%), and DENV-2 (1.5%). These samples were further investigated through viral genomic sequencing using a tiled amplicon PCR assay coupled with Oxford Nanopore Technologies' MinION platform. These data were analyzed using the viralrecon Nextflow pipeline to generate the genome sequences, which were genotyped using Genome Detective's Dengue Virus Typing Tool. Initial analysis revealed that DENV-4 samples were genotype IIB, consistent with reports from neighboring countries. Phylogenetic analysis of the DENV-4 samples in the context of all other DENV-4 sequences on GenBank from 2022-2024 indicated a monophyletic clade with distinct subclades. These subclades suggested circulation within El Salvador however two subclades were also related to autochthonous DENV-4 isolates from Florida, USA (2022 and 2023) and two Nicaragua isolates (2022). Work is ongoing to incorporate geospatial analysis with phylogenetic information to investigate how the viruses are circulating in Santa Ana department. This work is key to understanding the molecular epidemiology of DENV in El Salvador, which can be used to define introduction events and inform countermeasure development and deployment.

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ECOLOGICAL AND GENETIC DETERMINANTS OF WEST NILE VIRUS PERSISTENCE IN FORT COLLINS, COLORADO

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Despite being a semi-arid environment, Fort Collins, CO has emerged as a prominent hot spot for West Nile Virus (WNV) in the United States, with the 2023 season being one of the worst on record. To explore factors that contribute to successful introductions and persistence of West Nile virus in Fort Collins, we constructed a maximum likelihood time-resolved phylogenetic tree from 671 sequences derived from WNV-positive mosquito pools collected and sequenced from Fort Collins' surveillance program combined with 2,595 sequences from the rest of the United States. We found 91 discrete introductions of West Nile virus into Fort Collins with an average local persistence of 2.72 years. To investigate determinants of WNV persistence we developed a linear regression model. This preliminary analysis found a negative association between the persistence of West Nile virus and the year of introduction (estimate -0.41, CI 95%; -0.78, -0.04) indicating conditions become less favorable for WNV persistence with each passing year. These results are intriguing, given the rise in the incidence of West Nile cases despite a decrease in the persistence of new introductions, indicating that existing introductions have some advantages over novel introductions. A two-pronged investigation is ongoing to investigate these findings further. Firstly, computational modeling will scrutinize weather patterns, land types, avian immunity, and geographical locations during the introduction of these strains. Secondly, experimental analysis will explore strain phenotypes, focusing on replication under varying conditions. This interdisciplinary approach seeks to uncover critical insights into the factors influencing the introduction and persistence of WNV strains within a defined geographical focus. By combining advanced phylogeographic analyses with experimental investigations, we aim to inform targeted control strategies and contribute to a broader understanding of WNV transmission dynamics.

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GENOMIC EPIDEMIOLOGY OF RIFT VALLEY FEVER VIRUS INVOLVED IN THE 2018 & 2022 OUTBREAKS IN LIVESTOCK IN RWANDA

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Rift Valley Fever (RVF) caused by RVF virus (RVFV) is a mosquito-borne transboundary zoonosis which is endemic in many African countries and the Arabian Peninsula. This phlebovirus was first molecularly confirmed in Rwanda's livestock in 2012 and since then sporadic cases have been reported almost every year until 2018 when the first largest outbreak occurred followed by the second in 2022. The objective of this study was to determine the genetic characteristics of the circulating lineages and their

ancestral origin. Following the emergency of the 2022 RVF outbreak and the need to protect the public health, Rwanda established six temporary RVF testing centers to carry out the pre-slaughter screening by RT-qPCR of all animals arriving at slaughterhouses for meat production. A total of 157 initially RT-qPCR-confirmed livestock samples from 3 testing centers and 37 archived farm-collected samples from the 2018 outbreak were obtained via the Rwanda Veterinary Laboratory for virus sequencing. Overall, two whole genome sequences for the 2018 outbreak and 36, 41 and 38 virus sequences for S, M and L RVFV genome segments, respectively, from the 2022 outbreak were generated. Both Maximum Likelihood and Bayesian-based phylogenetic analyses as well as lineage assignment were performed. The findings demonstrated that viruses belonging to a single lineage C circulated during both outbreaks and shared a recent common ancestor with viral strains isolated in Uganda between 2016 and 2019, which were also genetically linked to the 2006/2007 largest East Africa RVF outbreak reported in Kenya, Tanzania and Somalia. Along-side the wild-type viruses, genetic evidence of RVFV Clone 13 vaccine virus in slaughterhouse animals was also found, emphasizing the importance of reinforcing the protection of public health during RVF outbreak as well as during vaccination campaigns using live-attenuated vaccines. The results provided further evidence of the ongoing cross-border widespread of RVFV lineage C in Africa and underscored the need for efficient national and international multi-disciplinary collaboration to fight and control this emerging hemorrhagic fever.

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SINGLE CELL TRANSCRIPTIONAL PROFILING OF DRY AND WET SEASON *PLASMODIUM FALCIPARUM*

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Persistence of malaria parasites in asymptomatic hosts is crucial in areas of seasonal transmission, where *P. falciparum* bridges wet seasons months apart. In the dry season, infected red blood cells (iRBCs) exhibit extended circulation with reduced cytoadherence, promoting splenic clearance of iRBCs and hindering parasitaemia increase. What determines longer circulation of iRBCs and asymptomatic persistence remains unknown. Here, we investigated transcriptional differences between parasites of similar developmental stage infecting asymptomatic Malian children at the transition from the dry to the wet season, and children showing symptoms of clinical malaria in the wet season. We generated a single cell RNAseq reference atlas of a lab-adapted line of *P. falciparum*, containing over 27000 iRBCs, capturing all asexual stages and developing gametocytes, allowing to infer pseudotime along the 48h asexual cycle. Then, we performed single cell RNAseq of iRBCs from 6 asymptomatic carriers at the transition from the dry to the wet season, and from 9 clinical malaria cases in the wet season, obtaining ~3600 and ~23000 *P. falciparum*-iRBCs, respectively, which were grouped by hours post invasion (hpi) through projection to the single cell reference atlas. Pseudotime of *P. falciparum*-iRBCsin clinical malaria samples ranged from 3.9 to 24.3 hpi (mode: 8.7 hpi), while the dry season parasites were 4.4 to 27.1 hpi (mode: 11 hpi). We then compared gene expression of 10 groups of cells with parasites between 6 and 11.25 hpi containing >100 cells of equivalent pseudotime from the dry season and malaria-causing parasites. We found 26 differentially expressed genes (DEGs, $p<0.05$ and fold change >1.5) across groups, which likely contribute to persisting infections in the dry season. DEGs upregulated in the dry season (n=14) encode parasite proteins exported to the host erythrocyte, and are linked to the remodelling of the host cell required for efficient cytoadhesion. Our data will help clarify the molecular mechanisms used by *P. falciparum* to adjust cytoadhesion and present the decreased virulence observed in persisting parasites during the dry season.

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THE DYNAMICS OF PARASITE GROWTH IN *PLASMODIUM FALCIPARUM* AND *P. KNOWLESI* CO-CULTURES

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In Malaysia, the incidence of human cases of *Plasmodium knowlesi* malaria has increased alongside the elimination of *P. falciparum* and *P. vivax*. However, whether the elimination of *P. falciparum* and/or *P. vivax* has contributed directly to the increase of *P. knowlesi* is unknown. We therefore utilised co-culture competition assays to investigate the *in vitro* interaction between *P. knowlesi* and *P. falciparum. P. knowlesi/P. falciparum* mono- and co-cultures were established in 6-well plates and maintained under standard conditions for 14 - 28 days. Total parasitemia was monitored by flow cytometry and maintained between 1-8%; samples were taken daily for digital (dPCR) targeting the 18S gene of each species to quantify the parasitaemia of each species. In the co-cultures, *P. falciparum* and *P. knowlesi* were seeded at *P. falciparum*: *P. knowlesi* parasitemia ratios of 90:10, 80:20, 70:30, 60:40 and 50:50. In all cases *P. falciparum* rapidly suppressed growth of *P. knowlesi*, accounting for >95% of parasites by day 10 and maintaining this dominance until the end of the assays. In subsequent experiments *P. falciparum/P. knowlesi* co-cultures were established in Transwell plates to prevent direct contact between the species. Growth rates of *P. falciparum* and *P. knowlesi* in the Transwell co-cultures were comparable to the growth rates of each species in the monocultures, with no inhibitory interaction observed. In summary, we have shown that *P. falciparum* suppresses growth of *P. knowlesi in vitro*, suggesting that *P. falciparum* may play a role in maintaining low prevalence of *P. knowlesi* in co-endemic regions, and that the removal of this suppressive effect may contribute to an increase in cases of knowlesi malaria. Further experiments evaluating the mechanisms of this inter-species interaction are underway, and data will be presented.

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DEFINING THE ROLE OF PIPECOLIC ACID IN THE ENCEPHALOPATHY OF CEREBRAL MALARIA

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Encephalopathy is the hallmark of cerebral malaria (CM), however the mechanism of coma is unknown. Our previous studies demonstrated elevated pipecolic acid (PA) levels in the blood of children with CM compared to children with mild malaria. We also found elevated PA levels in the brains of mice in the experimental cerebral malaria (ECM) model. Here we demonstrate that both *P. falciparum* and *P. berghei* ANKA generate PA using 13C-lysine metabolic tracing studies. To determine if other neuromodulatory metabolites are present in the brain in the animal model, we conducted whole metabolome analysis of ECM brains versus uninfected, and the only neuromodulatory molecule, pipecolic acid was increased ($p=0.0002$). ECM brains also demonstrated an increase in the lactate:pyruvate ratio ($p=0.003$), compared to controls suggestive of ischemia. Cerebral spinal fluid in children with CM compared to non-malaria controls demonstrated distinct metabolomic signatures, without differences in PA levels between the groups. To directly test if PA induces a decline in neurologic function, we administered PA subcutaneously into mice and observed a reversible neurological decline using the rapid murine coma and behavior scale ($p=0.02$). Our studies demonstrate that *Plasmodium* generates PA, brain metabolism during ECM is distinct and that PA induces a rapid and reversible effect on behavior.

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CEREBRAL MALARIA, THE BLOOD-BRAIN BARRIER AND BEYOND. THE IMPACT OF ICAM-1/EPCR DUAL BINDING PARASITES ON BARRIER DYSFUNCTION

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Cerebral malaria (CM) is characterised by parasite sequestration in the brain microvasculature triggering inflammatory responses, resulting in localised changes in surface receptor expression such (increased ICAM-1/decreased EPCR) culminating in increased barrier permeability and loss of tight junctions. In approximately 15-20% of cases, the disease is fatal with death occurring due to compression of the brain stem via sudden, excessive swelling of the brain. The exact mechanisms which trigger this swelling are not fully understood, nor is the impact of the adhesion of specific subsets of parasites on the blood-brain-barrier (BBB). We previously showed how ICAM-1/EPCR dual binding parasite can cross the blood brain barrier using 3D blood brain barrier organoids to model the human blood brain barrier, and that these dual binding parasites caused the organoids to swell in a PfEMP1 dependent manner. He we present further evidence of the negative impact of the interaction between dual binding PfEMP1s using defined parasites such as HB3VAR03 (ICAM-1/EPCR) and IT4VAR13 (ICAM-1/CD36) where binding impact not only the tight-junctions, but transcellular transport as evidenced by reduced efflux by P-glycoprotein. To investigate the secretory impact of parasites, we challenged the blood-brain barrier organoids with conditioned media, and again found differential responses suggesting heterogeneity in the secretory components of parasites to trigger increased barrier permeability. Taken together, these data highlight the complex nature of barrier dysfunction and interplay between parasite binding, secretory products, and immune responses contribute to barrier dysfunction.

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HETEROGENEITY IN PATHOGENIC BRAIN SEQUESTERED CD8$^+$ T CELLS DURING EXPERIMENTAL CEREBRAL MALARIA REVEALED BY SINGLE CELL SEQUENCING

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Brain sequestered CD8$^+$ T cells play a prominent role in the pathogenesis of experimental cerebral malaria (ECM) in mice and are found in the cerebrovasculature of young children with cerebral malaria. In mice, CD8$^+$ T cells accumulate in the brain during the effector phase of a *Plasmodium berghei* ANKA (*Pb–A*) infection and promote pathogenesis by inducing apoptosis of endothelial cells of the blood brain barrier. However, the molecular events associated with this CD8$^+$ T cell-mediated pathogenesis remain poorly understood. We performed single cell sequencing and bioinformatic analysis of brain sequestered CD8$^+$ T cells isolated from perfused tissue of *Pb–A* infected moribund and non-moribund mice and uninfected mice. We find that 42 genes associate with disease symptoms and 17 genes associate with *Pb–A* infection. Importantly, cluster analysis revealed that the brain sequestered CD8$^+$ T cells consists of two large clusters and ten small but distinct clusters indicating a large degree of heterogenicity in these cell populations during ECM. Furthermore, one of the large clusters is enriched in moribund mice and therefore associates with the symptoms of disease and the other large cluster preferentially expresses IFN–γ, a known biomarker of ECM pathogenesis. Lastly, we have created a transcriptional atlas of brain sequestered CD8$^+$ T cells by plotting the average expression and percentage of CD8$^+$ T cells that express various cytokines, chemokines, transcription factors, cell surface molecules such as checkpoint inhibitors, and other relevant molecules. The results of this study are being used to identify and test promising targets for adjunctive therapy to reduce the high mortality of human CM.

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METABOLITES ASSOCIATED WITH CEREBRAL MALARIA PATHOGENESIS AND PROTRACTED PRO-THROMBOTIC PROPENSITY IN CHILD SURVIVORS OF CEREBRAL MALARIA

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The pathogenic mechanisms of cerebral malaria and its sequelae remain poorly understood. Our previous transcriptomic and biomarker studies suggest that survivors of cerebral malaria have a prolonged period of risk for thrombosis, defective fibrinolysis, and vascular endothelium dysfunction, which may underlie post-recovery clinical sequelae. For this project, we aimed to determine the metabolic mediators associated with these biological processes. We collected plasma from Kenyan children aged 1-10 yrs with cerebral malaria (n=12), uncomplicated malaria (n=10), and acute febrile non-malarial illness (n=11) at presentation and 6 wks after clinical recovery. Untargeted metabolomics was performed using reverse phase C18 and hydrophilic interaction liquid chromatography mass spectrometry. MetaboAnalyst was used to analyze differential abundance of 1,612 metabolites. At presentation, children with cerebral malaria had significantly elevated levels of Neuroprotectin D1, a docosanoid metabolite derived from docosahexaenoic acid (DHA) in response to oxidative stress. Acute cerebral malaria was associated with decreased levels of citrulline, a known marker of gut barrier integrity, as well as with increased levels of gut microbial-derived metabolites phenylacetyl glycine (PAGLy) and indole-3-lactic acid (ILA), which directly correlated with Tie-2, a marker of endothelium dysfunction. At 6 wks, children with cerebral malaria had persistently elevated levels of metabolites associated with protracted coagulation and endothelial dysfunction, such as tryptophan pyrolysis product P2 (TrpP2), gamma-glutamylglutamic acid (GGA), and beta-aminoproprionitrile. TrpP2 and GGA directly correlated with markers of platelet activation. In summary, these data suggest that metabolic mediators of cerebral malaria pathogenesis may include gut microbial-derived metabolites and metabolites associated with pro-thrombotic propensity. We are currently validating our findings using quantitative targeted metabolomics and will correlate results with plasma markers of hemostasis, cerebral injury, and gut barrier integrity.

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TRANSCRIPTOMIC DATA ANALYSIS IDENTIFIES ACTIVE HOST UBIQUITIN-PROTEASOME PATHWAY IN KENYAN CHILDREN WITH SEVERE MALARIAL ANEMIA

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Malaria remains a significant global public health challenge, accounting for 249 million annual cases and 608,000 deaths. In western Kenya, severe malaria manifests primarily as severe malarial anemia [SMA, hemoglobin (Hb)<6.0 g/dL]. Our previous studies reported differential expression of host ubiquitination genes in children with malarial anemia, and temporal changes of ubiquitination gene expression following ingestion of hemozoin. Here, we report on transcriptome analysis of 1,761 genes that constitute the ubiquitin-proteasome system (UPS) in children with non-SMA (Hb≥6.0g/dl, n=41) and SMA (n=25), presenting at a rural Hospital in western Kenya. Total RNA isolated from peripheral blood of every child was sequenced using Illumina® NovaSeq 6000. Reads were mapped to the human genome (GR-Ch38) and differential gene expression analysis was performed using the EdgeR package. Gene Ontology (GO) enrichment analysis was performed to identify key domains, and the MetaCore™ network-building algorithm was used to identify functional interactions of differentially expressed genes (DEGs). A total of 659 UPS genes were differentially expressed in children with SMA versus non-SMA (*p*adj≤0.050): 404 up- and 255 down-regulated. GO enrichment analysis identified proteasome-mediated ubiquitin-dependent protein catabolic process (*p*adj=1.173E-76); ubiquitin ligase complex (*p*adj=1.290E-78); and ubiquitin-like protein ligase activity (*p*adj=3.321E-182) as top pathways in biological process (BP), cellular components (CC) and molecular functions (MF), respectively. Functional enrichment analysis using MetaCore™ identified protein modification by small protein conjugation or removal (*p*adj=3.781E-189) and ubiquitin-like protein transferase activity (*p*adj=7.782E-119) as top GO processes in BP and MF, respectively, with localization of the processes mapped to the cell cytosol (*p*adj=1.024E-94). Notably, the proteolysis ubiquitination pathway emerged as the most significantly enriched map (*p*adj=2.832E-19). Collectively, these results highlight active ubiquitin-proteasome-pathway in SMA pathogenesis.

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TO TEST OR NOT TO TEST: WHAT DETERMINES WHETHER CLIENTS TEST FOR MALARIA IN THE PRIVATE SECTOR IN KENYA AND NIGERIA?

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Nearly half of suspected malaria clients in Sub-Saharan Africa first seek care in the private informal sector. A randomized controlled trial was conducted among private retail outlets in Lagos, Nigeria and Western Kenya to assess whether anti-malarial price subsidies conditional on testing positive for malaria could improve the targeting of first-line antimalarials (malaria rapid diagnostic tests (mRDTs) were made available for purchase in the outlets during the study period). Although the subsidies did not improve targeting of antimalarials, we observed a large difference in malaria testing rates across study sites: 49% clients in Kenya tested, compared to 23% in Nigeria. We analyzed exit interview data from 2,441 clients in Nigeria and 5,696 clients in Kenya collected between August 2021-February 2023 to assess factors that might explain these differences in uptake of testing. This was supplemented with qualitative data collected from six focus group discussions (FGD) with outlet owners in Nigeria and four FGDs in Kenya. Client demographics were similar across both study sites. Levels of confidence in mRDTs were also similar in both sites: more than 95% of test-positive clients believed the test result was correct, while only 68% of test-negative clients in Kenya and 64% of test-negative clients in Nigeria believed the test result was correct. The proportions of untested clients who believed their illness was malaria were also similar in both countries (87% in Kenya, 83% in Nigeria). In both Nigeria and Kenya, the most common reason for not testing was that the client was sure the illness was malaria (38% in Nigeria and 17% in Kenya). However, one major difference between the countries was that 25% of untested clients in Nigeria said the test was not offered, compared to only 7% in Kenya. Moreover, FGDs indicated that while outlet owners understood the benefit of testing they had concerns about the accuracy and reliability of mRDTs as did many of their clients. Our results suggest that in addition to making testing more widely available, there is a need to increase awareness among outlet owners and clients about the accuracy and value of malaria testing.

6075

PERFORMANCE AND UTILITY OF HIGHLY SENSITIVE MALARIA RAPID DIAGNOSTIC TEST FOR DETECTING INFECTIONS THAT AFFECT HEALTH AND TRANSMISSION IN SCHOOL-AGED CHILDREN IN SOUTHERN MALAWI

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Over 325 million African children under the age of 14, including 200 million school-aged children, are at risk of malaria infection in endemic areas. Infections characterized by low levels of parasitemia are traditionally described as 'asymptomatic.' However, such infections can contribute to anemia-related cognitive deficits and decreased educational attainment in children. We aimed to assess the use of a high sensitivity rapid diagnostic test (hs-RDT) for detecting low density infections and to assess for evidence of possible *Plasmodium falciparum* histidine protein 2/3 (pfhrp2/3) gene deletions. We evaluated a hs-RDT (NxTek Eliminate Malaria Pf, Abbott Diagnostics Korea Inc.), a conventional-RDT (co-RDT) (SD Bioline Ag Pf, Abbott Diagnostics Korea Inc.), and a combination RDT (Biocredit Malaria Ag Pf (pLDH/HRP2), RapiGEN Inc.). All RDTs were compared to quantitative polymerase chain reaction (qPCR) as the reference standard. We hypothesized the hs-RDT would detect significantly more *P. falciparum* infections when compared to the other RDTs at the time of screening. Our analysis includes 474 children and 500 household members, of all ages, of children enrolled in a parent study (NCT05244954) evaluating intermittent screening and treatment. Out of 958 participants with a qPCR test result, 43.95% (421/958) tested positive by qPCR with a mean parasite density of 13.96p/uL. The prevalence estimated by NxTek was 54.79%, by SD Bioline was 44.04%, by Biocredit HRP2 was 46.91%, and by BIOCREDIT pLDH was 38.49%. The overall sensitivity of the NxTek RDT was 82.63% (195/236), SD Bioline was 73.27% (307/419), Biocredit HRP2 was 78.15% (329/421), and Biocredit pLDH was 68.33% (287/420). For parasite densities over 200p/uL, the sensitivity of the NxTek RDT was 100% (29/29), SD Bioline was 98.21% (55/56), Biocredit HRP2 was 94.64% (53/56), and Biocredit pLDH was 92.86% (52/56). The specificity of the NxTek RDT was 72.20%, SD Bioline was 79.55%, Biocredit HRP2 was 78.17%, and Biocredit pLDH was 85.45%. Participants that were positive by qPCR but negative by RDT are being analyzed for potential pfhrp2/3 gene deletions.

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WIDESPREAD PFHRP2/3 DELETIONS AND FALSE NEGATIVE RESULTS ASSOCIATED TO HRP2-BASED RDTS IN SOUTHERN ETHIOPIA

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HRP2-based RDTs have been widely used to diagnose malaria although the evolution and spread of *Plasmodium falciparum* parasite strains with deleted HRP2/3 genes have compromised it causing false-negative results. This study aimed to assess the prevalence of pfhrp2/3 deletions among symptomatic patients seeking malaria diagnosis at selected health facilities in southern Ethiopia. A cross-sectional study was conducted from July to September 2022. A purposive sampling strategy was used to enroll patients with microscopically confirmed P.falciparum infection. A capillary blood sample was obtained to prepare a blood film for microscopy and test the SD Bioloine TM Malaria Pf/Pv RDT. Dried blood spot samples were collected for further molecular analysis. Of 279 P. falciparum PCR-confirmed samples, 249 (89.2%) had successful msp-2 amplification, which was then genotyped for hrp2/3 gene deletions. The study revealed that pfhrp2/3 deletions were common in all health centers, and it was estimated that 144 patients (57.8%) across all health facilities had pfhrp2/3 deletions, leading to false-negative PfHRP2 RDT results. Deletions spanning exon 2 of hrp2, exon 2 of hrp3, and double deletions (hrp2/3) accounted for 68 (27.3%), 76 (30.5%), and 33 (13.2%) of cases, respectively. While the HRP2 RDT false-negative rate due to pfhrp2 exon-2 deletion was 27.3% (68/249), the population-level prevalence estimate of pfhrp-2 exon-2 deletion leading to HRP2 RDT false negatives was 24.3% (68/279). This study also showed that the sensitivity of the SD Bioline PfHRP2-RDT test was 76.5% when PCR was used as the reference test. In conclusion, this study confirmed the existence of pfhrp2/3 gene deletions, and their magnitude exceeded the WHO-recommended threshold (>= 5%). False-negative RDT results resulting from deletions in Pfhrp2/3 affect a country's attempts at malaria control and elimination. Therefore, the initiation of non-HRP2-based RDTs as an alternative measure is required to curb the grave consequences associated with the continued use of HRP-2-based RDTs in the study area in particular and in Ethiopia in general.

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PREVALENCE OF *PFHRP2/3* DELETIONS IN SOUTH SUDAN: RESULTS OF A 10-SITE NATIONAL SURVEY

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pfhrp2/3 deletions are recognized as a major threat to malaria control, particularly in the Horn of Africa. Data from South Sudan are lacking. We conducted a cross-sectional survey at 10 geographcially distinct sites across South Sudan to estimate the prevalence of *P. falciparum* with *pfhrp2/3* gene deletions. Patients under 15 years with suspected uncomplicated malaria were eligible for enrolment. After informed consent was obtained, capillary blood was taken, and a short questionnaire was administered. HRP2 and PfpLDH-based RDTs were performed in parallel and dried blood spots prepared. A positive test on either RDT triggered malaria treatment. Multiplex quantitative PCR will amplify *pfhrp2*, *pfhrp3*, *pfldh* and human tubulin genes simultaneously. Samples with ΔCq (Cq*pfhrp2* - Cq*pfldh* and Cq*pfhrp3* - Cq*pfldh*) values ≥ 3 will be classified as *pfhrp2* and *pfhrp3* deleted. Using the standard WHO protocol for surveillance of *hrp2/3* deletions, we targeted enrolling 200 suspected cases per site in order to have at least 80 pLDH-positive cases per site. From January 22 to March 27, 2024, a total of 1842 participants (53% males) were enrolled at the 10 sites. The median age of participants was 3 years (IQR 1-8). Overall HRP2 RDT positivity was 729/1842 valid tests (40%), and site-specific positivity rates ranged between 13% and 65%. Overall pLDH RDT positivity was 584/1839 valid tests (32%), and site-specific positivity ranged between 12% and 56%. A total of 15 of 584 (2.6%) pLDH-RDT positive samples were HRP2-RDT negative, a proportion that ranged between 0 and 5.4% by study site. To our knowledge, this is the first large-scale evaluation of *pfhrp2/3* deletions in South Sudan. Results of molecular testing will be available in September 2024 and will help inform policymaking around the continued use of HRP2-based RDTs in South Sudan.

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COUNTRYWIDE PFHRP2 GENE DELETION SURVEILLANCE IN MALI

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Malaria remains a public health concern with approximately 249 million cases in 2022 mainly in Sub-Saharan Africa. To prevent malaria-related death each malaria-endemic country should ensure that every suspected malaria case is tested, and confirmed cases are treated with quality-assured antimalarial medicine. The rapid, simple, and easy to use tests are the rapid diagnostic test (RDT). More than 90% of current available RDTs are based on the *Plasmodium falciparum* histidine-rich protein 2 (PfHRP2). Strain with PfHRP2 deletion may have serious consequences for malaria case management and threaten the use of such RDTs. WHO recommends switching to non-PfHRP2 RDTs when the prevalence of PfHRP2 deleted parasites reaches 5%. The objective of this study is to evaluate the countrywide prevalence of PfHRP2 deletion in Mali. We conducted a prospective, cross-sectional study including patients with suspected malaria based on clinical symptoms from September 2023 to January 2024 in 78 health centers from 13 health districts representing the 4 malaria transmission strata of the country. Dried blood spotted onto filter paper (DBS), HRP2-based RDT, and non-HRP2-based RDT (pLDH-based RDT) were used to collect samples from patients. RDT results were used directly to screen for discordant diagnoses. Real-time qPCR will be performed on DNA extracted from DBS to detect HRP2 deletion. The protocol has been approved by the Ethics Committee of the University of Science, Techniques and Technologies of Bamako, Mali. We have collected 22,778 samples out of the 28,080 planned (81.1%). The malaria prevalence by RDT was approximately 30%. The discordant samples i.e. Pfhrp2 (-) but PfLDH (+) ranged from 0.2% to 13.4% (average 2.9%). Molecular detection of pfhrp2 and pfhrp3 deletion is ongoing and results will be available by November 2024 and presented at the ASTMH annual meeting. This study will provide and update on the prevalence of pfhrp2/3 gene deletions across Mali, which will be critical data for malaria case management in the Country.

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ANALYTICAL PERFORMANCE ASSESSMENT OF THE AUTOMATED AND ARTIFICIAL INTELLIGENCE-ENABLED MILAB™ MAL MALARIA SYSTEM FOR THE DETECTION OF *PLASMODIUM FALCIPARUM* IN SUSPECTED MALARIA PATIENTS IN LAGOS, NIGERIA

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Accurate malaria diagnosis is a critical requirement of malaria case management for mandatory parasitological confirmation of all suspected cases before treatment. Progress in malaria testing is so far inadequate especially in Nigeria where cases tested is less than 40%. Poor quality of malaria microscopy, confidence in malaria rapid diagnostic tests and access to testing remain a challenge. Malaria microscopy has several limitations including high skills, long turn-around-time (TAT) that delay test results for patient management, work-load, and inadequate manpower, emerging and expanding histidine-rich protein 2/3 (HRP-2/3) deletions are challenges

that limit testing. We present preliminary analyses of the analytical clinical performance evaluation of the MiLab™ Malaria diagnosis system compared with expert microscopy among suspected malaria patients in Lagos, Nigeria. A total of 400 patients were assessed in this study. The MiLab™ diagnostic device is an automated optical malaria diagnostic system that detects *P. falciparum (Pf)* and *P. vivax (Pf)* using 5ul of blood in an automated thin film slide preparation by staining with modified Romanowsky stain and an artificial intelligence-enabled slide reading that provides results of the tests within about 15-25 minutes when set at 200,000 red blood cells (RBCs) or 300,000 RBCs. Expert Malaria microscopy was performed using standard protocol. Of 400 patients' preliminary analyses of 399 patients show that *parasite* detection by MiLab™ and expert microscopy was 96(24.1%) and 103 (25.8%) respectively. Performance of MiLab™ at 200,000 RBC among 251 patients was: sensitivity: 94.4% (95% CI:87.6;97.6); specificity (95% CI:94.7;99.4); positive predictive value (PPV):96.9% (95% CI: 90.5;98.8); negative predictive value (NPV): 96.9% (95% CI:93.0;98.7%); False positive (FP): 1.9% and False negative (FN): 5.6%. MiLab™ malaria diagnosis automated artificial intelligence (AI) capabilities for faster TAT and high-performance is a potential game changer in accelerating access to parasitological confirmation and an asset to Malaria control programs.

6080

END-USERS PERCEPTIONS ON THEORETICAL NON-INVASIVE MALARIA TESTING TOOLS

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Malaria remains a global health challenge in tropical and subtropical regions. Prompt and accurate diagnosis is crucial for effective disease management. Common diagnostic approaches include microscopy, lateral flow tests, and polymerase chain reaction. These methods rely on invasive sampling via venous or fingerpick blood draw, which can pose a level of risk to healthcare workers due to the handling of potentially infectious body fluids. Non-invasive tests based on saliva exhaled volatile organic compounds, and transdermal detection have the potential to revolutionize malaria diagnostics, increasing care linkage and case detection, and reducing bio-safety risks. Knowledge gaps exist on the feasibility and acceptability of these tools. This qualitative study aimed to generate evidence directly from end-users in the adoption of non-invasive diagnostic technologies to determine if these technologies are fit for purpose. This study was conducted across endemic and non-endemic areas in Indonesia, Rwanda, and Peru. Between October and November 2023, a total of 24 interviews were conducted with stakeholders and professionals working at borders, and 16 focus groups conducted with teachers, caregivers of children under five years old, healthcare workers, pregnant women, and community members (140 total participants). The comfort provided by non-invasive approaches to service recipients stands out, especially when compared to blood draw which is considered painful for children. Ease-of-use and the rapid diagnostic capabilities enabling real-time disease diagnosis were perceived as particularly beneficial in remote areas with limited healthcare infrastructures. Device portability was seen as a game-changer. The major concerns across the three countries were the lack of information on the accuracy of these non-invasive tools compared to established methods, the lack of reliance on tests targeting samples other than blood products, and the inability of the tools to differentiate between malaria species. This pioneering study shows the importance of engaging with end users early in the diagnostic development process.

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ANTIBODY-OMICS REVEALS DISTINCT HUMORAL PROFILES AND BIOMARKERS IN HIV/TB COINFECTION

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Despite the prevalence of antiretroviral therapy, HIV remains the strongest risk factor for developing Tuberculosis (TB), which is the leading cause of death among people living with HIV (PLHIV). Lack of accurate yet rapid and inexpensive diagnostics is a critical bottleneck in control of TB. Key challenges in TB diagnostics include difficulty in discrimination of the heterogenous spectrum of TB disease, which is further complicated in HIV/TB co-infection, and difficulty in obtaining and processing sputum samples for point-of-care (POC) diagnosis. Earlier, antibody (Ab)-based tests have failed due to poor specificity in discriminating past infection from current infection as well as latent TB infection (LTBI) from active TB (ATB). Recent work has shown that the inflammatory state of *M. tuberculosis* (Mtb)-specific Abs, driven by changes in Fc-glycosylation, differs across LTBI and ATB. Here we report the discovery of a Mtb-specific Ab Fc profile-based biomarker to distinguish ATB from LTBI in PLHIV. We have developed a multiplexed 'Ab-omics' platform for deep biophysical characterization (Fab and Fc) of a broad set of antigen-specific Abs including their isotype, subclass, glycosylation, and Fc receptor binding. We apply the Ab-omics pipeline to plasma from adults in South Africa with HIV and ATB (n=17) and LTBI (n=17) using multiple Mtb antigens (PPD, LAM, Ag85A, ESAT6, CFP10, HspX, PstS1) and non-Mtb antigens. Briefly, antigen-coated barcoded beads were incubated with plasma and probed with fluorescently labeled isotype probes, Fc receptors and lectins. With a total of 56 measured features (8 Ab Fc features 7 antigens) from each participant, machine-learning based analytics (LASSO-SVM) applied to this high-dimensional dataset revealed a minimal Ab Fc profile biomarker (AuRoC>0.9) distinguishing ATB vs LTBI. This included increased specific Ab isotypes (IgM-PPD, IgA-HspX), and Fc receptor binding (FcR3b-CFP10) and decreased Ab galactosylation (PstS1), in ATB vs LTBI. Our findings suggest that a non-sputum-based, purely Ab-based biomarker can achieve accurate diagnosis of ATB vs LTBI in PLHIV in endemic areas.

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DEVELOPMENT OF AMPLICON-BASED WHOLE-GENOME SEQUENCING OF *MYCOBACTERIUM TUBERCULOSIS*

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Tuberculosis (TB) is a leading cause of infection-related mortality worldwide, causing an estimated 1.13 million deaths in 2022. The majority of infections can be successfully treated with antibiotics, but the prevalence of drug-resistant TB and a lack of rapid and cost-effective drug susceptibility tests for many key antibiotics is a significant barrier to treatment. Whole-genome sequencing of *Mycobacterium tuberculosis* can be used for drug susceptibility testing and can provide valuable insight into transmission patterns. However, *M. tuberculosis* is slow to grow, meaning traditional sequencing methods which require culture can take many weeks to return results, greatly limiting the potential clinical benefits. Tiled amplicon sequencing is a low-cost method of amplifying target nucleic acid which has been used widely to sequence viruses such as SARS-CoV-2 and MPox directly from clinical samples. Extending this approach to *M. tuberculosis* would significantly reduce the cost, labor, and turnaround time for whole-genome sequencing, enabling more rapid determination of drug susceptibility and insight into transmission. We designed a tiled

amplicon panel consisting of 5128 primers, the largest tiled amplicon sequencing panel we are aware of to date, and employed the widely-used Illumina COVIDSeq protocol to enable sequencing of the full *M. tuberculosis* genome from minimal input samples. Compared to the same sample without amplification, we achieved >80% genome coverage with 500-1000x lower input DNA with our primer scheme. These findings indicate that tiled amplicon sequencing can be extended to bacterial pathogens to enable whole-genome sequencing from input DNA concentrations typical of clinical samples with minimal additional cost and laboratory effort. Using this approach to sequence *M. tuberculosis* could revolutionize TB control programs, enabling genomic epidemiology to be performed in resource-limited settings and reducing the time needed for comprehensive drug susceptibility testing from weeks to days.

6083

TWO DECADES OF MOLECULAR SURVEILLANCE OF MULTIDRUG-RESISTANT TUBERCULOSIS IN ARGENTINA: LATEST TRENDS AT THE DAWN OF THE GENOMIC ERA

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Multidrug resistant (MDR) tuberculosis (TB) poses a challenge to the global TB control. Argentina is a mid-incidence country for TB with a persistent 1% of MDR cases (~100 cases/year). Herein, we analyzed the genotypes obtained through an in-house PCR (5.9%), MIRU-VNTR15 (52.7%) or WGS (41.4%), of 1249 MDR isolates (of which 77.6% were newly diagnosed cases) collected in 2012-2022, compared to 2003-2009. East-Asian isolates were rare (1 %). Clustering rate remained high (76.3 % in 50 clusters) among new cases. Of the clustered cases, 442/739 (59.8%) were due to four major strains. Particularly, the Callao2 strain imported from Peru, caused a local outbreak, and displaced the historically dominant M strain. We classified 123 cases as preXDR and 9 cases as XDR, of which 76.1% and 44.4% belonged to a cluster, respectively, but were not associated to a particular genotype. PreXDR cases due to direct transmission were sporadic. The median time of persistence of the clusters was of 7 years (range: [0 - 30]) and median cluster size was 3 (range: [1 - 132]). Resistance conferring mutations in positions other than the most frequently found (*rpoB* codons 450, 445 or 435, and *katG*315 or -15*inhA*) were more common among unique isolates compared to clustered isolates (for *rpoB*: 16.7% and 3.6% respectively, Chi-sq test, $p < 0.01$; for isoniazid resistance: 31.2% and 11.2% respectively, Chi-sq test, $p < 0.001$; major strains excluded). Interestingly, no associations with cluster persistence time or size were observed (Chi-sq test, $p > 0.05$). Three provinces only had unique cases, while other three low incidence provinces only had clustered cases, mostly caused by strains circulating in the hot spots of the country. As expected, WGS revealed the intrinsic diversity of certain strains defined by classical genotyping methods, such as the O strain, which included four different subclusters. We conclude that underneath the relatively stable number of MDR-TB cases, epidemiologically relevant changes took place. This work provides the basis for the implementation of a real-time WGS-based surveillance which is expected to allow timely and fine-tuned interventions.

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PRELIMINARY OUTCOMES FROM A PROSPECTIVE OBSERVATIONAL COHORT OF ADULTS WITH DRUG-SUSCEPTIBLE CAVITARY TUBERCULOSIS IN HAITI

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Standard therapy for drug-susceptible pulmonary tuberculosis (TB) lasts 6 months due to the ability of *M. tuberculosis* (Mtb) to persist in a non-replicating state. Trials of treatment-shortening regimens often fail due to high rates of treatment failure and recurrence. Patients with cavitary TB or extensive disease involving >50% of lung are at increased risk of failure or recurrence with standard therapy and even higher risk in treatment-shortening trials. We are conducting a prospective observational study of adults with cavitary or extensive TB in Port-au-Prince, Haiti to seek biomarkers and immune correlates that may predict failure or recurrence in this population. Since May 2022, we have enrolled 137 adults without HIV with chest radiographic evidence of cavitary or extensive disease, with medium or high Xpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) and with no evidence of rifampin resistance, and who have not yet started treatment. Participants are treated according to World Health Organization (WHO) and Haitian national guidelines with 2 months of rifampin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampin and isoniazid. Of the 137 participants enrolled, median age is 27 (interquartile range (IQR) 21, 34). Fifty-six (41%) are female. Median BMI is 17.7 (IQR 16.3, 19.0). Twenty-five participants (18%) were sputum culture positive at month 2. Of n=114 participants who reached end of treatment, 95 (83%) were cured, 5 (4%) failed, 2 (2%) died and 1 (1%) had recurrence. In this prospective cohort of adults with cavitary or extensive TB, there was 18% sputum culture positive at 2 months and a high rate of failure. According to the WHO, globally <1% of HIV-negative people with drug-susceptible TB have treatment failure. Treatment failure among people with cavities may be due to several factors, such as inadequate drug penetration into the cavity or ineffective host immune response. People with cavitary TB represent a unique population who are at very high risk of poor outcome and are likely driving the need for 6 months of therapy.

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TUBERCULOSIS DRUG SUSCEPTIBILITY TEST WITH SNP-RESOLUTION USING SINGLE SAMPLE MELT ANALYSIS

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The global burden of tuberculosis (TB) disease is compounded by the emergence of drug-resistant strains. Determining TB drug susceptibility is essential to match disease-infected patients with effective drug regimens. High resolution melt (HRM) analysis offers a rapid and cost-effective screening solution for confirming susceptibility of polymerase chain reaction (PCR)-amplified nucleic acid products. However, a single base change can be difficult to detect by standard HRM. These limitations are particularly detrimental for TB drug susceptibility testing in which a single nucleotide polymorphism (SNP) can be sufficient to make a first-line TB drug ineffective. In this study, a reagent-based calibration strategy based on synthetic (L)-left-handed DNA, designated LHRM, was developed to confirm the drug-susceptible sequence of a PCR product with single base resolution. To test our LHRM approach, a constant amount of double-stranded L-DNA was used as a within-sample melt standard. LHRM and standard HRM were used to classify PCR products as drug-susceptible or not drug-susceptible with a test bed of nine synthetic *katG* variants, each containing single or multiple base mutations that are known to confer resistance to the first-line TB drug isoniazid (INH). Using a state-of-the-art calibrated instrument and multiple sample classification analysis, standard HRM performed at 33.3% sensitivity and 97.5% specificity. For this small data set, incorporating L-DNA for reagent-based calibration into every sample improved overall sensitivity to 77.8% and maintained high specificity of 98.7%. This improvement was due to improved classification of the most difficult S315T variant containing only a single base change. Notably, LHRM achieved sample classification only relying on within-sample melt differences between L-DNA and the unknown PCR product. LHRM shows promise as a high-resolution single sample method for validating PCR products in applications where the expected sequence is known and highly calibrated instruments are unavailable.

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RISK FACTORS ASSOCIATED WITH POST-TUBERCULOSIS SEQUELAE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Post-tuberculosis (TB) sequelae pose a significant challenge in managing TB survivors, often leading to persistent health issues post-treatment. This systematic review and meta-analysis aim to identify risk factors linked with long-term physical sequelae among TB survivors. We systematically searched Medline, Embase, PROQUEST, and Scopus for studies on long-term physical sequelae among TB survivors up to December 12, 2023. Included were all forms of TB patients experiencing long-term physical sequelae (respiratory, hepatic, hearing, neurological, visual, renal, and musculoskeletal). Narrative synthesis was used for risk factors reported once, and random-effect meta-analysis for primary outcomes with two or more studies. The review included 73 articles from 28 countries representing 31,553 TB-treated patients in the narrative synthesis, with 64 studies included in the meta-analysis. Risk factors associated with post-TB lung sequelae included older age (OR=1.62, 95% CI: 1.07-2.47), previous TB treatment (OR=3.43, 95% CI: 2.37-4.97), smoking (OR=1.41, 95% CI: 1.09-1.83), alcohol consumption (OR=1.84, 95% CI: 1.04-3.25), bacteriologically positive TB diagnosis (OR=3.11, 95% CI: 1.77-6.44), and presence of pulmonary lesions in radiology (OR=2.04, 95% CI: 1.07-3.87). Risk factors associated with post-TB liver injury included pre-existing hepatitis (OR=2.41, 95% CI: 1.16-6.08), previous TB treatment (OR=2.64, 95% CI: 1.22-6.67), hypo-albuminemia (OR=2.10, 95% CI: 1.53-2.88), and HIV co-infection (OR=2.72, 95% CI: 1.66-4.46). Risk factors linked with post-TB hearing loss included baseline hearing problems (OR=1.72, 95% CI: 1.30-2.26) and HIV co-infection (OR=3.02, 95% CI: 1.96-4.64). In conclusion, this review underscores that long-term physical post-TB sequelae, including respiratory, hepatic, and hearing issues, are linked with diverse socio-demographic, behavioural, and clinical factors. Identifying these risk factors is vital for targeting interventions to alleviate the post-TB treatment burden.

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TUBERCULOSIS TRENDS AMONG INDIGENOUS PEOPLE IN BRAZIL BEFORE, DURING, AND AFTER THE SARS-COV-2 PANDEMIC

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Despite some advances in tuberculosis control in recent decades, hotspots of transmission persist in some Indigenous communities. Delivery of healthcare to Brazil's Indigenous population was severely interrupted by the SARS-CoV-2 pandemic. The impact of this on tuberculosis transmission in these key vulnerable communities has not yet been investigated. We analyzed data from 2012-2022 from the Brazilian Ministry of Health database of notifiable disease (SINAN) to map the level of laboratory-confirmed diagnostics, multidrug-resistant TB, and disease outcome among the Indigenous population compared to the general population of Brazil and at state level. 964 cases of TB in Indigenous people were reported in 2022, the highest level since 2015. An increase in laboratory-confirmed TB diagnoses was registered for both the non-Indigenous and Indigenous population, but the level was significantly lower for the Indigenous population throughout the period (63.9% vs 68.4% in 2022). At the state level, the percentage of laboratory-confirmed diagnosis ranged widely - from 20-100% in 2022. Levels of cure were consistently higher, and level of fatality lower, among the Indigenous versus the non-Indigenous population. the percentage of Indigenous cases with multidrug-resistant TB has increased since the pandemic, from 0.44% (2019) to 1.94% (2021) and 1.11%(2022). In 2022, 5,91% of Indigenous cases of TB were recurrent episodes, and another 5.91% were re-treated after treatment abandon. Drug sensitivity testing was done for 9.02% of all Indigenous cases, and 14.04% of recurrent cases and people who had previously abandoned treatment. The dramatic increase in MDR-TB among the Indigenous population in Brazil demands urgent action considering the hyperendemic transmission levels in some communities. Diagnostics must be improved to ensure that TB treatment is given only to TB patients, and drug sensitivity testing must be carried out as a minimum for all patients returning to treatment after treatment abandon and for all recurrent episodes.

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COVID-19 COMMUNITY 'BANTABA': RAISING AWARENESS AND REDUCING MISINFORMATION ON COVID-19 A TWO URBAN LOCALITIES IN THE GAMBIA

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Omar Ceesay, Ebrima Manneh, Bakary Dibba, Effua Usuf.The COVID-19 pandemic has posed a significant challenge to global health, with over 3 million deaths worldwide as of April 2023. The Gambia, a small West African country, has not been immune to the impact of the pandemic, with over 10,000 confirmed cases. One of the challenges in the Gambia has been the spread of misinformation about COVID-19, which has contributed to low compliance with public health measures and hampered efforts to mitigate the spread of the disease. Community engagement employs participatory communication, a community development initiative that utilizes a bottom-up approach rather than a top-down approach in health interventions. Data collection was carried out between 17th February to 1st March 2022, when we conducted the Pre-test questionnaire. A post-community engagement was conducted nine months after the first community engagement and the result shows significant improvement in knowledge and understanding of the disease.The result shows that 79% of the participants know the signs and symptoms of covid. This shows engaging with the community with help in raising knowledge and awareness of the disease. 76% of the respondent shows fear of the covid 19 virus, while 90% shows feelings toward family member affected by the virus, because they think they can die anytime with the virus has it doesn't have a treatment.Community engagement is an effective strategy for raising awareness and reducing misinformation about COVID-19 within communities. Community leaders' engagement, public spaces for sensitization sessions, and dissemination of accurate information through various media channels are essential components of successful community engagement initiatives.

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THE EFFECT OF PANDEMICS ON DECENT WORK AND TASK PERFORMANCE AND ITS INFLUENCE ON THE LEADERS' EMOTIONAL INTELLIGENCE

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Pandemics poses unprecedented challenges for healthcare workers, impacting their work conditions, performance, and the role of leaderships emotional intelligence. Decent work, as defined by the International Labor Organization, encompasses opportunities for productive work with fair income, security in the workplace, social protection, and better prospects for personal development and social integration. The aim of this research was to assess the effect of the relationship between decent work and the task performance, the mediational role of leaders emotional intelligence, and the moderating effect of pandemics on health workers. This study, adopted a quantitative approach and utilized a cross-sectional survey design, collecting data from 2,000 healthcare workers. The data, obtained through stratified random sampling, were analyzed using the Structural Equation Modeling. We observed that pandemic dampens the positive relationship that exists between decent work and task performance of healthcare workers. Furthermore, the study identified that leaders emotional

intelligence played an appreciable mediating role in the relationship between decent work and task performance of health workers. Our data suggests and recommends that policies and practices to implement regulations to promote decent work standards (fair wages, safe conditions, work-life balance) across healthcare organizations should be developed. Additionally, training and assessment on emotional intelligence for healthcare workers, especially the leaders should be mandated. Further to this we encourage the development of emergency preparedness policies to address work conditions and employee support during pandemics/crises.

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QUANTIFYING THE IMPACT OF MODIFIABLE RISK AND PROTECTIVE FACTORS ON MORTALITY AMONG CHILDREN AND YOUNG ADOLESCENTS RECEIVING ANTIRETROVIRAL THERAPY

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Heterogeneity of mortality estimates of children who have received antiretroviral therapy (on-ART) exist across regions, with HIV mortality remaining much higher in resource-limited countries compared to resource-rich countries. An understanding of the factors influencing the risk of on-ART mortality could help explain the variation in mortality across locations and inform priorities for interventions. This research explores how modifiable risk factors influence mortality rates in children and young adolescents who have been initiated with ART. We perform a systematic review and meta-analysis to synthesize the existing literature on mortality among on-ART children using all global data sources. A list of biomedical, behavioral, and structural factors associated with HIV mortality are identified through literature review. We then perform a systematic procedure of covariates selection through the application of LASSO technique, which identifies the most statistically significant covariates. We also quantify the impact of these covariates on the mortality through counterfactual scenario simulation, which models and evaluates the potential effects of changes in these covariates on mortality. Variable selection has identified key covariates for the mortality among under-5 and over-5 age groups. For under-fives, PCV and antibiotics coverage for LRI are crucial, while for over-fives, hepatitis B vaccine, antibiotics, and PCV coverage are significant. A 10% increase in PCV and antibiotic coverage is associated with 5% and 15% mortality odds decrease for under-5 age groups. For the 5-14 age group, hepatitis B vaccine coverage shows pronounced effectiveness, reducing mortality odds by 8% with a 10% increase and 15% with a 20% increase. In conclusion, our study demonstrates that modifiable risk factors play a significant role in on-ART mortality among children and adolescents. The outcomes of this study are expected to contribute valuable knowledge to pediatric and adolescent healthcare and shape future health policies aimed at reducing mortality of children and adolescents living with HIV/AIDS.

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CHALLENGES AND LESSONS LEARNED WHILE COMPLETING/INITIATING VACCINE CLINICAL TRIALS DURING THE COVID-19 PANDEMIC IN A DEVELOPING COUNTRY: EXPERIENCE FROM NEPAL

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The global burden of vaccine-preventable infectious diseases is comparatively higher in developing countries. However, the safety and efficacious studies of vaccines in diseases prevalent countries are limited. Nevertheless, COVID-19 pandemic added many challenges in conducting clinical trials worldwide, especially in resource limited countries. This is an educational study where researchers from Nepal have shared their experiences while completing ongoing clinical trial and initiating the new clinical trial in Nepal using real time events, records, and secondary data. Lock down for rising case of COVID-19 affected the ongoing clinical trial for typhoid vaccine, sponsored by International Vaccine Institute (IVI). This clinical trial was first large scaled phase III clinical trial conducted in Nepal at 4 different sites. Out of 6 visits, 4th visits was almost completed and completion of remaining visits with retention of subjects in the study was challenging. The swift response from the IVI and proactive response from site staffs towards provided guidelines and study activities completed the study on time by fulfilling both government & protocol safety requirements. Similarly, conducting a clinical trial by Nepal for a novel vaccine during pandemic was quite more challenging than we presume. However, making necessary changes as per the local requirements, collaborating with local stake holders, conducting community engagement program, pre-screening activities, continuous subjects counselling, affiliating with various hospital departments, involving hospital staffs, etc. we were able to initiate & conduct the study amid the COVID-19 pandemic with highest enrolling sites among other countries & advance to continue the study. Conducting a clinical trial in Nepal during health crisis might be challenging, but it is possible. High subject enrollment rate, safety monitoring plans, rapid adaptability to new technologies, biological sample handling, active & passive surveillance of the subjects, etc. shows the optimal proficiency of sites and health professionals that needs to be explored more in Nepal.

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ADVANCING GEOSTATISTICAL METHODS FOR FUTURE STRATEGIES IN NEGLECTED TROPICAL DISEASE PROJECTS

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Neglected Tropical Diseases (NTDs) disproportionately affect the world's most vulnerable populations. The adoption of georeferenced survey results and recent advancements in geostatistical methods offer promising avenues for refining NTD project strategies, leveraging the growing inventory of GIS datasets. This presentation highlights the evolving landscape of geostatistical modeling, emphasizing its critical role in informing targeted interventions. Traditional methods often fail to capture spatial patterns inherent in NTDs. Cutting-edge geostatistical models, however, offer nuanced insights by accounting for spatial autocorrelation and heterogeneity. These models, such as Bayesian spatial approaches and geographically weighted regression, facilitate more accurate risk mapping and resource allocation. The integration of diverse GIS datasets, including environmental, demographic, and healthcare infrastructure layers, enhances the precision of NTD risk assessments. From high-resolution satellite imagery to crowd-sourced data, these resources provide invaluable context for optimizing intervention delivery. Despite significant progress, several challenges remain. Funds to develop geospatial datasets vital for effective geostatistical analysis of NTDs, such as accurate evaluation unit boundary files and georeferenced sampling frames, are needed. Further development of current tools, and strategies to extend them to more users, are also imperative. By harnessing the full potential of geostatistical methods, NTD projects can achieve greater impact with limited resources. From evaluating intervention effectiveness, to prioritizing endemic hotspots, or informing survey design strategies, these tools offer a paradigm shift in how we conceptualize and address NTDs. As we navigate the evolving landscape of global health, investing in robust geostatistical frameworks will be paramount to achieving sustainable progress in NTD control and elimination.

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FROM RESEARCH TO POLICY - LEVERAGING SCIENCE AND STRATEGIC COMMUNICATION TO TACKLE DENGUE IN BANGLADESH

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In 2017-18, icddr,b scientists documented significant resistance to permethrin in Aedes aegypti mosquitoes across several districts in Bangladesh, including Dhaka, and recommended alternative insecticide malathion and its combinations. The findings were disseminated to relevant stakeholders, including the Institute of Epidemiology, Disease Control and Research (IEDCR), Bangladesh in May 2018; however, resistance to these recommendations persisted and led to no immediate changes in vector control interventions. The dengue situation escalated into a severe outbreak in 2019, with cases dramatically increasing from 1,884 in June to a historical high of 101,354 for the year, the death toll was 164. icddr,b launched a strategic media advocacy campaign in mid-July, producing over 500 media outputs, including reports, talk shows, opinion articles. This campaign also involved targeted advocacy with entomologists and decision-makers to reinforce the scientific validity of the recommendations. The campaign gained momentum with support from the Honourable Prime Minister, leading to the Dhaka City Corporations adopting the recommended insecticides in the second week of August. This led to a temporal decline in cases, decreasing to 16,856 in September, and finally 4,011 in November. Despite these successes, in 2023, a staggering 321,179 dengue cases were reported across all 64 districts with a death toll of 1,705. This coincided with increased intermittent rainfall patterns, where average rainfall exceeded 120 mm from April to October, suggesting a link between the soaring dengue cases and the impacts of climate change. The severe dengue burden demands a multi-faceted response, combining public awareness and action, robust vector control, effective vaccines, and enhanced case management, supported by ongoing research. Engaging the mass media is crucial, as evidenced by icddr,b's 2019 advocacy success. This approach offers a proven model for implementing effective dengue control and prevention strategies throughout the year.

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Documentation And Analysis of the Social Contact Patterns Using Standardized Diaries Across Different Ages in Low-Income Settings in Vellore District, Tamil Nadu, Southern India

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Infectious diseases have a greater impact in low- and middle-income countries (LMICs), as evident from the COVID-19 pandemic. Human behaviors play an essential role in the transmission of infections. A study was conducted in urban and rural areas of Vellore district, Tamil Nadu, Southern India, to document and analyze social contact patterns using standardized social contact diaries across different ages in low-income settings. The study also documented symptoms of respiratory infections in this population. Using a symptomatic approach. The study identified acute respiratory infections and associated factors among 1257 index participants, of which 631 were from urban and 626 from rural Vellore. The mean number of contacts over two days was 15.86 ± 5.82 and 15.61 ± 6.9 for urban and rural areas, respectively. In both regions, the age group of 5-19 years ($p<0.001$) and school-goers ($p<0.001$) had significantly more contacts than all other age groups. On the other hand, the least number of contacts was observed among people of extreme ages (<6 months and ≥60 years). Overall, 10.8% of individuals experienced acute respiratory infections during a 3-month follow-up. The risk of respiratory infections was highest among children under 5 years of age, with other age groups having a significantly lower risk of ARI (OR 2.9, 0.21 – 0.47). Those without any education had a higher risk of ARI than those with any education (OR 2.8, 0.21 – 0.47). Pre-existing respiratory conditions like asthma increased the risk of ARI compared to those without them (AOR 6.07, 1.56 – 21.7). Participants from houses using biomass as fuel were also at a higher risk (OR 2.9, 1.96 – 4.48) of ARI than households using non-biomass fuel. Findings from this study will contribute to developing context-specific and targeted preventive and control strategies during infectious disease outbreaks. Understanding and quantifying social mixing patterns within communities will provide much-needed data for infectious disease modeling in LMICs.

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ENHANCING COMMUNITY HEALTH DIGITIZATION IN BURKINA FASO WITH ENTERPRISE ARCHITECTURE: ACHIEVEMENTS AND LESSONS.

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Malaria remains the leading cause of morbidity and mortality in Burkina Faso. In response, the government has implemented a 2019-2023 community health strategy with the digitization of service delivery as a priority intervention. To leverage the use of digital solutions, they must be developed, deployed, and scaled up in a coherent scheme and an optimum level of security to ensure a sustainable implementation. Thus, the Ministry of Health and Public Hygiene with support from Digital Square at PATH and the US Presidential Malaria Initiative , has developed an enterprise architecture to sustain the scale up of the community digital health solution (eSanteCom). The Open Group Architecture Framework (TOGAF) was implemented in a participative and collaborative way, involving relevant stakeholders from MoH, implementing organizations, civil society organizations, community health workers in an iterative process to describe the current state of the community health system through business, data, applications, technologies, and security domains, and envision the future state expected for a coherent scale up. The six-months intervention included stakeholders' engagement, framing workshop,10 key informants' interviews including five MoH information systems experts, and technical directors. Those actions resulted in a design of a general architecture document and a blueprint. Main outcomes include the stakeholder's awareness raising about enterprise architecture as an evidence-based approach to address the siloed and fragmented digital health interventions. Additional findings include a low maturity architecture capacity within MOH (<1/5), the lack of architecture governance framework. Some gaps and requirements were also highlighted to enhance the system security for all domains, leading to formulating recommendations and scenarios that will inform the new 2024-2028-health strategy. Overall, the lessons learned were endorsed by MOH who, accordingly, expressed interest in undertaking the extension of architecture from community health to the whole health system.

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CHIKUNGUNYA VIRUS RISK OF ACQUISITION, DIFFERENTIAL DIAGNOSIS AND VACCINE DEVELOPMENT: IMPACT OF INDEPENDENT ONLINE MEDICAL EDUCATION ON PHYSICIAN KNOWLEDGE AND CONFIDENCE

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Chikungunya virus (CHIKV) has a wide geographical spread and effective mosquito control is difficult to adopt for all individuals at risk. As previously reported, several vaccine approaches are being evaluated in clinical trials or are approved. Here, we assessed whether a short global online summary of an independent medical education symposium at the American Society

of Tropical Medicine and Hygiene 2023 meeting could improve primary care physicians' (PCPs) and infectious disease (ID) physicians' knowledge and confidence. Educational effect was assessed using a repeated-pairs design with pre-/post-assessment. Three multiple choice questions assessed knowledge, and one question assessed confidence. Statistical tests to assess significance included: Paired samples t-test for overall average number of correct responses and confidence. McNemar's test for individual questions and learning objectives (P<.05). Cohen's d estimated the effect size impact on number of correct responses (<.20 modest, .20-.49 small, .59-.79 moderate, ≥.80 large). From a total audience of 1115, there were 315 assessment completers. Overall, there were significant knowledge gains for ID physicians (P<.001; Cohen's d = 0.98) and PCPs (P<.001; Cohen's d = 0.78). Significant knowledge gains regarding symptoms that differentiate CHIKV from other arboviruses were found (PCPs P<.001; ID physicians P<.01). Very high knowledge gains regarding vaccine data were seen with a relative percentage change in knowledge of 1225% for ID physicians (P<.001; 31% improved) and of 1033% for PCPs (P<.001; 51% improved). A considerable proportion of PCPs (56%; confidence shift 101%; P<.001) and ID physicians (56%; confidence shift 87%; P<.001) increased their confidence regarding their ability to advise travellers about their risk of CHIKV acquisition. Online medical education significantly improved physicians' knowledge and confidence regarding diagnosis, vaccine data and their ability to advise travellers of the risk of CHIKV. As a CHIKV vaccine development continues, it is critical that physicians are aware of the need for a vaccine and to optimally advise individuals.

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AN EXPLAINABLE MACHINE LEARNING APPROACH FOR PREDICTING LINEAR GROWTH FALTERING FOLLOWING A DIARRHEAL ILLNESS AMONG CHILDREN AGED 6-35 MONTHS IN WESTERN KENYA

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Stunting affects one-fifth of children globally with diarrhea accounting for an estimated 13.5% of stunting. Identifying risk factors for its precursor, linear growth faltering (LGF), is critical to designing interventions. Moreover, developing new predictive models for LGF using more recent data offers opportunity to improve model performance and capture new insights. We employed machine learning (ML) to derive and temporally validate a predictive model for LGF among children enrolled with diarrhea in the Vaccine Impact on Diarrhea in Africa (VIDA) study and the Enterics for Global Heath (EFGH) *Shigella* study in rural western Kenya. We used 7 ML algorithms to retrospectively build prognostic models for the prediction of LGF (≥0.5 decrease in height/length for age z-score [HAZ]) among children 6-35 months. We used de-identified data from the VIDA study (n=1,473) combined with synthetic data (n=8,894) in model development, which entailed split-sampling and K-fold cross-validation with over-sampling technique, and data from EFGH-Shigella study (n=655) for temporal validation. Potential predictors included demographic, household-level characteristics, illness history, anthropometric and clinical data chosen using an explainable model agnostic approach. The champion model was determined based on the area under the curve (AUC) metric. The prevalence of LGF in the development and temporal validation cohorts was 187 (16.9%) and 147 (22.4%), respectively. The following variables were associated with LGF in decreasing order: age (16.6%), temperature (6.0%), respiratory rate (4.1%), SAM (3.4%), rotavirus vaccination (3.3%), breastfeeding (3.3%), and skin turgor (2.1%). While all models showed good prediction capability, the gradient boosting model achieved the best performance (AUC% [95% Confidence Interval], 83.5 [81.6-85.4] and 65.6 [60.8-70.4]) on the development and temporal validation datasets, respectively. Our findings accentuates the enduring relevance of established predictors of LGF whilst demonstrating the practical utility of ML algorithms for rapid identification of LGF among at-risk children.

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ANALYSIS OF CARE-SEEKING PATHWAY AND FACTORS INFLUENCING EARLY AND APPROPRIATE CARE-SEEKING FOR MALARIA PATIENTS IN THE REPUBLIC OF GUINEA, 2022-2023

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The main aim of this study was to analyze the care pathway and the factors associated with early and appropriate care-seeking for malaria patients in the Republic of Guinea. A cross-sectional study was carried out between November 2022 and March 2023 among 3300 patients diagnosed with malaria in nine health districts. Axel Kroeger's conceptual framework was used. The conventional recourse was defined as the use of a public or private health facility or at the community services. Then an early and appropriate care-seeking as seeking care within 24 hours of the onset of symptoms in the conventional recourse. Sankey's alluvial diagrams were used to represent patients' pathways and logistic regression models identified factors associated with early and appropriate care-seeking. A total of 1632 (49.45%) was female and 1132 (34.30%) were under 5 years of age with mean age of 27.46 months. For those aged 5 years and older, the mean age was 27.03 years. At time of interview, 1337 (40.52%), 1423 (43.12%), 437 (13.85%) of patients were respectively in their first, second and third recourse. Of all patients, 1757 (53.25%) had sought care within 24 hours and 28.55% had sought care within 24 hours at a conventional recourse. Individually and as a first intention, self-medication was the main modality with 1214 (37.30%). In 1992 (60.36%) patients had a conventional care pathway. Overall, the health districts of Boffa (Lower Guinea, coastal region) OR = 0.48 95% CI 0.33 – 0.70 (p <0.001), Dabola (Savanna region) OR = 0.43 95% CI 0.30 – 0.63 (p<0.001), and Labe (Mountain region) OR = 0.43 – 0.91 (p=0.016) were at risk of delaying appropriate care seeking (final ORs) for all group, regarding Dixinn district in Conakry. Low rates of early and appropriate care-seeking were observed. Patients generally sought care through multiple means, often resulting in a delay in adequate management. The risk associated with certain health districts in the care-seeking behavior shows the need to deploy strategies adapted to the needs of communities through an in-depth community diagnosis of health service utilization.

6099

SCREENING, VACCINATION, AND AWARENESS CREATION FOR HEPATITIS B VIRUS INFECTION IN ACCRA, GHANA

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Viral hepatitis remains a major public health threat, affecting millions globally. For over a decade now, 28th July is observed as World Hepatitis Day (WHD), with the goal of raising awareness of viral hepatitis, intensifying screening efforts, increasing vaccination coverage, and mobilizing global efforts towards control. We present a report of our 2021 and 2022 WHD medical outreach activities in Accra. The activities took place in the Legon and Maamobi communities in 2021 and 2022 respectfully. The Advanced

quality one-step multi-HBV test was used to test for HBV surface and envelope antigens, as well as surface, core and envelope antibodies. Positive persons were recommended for management while negative persons were encouraged to take up vaccination. In 2021, 297 participants were screened at Legon – 19 (6.4%) tested positive for HBsAg, and 278 (93.6) were negative. Of these, 246 (82.8%) were offered free vaccination. In the end, 66% (163/246) completed all three vaccinations whereas 34% (83/246) were lost to follow-up after either the first or second vaccination. In 2022, 388 participants from 2 communities (Legon, Maamobi) were screened and 25 (6.4%) tested positive for HBsAg - 21 (5.4%) from Maamobi and 4 (1.0%) from Legon. A total of 204 (64.8%) received all 3 vaccine doses while 111 (35.2%) were lost to follow-up. Our activities align with the WHO's agenda to reduce the global burden of viral Hepatitis by 2030 through active case search, improved clinical care, and increased access to HBV vaccination. Additionally, generated data shed light on participants commitment to full dose completion which could be useful for HBV screening and vaccination activities in other areas across the continent.

6100

SUSTAINING MALARIA CONTROL THROUGH WARD DEVELOPMENT COMMITTEES IN NIGERIA

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Nigeria has a high malaria burden. Ward Development Committees (WDC) are government-constituted governance structures to encourage community participation and increase access to primary health care services at the ward level. However, there is little documentation of their potential contributions to malaria programs. In 2022, the USAID-funded Breakthrough ACTION-Nigeria Project (BA-N) trained 219 WDC representatives from 219 wards in 5 states to conduct community discussions about malaria prevention and treatment; refer, and follow up with eligible community members for fever care and antenatal (ANC) services; address barriers to malaria service provision and uptake; and mobilize resources for community health. WDC representatives are respected community members who volunteer their time and only receive transport stipends for activities. They submitted monthly reports on the number of community members in attendance and numbers referred and participated in monthly review meetings with BA-N and the State Malaria Elimination Programme officers, who provide supportive supervision. Between October 2022 and September 2023, WDCs conducted 5,748 community discussions and reached 108,098 participants (47,527 males (46%) and 60,571 females (54%)). Of these numbers, 26,218 were referred to health facilities for fever care and ANC services (24,320 and 1,898 respectively), with 22,800 (21,206 fever and 1,594 ANC) completing these referrals. Completed referrals were equivalent to 1% and 2% of the total number of cases seen at their focal facilities for fever and ANC. The overall referral completion rate was 87% for fever and 84% for ANC. The results suggest that WDCs can reach community members with malaria messages and are successful at engaging both males and females. While their contribution to overall service uptake for both services was minimal, they achieved high referral completion rates, suggesting high trust in WDCs. Future initiatives should measure WDCs' influence on community perceptions and other malaria behaviors and explore ways to cost-effectively scale the use and reach of WDCs for malaria social and behavior change.

6101

CALL FOR A FAIRER APPROACH TO AUTHORSHIP PRACTICE IN THE REPORTING OF BIOMEDICAL RESEARCH

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Authorship of academic publications confers credit, responsibility, ownership, and accountability for published research work. However, significant inequities currently exist in the research landscape concerning authorship practices. Current guidelines and practices disadvantage field workers, early career researchers (ECRs), those whose English is not their first language, and researchers from low-resource settings who do not have protected time for research or training in academic writing. For biomedical researchers, the most commonly used guidelines are the 'International Committee of Medical Journal Editors' (ICMJE) guidelines. However, the ICMJE guidelines and current practice do not adequately reflect the reality of contributions in such research and could exacerbate existing inequalities among researchers. Many contemporary teams are multidisciplinary and consist of individuals with varying abilities and existing inequalities. As such, not all individuals, such as ECRs, can or should be 'accountable for all aspects of the work' (criterion 4) as required by the ICMJE. Additionally, not all intellectual contributions meriting authorship require 'drafting the article or reviewing it critically for important intellectual content' (criterion 2). Our paper gives arguments for calls for a revision in the ICMJE guidelines, particularly in criteria 2 and 4, as well as current practices, to enable deserving individuals to be given the opportunity to be authors. For the latter, we urge lead and senior researchers to engage and support less privileged members of the team, ECRs, those who face language barriers, and those with limited experience to enable their enhanced contributions. We are not calling for a loosening of authorship requirements but rather, for recognition of those who have substantially contributed to be given the opportunity to be authors.

6102

UNDERSTANDING THE VIEWS OF PREGNANT AND LACTATING WOMEN ON CHILD BREASTFEEDING. A QUALITATIVE STUDY IN EASTERN ETHIOPIA.

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Malnutrition is a common cause of death among children in Ethiopia. Exclusive breastfeeding is crucial for children survival, but fewer than half of children under six months old are exclusively breastfed. Child malnutrition can result from early weaning from breast milk. In Ethiopia, little is known about how socio-cultural factors impact breastfeeding. The paper explores how mothers conceptualise breastfeeding practices and strive to prevent child malnutrition. The study was conducted from May 2023 to July 2023 using ethnographic and phenomenological approaches, including in-depth interviews, focus group discussions, and participant observations. The study was conducted in the mother's home and nearby health facilities, where confidentiality was maintained. All the data was collected with the consent of the participants. The study found misalignment between biomedical and community understandings of breastfeeding. The three main obstacles to breastfeeding were: mothers' assumptions that breastmilk alone does not cover their children's nutritional needs; social and cultural burden to wean children from breastfeeding quickly; and the perception that breastfeeding during pregnancy could lead to child malnutrition, particularly kwashiorkor malnutrition. This dilemma is made worse by the impact of this misalignment because breastfeeding is not understood by communities or health workers in the same way. The study conceptually explores what is at stake when mothers and healthcare professionals don't speak the same language when it comes to breastfeeding. Open dialogue and engagement between socio-cultural and biomedical perspectives could lessen pervasive misconceptions and support mothers in breastfeeding.

6103

LESSONS FROM THE FIELD: MINIMUM SERVICE STANDARDS ASSESSMENT TOOL AND THE HOSPITAL STRENGTHENING PROGRAM: A NOVEL FIRST STEP TOWARDS THE QUALITY IMPROVEMENT OF NEPAL'S GOVERNMENT HOSPITALS

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District hospitals in Nepal, as in other LMIC settings, struggle to provide quality care due to inadequate investments in equipment, human resources, and hospital infrastructure. To address these challenges, the novel Minimum Service Standards (MSS) assessment tool was developed by the Nick Simons Institute in partnership with the Ministry of Health and Population to routinely assess hospital readiness through a detailed checklist evaluating governance, clinical services, and support services. The Hospital Strengthening Program (HSP) then provides a mechanism to close the identified gaps through a small annual grant, thus together providing knowledge and resources to improve healthcare at the district hospital. Nepal is a mountainous, low-income country in South Asia which faces significant health challenges, including high maternal and under-five mortality rates. Since its inception in 2014, MSS/HSP has expanded to 127 government hospitals as of 2023. The MSS/HSP program provided a blueprint for hospitals to pursue excellence and has tracked and motivated substantial improvements in services, such as 24hr emergency (+14%), X-ray (+23%) and Cesarean service (+31%). Additionally, the program has profoundly impacted policy and management within the healthcare sector, influencing key areas such as budget allocation, insurance payments, and hospital upgrade criteria. The MSS/HSP program has given hospitals in Nepal a blueprint towards success through the use of the novel MSS assessment tool and the financial support to address gaps in the LMIC setting. Due to the close collaboration with the MoHP, the program has secured support at all levels of government, thereby ensuring its sustainability, and impact.

6104

PHYSICIAN KNOWLEDGE, ATTITUDES, AND PERCEPTIONS OF FACILITY-WIDE ANTIBIOGRAMS IN SOUTHERN SRI LANKA: A PRE-IMPLEMENTATION STUDY

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Antimicrobial resistance (AMR) poses significant challenges to global public health. Critical drivers of AMR are the misuse and overuse of antimicrobials for human health. Antibiograms are paper-based or electronic tools that display summary data of local antibiotic susceptibility trends, aiding physicians in selecting empirical antimicrobial therapies for a specific patient when microbiologic culture data are unavailable. However, scant literature exists on the feasibility and challenges of developing and implementing antibiograms in low- and middle-income countries (LMICs) with limited microbiological and antibiogram implementation capabilities. This qualitative study, conducted at the most prominent public tertiary care hospital in southern Sri Lanka from June to August 2023, explored physicians' knowledge, attitudes, and perceptions towards antibiograms. Through convenience sampling, 31 critical informant physicians were recruited from pediatric and adult medical wards. Interviews were conducted in English, audio recorded, transcribed, and analyzed using thematic analysis. Most physicians were unaware of antibiograms. However, almost all (96%, 29/31) physicians expressed enthusiasm for using antibiograms in their facility, citing the potential to refine antibiotic prescriptions, curb antibiotic resistance, and improve patient care. One-third (33%,10/31) expressed skepticism about antibiogram implementation, citing time and resource constraints. The physicians recommended that a multidisciplinary team in small, discussion-based groups conduct antibiogram training. These findings offer insights for developing and implementing antibiograms in an LMIC setting to optimize antibiotic prescribing practices and combat AMR globally.

6105

EFFECTS OF A SCHOOL-BASED PHYSICAL ACTIVITY PROGRAM AND MULTI-MICRONUTRIENT SUPPLEMENTATION ON BODY COMPOSITION AMONG SCHOOLCHILDREN IN THE KILOMBERO DISTRICT, TANZANIA

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Over the past decade, there has been a sharp rise in childhood obesity and overweight in low- and middle-income countries, including Tanzania, mainly governed by rapid changes in lifestyle and dietary patterns. We examined the effects of a school-based physical activity program and multi-micronutrient supplementation on body composition among schoolchildren in the Kilombero district, Tanzania. Children aged 6-12 years were cluster-randomized by class into one of four groups: (i) physical activity (PA) (n=236); (ii) a multi-micronutrient supplementation (MMNS) (n=263); (iii) physical activity plus multi-micronutrient supplementation (PA+MMNS) (n=257); and (d) control group (n=248). Children were followed over 2 years and assessment done at 12 and 24 months post-intervention. Generalized estimated equations (GEE) with random intercepts for school classes were employed to examine the intervention groups association with fat mass (FM), fat-free mass (FFM), truncal fat mass (TrFM), and truncal fat-free mass (TrFFM) during the second (T2) and third assessment (T3). A secondary set of GEE analyses were conducted, adjusting for children's sex, age, and height-for-age z score (HAZ) at the respective data assessments. In the unadjusted model, both boys and girls had decreased TrFM associated with PA promotion. In the adjusted model PA promotion among boys was significantly associated with reduced TrFM and FM. Boys engaged in the PA+MMNS arm also notably reduced FM. Girls in the MMNS arm had significant FM reductions, whereas those in PA arm had significant decreases in FM, TrFM and increases in FFM at T2. Girls in PA arm showed decreased in TrFM in the unadjusted model, while boys in PA+MMNS exhibited declined TrFFM. However, after adjustment, boys in the PA+MMNS arm had significant FM and TrFM declines. Furthermore, significant TrFM reduction in females assigned to the PA intervention at T3. Our research indicates that among Tanzanian schoolchildren in the Kilombero district, micronutrient supplementation and school-based physical activity programs were associated with decreased FM and enhanced FFM.

6106

CHARACTERIZATION OF MICROBIAL ISOLATES IN ANTIMICROBIAL STEWARDSHIP PROGRAM (ASP) OF A TERTIARY HEALTHCARE FACILITY IN SOUTHEAST NIGERIA - THE MONITORY PROJECT

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The emergence of antimicrobial resistance (AMR) poses a significant threat to global public health, challenging the effectiveness of traditional antibiotics. This section introduces the MONITORY project, which investigates AMR

within an Antimicrobial Stewardship Program (ASP) at a tertiary healthcare facility in Southeast Nigeria. The study employed a hospital-based descriptive approach, analyzing 235 clinical isolates collected from the microbiology laboratory of Nnamdi Azikiwe University Teaching Hospital. Isolation techniques, microbial identification, and antimicrobial susceptibility testing methods are described, alongside molecular analysis procedures. Gram-negative organisms predominated among clinical isolates, with notable resistance patterns observed. Staphylococcus aureus displayed significant methicillin resistance (MRSA), and molecular analysis confirmed the presence of ermC genes associated with macrolide resistance in the majority of S. aureus isolates. The findings highlight the urgent need for comprehensive ASPs to address AMR, particularly in resource-limited settings. Challenges in ASP implementation and the importance of strategic policy interventions, interdisciplinary collaboration, and international cooperation are discussed. Recommendations for responsible antimicrobial use, surveillance, and research efforts are provided. The MONITORY project underscores the critical importance of addressing AMR through collaborative efforts across healthcare sectors and global partnerships. Responsible antimicrobial stewardship, surveillance, infection control measures, and research and development initiatives are essential to mitigate the growing threat of AMR and safeguard public health.

6107

PRECARIOUS HUMANITARIAN SITUATION RISKING INFECTIOUS DISEASES OUTBREAKS FOR INTERNALLY DISPLACED PERSONS IN PORT-AU-PRINCE, HAITI

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Since 2018, the humanitarian situation in Haiti has deteriorated through a series of escalating sociopolitical crises. This includes gang violence, internal displacement, migration, fuel stockouts, closing of schools, businesses and hospitals, and rising living costs. As of Dec 2023, 310,000 people were reported as forcibly displaced in Haiti due to violence and insecurity. A cholera outbreak resurged in Haiti in late 2022. Displaced persons are at particular risk of exacerbation of chronic diseases and of acute illnesses such as infectious diseases. We sought to better understand the living situations, motivations for displacement, and health risks of a population of displaced persons in a spontaneous camp in Carrefour Feuille, Haiti, a neighborhood of Port-au-Prince. We interviewed 100 camp residents in Sept 2023. The mean age of respondent was 37.5 years (range 19-78), 53% were male. More than half had been property owners. 69% were displaced due to gangs taking over their neighborhood, at least 20% experienced their home being set on fire. Regarding their home neighborhood, 88% reported never seeing a government representative, 75% were unaware of any support or services there. Only 18% reported a visit from any official to the camp, however 61% did receive some assistance. Regarding health and hygiene, 10 respondents (10%) reported being aware of someone with a diarrheal illness that resembled cholera. 84% reported the presence of latrines. Only 43% reported having access to a place to bathe, 44% had access to water, but only 16% had access to potable water in the camp. 42% reported being aware of someone who was ill, yet only 2 people reported that there had been a mobile clinic at the camp. Displaced persons in greater Port-au-Prince, Haiti in Sept 2023 were in precarious humanitarian conditions, vulnerable to infectious diseases outbreaks and other ill-health as a result of lack of appropriate shelter, water and hygiene facilities, health care and potable water access. In the context of an ongoing cholera epidemic and worsening socio-political crisis there is an urgent need for appropriate humanitarian support for displaced persons in Haiti.

6108

AWARENESS AND PRACTICE OF MEDICAL WASTE MANAGEMENT AMONG HEALTHCARE PROVIDERS AT SALAVANH AND SEKONG PROVINCIAL HOSPITAL, LAO PDR

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Globally, medical waste management is a crucial public health concern. This descriptive cross-sectional study aimed to explore the amount of medical waste, and healthcare providers' awareness, knowledge, and practice in handling medical waste at Salavanh and Sekong provincial hospitals, from September 1st to December 31st, 2022. Every days waste was weighed and record from 2016-2022 for Salavanh Provincial Hospital, and from 2018-2022 for Sekong Provincial Hospital. All nurses (115), doctors (64) and the garbage collectors (2) for the inpatient departments were interviewed. Interviews were face to face using a Lao Language adaption of Zimba Letho's (2021) waste management surveys including their demographics questionnaire and medical waste management awareness and knowledge questionnaire previously used in Bhutan. Waste management practices were observed during the busiest hour of the day from 9:00-10:00 AM on seven consecutive workdays (Monday-Friday). Zimba Letho's (2021) observation check list was adapted to Lao Language and used in inpatient departments and at medical waste collection point to document the condition of waste receptacles, segregation of waste and how waste was transported. STATA version 13 was used for analysis. Salavanh Provincial Hospital produced was 0.68 kg/bed/day, and 0.80 kg/bed/day for Sekong Provincial Hospital with increasing amount of waste during time tracked. Most of the respondents had not received prior medical waste management training (71.8%). They knew some hazards of medical waste (blood-borne pathogens, sharps disposal, personal protective equipment, and waste disinfection). Most of them had difficulties following the medical waste management guidelines due to insufficient equipment for waste collection, storage, and disinfection. The observation results corresponded well with the interviews. Both hospitals lacked medical waste management training and Hepatitis B virus vaccination for their staff. There were several opportunities for improvement in medical waste management, especially in disinfection of transport vehicles.

6109

UNVEILING LIVES: EXPLORING THE DAILY ROUTINES OF LEPROSY-AFFECTED INDIVIDUALS IN MALAYSIA THROUGH VIDEO ETHNOGRAPHY

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The study employed video ethnography, utilising the "walk and talk" technique, to invite individuals affected by leprosy to lead the researcher through their daily routines as part of a broader research on the lived experiences of individuals affected by leprosy in Malaysia. This method allowed participants to share their stories on their own terms, capturing spontaneous moments and insights that might not emerge in structured settings. The research aimed to understand the everyday routines and needs of leprosy-affected individuals and how they navigated challenges, societal expectations, and personal aspirations, using visual and auditory elements to provide nuanced exploration. Video ethnography typically involves smaller sample sizes, and participants were selected through purposive and convenience sampling based on leprosy diagnosis. Six participants volunteered, three each from Kelantan and Sungai Buloh Leprosarium, ensuring diverse data and some generalisability.

Participants were not choreographed but were given some instructions and information, and they were free to select their study locations. The walkabout resulted in 3 to 4 hours of video footage each, capturing verbal and nonverbal expressions. The videos, audio recordings, and field notes were transcribed and analysed using NVivo 12 software, revealing themes of resilience, economic engagement, stigma, supportive family dynamics, and community support. Despite challenges, participants demonstrated determination to lead productive lives, emphasising the importance of work for sustaining families and communities. Self-imposed stigma hindered confidence and societal participation, but strong family bonds and community support promoted social inclusion and combatted stigma. Overall, the study sheds light on the daily struggles, aspirations, and resilience of individuals affected by leprosy. It advocates tailored interventions for their overall well-being.

6110

EMPOWERING WOMEN AND GIRLS: A PATH TO GENDER EQUITY IN HEALTH AND WELLBEING

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Women's health remains a critical global challenge, with significant disparities in access to healthcare, and diagnostic services especially in less-resourced settings. Empowering women and girls is not only a moral imperative but also a strategic investment in achieving gender equity in health and wellbeing. Despite significant progress in recent decades, gender disparities persist in access to healthcare, education, and decision-making power, disproportionately affecting women and girls in many parts of the world. Building upon the success of the "What Women Want" (WWW) campaign initiative conducted between 2018 and 2023 across eight countries, primarily in South-East Asia and Sub-Saharan Africa, FIND and White Ribbon Alliance (WRA), Kenya would like to embark on an initiative to understand how women and girls define health and wellbeing in Kenya. This endeavour aims to explore how women and girls define health and wellbeing in Kenya, with the goal of reshaping the understanding and response to their needs aiming to increase their decision-making rights agency for their health and wellbeing. Employing the WRA Kenya programming framework of 4Ps (people-practice-policy-products) within the Ask-Listen-Act approach, the initiative will ensure that women and girls receive quality, dignified, and equitable health services tailored to their needs at all levels. Key informant interviews and 'listening sessions' with adolescent girls, and women across the life continuum will be conducted. Additionally, the initiative will capture and document the lived experiences of women and girls through digital and multimedia storytelling to gain insights into their needs. The findings will inform community engagement, advocacy with duty bearers, and collaboration with key stakeholders to raise awareness among women and girls about their right to health, wellbeing, and self-care. Furthermore, the initiative aims to empower women and girls to demand and access quality, equitable, and dignified healthcare while advocating for policy reforms and resource allocation to prioritize women and girls' health and wellbeing throughout their lives.

6111

EXPLORING RESILIENCE AND WELL-BEING AMONG COMMUNITY HEALTH WORKERS: AN EXPLORATORY STUDY IN THE UPPER EAST REGION, GHANA

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Community Health Workers (CHWs) play a pivotal role in the execution of health interventions for neglected tropical diseases (NTDs) and routine health services in low-resource settings. However, they encounter challenges and stressors that may impact their resilience and well-being. While the importance of resilience and well-being is increasingly recognized, most quantitative research can not fully capture how these concepts are expressed in the African context, identify factors that shape and maintain them or account for the diversity and complexity of experiences. To address this gap, a phenomenological approach was used to explore the meaning of resilience and well-being of CHWs in the Upper East Region of Ghana and to identify contextual factors that contribute to their ability to cope with challenges and serve their communities. Twenty in-depth interviews were conducted: 16 with CHWs and 4 with community stakeholders. Interviews were transcribed verbatim into English and analyzed in NVivo (Version 14). Findings showed that resilience emerges as expressions of reciprocal altruism, personal drive, community solidarity, and spirituality amidst adversity. Well-being is perceived by participants as holistic, encompassing physical health, mental state, spirituality, and social harmony. Resilience and well-being among CHWs are shaped and maintained by how they navigate individual strengths, relationships, resources, beliefs, and seasonal challenges. For instance, heavy rains disrupt CHWs' daily routines, create competing demands, and introduce stressors into their work. Resilience and well-being are essential aspects of the human experience, yet their expression and interpretation differ globally. To boost the resilience and well-being of CHWs, interventions must be context-specific. Among CHWs in Sub-Saharan Africa, understanding their unique needs and experiences is essential to fostering resilient CHWs and ensuring that they can effectively serve their communities for NTDs and routine healthcare interventions.

6112

THE COST OF ACCESS TO HEALTH CARE FOR CHILDREN UNDER-FIVE YEARS WITH SEVERE ANAEMIA - A COSTING STUDY OF REFERRAL HOSPITALS IN MALAWI KENYA AND UGANDA

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Severe anaemia is a major cause of hospital admissions in African children under five years of age and the condition bears a high cost of access to health care. This study estimates the household costs of accessing care for severe anaemia at referral hospitals in Malawi (Zomba and Kamuzu Central Hospitals), Kenya (Kisumu and Busia Referral Hospitals) and Uganda (Jinja and Kitgum Hospitals). We prospectively collect data on the costs incurred when accessing services for severe anaemia alongside the randomized controlled trial, titled: Dihydroartemisinin-piperaquine and azithromycin for the post-discharge management of children with severe anaemia in Malawi, Kenya and Uganda. After enrolling children under five with severe anaemia, their guardians report direct and indirect costs encountered during their hospital admission. Since August 2023, 192 participants have been enrolled across the six study sites. Among these, subsistence farming 79/192 and informal trading 50/192 were the main sources of income of guardians supporting children with severe anaemia while 129/192 paid for part of the services accessed. About 88/192, needed a loan and 29/192 had to sell their assets to cover costs for the illness. Motorcycle taxis, 104/192 and ambulances, 25/192 were the main modes of transport used to get to a referral facility. Across all study sites, the major costs incurred were for transportation $2.9 (on average) and food $3.8. Medication cost was a common cost in Uganda with 58/64 of participants paying an average of $6.31. Opportunity costs were high as primary guardians did not work for 6 days (inter-quartile range: 3-7 days) during the illness and a secondary guardian was commonly involved during the hospital stay for 4 (3-5) days. This amounts to a mean productivity loss of $21 in Malawi, $38 in Kenya and $11 in Uganda during an illness with severe anaemia. The mean total cost for access to care was $30 in Malawi, $45 in Kenya and $36 in Uganda. In conclusion, transport, medication and nursing care are major sources of catastrophic health expenditure in this population.

6113

MORTALITY ESTIMATES IN SOUTH AND SOUTHEAST ASIA BY ELECTRONIC VERBAL AUTOPSIES

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In low- and lower-middle income countries in Asia most deaths happen outside of the healthcare system with no cause of death (COD) assigned. Cause-specific mortality data are crucial for designing public health policies. Alongside a rural febrile illness etiology study of Southeast Asian patients, we sought to understand the underlying major COD in these underserved populations using electronic verbal autopsies (VA). Between 2021 to 2023, mortality surveys were conducted at rural sites in Bangladesh, Myanmar, Lao PDR, Thailand and Cambodia using standardized WHO VA questionnaires and ICD-10 codes, ascertained by the physicians' review. Over 3,000 adult deaths were identified across the sites with 80-95% completeness of death reporting. Following a death, most interviews were scheduled between three and six months in order to minimize recall bias. In all countries, men accounted for about 1,748 (60%) of the recorded deaths. The majority of cases died at home 2,290 (76%) and the deceased individuals used a variety of healthcare facilities, primarily government hospitals and health centers. At all sites non-communicable diseases predominated and the three leading COD among adults were conditions relating to the digestive system, cardiovascular disease, and neoplasms. Our research highlights the necessity of regional and country-specific strategies to address the growing burden of non-communicable diseases. To monitor changes over time, verbal autopsies could be integrated into countries' civil registration and vital statistics systems at the time of national surveys.

6114

UNDERSTANDING THE IMPACT OF WORKING HOURS ON MEDICAL DOCTORS IN NIGERIA. A STUDY ON MENTAL HEALTH AND DECISION-MAKING

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This study seeks to comprehensively examine the impact of working hours on the mental health and decision-making of medical doctors in Nigeria. The hypothesis is that prolonged working hours may lead to increased stress, and impaired decision-making among medical doctors, ultimately influencing the quality of healthcare delivery. A quantitative approach was employed, utilizing a survey questionnaire to gather data from 58 medical doctors in a tertiary hospital in Nigeria. The questionnaire encompassed items related to expected working hours, self-reported mental health status, and perceived impact of long working hours on decision-making. Participants were selected through convenience sampling. Preliminary findings indicate that 86% of doctors start work by 8 am, with 55% only closing when they are done with work. 53% reported working 5 days a week, 26% work 7 days a week, and 50% reported working even on weekends. Additionally, 95% reported not having scheduled breaks during their workday, and 97% reported taking multiple in-hospital calls a week. 97% believe the impact of long working hours on them affects their patients care and 86% believe it drives their decision-making. A significant number, 60% reported their hospital not having policies guiding their working hours. Notably, 100% believe that revising and regulating working hours would positively impact their physical and mental well-being, as well as improve healthcare delivery to patients. These findings underscore the urgency of addressing working hour policies to safeguard the mental and physical well-being of medical practitioners and enhance patient care. Further analysis of the data is underway to provide a comprehensive understanding of the impact of working hours on medical doctors in Nigeria.

6115

THE ROLE OF GENDER IN MALARIA HEALTHCARE PROVIDER PERFORMANCE

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Gender dynamics shape interpersonal interactions between healthcare providers and supervisors and influence provider recruitment, retention, and performance. Providers of different genders receive different professional development opportunities and face different constraints which impact their performance. PMI Impact Malaria conducted a secondary analysis of malaria service delivery training data and supervisory data to examine how the gender of training participants, supervisors, and supervisees influenced training participation, and training and supervisory performance. The study examined 491 supervisory observations across three countries, and 23,671 training observations across 11 countries using descriptive statistics, multivariate regression, and qualitative data validation with country teams. The study found that women improve more between pre- and post-test when trainings are at parity with regard to participant gender; for example, case management trainings in Rwanda had roughly equal numbers of female and male participants, and women had greater gains than men by 3.58% (p=0.02). Country team validation meetings noted that parity is difficult to achieve due to gender barriers to women entering the cadres targeted for the trainings, or preference by predominantly male managers to select male participants even within predominantly female cadres (e.g. nursing). Teams noted that women often make fewer training gains and perform worse overall due to household and childcare responsibilities (such as bringing infants to trainings or leaving early to complete household tasks) and having less experience or seniority in the field than male counterparts. Analysis of supervisory data did not indicate significant differences in competency scores based on supervisor or supervisee gender; however, this analysis was limited due to sample size, and it is recommended that supervisory checklists include gender of supervisor and supervisee to further this analysis. Both global and country-level analysis of these results can help programs understand and address gaps in malaria provider performance.

6116

EVALUATION OF PHYSICAL ACTIVITY AND DIET INTERVENTIONS IN PREVENTING CHILDHOOD OBESITY IN THE UNITED STATES OF AMERICA: A SYSTEMATIC REVIEW

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In the United States (US), ethnic/racial minorities and poor socioeconomic status children are disproportionately affected by childhood obesity. Among Organization for Economic Cooperation and Development member states, the US has the highest obesity rate in the world. In an investigation of the prevalence of childhood obesity in the US, no age group showed indications of a decrease. Obesity prevention in children is a global priority. Diet and physical activity are considered to be changeable behavioural factors that affect overweight and obesity. A significant body of research on behavioural risk factors associated with childhood obesity implies that physical activity and eating behaviours are related and likely bidirectionally causal, and hence should be explored simultaneously in this study. A narrative synthesis for quantitative studies was chosen to answer the research questions in this systematic review. The search utilised specified

combinations of MeSH words, Boolean operators, and Truncation and was conducted using three databases: PubMed, MEDLINE, and Child Development & Adolescent Studies and covered between the year 2016 and 2022. The Critical Appraisal Skills Programme for Randomised Control Trial (RCT) research appraisal instrument was utilised to evaluate the study's quality. Included were ten studies from across the US between the year 2016 to 2022. These studies were undertaken primarily in two distinct settings: the school and the community. The review found that childhood obesity is still pervasive in the US, especially among racial/ethnic minorities and low-income groups, and will continue to rise if not adequately addressed. The current behavioural interventions, which include physical activity and nutrition education, are capable of positively influencing weight-related outcomes and BMI among 5 to 18-year-old children in the US, but an integrated multicomponent strategy will achieve better results. Nonetheless, future RCT research should focus a greater emphasis on systemic therapies, such as policy and socioeconomic interventions.

6117

NAVIGATING THE LOW COVID-19 VACCINATION RATE NEXUS: BIBLICAL INTERPRETATIONS AND PRACTICES OF PENTECOSTAL CHRISTIANS IN DMV

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The development and release of a vaccine during an epidemic or pandemic is aimed at mitigating the adverse effects of infection, transmission, and spread of the disease. However, the development and availability of a vaccine does not always guarantee the acceptance of the vaccine by the entire population. This is the case of COVID-19 vaccine that was approved and released by FDA in August 2021. The low COVID-19 vaccine rate within the Black Pentecostal Christian community in the DMV area is a public health concern. The decision by many in this subpopulation to reject the vaccine would continue to adversely impact the development of herd immunity and may likely extend the spread of the disease. Some factors that might have influenced the decision of this population to accept or reject the vaccine have been linked to politics, anti-COVID-19 vaccine sentiments, and religion. Though research findings have reported that belief in God has led to a delay or refusal of COVID-19 vaccine, the research focused on only one aspect of the image of God - how individuals conceptualize God and how this could influence the acceptance of the vaccine. This calls for further research on other aspects of the image of God. This study therefore aimed at exploring and elucidating the convoluted relationship between religious beliefs, practices, and leadership guidance in the context of COVID-19 vaccination within the Black Pentecostal Christian community in the Washington D.C. Metro area. The qualitative study uses the phenomenological approach with in-depth interviews and the theory employed is the health belief model. Findings of this study are significant in bridging the gap in knowledge with regards to health, religious studies, and community engagement. The findings would also have the potential to enact positive social change both at personal and community level. Moreso, the findings would help policy makers, public health professionals, and researchers to make informed decisions. The author is finalizing on the interview and wishes to present the results and findings of this study in November 2024 in New Orleans, USA during the ASTMH annual conference.

6118

MASS CYTOMETRY DATA INTEGRATION METHODS REVEAL RURAL-URBAN GRADIENT OF IMMUNE PROFILES ACROSS GEOGRAPHY

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The human immune system strongly varies across populations and is impacted by a range of host and environmental factors. As such, a rural, compared to urban lifestyle, has previously been associated with baseline differences in immune profiles and reduced vaccine responsiveness. Here, using three mass cytometry datasets, we studied shared and population-specific immune characteristics of healthy rural- or urban-living Indonesian, Senegalese and Tanzanian adults and urban-living Europeans. After harmonized preprocessing and quality control, 75.4 million cells were integrated using in total four data-integration methods, including CytoNorm, Harmony, CytofIn and quantile-normalisation. Using the best performing integration method (CytoNorm), we were able to assess in detail cellular immune profiles associated with rural- or urban-lifestyle shared across geography. Generally, rural-living individuals showed an immune profile that showed an overall highly differentiated and activated state. Using machine learning models, we were able to discriminate rural- and urban-living individuals based on these profiles with moderate to-high accuracy. The current study serves is an example on the integration of different large mass cytometry datasets. The findings presented here may guide future studies on the shared or population-specific environmental drivers of baseline immune profiles and how this impacts vaccine immunogenicity in low-responding populations.

6119

SUCCESSFUL RECRUITMENT STRATEGIES FOR ENGAGING PREGNANT WOMEN IN CLINICAL TRIALS: LESSONS LEARNED FROM TWO INDIVIDUALLY RANDOMIZED CONTROLLED TRIALS CONDUCTED IN KENYA

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Experiencing a low recruitment and high attrition rate among participants has been a persistent challenge in numerous clinical trials involving pregnant women and may introduce bias into the trial's findings. Although barriers to effectively recruiting pregnant women to clinical trials are well documented, little is known about how to succeed. The Improving Pregnancy Outcome (IMPROVE) trials were individually randomized clinical trials targeting HIV-negative and HIV-positive pregnant women between 16-28 weeks gestation. Women gave their consent at enrolment, and an obstetric ultrasound was performed to estimate gestational age. Afterward, participants attended regular scheduled study clinic visits every four weeks up to six or eight weeks after delivery. Venous blood and urine samples were collected at each visit. Overall, we enrolled 1925 participants, with 96.7% of scheduled visits attended and 99.0% of participants contributing to the primary analysis. Recruitment strategies reported included: home pregnancy testing by community health workers and referral to the study clinics; establishing group antenatal care tailored towards the studies' inclusion criteria; utilizing key community stakeholders to spread messages about the study; establishing community advisory board (CAB) to help disseminate information about the study and support to curb negative perceptions about the study in the community; site networks, which made it possible for the study to get referrals from other facilities. Retention strategies included: proper consenting using a language a participant is comfortable with and assessing comprehension after consenting; involving guardians and spouses during consenting; regular phone calls to remind the participants about visits; realistic trial timelines; a wide scheduled visit window; free obstetric ultrasound at enrolment; compensation of participants for their time and transport. IMPROVE clinical trials experiences

provide additional evidence of successful recruitment and retention of pregnant women and reinforce more of what has previously been documented.

6120

ESTABLISHING A NATIONAL DEEP VEIN THROMBOSIS NETWORK IN GHANA: RESULTS FROM A PROSPECTIVE MULTI-CENTER STUDY

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Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a leading cause of morbidity and mortality worldwide. Nevertheless, data on VTE in sub-Saharan Africa are scarce. This observational study was carried out in a national capacity development project aiming to improve the diagnosis and treatment of patients with DVT in Ghana. Between 2018-2022, we established a “National DVT Network” comprising nine hospitals across Ghana. “DVT teams” were trained and equipped with technical infrastructure to enable DVT diagnosis. A total of 1422 adult patients with suspected DVT were screened. DVT was confirmed by ultrasound in 626 patients (44%), including 619 patients with lower extremity DVT (LEDVT) and 10 patients with upper extremity DVT. Among the 619 cases of LEDVT, 77% were inpatients. Among 240 patients with suspected DVT and PE, PE was confirmed in 59 (25%) by computed tomography. Anticoagulants were administered to 223 out of 1422 patients (16%) with suspected DVT prior to the onset of suspicious symptoms. This included 25% (37/146) of inpatients with active cancer, 23% (57/244) of inpatients with lower extremity immobilization, and 27% (8/30) of inpatients with a history of DVT. Study phase 2 (2020-2022) comprised 930 patients, including 379 with VTE. Out of 930 patients, 81 died (9%) primarily while hospitalized. Anticoagulation was received by 96% (365/379) of patients with confirmed VTE. The fatality rate was significantly higher among patients with confirmed VTE (17%, 65/379 versus 3%, 16/551, $p<0.001$). Excluding individuals who were not deceased, only 16% (45/310) of patients diagnosed with DVT received follow-up after 6 months. Among these, DVT was completely resolved in 71% (32/45). The prevalence of DVT among Ghanaians with clinical suspicion is high, suggesting that DVT is a common disorder in Ghana. Increased awareness among healthcare professionals for indicated prophylactic anticoagulation is needed. The follow-up of patients with DVT was insufficient and needs to be improved. However, in most patients receiving treatment and follow-up, DVT might be completely resolved after 6 months.

6121

THE FIRST AFRICAN CENTER OF EXCELLENCE IN BIOINFORMATICS & DATA SCIENCE (ACE-MALI): TEN-YEAR ACCOMPLISHMENTS

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The April 2, 2015, was the opening ceremony of the First African Center for Excellence in Bioinformatics and Data Science at University of Sciences, Techniques and Technologies of Bamako, (USTTB) Mali. The goal of the ACE initiative is to leverage in-kind donations to provide a sustainable, reliable, and local infrastructure of high-performance computing hardware coupled with bioinformatics tools, training, and mentorship designed to improve the quality of infectious disease research in Africa by Africans. ACE aims to carry out relevant research based on high-quality training in Bioinformatics and Data sciences at MSc and PhD levels that takes into consideration the needs of Public health and industry in west Africa. The program has obtained different Research and training grants from NIH, H3Abionet and USTTB to support research and Msc and PhD. Some Students were supported by different programs such us NIH-Fogarty training Grant, H3ABioNet and Welcome Trust funded DELGEM program.In collaboration with Tulane University (USA), we organized annual bioinformatics and data science symposia and workshops, student and faculty exchange program at Tulane University, careers enhancement, grant writing and submission. ACE hosts different short-term training from H3ABionet such us IBT, NGS, AGMT, etc.Today 42 students are graduated in Msc in Bioinformatics from Mali, Gabo, Burundi and Nigeria, 12 of them are enrolled in PhD programs in Mali, in UK or USA and 10 of them have position of Research Assistants in different national Research institutions and research program in Mali. A couple of PhD students are ready to defend their thesis by the end of this year, Their works were focused on malaria vaccine and drug target development in silico, proposing some good targets with their inhibitors. Faculty and student have produced up to twenty scientific publications in international reviews. This work summarizes the highlights of main achievements of the program and developed approaches can serve as a model to build or strengthen capacity in research training program in Africa.

6122

EXAMINING THE PRESENCE OF MONKEYPOX IN A GHANAIAN COMMUNITY: A CASE STUDY AT PENTECOST HOSPITAL

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The Greater Accra region of Ghana has historically been regarded as nonendemic for monkeypox. Nonetheless, the evolving interplay of factors such as climate change, and urbanization raises uncertainties regarding its current transmission status. The La-Nkwantanang Madina Municipal Health Directorate was notified of a suspected monkeypox case involving a 13-day-old infant, Priceless Danso, at Pentecost Hospital, Madina. Upon admission, the infant presented with a temperature of 37.2°C, pulse rate of 155 bpm, respiration rate of 36 cpm, SpO2 of 64%, and RBS of 9.7 mmol/L. Multiple vascular rashes (approximately 0.5 cm × 0.5 cm) were distributed evenly over the body, and the child was dehydrated. Diagnostic tests confirmed impetigo/monkeypox and sepsis, with a positive result for monkeypox. The infant was treated with oxygen, intravenous antibiotics (ampicillin, flucloxacillin), and intravenous fluids. The mother and grandmother received counseling and reassurance, and health education was provided on the disease condition, signs, and symptoms. A cross-

sectional design involving interviews with a structured questionnaire was used for contact tracing. The survey purposefully sampled individuals who got contact with the infant. Tragically, the infant, Priceless Danso, passed away the following morning. Contact tracing and preventive measures were initiated, including self-observation for involved staff and the provision of a contact number for follow-up information or clarification. The La-Nkwantanang Madina Municipal Health Directorate collaborated with various specialties, including Disease Control, Community Health Nurses, Nutrition Management, Nursing Administration, Clinical Coordinators, and other districts, to break the chain of transmission and avoid a public health emergency.

6123

INVESTIGATING THE INFLUENCE OF HUMAN MILK OLIGOSACCHARIDES ON CHILD GROWTH DEVELOPMENT

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Detecting growth deficiencies in children early on is imperative for implementing effective interventions and, averting potential long-term health complications. Human Milk Oligosaccharides (HMOs) are vital for infant nourishment, fostering a healthy gut microbiome and strengthening the immune system. Research indicates they positively influence infant growth, leading to healthier outcomes by 24 months of age. Their role in promoting optimal growth and development underscores the significance of breastfeeding in early infancy. Our investigation constitutes a supplementary study to the SAGE birth cohort, an established research initiative comprising 444 mother-infant pairs located in Leon, Nicaragua. Breastmilk collected from mothers after childbirth at one month was analyzed using fluorescent high-performance-liquid-chromatography, where the composition of 19 HMOs was quantified. Linear Regression Models were conducted to examine the relationship between HMO composition and infant growth using the rate of change in the child's Z scores between one and 24 months of age. The assessment of HMO levels revealed distinct patterns between secretor and non-secretor mothers, with varying HMO abundances. In the crude analysis, higher concentrations of 3-sialyllactose (3'SL) were significantly associated with positive changes in Weight-for-Age Z-score (WAZ) and Length-for-Age Z-score (LAZ) over time in infants, underscoring the importance of this HMO in infant growth. Additionally, positive associations were found between difucosyllactose (DFLac), difucosyllacto-N-tetrose (DFLNT), disialyllacto-N-tetraose (DSLNT), and fucosyllacto-N-hexaose (FLNH) concentrations and WAZ rate changes, while promising trends were observed in fucodisialyllacto-N-hexaose (FDSLNH) and sialyl-lacto-N-tetraose c (LSTc) concentrations in relation to WAZ and LAZ rate changes, respectively. These findings underscore the significance of understanding the specific HMOs' impact on infant growth and development, advocating for increased breastfeeding to optimize children's health outcomes.

6124

DETERMINANTS FOR EARLY CARE SEEKING FOR MALARIA AMONG CAREGIVERS OF CHILDREN UNDER FIVE YEARS IN UGANDA

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Following decades of implementing malaria prevention and treatment interventions, the Demographic Health and Malaria Indicator Surveys showed a positive trend in prompt care-seeking for children under five years in Uganda from 75% in 2016 to 87% in 2019. A cross-sectional study conducted in West Nile and Karamoja regions in November-December 2022 assessed the determinants for early care seeking practices. The mixed methods study with caregivers included 803 surveys, 18 focus group discussions, 24 in-depth interviews. STATA 17 and Atlas.ti 23 were used for analysis. From the survey, 54% of the caregivers had children under five who had a fever in the past 30 days, 76% sought treatment and advice from providers, 84% indicated a preference for government health care rather than traditional healers. 69% reported being happy with malaria services for children under five at the visited health facility, and the odds of practicing positive malaria behaviors such as prompt care-seeking for children with a fever in 24 hours of onset were significantly higher among those who reported being satisfied with the services and provider interactions (OR 5.9, 95% CI: 2.86 - 12.28). The reasons for prompt care seeking described in focus group discussions and interviews included previous encounters with malaria among children, the need to avoid complicated illnesses, saving the child, fear of treatment costs, the need to avert malaria deaths, and positive results from completing a full course of malaria treatment. The perceived motivators of health facility utilization included advice on malaria prevention, ability to provide diagnostic and appropriate treatment services, availability of free services, proximity of health facilities, availability of community health workers. Accompanying one another to the hospital and taking care of the neighbor's children were common ways of practicing shared compassion. Service delivery programs need to improve client experience by making services more accessible, building provider-client relationships, and encouraging compassionate actions to improve malaria case management.

6125

TRADITIONAL HEALERS REFERRING FOR MALARIA IN UGANDA: RESULTS FROM RAPID ETHNOGRAPHIES

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Available evidence on Uganda suggests that traditional healers are common, however, few studies document the emergence of acquiescence for, and collaboration with, modern medical services. This study investigated traditional healer practices which promote malaria prevention and treatment. Between 27 November and 10 December 2022, a cross-sectional design comprising seven key informant interviews (KIIs) and six rapid ethnographic observations was conducted with traditional healers from the West Nile and Karamoja regions of Uganda. Participants were purposively selected using snowball sampling in areas of high malaria positivity. KIIs were used to collect individual perspectives while ethnographic observation triangulated with contextualized data. Results illustrated that traditional healers were appreciative and supportive of ongoing referrals and linkages with the health facilities. Traditional healer skills were used by health facilities under supervision, to address shortages of staff, for example in the maternity ward where they observed pregnant women progression towards delivery and alerted the midwife. Observation data revealed; a traditional healer tendency for testing for malaria from the facility before complimentary herbal healing was commenced; that traditional healers do not treat conditions they do not understand because they want to avoid wasting herbs and time and fear the consequences of adverse client outcomes. Traditional healers request clients to first get a test at a health facility to ensure the specificity of their treatment methods. KII data revealed that traditional healers were mostly confident of facility-based test results and medicines, which they perceived as fast in healing compared to "slow" herbs. From this study, traditional healers were receptive towards a referral role to health facilities for confirmation of malaria before herbal treatments commence. Potential interventions among traditional healers may include; engagement as partners and referral agents.

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ENHANCING CHILD MORTALITY SURVEILLANCE AND PREVENTION STRATEGIES IN LOW MIDDLE-INCOME COUNTRIES: THE CHAMPS NETWORK APPROACH IN PAKISTAN

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Child mortality is a pressing issue in countries, like Pakistan, where under-five mortality rates are nearly double the global average. Many more deaths, particularly those at home, go unaccounted for—with incomplete determination of the cause of death (CoD). The Child Health and Mortality Prevention Surveillance (CHAMPS) site in Pakistan aims to establish mortality surveillance of children under five years in three peri-urban areas in Karachi. The goal is to collect robust data on CoD through lab testing of post-mortem minimally invasive tissue samples (MITS) alongside clinical and verbal autopsy (VA) data. Implementation began in July 2023 with a target of 100 MITS samples in a year. Preliminary socio-behavioral science (SBS) investigations informed our strategy. On-going community engagement and liaison with stakeholders helped establish a network of key informants to provide timely death alerts. Mobile vans, specifically designed for MITS procedures, are deployed in catchment areas for flexible sample collection outside households or hospitals, addressing the gap in accounting for home deaths. A rapid response time and collection outside households also help reach the target population within the narrow window between death and shrouding/burial common to Muslim communities—after which the body cannot be disturbed. Grief support for bereaved parents and a CoD report are provided as incentive for study participation. The van can also be used to aid families in ritual bathing, shrouding and transport of the body following collection. A total of 180 microbiology, histology and molecular tests are conducted on samples. Lab data is reviewed in conjunction with available child and maternal clinical and VA data by a panel of physicians to determine CoD. To date, 31 MITS samples have been collected. 45% were collected from home deaths. MITS data on community deaths should provide an in-depth understanding of pediatric CoD in Pakistan to help tailor interventions and policies to reduce under-five mortality. Our approach may benefit others looking to overcome challenges in community-oriented surveillance and sample collection.

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ASSESSING TENSION AND ALIGNMENT OF COMMUNITY VALUES AND CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) IN URBAN NEIGHBORHOODS OF KARACHI, PAKISTAN

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The Child Health and Mortality Prevention Surveillance (CHAMPS) networks conducts mortality and pregnancy surveillance in Africa and South Asia to understand and prevent child mortality. A key data component is the collection of minimally invasive tissue samples (MITS) to determine cause of death. We assessed the feasibility, acceptability, and implementation of CHAMPS through a series of participatory workshops within the communities of three peri urban areas of Karachi, Pakistan. Participatory Inquiry into Community Knowledge for Child Health and Mortality Prevention (PICK-CHAMP) workshops introduce CHAMPS to target communities and assess how well study activities align with community perceptions and priorities. Ten workshops were conducted from May to June 2023 with both community members and leaders, selected to participate through purposive and snowball sampling. PICK-CHAMP workshop exercises identified participants' health concerns and explored their attitudes towards mortality and pregnancy surveillance. Data was thematically analyzed and the degree of alignment or tension between community priorities and CHAMPS goals was scored using the CHAMPS tool. Results demonstrated strong alignment with CHAMPS pregnancy surveillance and moderate alignment, with minimal tension, with CHAMPS MITS. Most antenatal and child health concerns expressed by participants were alleviable through medical/public health interventions, highlighting compatibility with study aims. 99.1% of respondents believed pregnancy surveillance fit with community priorities, and 56.1% believed the same for MITS. We found moderate-high alignment for pregnancy surveillance (81.5%) and MITS (76.1%) when participants were asked about community supportiveness. Understanding the alignment and misalignment of community priorities and CHAMPS aims allowed us to tailor advocacy strategies to meet community values. Moreover, community engagement facilitated through PICK-CHAMP activities improved our connections with stakeholders and spread valuable awareness about the study.

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ENHANCING THE IDENTIFICATION OF CAUSES OF DEATH THROUGH COMMUNITY-BASED VERBAL AUTOPSY METHODS DURING THE COVID 19 OUTBREAK

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In a resource constrained settings like Pakistan, obtaining accurate mortality data can be challenging due to limited autopsy practices and a significant proportion of deaths occurring outside of hospital facilities. This study utilized a community-based verbal autopsy approach in two peri-urban sites in Karachi, Pakistan to obtain cause of death (CoD) data at the household level. The two sites, Ali Akbar Shah and Bhains Colony, are part of a health demographic site surveillance (HDSS) system that was established in 2003. Rigorous interviewer training ensured sensitive data collection using the

WHO 2016 Questionnaire. Verbal autopsy (VA) data underwent physician review to determine causes of death in accordance with ICD-10 codes. VA was conducted on 1500 deaths, with a male: female ratio of 1.12:1. 41.6% of deaths occurred at home. For children under 5 years, 31.5% of deaths occurred at home. Non-communicable diseases were most common, accounting for 39.3% of deaths with acute cardiac disease (12.6%), liver cirrhosis (7%), and stroke (4.3%) being the three most common causes. Major causes of death associated with communicable diseases included diarrheal disease (6.4%), pneumonia (4.1%), and sepsis (3.4%). Among adults (>18 years) acute cardiac disease (25.1%) and liver cirrhosis (13.4%) were top causes of mortality. There was a higher prevalence of liver cirrhosis among females (14%) compared to males (10.1%). Neonatal sepsis (12.8%) and perinatal asphyxia (11.7%) were prominent CoD in children under five. Pneumonia (8.8%) and road traffic accidents (8.8%) were the two major CoD in children between 5-18 years. The considerable proportion of deaths, particularly in children, taking place at home underscores a potential gap in health access and utilization which needs to be explored. Understanding trends in disease burdens across varying demographic groups can help tailor interventions to improve public health outcomes in resource-constrained settings.

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COMMUNITY BEHAVIORS AND PRACTICES TOWARDS ROUTINE IMMUNIZATION IN POLIO HIGH RISK UNION COUNCILS OF PAKISTAN

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Behavioral and Social Drivers of Vaccination (BeSD) are people's beliefs, experiences, andcircumstances influencing vaccination decisions. BeSD are categorized into four domains: attitudes towardsvaccines, social influences, motivation (or hesitancy) to vaccinate, and practical considerations. This studypresents the BeSD findings about essential childhood vaccinations from seven districts over three provincesthat hold the polio super-high-risk union councils (SHRUCs) in Pakistan. A cross-sectional survey was conducted in 2023 in 39 SHRUCs over 7 districts using a two-stage stratified cluster sampling technique. Altogether, 7,829 caregivers across the SHRUCs districtsresponded to the BeSD childhood vaccination survey for caregivers, designed to assess the drivers ofvaccination for children under age 5. Of the respondents, 43.3% wanted their child to receive all vaccines according to Pakistan'sschedule, with notable differences across SHRUC districts: 84.9% in Sindh, 33.2% in Balochistan, and only2.6% in Khyber Pakhtunkhwa. Nearly two-thirds of respondents (65%) considered vaccines are veryimportant for their child's health, but opinions varied by district, ranging from 84.6% in Sindh to 41.5% inBalochistan. Altogether, 91.8% reported encouragement from family and friends to vaccinate their child,and 93.4% knew where to access vaccination services. Affordability varied greatly, with 59.3% finding itvery easy, ranging from 35.9% in Balochistan to 81.2% in Sindh.Challenges in accessing vaccination services were reported by 1,644 respondents, primarily due to difficultyreaching clinics (73.4%) and long waiting times (63.9%). Dissatisfaction with vaccination services wasexpressed by 2,434 respondents, centred on long waiting times (62.7%), insufficient staff interaction(41.0%), and vaccine unavailability (38.0%). Despite caregivers' willingness, access and affordability barriers remain, includingtransportation challenges and long wait times. Targeted interventions addressing these issues are crucial toimproving vaccination coverage.

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OPTIMIZING COMMUNITY HEALTH RESOURCES FOR UNIVERSAL ITN COVERAGE IN THE DRC: OUTCOMES OF A *TRINÔME* TO*BINÔME* PILOT IN LUALABA PROVINCE, 2023-2024

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The USAID End Malaria Project has supported the National Malaria Control Program in the Democratic Republic of the Congo (DRC) in distributing insecticide-treated nets (ITNs) through door-to-door mass campaigns since 2021, employing teams of three community health workers (CHWs), known as *trinômes.* The *trinôme* approach, consisting of a designated sensitizer, carrier, and investigator, became national policy for ITN campaigns during the COVID-19 pandemic. In response to financial constraints, the project piloted a transition in August 2023 to a *binôme* model that combined the roles of sensitizer and carrier in seven health zones in Lualaba province before scaling up to Lualaba's remaining seven health zones. Feasibility and cost-effectiveness were assessed by evaluating time taken to distribute an ITN to a household and the number of households covered per day against national targets set based on *trinôme* performance in previous campaigns. Cost savings were also calculated comparing the *binôme* and *trinôme* approaches. Instead of the 8,175 expected *trinôme* CHWs, 5,450 CHWs formed the *binôme* teams. Across the pilot and scale-up phases, similar outcomes and outputs were achieved. Teams successfully reached 97% of targeted households with a total of 2,132,389 ITNs benefitting 3,959,639 individuals. Teams spent between 12-15 minutes distributing in each household against the national target of 10-15 minutes. Daily *binôme* output was between 25-30 households per day in rural areas against a target of 30, and between 40-50 households in urban areas against a target of 50. There were direct cost savings of 30% ($221,997) on both labor and training. The operational distribution cost (which excludes the physical ITN cost) in the province also dropped to $1.53 per ITN distributed against the planned target of $1.81. The *binôme* approach for door-to-door mass distribution campaigns proved viable in the DRC; significant cost savings were realized without impacting the target output coverage. This approach also frees up CHWs to concentrate on delivery of other health services, allowing for better delivery of routine care during ITN campaign periods.

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INSIGHTS FROM CHILD HEALTH & MORTALITY PREVENTION SURVEILLANCE (CHAMPS) NETWORK - PAKISTAN SITE

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Child mortality is a global public health concern. It disproportionately affects emerging nations in Sub-Saharan Africa and South Asia, accounting for over 80% of five million under-5 deaths per year. In Pakistan, the under-five child mortality rate is 63.3 deaths per 1,000 live births. Pakistan was added to the Child Health and Mortality Prevention Surveillance (CHAMPS) network to investigate and address this high rate of under-five mortality. Study implementation began in July 2024 at three peri-urban sites in Karachi aiming to enumerate all stillbirths and under-5 deaths and collect data on cause of death (CoD). Data collected from consenting families includes minimally invasive tissue samples (MITS) and available (non-MITS) data from clinical records and verbal autopsy (VA). Our target is to collect 80 MITS this year. Following lab testing, data is reviewed by a panel of physicians to determine CoD. We are presenting preliminary findings from our study. As of March 31st, 2024, we documented 302 under-five deaths. We completed 31 MITS cases, consented 166 non-MITS cases, and conducted 156 VA. Of 31 MITS cases, 12 (38.7%) were stillbirths, 10 (32.2%) neonates, 7 (22.5%) post-neonates, and 2 (6.4%) were 1-5yrs. 45% of samples were collected from deaths occurring at home. 58% of MITS cases were male. Blood microbial testing showed eight positive cases of *K. pneumonia*, four for *Staphylococcus species* and two for *P. aeruginosa*. CSF microbial testing showed six positive cases for *Acinetobacter baumannii* and four positive for *E. Coli*. Pathology reports showed presence of aspiration pneumonia in neonatal and 1-5yrs groups. Intrauterine fetal distress was reported among stillbirths. MITS has been helpful in providing a concrete

understanding of child mortality causes. Following case- review by physician panels and determination of CoD, data trends will help inform interventions and policies aiming to reduce regional child mortality.

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ENHANCING DISEASE SURVEILLANCE AND RESPONSE SYSTEMS IN THE GAMBIA AND SENEGAL: A CROSS-BORDER COLLABORATION

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Effective disease surveillance is crucial for early detection and response to disease threats. However, resource constraints, including infrastructure and financing gaps, can create hurdles, particularly in low- and middle-income countries. These difficulties are compounded by increased population mobility in border areas, which exacerbates the risk of infectious disease spread. Cross-border collaboration offers an opportunity to enhance disease surveillance and response, particularly in countries such as The Gambia and Senegal, which have long open borders. In these contexts, communication, data sharing and mapping population movement, which may require substantial investment, are critical for minimizing disease transmission. This study evaluates the costs and financial implications of a cross-border surveillance strategy between The Gambia and Senegal, for earlier detection and response to disease outbreaks. Employing a mixed methods approach, the study assesses existing surveillance systems and identifies changes needed in resource allocation, infrastructure, and institutional arrangements. A micro-costing assessment estimated implementation costs, with a focus on identifying sustainable co-financing models. A multi-criterion mapping exercise will facilitate the co-development of a cross-border collaboration strategy. Initial findings indicate suboptimal performance of the Integrated Disease Surveillance and Response systems at facility levels, with weaknesses in outbreak investigation and timeliness of reporting. Qualitative inquiry revealed that inadequate laboratory capacity hampered early detection and confirmation of outbreaks, compounded by insufficient funding. Recommendations for enhancing cross-border collaboration included: improving funding and timely access to funds and implementing district to district collaboration. This research identifies barriers and enablers to cross-border surveillance, and proposes strategies for effective implementation, informing analyses on the financial implications of operating a cross-border surveillance system in the subregion.

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IDENTIFYING DISTRICT-LEVEL RISK FACTORS FOR DELAYS IN YELLOW FEVER SPECIMEN COLLECTION AND ARRIVAL FOR TESTING IN GHANA

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Delayed diagnosis of yellow fever (YF) leads to increased morbidity and mortality during outbreaks, but the steps in the YF diagnostic pathway which cause the greatest delays in case detection are not well known. Ghana is classified as a high-risk country for YF by the WHO Eliminate Yellow Fever Epidemics strategy. When a patient meets the case definition for suspected YF, a specimen is collected and sent to the National Public Health and Reference Lab (NPHRL) for testing. Our interviews with 148 clinicians at 53 health facilities in Ghana revealed perceived delays in YF testing. We therefore explored district-level risk factors contributing to differences in specimen collection and arrival at the NPHRL for YF testing. We conducted a cross-sectional sample of 12 districts in Ghana with patients tested for suspected YF from 2018-2022. Districts were stratified by ecological zone, patient volume, and distance of highest tier health facility from a reference zonal laboratory. A total of 298 patients were tested for YF from 190 health facilities in the sampled districts. We used descriptive statistics to compare time from symptom onset to specimen collection and time from specimen collection to arrival at the NPHRL. We used multivariable linear regression to identify district-level risk factors associated with diagnostic delays including distance from districts to NPHRL, population density, and poverty level. The mean duration from symptom onset to specimen collection was 5.1 days (range 0-30, standard deviation 4.4), and from collection to arrival at NPHRL was 8.9 days (range 0-94, standard deviation 11.8). There was a significant relationship between distance and time to specimen arrival at the NPHRL, with arrival time delayed by 1.5 days for every 100 kilometers from the NPHRL. We conclude that the timing of specimen collection and arrival for YF testing differs across districts in Ghana. Improving access to YF testing, including through decentralized testing and improved specimen transport, could lead to earlier detection of YF outbreaks.

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SEROPREVALENCE OF ELEVEN NEGLECTED DISEASES OF PUBLIC HEALTH INTEREST IN NAURU

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Nauru is a small island nation in the western Pacific region, approximately 1800 miles northeast of Australia. Here we share the results of a 2019 integrated serosurvey conducted using dried blood spots collected during a trachoma survey in Nauru. Antibody data are presented for six neglected tropical diseases (NTDs) and five additional parasitic diseases of public health interest to the Nauru Ministry of Health. This was a nationally representative, randomized, two-stage cluster survey, with 769 samples analyzed from children ages 1-9 years. For NTDs, less than 5% of children were antibody positive to any of three lymphatic filariasis (LF) antigens included, with two children double positive and none triple positive. No children tested antibody positive to both yaws antigens. For trachoma, 32.5% (95% CI, 29.2% - 35.8%) of children were antibody positive. One quarter (25.6%, 95% CI, 22.5% - 28.7%) of children were seropositive for *Strongyloides stercoralis*. For the parasite *Taenia solium*, 6.6% (95% CI, 4.9% - 8.4%) were seropositive for cysticercosis marker T24H and 1.2% (95% CI, 0.4% - 1.9%) were positive for the taeniasis infection marker ES33. Toxoplasmosis seropositivity was significantly high, at 44.3% (95% CI, 40.8% - 47.9%) as was toxocariasis at 28.9% (95% CI, 25.7% - 32.1%). Approximately a quarter of children surveyed were seropositive for giardiasis, 23.2% (95% CI, 20.3% - 26.3%) and cryptosporidiosis, 26.8% (95% CI, 23.7% – 29.9%) respectively. Less than 5% of children were seropositive for amebiasis, 4.3% (95% CI, 2.9% - 5.7%). In addition to confirming the need for trachoma interventions, the use of the multiplex bead assay identified high seroprevalence to several parasitic and water-borne diseases that can guide programmatic intervention. The serological data lends support to epidemiological data indicating LF and yaws are not present in Nauru. Taking advantage of specimens collected during a vertical trachoma survey provided added public health benefits by providing data to guide programs that would have required additional funding to collect otherwise.

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COVID-19 VACCINE HESITANCY: A GLOBAL SURVEY ON KNOWLEDGE, EXPERIENCE, ATTITUDE, AND PSYCHOLOGICAL STRESS

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The COVID-19 pandemic has underscored the urgency of rapid vaccine development and availability. However, vaccine hesitancy remains a significant barrier to global efforts to curb the pandemic, despite extensive public health campaigns. The present study aimed to explore the factors that may contribute to COVID-19 vaccine hesitancy. A global online cross-sectional survey was conducted in 2023, involving 102,481 adult participants from 189 countries. The 48-question survey, translated into 33 languages, examined the effects of various factors such as demographics, knowledge, attitude, experience, and psychological stress (egocentricity, callousness, and antisociality) on COVID-19 vaccine hesitancy. The cohort's mean age was 27.3±9.9 years, with about 58% of respondents identifying as female. A notable proportion of respondents, 18%, reported being unvaccinated against COVID-19, while over 31% expressed disagreement with COVID-19 vaccination. Furthermore, the optimal structural equation model (RMSEA=0.032/CFI=0.955/TLI=0.950) incorporated gender, level of education, and family member's COVID-19 severity. The model elucidated 45.34% of the observed variance, suggesting that female participants and those with family members experiencing more severe COVID-19 conditions tended to express lower levels of hesitancy related to vaccine reactions (HRVR), in contrast to individuals with higher levels of education. Regarding psychological stress, antisociality was significantly associated with increased concern about COVID-19 vaccine information (CVI) and HRVR (OR=1.19 and 1.08, 95%CI:1.17-1.2 and 1.06-1.09, p<0.001, respectively). Conversely, both egocentricity (OR=0.97, 95%CI:0.96-0.98, p<0.001) and callousness (OR=0.76, 95%CI:0.75-0.77, p<0.001) were associated with reduced concern about CVI. Egocentricity was also associated with increased HRVR (OR=1.12, 95%CI:1.10-1.14, p<0.001). These findings offer global evidential insights to enable policymakers to develop multitiered interventions to combat COVID-19 vaccine hesitancy that could be scaled up to other vaccine-preventable diseases.

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COMPARATIVE ANALYSIS OF STATE-LEVEL POLICY RESPONSES IN GLOBAL HEALTH GOVERNANCE: COVID-19 AS A CASE

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States are key actors in global health governance, particularly in the prevention and control of infectious diseases. The emergence and re-emergence of infectious diseases in recent decades pose profound challenges to global health security. As the first coronavirus pandemic, the COVID-19 caused significant damage worldwide, but responses and outcomes varied greatly among states. Using COVID-19 as an example, this study aims to compare the policies and measures implemented by different states during the COVID-19 pandemic and to synthesize experiences to strengthen global health governance for future infectious disease crises. We selected the United States, Sweden, India, and Nigeria as the representative states with different economic development and impact of COVID-19 prevention and control strategies. We systematically collated data on the policies adopted by these states to control COVID-19 from literature, reports, authoritative media and official websites. A comparative analysis was then conducted to analyze the differences, rationale, and challenges of the approaches taken by these states. The management of COVID-19 by states is divided into domestic and international governance. Domestically, the United States and India have taken more measures, yet notable disparities in infection source control, transmission interruption, vulnerable population protection, collaborative governance, and so on were observed among all four states. Internationally, the United States and Sweden were more proactive in international governance, and all four states have variations in their adherence to global regulations, information sharing, resource distribution, and cooperative engagement. Significant disparities occurred during the response to early COVID-19 in four states, which may be due to differences in politics, economy, and culture. To prevent and mitigate the impact of infectious diseases, states should prioritize solidarity and cooperation, and improve governance domestically and internationally based on national contexts and global health principles in the future.

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SEARCH FOR ACTIVE CASES OF YAWS IN PARTS OF IMO STATE, SOUTHEAST NIGERIA

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Yaws was previously eradicated in Nigeria but Nigeria belongs to the WHO Yaws epidemiological category B countries. This study focused on active search for cases of Yaws amongst adults in two communities in 2 local government areas of Imo State respectively in Ehime Mbano and Mbaitoli. Informed written consents and appropriate ethical clearance were duly obtained from relevant authorities. Sampling method was purposive and medical screening were conducted among the participants using the WHO SkinNTD toolkit. Blood samples (2mls) of participants were collected and subjected to serological and VDRL test. Pre-tested questionnaires were used for demographic data as well as data on their knowledge and practices. A total of 125 adults (75 adults from Ehime Mbano, 50 adults from Mbaitoli) participated. From Ehime Mbano, despite high presumptive cases of yaws 49(65.3%), only 28(37.3%) was reactive to serological test strip and 47(62.7%) showed no symptoms. Clinical examination of the seropositive participants showed that 5(17.9%) papiloma virus, 8(28.6%) ulcer, 3(10.7%) swelling bones and 12(42.9%) hyper keratosis on feet and palms. Findings from Mbaitoli LGA showed that despite high presumptive cases of yaws 35(70%), only 3(6%) was reactive to serological test strip and 47(94%) showed no symptoms. Knowledge on Yaws from the data collected from the total 125 participants, indicated that 14(11.2%) insect bites caused the disease, 4(3.2%) bad drinking water source, 7(5.6%) bathing cold water, 10(8%) enemies and 90(72%) unidentified causes. On their practices, 40(32%) among participants visit the clinic for their treatments, 17(13.6%) visit herbalist, 5(4%) and 3(10.7%) consults oracle and spiritualists respectively while 30(24%) use more than one treatment method. Active search for Yaws yielded positive results in Ehime Mbano which require further confirmation and follow up. In conclusion, this study confirmed that there had been considerable progress in the treatment of yaws in the last decade, but the danger of re-emergence exists. Thus the need for more attention on yaws in Nigeria is advocated.

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IDENTIFICATION OF ANTHRAX AS THE CAUSE OF A CLUSTER OF UNEXPLAINED DEATHS, UGANDA, 2023: THE ROLE OF METAGENOMIC NEXT GENERATION SEQUENCING AND POSTMORTEM SPECIMENS

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Several deaths of unknown etiology were reported in Kyotera District of Southern Uganda in August of 2023. Patient symptoms included fever, shortness of breath, abdominal pain, vomiting, loss of appetite, profuse sweating, body aches, swelling of limbs, and blisters with a black center. Field response teams deployed by the Uganda Ministry of Health (MOH) collected clinical and epidemiological data and specimens. The Mortuary Surveillance Program, a collaborative effort between the MOH, the Abbott Pandemic Defense Coalition (APDC) and Uganda Virus Research Institute (UVRI), analyzed postmortem specimens to explore potential infectious causes of death. Blood specimens from deceased individuals with unknown cause of death from Kyotera District were PCR screened for viral hemorrhagic fevers: Ebola, Marburg, Rift Valley and Crimean Congo. Metagenomic Next Generation Sequencing (mNGS) was performed on PCR-negative specimens using the Illumina DNA Prep kit on the MiSeq NGS platform. Data was analyzed with an Abbott-internal bioinformatics pipeline, DiVir. Results were confirmed by an alternate NGS library prep method, the Respiratory Pathogen ID/AMR Enrichment Panel (RPIP). Deep sequencing identified the presence of *Bacillus anthracis* reads in only one of the index patients from August, and thus cases were deemed unrelated. By November 2023, a cumulative total of 27 human and 22 animal deaths had been reported in the Kyotera District for which symptoms were consistent with anthrax infection. For six additional cases subjected to mNGS and RPIP enrichment, an anthrax diagnosis was confirmed by UVRI and DiVir pipelines. Notably, only 3/7 were positive for anthrax using an in-house PCR assay. Utilizing mNGS of postmortem specimens through the Mortuary Surveillance Program, was a powerful tool for identifying an otherwise unrecognized Anthrax outbreak in Uganda. Building and sustaining the infrastructure for mortuary surveillance and NGS should be prioritized for control of emerging and re-emerging pathogens and integrated into public health programs in sub-Saharan African countries.

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SARS-COV-2 TRANSMISSION POTENTIAL AND CONTROL MEASURES IN ZIMBABWE: AN ECOLOGICAL ANALYSIS

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This ecological study aimed to investigate the SARS-CoV-2 transmission potential in Zimbabwe from Mar 20, 2020, through Mar 9, 2023, and its ten provinces from Mar 20, 2020, through May 11, 2022. The association between the transmission potential and policy interventions was accessed until Feb 28, 2021, before the introduction of vaccines. Datasets from Johns Hopkins University, African Surveyors Connect, and the Zimbabwe Ministry of Health and Child Care were analyzed. Negative and zero incident case counts were imputed, infection dates were estimated from report dates via deconvolution, and infection counts were estimated via a Poisson-distributed multiplier of 4. The time-varying reproduction number (Rt) was estimated by the R package 'EpiEstim' using the 7-day sliding window and non-overlapping time windows. Between Mar 2020 and Dec 2022, Zimbabwe and its ten provinces experienced three case surges corresponding with the Beta (Nov 2020), Delta (Jun 2021) and Omicron (Dec 2021) waves. In alignment with the waves, Rt>1 was observed during case surges, and Rt<1 was observed during case declines between waves. Secondary to low incident cases (Mar-Jun 2020), Rt estimates showed greater uncertainty. On the national level, Zimbabwe's 'dusk-to-dawn' daily curfew on July 21, 2020, was associated with a decrease in Rt (-11.39%, 95%CrI: -17.00%, -6.02%). On the provincial level, the daily curfew was associated with a statistically significant decrease in Rt in Harare (-16.89%, 95%CrI: -25.38%, -10.04%), Manicaland (-10.01%, 95%CrI: -19.03%, -1.17%), Midlands (-10.40%, 95%CrI: -19.94%, -1.60%), Matabeleland South (-13.54%, 95%CrI: -22.88%, -5.65%), and Bulawayo (-16.20%, 95%CrI: -24.49%, -8.04%). This study highlighted how non-pharmaceutical interventions impacted the SARS-CoV-2 transmission in Zimbabwe. It emphasizes the importance of public health interventions implemented at national and sub-national levels in different countries. Tailoring interventions to specific locations and populations is crucial, as various factors can affect their effectiveness.

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ONE-YEAR PATTERN OF ANTIMICROBIAL RESISTANCE IN *ESCHERICHIA COLI*, *KLEBSIELLA PNEUMONIAE* AND *PSEUDOMONAS AERUGINOSA* ISOLATES IN OSOGBO, NIGERIA

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Escherichia coli, Pseudomonas aeruginosa and *Klebsiella pneumoniae* are gram-negative bacteria that have been linked with various healthcare-associated and community-acquired infections. These three organisms have been identified by MAAP survey as critical multi-drug resistant pathogens that require new drugs to combat their infections in humans. Therefore, antimicrobial resistance patterns of *E. coli*, *K. pneumoniae* and *P. aeruginosa* isolates from clinical specimens submitted for microbial culture and sensitivity test were analyzed between January and December 2022. 286 bacterial isolates including 171, 83 and 32 of *E. coli*, *K. pneumoniae* and *P. aeruginosa* respectively were identified. All *P. aeruginosa* isolates exhibited resistance to at least one antibiotic. Essentially, 75% of *P. aeruginosa*, 66.1% of *E. coli* and 71.1% of *K. pneumoniae* demonstrated multidrug resistance pattern. *E. coli* 63.69% and *P. aeruginosa* 14.65% showed highest resistance to ZEM, and least resistance to LBC. Whereas, *K. pneumoniae* showed highest resistance to IMP 30.19% and least resistance to GEN 23.99%. AUG-CIP-CRO-CTX-CXM-GEN-IMP-LBC-ZEM antimicrobial resistance pattern occurred in urine, wound specimens for *P. aeruginosa* isolates. The same pattern was also found in *E. coli* isolated from vagina swab. The 3 bacteria isolates demonstrated a considerable high prevalence of resistance to antibiotics under study. The resistance to Imipenem is noteworthy as it is often reserved for the treatment of multidrug resistant pathogens. *P. aeruginosa* has always shown higher rate of multidrug resistance (MDR) and this was also established in this study. ZEM and CIP are often used in the treatment of *P. aeruginosa* infections but this study indicated that the resistance by *P. aeruginosa* to both antibiotics is very high. This study shows that antimicrobial resistance among these organisms is on the increase. As such, there is need for community-based sensitization on proper use of antibiotics as well as regulated sale of antibiotics to lower the rate of antimicrobial resistance.

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COMMUNITY PERCEPTIONS OF HEALTH-RELATED RISK FACTORS, HEALTH STATUS, AND HEALTHCARE SERVICE IN RURAL SOUTHEAST ASIA: INSIGHTS FROM A CROSS-SECTIONAL HOUSEHOLD SURVEY IN BANGLADESH, CAMBODIA, AND THAILAND

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To guide rural disease control priorities the South and Southeast Asia Community-based Trials Network conducted cross-sectional household health surveys in Bangladesh, Cambodia, and Thailand during 2022-2023. We used two-stage cluster sampling to recruit participants of all ages to assess disease prevalences and identify community-perceived concerns related to risk factors, health status, and health services. Adult participants' (≥ 15 years old) demographic and socioeconomic characteristics, concerns about health-related factors, and previously diagnosed diseases were collected through questionnaire interviews. Among adults (Bangladesh: n=1168, Cambodia: n=937, Thailand: n=1210), the majority were women (Bangladesh: 57.9%, Cambodia: 54.3%, Thailand: 59.5%), aged 15-44 years in Bangladesh (71.8%) and Cambodia (60.4%), and 45 years or older in Thailand (70.7%). Many had no formal education (Bangladesh: 33.8%, Cambodia: 21.6%, Thailand: 28.2%). The self-reported prevalence of raised cholesterol, hypertension, and diabetes was highest in Thailand (cholesterol: 17.2%, hypertension: 25.2%, diabetes: 10.2%), followed by Cambodia (cholesterol: 4.2%, hypertension: 13.1%, diabetes: 4.6%) and Bangladesh (cholesterol: 0.8%, hypertension: 10.9%, diabetes: 4.3%). Healthcare costs were the leading concern in Cambodia (82.1%) and Bangladesh (46.1%), and were most likely to be reported by Bangladeshi adults with hypertension (57.5% vs. 44.7%, p=0.006). No specific concern was most commonly reported (38.8%) in Thailand, but timeliness of health service delivery (20.9%) was more frequently mentioned by those reporting hypertension (24.9% vs. 19.3%, p=0.038) or diabetes (29.8% vs. 18.7%, p=0.008). This survey highlights the large variation in self-reported disease prevalences and community concerns, and the need for healthcare interventions tailored to local contexts. Further laboratory assays will confirm disease status and identify the extent of undiagnosed and untreated conditions, and determine associations between non-communicable and infectious diseases by sero-epidemiological assays.

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DEVELOPING THE CONCEPT AND PRACTICE OF ANTICIPATORY ACTION FOR EPIDEMICS A THE HUMANITARIAN SECTOR

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Within the humanitarian sector, a novel anticipatory approach to climate and disaster risk management is emerging. 'Anticipatory action' makes use of climate or weather forecasts and observations as well as in-depth risk analysis to predict where and when a disaster may unfold in order to intervene in advance and prevent or reduce negative impacts. Specifically, it codifies the release of pre-emptive emergency funding to enable pre-agreed actions based on predefined triggers within a forecast of a hazard. Advances in the understanding climatic drivers of infectious disease mean that developing anticipatory action as part of epidemic prevention, preparedness, and response can help humanitarian actors and their partners increase the effective timing of outbreak interventions, reduce the delay to response, prioritise and allocate the use of limited resources, and improve coordination and clarification of roles and responsibilities amongst relevant actors. Specifically, climate-informed early warnings for climate-sensitive infectious diseases can provide information on (1) a change (earlier or later) in the onset or cessation of the transmission seasons in endemic areas, (2) geographic locations that are at higher risk, and (3) the likely magnitude of cases (including the potential surpassing of the epidemic threshold) in a forthcoming season. Anticipatory action for epidemics does not necessarily entail designing new interventions, rather it helps improve decision-making on the optimal timing of existing disease control and prevention. This paper contributes to building a common understanding on the concept of anticipatory action for epidemics for humanitarian practitioners. We detail the three main triggering methods that can be used to establish anticipatory action for epidemics and provide purposively selected case studies to illustrate the methods.

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ASSESSMENT OF COMMUNITY AWARENESS, CONDUCT AND HABITS ON YELLOW FEVER IN THE UPPER EAST REGION OF GHANA

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Recent update by WHO revealed that from January, 2021 to December, 2022, Ghana recorded 62 confirmed cases and 12 confirmed deaths as a result of Yellow Fever (YF) outbreak. Designing efficient control and preventive methods requires a thorough assessment of the community's awareness, knowledge and practices on YF. We determined community's knowledge, practices and awareness on YF using structured questionnaire with a data collection application software KOBO collect. A total of 1000 participants from two municipalities and two districts in the Upper East Region, were selected for the survey from May to July 2023. Seven hundred and ninety-two (79.2%) of the participants indicated they have heard about YF. Four hundred and fifteen participants, 415 (41.5%) had knowledge that transmission of YF is through mosquito bites. Participants from two districts; Bulsa North District, 158 (15.8%) and Kassena Nankana West District 153, (15.3%) showed very little knowledge on YF, (Mann-Whitney test =19523.000 $P = 0.567$) as well as in Bolgatanga Municipal, 295 (29.5%) and Kassena Nankana East Municipal, 186 (18.6%) (Mann-Whitney test=32300.000, P=0.000). Preventive measures used by participants to reduce spread of YF include sleeping in mosquito net, 303 (30.3%) clearing of bushes, 110 (11.0%) and vaccination, 170 (17.0%). The vaccination of respondents was not influenced by time taken to access health service

(Spearman Rho correlation coefficient=0.311). Continuous education and sensitization of inhabitants in the Upper East Region is required to create the needed awareness on YF outbreak preparedness and control.

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ECOLOGICAL STUDY OF TERRESTRIAL SMALL MAMMALS IN AN ENDEMIC PLAGUE FOCUS IN THE CENTRAL HIGHLANDS OF MADAGASCAR, IMPACT ON SURVEILLANCE STRATEGIES

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In Madagascar, human plague outbreak occurs almost every year in endemic foci and the extent of its burden may vary according to localities, case management and response. In order to investigate the implications of reservoirs in plague maintenance, we implemented a longitudinal survey. Six small mammal trapping sessions were conducted in six areas in Ankazobe during two years. Spleen from each individual of small mammals was used for Yersinia pestis detection by bacteriology and qPCR. Further, the presence of anti-F1 IgG antibodies was investigated by ELISA. A total of 2,762 small mammals were trapped and R. rattus represented 88% of all captures, with their relative abundance being significantly between trapping sessions and plague seasons. A pic of reproduction was observed during the dry and humid season. None of the tested individuals were neither PCR nor culture positive and a global seroprevalence of 0.4% was observed. Although Y. pestis appeared to circulate at low levels during the present survey, our study highlighted marked seasonal variations of R. rattus abundance and reproduction, thus allowing us to assess the most valuable periods to implement rodent reservoirs management in this recurrently active endemic focus of plague.

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RETROSPECTIVE EVALUATION OF THE DIAGNOSTIC ACCURACY OF THE RELASVPAN LASSA ANTIGEN RAPID DIAGNOSTIC TEST FOR THE DETECTION OF ACUTE LASSA VIRUS INFECTION IN NIGERIA USING REAL TIME POLYMERASE CHAIN REACTION AS REFERENCE STANDARD

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Lassa virus (LASV) is a biosafety level 4, priority pathogen under the World Health Organization R&D Blueprint. LASV infects up to 300,000 persons annually across West Africa, causing a zoonotic, potentially severe viral hemorrhagic fever known as Lassa fever (LF). The LASV Rapid Diagnostic Test (RDT) landscape is currently not only limited, there is also limited independent performance data on the available LASV RDT to inform their use. This study was set up to assess the diagnostic accuracy of a LASV antigen RDT to determine its suitability for widespread use as a potential screening tool for acute LASV infection. This was an observational, retrospective, diagnostic accuracy study to determine the performance of the ReLASV™ Pan Lassa Antigen RDT (Zalgen Labs, LCC, Germantown, USA) using archived, frozen blood samples collected from individuals in Nigeria. The overall performance of this RDT was measured against the reference test, Altona RealStar LASV qRT-PCR 2.0 (Altona Diagnostics, Hamburg, Germany). Point estimates were calculated based on standardized definitions and the 95% confidence interval for each point estimate was derived based on Wilson's score method. With an observed PPA and NPA of 65% and 50.7% respectively, this test performed below the average expected performance. This test might therefore not be suitable for making critical diagnostic or treatment decisions without further validation or improvement. These findings underscore the importance of thoroughly assessing the performance characteristics of tests, to ensure their reliability and accuracy in real-world applications, especially in healthcare settings where diagnostic accuracy is critical.

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COMPARISON OF KNOWLEDGE, ATTITUDES AND PERCEPTIONS ON RESPONSE TO THE COVID-19 PANDEMIC BETWEEN RURAL AND URBAN COMMUNITIES IN DEMOCRATIC REPUBLIC OF CONGO

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SARS-COV-2 outbreak highlighted difficulties experienced by DRC population, a country of more than 90 million inhabitants located in central Africa. As soon as the first positive national case was diagnosed, the government implemented measures to protect the public. However, there are great differences between the large cities and the hinterland, which sometimes lack everything: access to water, electricity and quality health care. This project aims to compare knowledge, attitudes and practices on the government response to the COVID-19 pandemic between urban and rural communities in the DRC. This is a mixed study on knowledge, attitudes and practices conducted in two sites: Kinshasa for the urban area and at Kimpese, for the rural area. Data were collected through individual questionnaires administered to medical staff and group interviews with patients' carers. The study included 90 participants, 46 from the Kinshasa site and 44 from the Kimpese site. While 67% of Kinshasa residents surveyed trusted government reports on the spread of the epidemic and statistics on the number of cases of COVID-19 and deaths, that perception in Kimpese was lower (47%). Of the various government measures taken, the most popular were face masks (97%), lockdowns (97%) and travel restrictions (82%). Economic and social intervention policies, at 12% and 22%, were the least known. Just over six out of ten people questioned were satisfied with these measures. Proactive government management and logistical organisation prevented the spread of the C0VID-19 pandemic throughout the country. However, government management was marred by setbacks: communication crisis and financial mismanagement. Lack of contextualisation to national realities could be one of the causes of the non-appropriation of communities more concerned with their survival to the point of denying the existence of the disease. COVID-19 pandemic response in the DRC has taken into account the gap existing between urban and rural communities. An assessment of the consequences should be made. An epidemic risk management plan is needed to avoid making the same mistakes in the future.

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A MIXED-METHOD STUDY TO DETERMINE CAUSES OF DEATH USING MINIMAL INVASIVE TISSUE SAMPLING AND VERBAL AUTOPSY IN THE BONO EAST REGION, GHANA.

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High-quality mortality data is needed for decision-making in health delivery. However, this is lacking in most low and middle-income countries. The Kintampo Health and Demographic Surveillance System (KHDSS) records all deaths of registered members and uses the WHO Verbal Autopsy (VA) tool to determine causes of death, but this process is limited by imprecise diagnosis and recall bias which ultimately reduces data quality and hampers evaluation of health policies. Minimal Invasive Tissue Sampling (MITS) is proven to improve the accuracy of cause-of-death (CoD) determination in low-resource settings. This study aimed to combine MITS and VA techniques to determine CoD in 300 cases involving stillbirths, children under five, and adults 60 years and above in the Bono East Region of Ghana. Initiated in May 2023, this study will explore the feasibility of integrating MITS into KHDSS to determine CoD and the acceptability of the MITS procedures. The inclusion criteria are deaths among individuals registered in the KHDSS occurring at the study hospitals or brought to study hospitals within 12 hours of death and written informed consent given by relatives. Cases of legal issues such as murder and accidents are excluded. Tissues and fluid samples are collected for molecular, microbiological, and histopathological analyses; placenta and umbilical samples are included in stillbirths and neonatal deaths. A multi-disciplinary panel of experts determines the CoD based on laboratory results, VA open narratives, and whenever available, clinical history. A total of 90 cases have been completed in the preceding 11 months since study initiation:15 stillbirths (66.7% females), 13 children under five (61.5 % males), and 62 adults (51.6% females). Thirty-one percent of these cases have been assigned causes of death (28/90) and the main CoD in stillbirth and adults are septicemia and pneumonia, respectively.

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USING MINIMALLY INVASIVE TISSUES SAMPLING TO DETERMINE CAUSES OF DEATHS IN THE MIDDLE-BELT OF GHANA: IMPLEMENTATION SUCCESSES, CHALLENGES AND OPPORTUNITIES

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Determination of underlying Causes of Death (CoD) and death registration remains a challengein low-resource settings. Minimal invasive tissue sampling (MITS) is an innovative interventionthat improves the accuracy of CoD information, is more culturally acceptable, and is less costlycompared to the conventional autopsy. A mixed-method study is currently being conducted inGhana to determine CoD among stillbirths, children under five, and adults 60 years and aboveusing MITS. The study team presents challenges and successes to inform future implementationof MITS in similar settings. Several challenges were identified as part of the baseline capacityassessment of health facilities and mortuaries, notable among them was the absence of apathologist in study sites. Others include 1) deficiencies in infrastructure like mortuaries, 2) lackof temperature-controlled cold boxes for transporting tissue samples, and 3) relatives' hesitancy toconsent to MITS on their deceased family members. To address the limited pathology expertise,following training, MITS sample collection was task-shifted to non-pathologists including medicalofficers, midwives, nurses, and laboratory scientists. Additionally, a virtual network of expertsincluding a pathologist provided technical support in sample analysis and interpretation. Otherstrategies implemented to address the challenges included: 1) improving the physical infrastructureby renovating mortuaries to ensure suitable environments for MITS sample collection, 2)establishing an electronic death notification system at hospitals and mortuaries, and, 3) conductingextensive community engagement involving stakeholders and developing context-specificguidelines to support the MITS consent process. Task-shifting of sample collection to non-pathologists, leveraging virtual networks to enhance capacity, optimizing existing facilities, andeffective community stakeholder engagement strategies have been key to implementing MITS inthis setting and are relevant considerations for scaling MITS within Ghana.

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COLLABORATING WITH KEY COMMUNITY ACTORS TO PREPARE FOR FUTURE OUTBREAK RESPONSES: LESSONS FROM LIBERIA

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The West African sub-region was unprepared to manage the 2014-2016 Ebola outbreaks. The outbreaks exposed many systemic and structural challenges within the health sector, including limited recognition of community engagement and preparedness. In Liberia, the virus spread via person to person transmission, household clusters, and community transmissions. There were fears and misconceptions among community dwellers leading to lack of trust in the health care systems. Although Liberia and other regions are currently Ebola-free, the risk of another epidemic remains eminent thereby justifying the need for community preparedness to prevent, respond to, and contain any future outbreaks. We conducted a mixed methods quantitative and qualitative study design. This presentation focuses on the qualitative components conducted in three prevalence counties for EVD to identify the determinants of community preparedness for outbreak response, readiness for Merck ZEBOV vaccination, and the roles of informal and formal community structures. We used purposive sampling methods to conduct key informant interviews and focus group discussions with community groups, and leaders of informal and formal structures. Most of the participants described the communities as not being prepared to manage outbreak response. High death rates led communities to adhere to preventive measures although others were still engaged in traditional practices. Community leaders developed preventive measures including washing buckets at major intersections to prevent the spread of the virus. They highlighted limited trust in health authorities. Participants expressed varying opinions on Ebola vaccine, with some hesitant to take it due to lack of information, mistrust, and cultural beliefs and practices. They described community engagement and awareness as crucial for addressing mistrust and misinformation about the Ebola vaccine. There is a need for collaboration with key community leaders to prevent, detect and respond to threats from emerging and reemerging pathogens, build robust and resilient health systems, and strengthen community response.

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SEROLOGICAL SURVEY OF A COMMUNITY IN GHANA INVADED BY BLACKFLIES

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The Greater Accra region of Ghana is nonendemic for onchocerciasis, however, due to climate change, illegal mining activities, urban migration, and other factors, the transmission status is uncertain and confirmation may be required. The recent upsurge of blackflies in the La Nkwantanang Madina Municipality were investigated to ascertain the infectivity of

onchocerciasis among community members. The Neglected Tropical Disease program of the Ghana Health Service commenced a serological and entomological assessment in the identified communities to confirm or otherwise the onchocerciasis infectivity. This was a cross-sectional design involving interviews with a structured questionnaire. The survey purposefully sampled three firstline communities near the breeding sites of the blackflies. A total of 100 adults of 20 years and above were finger prick and dried blood spots collected for laboratory confirmation. Of the 602 samples, 24 were positive for onchocerciasis giving an overall prevalence of 3.9%. The seroprevalence of onchocerciasis in the community was 4.97%. Among the persons who tested positive for onchocerciasis, 50% were males and 21% were 60 years old and above. Two areas in the community attained the statistical threshold for mass drug administration with ivermectin for onchocerciasis.

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THREAT OF URBAN ARBOVIRAL DISEASES FROM *AEDES AEGYPTI* IN COLOMBIA

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Several arboviruses have emerged and/or reemerged in the New World in the past decades. While yellow fever and dengue are historical diseases which continue to cause deadly epidemics, chikungunya and Zika have recently invaded the South American continent, causing great concern. In Colombia, unplanned urbanization combined with growing demographics produce conditions suitable for the proliferation of *Aedes aegypti*, setting the scene for arbovirus epidemics. We collected eggs and adults of *Ae. aegypti* in Medellin, Colombia (from February to March 2020) for mosquito experimental infections with dengue (DENV), chikungunya (CHIKV), yellow fever (YFV) and Zika virus (ZIKV) and viral detection using the BioMark Dynamic arrays system. We show that *Ae. aegypti* from Medellín was more prone to become infected, to disseminate and transmit CHIKV and ZIKV than DENV and YFV. Thus, in Colombia, chikungunya is the most serious threat to public health based on our vector competence data.

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DEMONSTRATION OF RNA ACTIVATION IN TICKS

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RNA activation (RNAa) is burgeoning area of research in which small activating RNAs (saRNAs) mediate the targeted upregulation of specific genes. So far, the phenomenon has been limited to mammals, plants, bacteria, *Caenorhabditis elegans* and recently, *Aedes aegypti,* with no indication of its presence in other arthropods including ticks, despite the presence of Argonaut 2, an indispensable requirement for the formation of RNAinduced transcriptional activation complex. In this study, we demonstrated the presence of RNAa phenomenon for the first time in the Asian longhorned tick, *Haemaphysalis longicornis.* We targeted the 3'-UTR of a novel endochitinase-like gene in embryogenic eggs, for dsRNA-mediated gene activation. Our results showed an increased expression of the gene in *H. longicornis* endochitinase-dsRNA (dsHI-CHT) tick eggs at day-13 post-oviposition. Furthermore, we observed that the dsHI-CHT tick eggs exhibited relatively early egg development and hatching. Results therefore suggests that the dsRNA-mediated gene activation of HI-CHT led to the early development and hatching of dsHI-CHT tick eggs. This is therefore the first evidence of RNA activation in ticks and the outcome of this study provides new opportunities, based on the usefulness of RNAa as a tool for over expression of genes, for future research in tick biology, to reduce the global burden of ticks and tick-borne diseases.

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TICKS ON DROMEDARY CAMELS (*CAMELUS DROMEDARIUS*, LINNAEUS, 1758) FROM SOMALIA

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Ticks are prominent parasites and competent vectors of pathogens that may affect both humans and animals. Dromedary camels (*Camelus dromedarius*, Linnaeus, 1758) are vital livestock in Somalia but are susceptible to tick infestations, which pose health risks to both animals and humans due to pathogen transmission. Understanding tick diversity and prevalence in camel populations is crucial for effective management strategies. Therefore, this study aimed to collect and identify tick species parasitizing dromedary camels. A cross sectional study was utilized, involving the examination of 155 dromedary camels from Mogadishu and Lower Shabelle regions of Somalia. Ticks were removed from dromedaries using a commercial hook and kept in absolute ethanol labeled tubes for identification according to morphological taxonomic keys. A total of 346 (223 M, 112 F, and 11 nymphs) ticks were collected from 79/155 (50.9%; 95% CI: 42.8-59.1%) dromedary camels with a mean of 4.4 ticks per animal. Ticks were identified as *Rhipicephalus pulchellus* (174/346; 50.3%), *Hyalomma dromedarii* (103/346; 29.8%), *H. rufipes* (35/346; 10.1%), *H. marginatum* (16/346; 4.6%), *R. humeralis* (14/346; 4.0%), *Amblyomma lepidum* (2/346; 0.6%), *A. gemma* (1/346; 0.3%,), and *Ornithodoros* sp. (1/185; 0.5). The study identifies tick species infesting dromedary camels in Somalia, including the first report of *A. lepidum* and *R. humeralis* ticks in dromedary camels in the country. The economic importance of *Amblyomma* and *Rhipicephalus* ticks has long been recognized due to their ability to transmit multiple pathogens to humans and animals. Our data highlights the need for targeted control measures to mitigate health risks for animals and humans, emphasizing the importance of further research for comprehensive tick management and disease prevention in camel populations.

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UNDERSTANDING BARRIERS IN TRIATOMINE SURVEILLANCE: CHALLENGES AND COMMUNITY - DRIVING SOLUTIONS IN AREQUIPA, PERU

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Vector-borne diseases remain a significant public health challenge globally, yet funding and support for vector control programs are diminishing. This study explores the systemic barriers to effective triatomine surveillance in Arequipa, Peru, by analyzing existing surveillance strategies and identifying critical inefficiencies that compromise their efficacy. Using qualitative methods, we conducted interviews and focus groups with stakeholders, applying purposive sampling to capture diverse perspectives. Our findings highlight significant systemic barriers, including inadequate community engagement, administrative inefficiencies, and resource constraints, which hinder the efficacy of both passive and active surveillance systems. We developed "AlertaChirimacha", an internet-based surveillance innovation,

to streamline the reporting process and expedite response times. "Alertachirimacha" was received positively and demonstrates the capacity of digital tools to improve the efficiency and reactivity of vector surveillance in environments with constrained resources. Our findings underscore the need for a systems thinking approach to reevaluate and enhance triatomine surveillance and control strategies. Integrating better training, improved resource allocation, and enhanced community participation are essential.

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AEDES AEGYPTI AND OTHER MOSQUITO SPECIES COHABITATING IN THE CHEKWOPUTOI CAVE, UGANDA

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Aedes aegypti is a major mosquito vector of globally significant human pathogens. *Ae. aegypti* can transmit viruses such as dengue (DENVs), Zika, chikungunya, and yellow fever. *Ae. aegypti* exhibits a complex genetic structuring among populations in Africa. Significant knowledge gaps remain pertaining to the sylvatic larval habitats of *Ae. aegypti*. We opportunistically collected mosquito larvae (n=113) from a rock pool at the entrance to Chekwoputoi cave located in the Kween District, Uganda. This cave is is the known roosting site for a large colony of the African sheath-tailed bat, *Colura afra* and is regularly utilized by domestic and other wild mammal species. Mosquitoes were reared to adults at the Uganda Virus Research Institute and morphologically identified. This collection comprised seven species: *Ae. aegypti formosus* (n=5), *Anopheles rhodesiensis*, and five additional *Culex* and *Aedes* species. Species identifications were confirmed using molecular techniques (ND4 and COI) and documented using high resolution photography. These observations represent unique ecological insight into the larval habitat and mixed-species larval community of medically-important mosquito species in Uganda. We hope to utilize this information to understand mosquito vector ecology in this poorly-studied area, and how these vectors cohabitate with each other.

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MULTIDIMENSIONAL EVALUATION OF FACTORS ASSOCIATED WITH TICK INFESTATION AMONG DOGS LIVING IN ECOTONES OF MADRE DE DIOS, PERU

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Tick-borne pathogens circulate among humans, pets, and ectoparasites in Madre de Dios (MdD), Peru, and domestic dogs may act as a major host and reservoir. Identification of the risk factors associated with tick infestation in dogs, especially species involved in the transmission of human pathogens, is critical for a proper estimation of zoonotic transmission risk. We conducted a cross-sectional study in 120 houses in ecotones of MdD, systematically checking 170 dogs from 84 houses for ticks. We evaluated factors potentially associated with tick infestation among dogs: owners' socio-demographic information, housing characteristics (main wall and floor materials, nearby trash accumulation, etc.), dogs' signalment and acaricide use. MapBiomas Amazonia was used to determine the land coverage in a 100 meters-radius buffer around houses. Ticks were morphologically identified, and bivariate mixed effects logistic regressions were used to determine the association between these factors and tick infestation. Forty-one percent of dogs were infested with ticks (*R. sanguineus*: 90%; *A. ovale*: 4.3%, both: 4.3%). Living in houses surrounded with at least some land covered by urban infrastructure and houses close to trash accumulation were associated with higher odds of tick infestation in dogs. In contrast, dogs with owners with outdoor occupations in rural environments, dogs who live in houses surrounded with at least some land covered by a mosaic of uses (agriculture and/or pasture), and dogs who live in houses with floors built mainly with wood had lower odds of tick infestation. Our results suggest that the environmental factors and owners' outdoor habits are driving the odds of tick infestation in dogs, with no significant contribution of dog characteristics. Land coverage may be associated with microenvironmental variables or may be a proxy of other factors, like dog density. Owners who work outdoors in rural areas may be more aware of the risks associated with tick infestation. Our findings characterize the impact of individual- and community-based factors on tick infestations and highlight strategic targets for tick control interventions.

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TRACKING THE SOURCE POPULATION OF *SIMULIUM* BLACKFLY INVASION IN URBAN SETTINGS IN GHANA: A GENOMICS APPROACH

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Simulium blackflies of the *damnosum* species complex exhibit long flight ranges of 20 to 600km when assisted by wind. They are vectors of the parasitic nematode that causes human onchocerciasis (river blindness), characterised by severe skin lesions, irreversible blindness, and epilepsy. Onchocerciasis occurs predominantly in remote rural areas in sub-Saharan Africa, Yemen, and small foci in Brazil and Venezuela. Control is by community-based mass drug administration (MDA) with ivermectin. Extensive small-scale mining in the Eastern Region have led to the pollution of fast-flowing rivers, which serve as natural breeding habitats for the *Simulium* vectors. These blackflies are likely to migrate in search of suitable breeding habitats, posing a potential risk of onchocerciasis transmission in areas previously unaffected by the disease. Reports of blackflies in parts of the capital city, Accra (an onchocerciasis naïve area) in June 2023, where blackflies had not previously been found, warranted prompt investigation of the source of the blackflies invading urban areas to assess risk of onchocerciasis transmission. We collected 270 female adult blackflies by human landing catch (HLC) from 14 communities in Ghana. Whole genome sequences were obtained from genomic DNA extracted from the blackflies. Based on principal components analysis (PCA) of 138,128 SNPs, the blackflies from two communities in the Volta region (Elavayno, n=10; Holuta, n=10) were genetically distinct from those collected from Accra (Paradise Valley, n=10; Teiman Borga Town, n=9) and the Eastern region (Asuoyaa, n=14), and elsewhere in Ghana. A PCA and k-means clustering of these distinct groups showed that the blackflies from Accra exhibited greater genetic similarity to those from the Eastern region. This implies a potential origin in southeastern Ghana. Despite the small sample size, we further identified potential migration of flies northward from the south. Further investigation into the corridors for fly movement and the implications of urban migration on the risk of onchocerciasis transmission is warranted.

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LAND REVERSION AND PALM FEATURES ARE MAJOR DRIVERS INFLUENCING THE OCCURRENCE OF A CHAGAS DISEASE VECTOR IN RURAL AREAS IN PANAMA

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In tropical countries, Royal Palms (*Attalea* spp.) constitute the most important element in the common arrangement defining the ecological niche of kissing bugs of the genus *Rhodnius*. The presence of palm-dwelling kissing bugs near human settlements, coupled with high infection rates with *T. cruzi* serve as indicators of the risk of transmission in rural areas. In this study, we assessed the impact of land use changes and palm characteristics on the occurrence, abundance, and infection status of *Rhodnius pallescens*, the primary vector of Chagas Disease in Panama. We sampled Kissing Bugs from Royal Palms in 12 communities distributed along a landscape gradient, with varying percentages of native forest, grassland, cropland, and early successional forest cover in Central Panama. Genomic DNA was extracted from whole bodies, and real-time PCR (RT-PCR) assays were performed using probes targeting the 28S ribosomal RNA (rRNA) genes of *Trypanosoma* parasites. We used robust design occupancy modeling to evaluate hypotheses for factors that might correlate with the occurrence of *R. pallescens* on Royal Palms, using 10 m resolution land cover data at 100 and 300 buffers, as well as specific palm traits. To account for potential spatial autocorrelation, we ran spatial occupancy model versions of the top-performing models and compared the outputs. We tested infection in populations of *R. pallescens* and found prevalence to be over 70%. We observed that elevation, amount of palm infructescence and successional forest cover have a positive effect on the probabilities of the presence of *R. pallescens* in these areas, whereas the percent of native forest showed a significant negative effect on these probabilities. Our models with quadratic effects outperformed those with linear effects for landscape metrics, indicating that predicted occupancy peaks at optimal amounts of these cover types and palm features. Our findings suggest that, in rural areas of Panama, anthropogenic landscape alterations, mainly forest regeneration, are associated with higher probabilities of palm infestation by Chagas disease vectors and with higher vector population densities.

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INSECT CELL LINES DERIVED FROM OLD AND NEW WORLD VECTORS OF TRYPANOSOMES

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Continuous insect cell lines play important roles in research into biology and control of vectors of human and livestock pathogens. In sub-Saharan Africa, tsetse flies of the genus *Glossina* transmit the salivarian trypanosomes that cause sleeping sickness in humans and nagana in domestic animals, while in Central and South America triatomine bugs of the genera *Triatoma* and *Rhodnius* are major vectors of *Trypanosoma cruzi*, causative agent of Chagas disease in humans. Part of the remit of the Tick Cell Biobank is to generate new cell lines from neglected tropical disease vectors for distribution to the global research community as research tools. We have recently established new cell lines from three trypanosome vectors: *Glossina morsitans morsitans*, *Triatoma infestans* and *Rhodnius prolixus*. The *G. m. morsitans* cell line GMA/LULS61 is derived from tissues of adult female tsetse flies. Three *T. infestans* cell lines, TIE/LULS54, TIE/LULS65 and TIE/LULS69, and three *R. prolixus* cell lines, RPE/LULS53, RPE/LULS57 and RPE/LUCH66, were generated from embryonic tissues. With a view to their possible application in development of vector control strategies, GMA/LULS61, TIE/LULS54 and RPE/LULS53 have been tested for susceptibility to infection with *Wolbachia*. GMA/LULS61 cells supported infection and growth of 6/7 insect-derived *Wolbachia* strains, whereas neither of the triatomine bug cell lines became infected. TIE/LULS54 and RPE/LULS53 cells do not harbour Triatoma virus, and GMA/LULS61 cells do not harbour salivary gland hypertrophy virus, indicating that the cell lines could be used to propagate these previously uncultured viruses proposed as possible biological control tools. All the cell lines described here are available, subject to Material Transfer Agreements, from the Tick Cell Biobank https://www.liverpool.ac.uk/research/facilities/tick-cell-biobank/.

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DETERMINING *TRYPANOSOMA CRUZI* INFECTION PREVALENCE, BLOOD-MEAL PREFERENCE AND MICROBIOME COMPOSITION IN *TRIATOMA RUBIDA, TRIATOMA RECURVA, TRIATOMA PROTRACTA* AND *PARATRIATOMA HIRSUTA* COLLECTED BY *I*-NATURALIST CITIZEN SCIENTISTS IN THE AMERICAN SOUTHWEST

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Triatomine bugs are vectors of *Trypanosoma cruzi,* the etiological agent of Chagas disease. There are 11 species of triatomines reported in the US, with seven reported in the Southwest. Autochthonous *T. cruzi* transmission in the US is rare, owing to the sylvatic nature of triatomine species present and the inefficient mode of transmission. With ever-expanding anthropogenic land-use changes, the overlap between human and triatomine habitat is increasing and it is important to study triatomine bionomics and spatial distributions to update estimates of regional transmission risk. Citizen scientists who documented triatomine species observations on the i-Naturalist website from May-September 2023 were contacted with a request to safely collect, kill, and mail triatomine specimens to UNLV along with information regarding location and date of collection. Triatomine specimens were identified morphologically using standard keys before DNA was extracted from the abdomen of individual bugs and *T. cruzi* infection prevalence assessed using qPCR. A multiplex amplicon-sequencing assay has been designed to simultaneously characterize triatomine genetic diversity (CytB, ITS2), triatomine vector blood meal preferences (vertebrate 12S rRNA, CytB) and microbiome composition (16s rRNA, 18s rRNA). Overall, 449 triatomines were received, with all specimens from California being *T. protracta protracta* (n=17), while *P. hirsuta* (n=35) and *T. protracta* (n=10) were received from Nevada, and *T. rubida* (n=161) and *T. recurva* (n=206) were the predominant species from Arizona. *T. cruzi* infection prevalence by species was *T. recurva*: 94.7%, *T. rubida*: 92.9%, *T. protracta*: 72.2%, and *P. hirsuta*: 71.9%, for an overall infection prevalence of 90.7%. This is believed to be the first reported natural infection of *P. hirsuta* with *T. cruzi.* Amplicon sequencing characterization is ongoing, with results forthcoming. Additionally, entropy-based habitat models are being developed for the Southwest based on the spatial distribution of samples received, to identify putative hot spots of triatomine bug infestation for targeted surveillance efforts.

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RHIPICEPHALUS MICROPLUS SERPINS RMS-3 AND RMS-17 AND *IXODES RICINUS* SERPIN IRIPIN-3 EMPLOY DISTINCT MECHANISMS TO INHIBIT PROLIFERATION OF MOUSE T CELLS

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While feeding on hosts, ticks secrete saliva containing immunosuppressive molecules. These molecules enable ticks to attenuate hosts' immune responses, thereby facilitating the acquisition of a full blood meal. Proteins contained in tick saliva include serpins, which act as inhibitors of serine proteases. Two serpins from the tick *Rhipicephalus microplus* (RmS-3 and RmS-17) and one serpin from the tick *Ixodes ricinus* (Iripin-3) have been demonstrated to inhibit T cell proliferation. However, the mechanisms underlying the anti-proliferative activities of these serpins remain unknown. To elucidate the mechanism of action of the serpins, we treated mouse spleen cells with RmS-3, RmS-17, and Iripin-3. Subsequently, we stimulated T cell proliferation by adding the mitogen concanavalin A (ConA) to the cell cultures. Using flow cytometry, we assessed the expression of the T cell growth factor interleukin-2 (IL-2), the alpha-chain of the receptor for IL-2 (CD25), and the proliferation marker Ki-67 by T cells 24 h after the addition of ConA. Simultaneously, we measured the amount of secreted IL-2 using the ELISA method. Lastly, we employed flow cytometry to analyze the distribution of T cells within the G0/G1, S, and G2/M phases of the cell cycle at 48 h and 72 h after ConA addition. The experiments showed that the treatment with RmS-3 and RmS-17 led to a decrease in IL-2 production and CD25 expression by T cells. Consequently, the expression of Ki-67 was reduced in the presence of both serpins, and the cell cycle was arrested in the G0/G1 phase. In contrast, Iripin-3, while diminishing IL-2 production, did not affect the ability of T cells to express CD25. Initially, the entry of T cells into the cell cycle was hindered by Iripin-3, as indicated by decreased expression of Ki-67. However, cell cycle analysis performed at 48h and 72h time points revealed that T cells were eventually able to resume progression through the S and G2/M phases. Altogether, these results indicate that the *R. microplus* serpins RmS-3 and RmS-17 and the *I. ricinus* serpin Iripin-3 inhibit T cell proliferation through distinct mechanisms.

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EXPLORING THE TRANSCRIPTOME OF IMMATURE STAGES OF *ORNITHODOROS HERMSI*, THE SOFT-TICK VECTOR OF TICK-BORNE RELAPSING FEVER

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Ticks affect host's hemostasis, immunity, and tissue repair processes by injecting saliva into skin. Soft ticks exhibit a rapid-feeding strategy, completing blood meals within minutes, and possess powerful bites, causing discomfort and skin disorders. However, studies on bite effects and the genetic mechanisms underlying their feeding strategy are limited. Here, we focused on *Ornithodoros hermsi*, the vector of the tick-borne relapsing fever in the U.S. Through a combination of histopathological and whole-body transcriptomic analyses, we aimed to gain insights into *O. hermsi* feeding behavior across various feeding (unfed, 6h, 12h, 24h, and 5 days post-feeding) and developmental stages (larvae, 1st-, and 2nd-nymphs). Analysis of mouse-bitten skin showed extensive subcutaneous hemorrhages at the bite site, suggesting the presence of potent proteolytic enzymes and anti-hemostatic agents in tick saliva. By transcriptomics, we identified a diverse array of proteases, e.g., metalloproteases (M12B and M13) and serine-proteases (S01A), suggesting a potential involvement in host tissue degradation. We also identified homologs of anticoagulants described in other soft ticks, including factors Xa, thrombin, and platelet aggregation inhibitors. Clustering revealed distinct transcriptional profiles: unfed, early-fed (6h–24h), and late-fed (5d) across all developmental stages. Modulation in the expression of most annotated protein functional classes displayed a similar pattern: high expression in unfed, followed by a sharp decline in early-fed, then a subsequent increase as digestion progresses, akin to baseline expression at late-fed as seen in unfed groups. While the classical salivary genes (e.g., metalloproteases, lipocalins, proteases, and mucins), exhibited the same pattern, a gene expression switch between unfed and late-fed groups suggests a yet-to-be-elucidated strategy to alter the molecular repertoire for subsequent blood meals. Overall, our findings highlight the intense pre-feeding transcriptional activity of *O. hermsi*, providing valuable insights into its rapid-feeding strategy.

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ECTOPARASITE BURDEN OF SMALL MAMMALS LINKED TO LAND USE AND LAND COVER IN THE SOUTHEASTERN PERUVIAN AMAZON

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Rodents are known reservoirs of zoonotic vector-borne pathogens. Understanding their ecology and infestation patterns is pivotal to accurately assess disease transmission risk. We studied the association between land use/land cover (LU/LC) types, host characteristics and ectoparasite burden in rodents through a cross-sectional study in Madre de Dios (MdD), Peru. Ectoparasites were collected from 207 rodents and taxonomically identified. LU/LC type of the capture location was obtained from MapBiomas Amazonia. Bivariate logistic and negative binomial regression models were used to characterize infestation patterns across ectoparasite groups (mites, fleas, lice, and ticks) and at the genus level. In total, 159 (76.81%) small mammals were infested with ectoparasites: 150 (72.46%) with mites, 15 (7.25%) with ticks, 10 (4.83%) with lice, and 8 (3.86%) with fleas. We found the presence of ticks, lice, and mites to be positively correlated with the presence of vegetation. Forest formation and proximity to water bodies were associated with specific patterns on infestations for various mites (Demodecidae, *Gigantolaelaps* spp., *Androlaelaps* spp., *Mysolaelaps* spp.). Looking at host characteristics, louse abundance was lower in male rodents, and mite abundance was lower in animals with higher body weight for all the species captured. While our results on factors associated with tick abundance are in accordance with published literature, they are conflicting with reports on louse abundance, which might vary according to proximity to dwellings. We confirm the role of the vegetation and water bodies in promoting rodent infestation with various ectoparasites, which serve as a strategic environmental target to reduce the risk of transmission of zoonotic rodent-borne pathogens.

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CHARACTERIZATION OF TICK-BORNE ENCEPHALITIS VIRUS SAMPLES FROM *IXODES* TICKS COLLECTED IN MONGOLIA

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Tick-Borne Encephalitis Virus (TBEV) can cause neurological disease in humans with a range of clinical severity including death, depending on the subtype. Far-Eastern subtype has the highest mortality rates while Siberian is more likely to cause chronic disease. Tick-Borne Encephalitis (TBE) is endemic in Mongolia including both Siberian and Far-Eastern TBEV subtypes and has been detected since the 1980s. *Ixodes persulcatus* is the main vector of TBEV in Mongolia but this flavivirus has also been found in *Dermacentor* species. Understanding the epidemiology and evolutionary dynamics of TBEV is necessary in shaping the public health response to this deadly disease in Mongolia. Thirteen hundred *Ixodes persulcatus* ticks were collected in May 2020 from Eruu, Khuder, and Mandal in Selenge using the dragging and flagging method. Tick samples were homogenized, pooled (pool sizes ranged from 20-50), and then the supernatant was inoculated into Vero cells. Upon observing cytopathic effect (CPE), two reverse transcription polymerase chain reactions (RT-PCRs) were conducted on cell supernatant; one was to detect TBEV and the second was to subtype TBEV. Lysed cell culture supernatant was processed with Next-Generation Sequencing (NGS) using Illumina technology to obtain FASTA files for analysis. TBEV was detected from these samples and identified as the Siberian subtype using PCR. Ongoing phylogenetic analysis of NGS results will analyze genomic changes of TBEV to previously published TBEV sequences in the region. Subtype analysis of TBEV and tracking the viral evolution in ticks, specifically *Ixodes persulcatus* in Selenge, is vital to understanding the risk to the local populations. Current vaccines have been developed based on the European and Far-Eastern strains and genomic analysis of wildtype TBEV can inform vaccine strategies. Given the high concentration of this tick species and previous documentation of TBE infection in humans and ticks in this province, further characterization of TBEV in Mongolia is needed.

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GENOMIC INSIGHTS INTO THE *SPIROPLASMA SYMBIONT* OF *GLOSSINA FUSCIPES FUSCIPES*: IMPLICATIONS FOR TRYPANOSOME TRANSMISSION CONTROL

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Tsetse flies (*Glossina* spp.) are primary vectors of parasitic trypanosomes responsible for human and animal African trypanosomiasis in sub-Saharan Africa. In addition to trypanosomes, tsetse flies harbor both obligate and facultative symbionts, which play crucial roles in host physiology and vector competence. *Spiroplasma*, a bacterium found in the tsetse fly species *Glossina fuscipes fuscipes* (*Gff*), has emerged as a potential candidate for reducing trypanosome transmission in its tsetse host. Previous research demonstrates a negative correlation between *Spiroplasma* presence and trypanosome infection in *Gff* flies and has shown *Spiroplasma* to be an apt manipulator of *Gff* physiology. However, the mechanisms behind the putative *Spiroplasma*-induced trypanosome resistance remain unknown. Here, to better understand the *Spiroplasma* strain that infects *Gff* flies, we conducted comparative genomics of *Spiroplasma* collected from the colony located at the FAO/IAEA Insect Pest Control Laboratory (IPCL) in Seibersdorf Austria and from a population located at Toloyang village in Northwestern Uganda. Leveraging Oxford Nanopore (ONT) sequencing technology, we generated closed *Spiroplasma* genomes from individual *Gff* flies. Both the colony and field assemblies had a high degree of similarity in gene content and structure, suggesting they belong to the same strain, denoted as *s*Gff. Phylogenomic analyses placed *s*Gff within the *Spiroplasma poulsonii* clade, which is a clade predominantly comprised of other Dipteran-infecting strains. Within the *s*Gff genome, we found genes involved in nutrient transport showing that *s*Gff relies on its host for many essential metabolites. We also identified numerous mobile genetic elements and putative defensive genes, including prophages, plasmids, and toxin genes, that could be responsible for the *s*Gff-induced resistance to trypanosomes. This study enhances our understanding of the *s*Gff strain and its potential role in modulating trypanosome transmission in its *Gff* host and highlights the efficacy of ONT sequencing to rapidly unravel the biology of symbionts.

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MICROBIAL DIVERSITY OF *CULICOIDES REEVESI* FROM CHIHUAHUA, MEXICO: A METAGENOMIC ANALYSIS OF RRNA 16S

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This study aimed to investigate the microbial diversity of bacteria in the composite microbial community associated with *Culicoides reevesi* biting midges from Buenaventura municipality in the state of Chihuahua, Mexico, using a Sanger sequencing 16s rRNA metagenomics approach. Adult females of *Culicoides reevesi* were collected by human landing catches in the rainy season of 2023 and morphologically identified. They were grouped into pools of 25 individuals from which genomic DNA (gDNA) was extracted. Sanger sequencing of 16S rRNA was performed for a total of 4 pools, and the amplicon sequencing of the V3-V4 hypervariable region was done on Illumina Mseq platform to detect bacterial communities. The bioinformatic analysis included quality assessment, taxonomic classification, and visualization. The evaluation of the microbial community involved assessing taxa abundance and diversity using Mothur and QIIME2 software included in Galaxy Tool Shed (https://usegalaxy.eu/). Our study presents, for the first time in México and worldwide, an in-depth analysis of the bacteriome composition in *C. reevesi*, utilizing a 16S rRNA metagenomic approach. We emphasize the prevalence of dominant bacterial phyla, particularly Proteobacteria, alongside varying abundances of Actinobacteria, Firmicutes, Acidobacteria, and Bacteroidota, with a notable occurrence of Tenericutes. We identified intriguing species of both human and animal pathogenic bacteria. Moreover, we observed the absence of unidentified bacterial sequences, alongside the presence of other bacterial groups associated with the environment or plants. This has implications for both healthcare and ecological management, potentially simplifying control measures but also posing risks if the dominant species are harmful. This research enhances our understanding of the microbiome associated with *Culicoides* species, such as *Culicoides reevesi*, underscoring the need for further investigation to fully grasp their ecological importance and impact on public health.

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ASSESSING FINE-SCALE ENVIRONMENTAL INFLUENCE ON COMMUNITIES OF CUTANEOUS LEISHMANIASIS VECTORS IN SOUTHERN IN PERU

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The departments of Madre de Dios and Cusco have the highest incidence of cutaneous leishmaniasis (CL) in Peru, accounting for about 30% of cases annually. Despite the significant public health impact of CL in this region, knowledge on sand fly ecology and distribution is still lacking. To better understand the transmission risks, it is crucial to examine the fine-scale environmental factors that favor the abundance of the potential vectors of CL. Therefore, our goal was to use a novel light trap to investigate the structure of sand fly communities across habitats with differing levels of anthropogenic impact at Manu Biological Station, located within the Manu Biosphere Reserve in Southern Peru. We hypothesized that the proportion of potential vector species would be greater in habitats with less canopy cover and associated with human activity. The low-cost light trap (Katchy UV light trap) was validated by comparing the abundance and species richness of phlebotomine sand flies to collections with standard CDC light traps using a Latin square design. The Katchy trap was then used to sample five habitat classes: secondary forest, bamboo dominated forest, riparian forest, abandoned fruit crops and peridomicile. For each trapping location, temperature, relative humidity, foliage cover and basal area were recorded. A total of 1184 sand flies were collected during the trap comparison and our results suggest that the Katchy light trap offers a viable low-cost alternative for phlebotomine sand fly sampling. Across the five habitat types, a total of 3047 sand flies belonging to 31 species were collected. *Nyssomyia shawi* was the most abundant species across all sites, representing 36.9% of all sand flies collected. Preliminary results indicate variation in community composition and abundances across different habitat types. Quantifying the influence of fine-scale environmental factors on phlebotomine sand fly communities across anthropogenically impacted habitats can provide insights relevant to understanding potential transmission risks and improve prevention and management of CL in Peru's endemic sylvatic regions.

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FIRST REPORT OF NATURAL INFECTION OF *ANOPHELES GAMBIAE S.S.* AND *ANOPHELES COLUZZII* BY WOLBACHIA AND MICROSPORIDIA IN BENIN: A CROSS-SECTIONAL STUDY

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Recently, bacterial endosymbiont, including *Wolbachia* and Microsporidia were found to limit the infection of *Anopheles* mosquitoes with *Plasmodium falciparum*. This study aimed to investigate the natural presence of key transmission-blocking endosymbionts in *Anopheles gambiae* and *Anopheles coluzzii* in Southern Benin. The present study was conducted in seven communes of Southern Benin. Anopheles were collected using indoor/outdoor Human Landing Catches (HLCs) and Pyrethrum Spray Catches (PSCs). Following morphological identification, PCR was used to identify *An. gambiae* sensu lato (*s.l.*) to species level and to screen for the presence of both *Wolbachia* and Microsporidia. *Plasmodium falciparum* sporozoite infection was also assessed using ELISA. Results: Overall, species composition in *An. gambiae s.l.* was 53.7% *An. coluzzii*, while the remainder was *An. gambiae* sensu stricto (*s.s.*). Combined data of the two sampling techniques revealed a mean infection prevalence with *Wolbachia* of 5.1% (95% CI 0.90–18.6) and 1.3% (95% CI 0.07–7.8) in *An. gambiae s.s.* and *An. coluzzii*, respectively. The mean infection prevalence with Microsporidia was 41.0% (95% CI 25.9–57.8) for *An. gambiae s.s.* and 57.0% (95% CI 45.4–67.9) for *An. coluzzii*. *Wolbachia* was only observed in Ifangni, Pobè, and Cotonou, while Microsporidia was detected in all study communes. Aggregated data for HLCs and PSCs showed a sporozoite rate (SR) of 0.80% (95% CI 0.09–2.87) and 0.69% (95% CI 0.09–2.87) for *An. gambiae* and *An. coluzzii*, respectively, with a mean of 0.74% (95% CI 0.20–1.90). Of the four individual mosquitoes which harbored *P. falciparum*, none were also infected with *Wolbachia* and one contained Microsporidia. This study is the first report of natural infections of field-collected *An. gambiae s.l.* populations from Benin with *Wolbachia* and Microsporidia. Sustained efforts should be made to widen the spectrum of bacteria identified in mosquitoes, with the potential to develop endosymbiont-based control tools; such interventions could be the game-changer in the control of malaria and arboviral disease transmission

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INTRA-POPULATION DIFFERENCES IN CTMAX AND EGG SURVIVAL IN USA POPULATIONS OF THE TIGER MOSQUITO, *AEDES ALBOPICTUS*: IMPLICATIONS FOR CLIMATE ADAPTATION?

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In recent decades, we seen increases in the number of reported cases of vector-borne disease as well as vector range expansions in the USA. These increases have, in part, been attributed to climate change. Extreme weather events, such as heat waves and droughts, are also becoming more common and have the potential to negatively impact vectors if temperatures regularly go above, or humidity goes below, the thresholds to which ectothermic vectors can withstand. Very little is known about what these thresholds are for different vector species, and less is known about population differences within species. To address these gaps in knowledge, we established eight populations of the tiger mosquito, *Aedes albopictus,* from urban locations across its range in the eastern United States spanning four climate zones. Using a series of common garden experiments, we experimentally determined CTmax for adults and larvae, and survival rates of eggs exposed to different temperatures and relative humidities. We found significant population differences in CTmax for both adult males and females that were not correlated with latitude or longitude. Larvae had, on average, significantly higher CTmax (mean 44.8C) than adults (37.7C) and population differences were less pronounced for larvae. We interpret these results as larvae living below their thermal maximum and being less locally adapted than adults. We also found significant differences by population in egg survival but only when eggs were exposed to a higher temperature and lower humidity treatment (31C and 65% RH). Interestingly, the adult populations with the highest CTmax were not the same populations with the highest egg survival indicating that different selection pressures may be acting on the different life stages potentially because adults are mobile and eggs are sessile. These results present evidence of genetic based differences in heat tolerance at broad spatial scales for an important species with a near global distribution. As genetic variation is critical for thermal adaptation, this work implies that *Ae. albopictus* may be able to adapt to higher temperatures than they currently experience.

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PYRUVATE KINASE AND SIRTUIN 2 PROTEIN INTERACTION TIGHTLY REGULATES CARBON AND NITROGEN METABOLISM IN *AEDES AEGYPTI* MOSQUITOES

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Aedes aegypti females are vectors of pathogens that cause serious human diseases. The implementation of better mosquito mitigation strategies requires a better understanding of mosquito metabolism. Previously, the application of positional 13C-stable isotope tracer analysis allowed us to provide evidence that *Ae. aegypti* mosquitoes use the carbon skeleton of glucose for ammonia detoxification and uric acid synthesis *via* multiple metabolic pathways, including glycolysis. Later, the kinetic characterization of the recombinant pyruvate kinase 1 from *Ae. aegypti* (AaPK1), the enzyme that catalyzes the last step of the glycolytic pathway, showed that AaPK1 is allosterically regulated by specific amino acids and phosphorylated sugars. Mass spectrometry-based target metabolomics, stable-label isotope tracing coupled with reverse genetics provided evidence that AaPK regulates both carbon and nitrogen metabolism. Recently, we discovered that AaPK is a lysine-acetylated protein post-translationally regulated by sirtuin 2 (AaSirt2), an NAD^+-dependent deacetylase that catalyzes the removal of acetyl groups from acetylated lysine residues. Western blotting of immunoprecipitated proteins showed that AaPK binds with AaSirt2 in the cytosolic fractions of tissues dissected from non-starved and starved females. In addition, knockdown of AaSirt2 by RNA interference significantly decreased AaPK protein abundance in fat body of starved females indicating that both AaPK and AaSirt2 tightly modulate how mosquitoes respond to starvation. We also found that AaSirt2 localized in both cytosolic and mitochondrial cellular compartments of mosquito tissues. To identify potential additional targets of AaSirt2, we took a proteomics-based approach to analyze immunoprecipitated lysine-acetylated proteins from cytosolic and mitochondrial fractions isolated from non-starved and starved mosquitoes. Our acetylomics data indicate that AaPK and other lysine-acetylated proteins significantly change their relative abundance in females deprived of sugar to cope with starvation.

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EXPLORING THE IMPLICATIONS OF TRAIT VARIATION AND LIFE HISTORY TRADE-OFFS FOR VECTOR-BORNE DISEASE TRANSMISSION

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Vector-borne diseases pose significant challenges to public health worldwide and our current understanding of mosquito-borne disease transmission relies heavily on mechanistic mathematical models that can vary in complexity. One limitation to these models is a lack of incorporation of trait variation associated with dynamic environments more characteristic of field conditions. Additionally, it is assumed that these traits are often varying independently of each other. Yet, life history theory and evidence from a diversity of vertebrate and invertebrate systems suggest organisms experience life history trade-offs resulting in negative correlations across life history traits. To interrogate these assumptions, we explored the integration of life history theory into transmission models to investigate how accounting for life history trade-offs affects our understanding of vector-borne disease transmission. We utilized the basic reproductive number of a mosquito-borne pathogen (R_0) as a simple heuristic model to examine the effects of life history trade-offs that have been well established in other systems, specifically trade-offs between mosquito current reproduction (e.g., lifetime egg production) and immune defense (e.g., with consequences for vector competence and the extrinsic incubation period) as well as current reproduction and future survival. We found that incorporating correlations across traits, such as reproduction and immunity, leads to a substantial change in vectorial capacity and subsequently the predicted relative R_0 compared to a model that does not account for these trait correlations. This study underscores the importance of considering ecological and evolutionary factors in disease transmission dynamics and highlights the potential of integrating life history theory into epidemiological research for more robust disease control strategies.

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EXPLORING HOW LARVAL DIET AND REARING WATER INFLUENCE *AEDES AEGYPTI* FITNESS, MICROBIOTA AND VECTOR COMPETENCE

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Mosquito rearing optimization in laboratory conditions is crucial for both vector research and control. Although the addition of nutriments is important for *Aedes aegypti* development from immature stages to adult mosquitoes, little is known about the nutriment composition of commercial diets used for mosquito rearing and their influence on *Ae. aegypti* life traits and ability to transmit pathogens. Here, we evaluated the influence of diets commonly used in laboratory rearing on *Ae. aegypti* fitness, lifespan, microbiota and vector competence. First, we characterized the effect of four diets and two different rearing waters (laboratory *versus* field-collected waters) on *Ae. aegypti* development, lifespan and microbiota. Our investigations demonstrated that nutriment composition (protein, lipid, carbohydrate) of the diets tested influenced *Ae. aegypti* development (time to pupation and emergence), size and survival. Metagenomic analysis revealed specific modulations of adult microbiota composition according to both diet and rearing water. Indeed, in laboratory water, if new emerged females demonstrated a high proportion of *Chryseobacterium* after independent rearing with three different diets, mosquitoes reared with yeast contained a more diverse microbiota composition. For field collected water, the diversity of the microbiota composition was high for three diets. However, for TetraMin condition, female microbiota was mainly composed by *Shingobacterium*. Then, we investigated the influence of the larval diet on *Ae. aegypti* vector competence for dengue virus (DENV). Our results highlight differences on vector infection and virus dissemination according to the diet used. Mosquitoes reared at larval stage with diets containing a higher concentration of protein seemed to be more susceptible to DENV infection and dissemination. Taken together, these results emphasize the importance of the standardization of arbovirus transmission estimation protocols to be as close as possible to field conditions and obtain accurate transmission risk estimations.

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HARNESSING MOSQUITO SYMBIONTS FOR MALARIA TRANSMISSION BLOCKING

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A possible malaria control approach involves the dissemination in mosquitoes of inherited symbiotic microbes to block *Plasmodium* transmission. However, in the *Anopheles gambiae* complex, the primary African vectors of malaria, there are limited reports of inherited symbionts that impair transmission. We have established the SYMBIOVECTOR project to investigate the prospect of deploying a recently discovered Anopheles symbiont, *Microsporidia MB*, as a *Plasmodium* transmission blocking tool. The ability of *Microsporidia MB* to block *Plasmodium* transmission together with vertical transmission and avirulence makes it an excellent candidate for symbiont-based transmission blocking. We show that a vertically transmitted microsporidian symbiont (*Microsporidia MB*) in the *An. gambiae* complex can impair *Plasmodium* transmission. *Microsporidia MB* is present at moderate prevalence in geographically dispersed populations of *An. arabiensis* in Kenya, localized to the mosquito midgut and ovaries, and is

not associated with significant reductions in adult host fecundity or survival. We investigated the mechanistic basis and efficiencies of *Microsporidia MB* transmission between *Anopheles arabiensis* mosquitoes. We show that *Microsporidia* can be transmitted both vertically (mother to offspring) and sexually between adult mosquitoes. The dynamics of spread and optimal dissemination strategies have been investigated under semi-field conditions and used to determine the likely outcomes of releasing *Microsporidia MB* in the field.

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CULEX MODESTUS CAN TRANSMIT USUTU VIRUS AND CAN BE COLONIZED IN A LAB SETTING

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Usutu virus is an emerging pathogen transmitted primarily by *Culex* mosquitoes. Recent preliminary data suggested that *Culex modestus* from Belgium may be strong Usutu virus vectors, potentially more efficient than the primary vector *Culex pipiens*. Yet, *Culex modestus* is a poorly understood species, despite their potential role in pathogen transmission and widespread establishment across Europe, Asia, and Northern Africa. Here we captured *Culex modestus* from Belgium to investigate their vector competence for Usutu virus and to establish a lab colony. Larvae and pupae were collected from a reedbed pond and brought to the lab to rear to adulthood. Adult *Culex modestus* were placed in cages and allowed to mate, lay autogenous egg rafts, and produce new generations. Testing different rearing conditions revealed that this species has specific requirements for larval diet, breeding water, and blood-feeding hosts. For example, despite readily feeding on chicken and rabbit blood, only females that fed on live mice effectively produced offspring. Through the establishment of the colony we experimentally designed a rearing protocol and gained insights into novel aspects of their biology, including their mating in confined spaces, small body size, and active and aggressive behavior. Meanwhile, female *Culex modestus* from the third generation were experimentally infected with a Belgian strain of Usutu virus via a blood meal. After 14 days of incubation at 25°C, the Usutu virus transmission capacity was evaluated by measuring infectious titers in a plaque assay and RNA copies by qRT-PCR. Most *Culex modestus* had an Usutu virus infection in their abdomen and heads (61%; n=17/28) with relatively high median titers (5560 PFU/abdomen and 778 PFU/heads). We observed a transmission efficiency of 54% (n=15/28) based on the presence of infectious Usutu virus in the mosquito saliva. This research offers compelling evidence that Belgian *Culex modestus* are potent vectors for Usutu virus, highlighting their potential role in Usutu virus circulation. In addition, we hope this study aids future researchers who wish to establish lab colonies of these mosquitoes.

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TIME TO LOSS OF PHYSICAL INTEGRITYOF ATTRACTIVE TARGETED SUGAR BAIT STATIONS IN WESTERN PROVINCE, ZAMBIA: A SURVIVAL ANALYSIS

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The Westham Attractive Targeted Sugar Bait (ATSB) stations are a potential addition to the integrated vector management strategy against malaria. Each station, measuring approximately the size of A4 paper, consists of 16 cells filled with a bait sugar paste and ingestion toxin (dinotefuran), contained between a white plastic backing and a black perforated membrane to allow mosquito feeding. This study measured the length of time ATSB stations maintained physical integrity when hung on external walls of residential structures in a field setting in Western Province, Zambia as part of a Phase III cluster-randomized trial of ATSB efficacy. Loss of physical integrity was defined according to pre-defined criteria for bait station replacement due to damages which included tears, mold, leakage, and depletion of bait. A total of 5696 visits were made to 1107 ATSB stations, that were placed on 304 eligible structures to assess for their physical presence and condition using pre-defined criteria. Kaplan-Meier curves and Cox-Proportion Hazard models were used to assess survival probabilities, including risk factors associated for increased physical deterioration. The overall median ATSB station survival time was 149 days, or equivalent to 5 months. It was evident that the most documented damage on bait stations were holes/tears, and mold. Longevity of ATSB station survival was extended on those that were hung on structures that had “excellent protection” (Hazard Ratio 0.36, 95% CI {0.25-0.49}, p<0.001) compared to bait stations that had “no protection”. Thatched roof also extended ATSB station survival, and resulted in median survival time of 218 days (HR 0.37, 95% CI {0.26, 0.47}, p<0.001), or equivalent to 7 months, when compared to roofing made of iron sheets. Results suggest that ATSB stations may remain intact over the malaria transmission season in this setting in rural Zambia, and that longevity increases when housing characteristics provide sufficient protection from the weather, such as when placed under wide thatch roofs. Further research is needed to understand the relationship between physical damage of the bait station and efficacy.

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IDENTIFICATION OF NOVEL *WOLBACHIA* INFECTIONS IN FLORIDA MOSQUITOES

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Mosquito-transmitted diseases, such as malaria, dengue fever, and mosquito-borne encephalitis, cause thousands of deaths annually. Scientists have been developing novel approaches to reduce the incidence of these diseases and several rely on artificial transinfections with *Wolbachia*, an endosymbiotic bacterium. *Wolbachia* can spread rapidly through mosquito populations and block infection and transmission of important pathogens like dengue virus. Critically, it is unclear which mosquito species harbor native *Wolbachia* infection and how the prevalence of such infections varies across mosquito populations. This is important because laboratory studies show that native *Wolbachia* can have variable impacts on pathogen infection. For instance, some native *Wolbachia* infections decrease mosquito susceptibility to arbovirus and reduce the rate of transmission, while others have no effects. To better understand mosquito-*Wolbachia*-pathogen dynamics in nature, it is first necessary to establish which mosquitoes naturally harbor *Wolbachia*. Florida is a prominent site for arboviral disease in the United States. It is also home to approximately 90 different mosquito species. We have collected and screened approximately 35 of those species for the presence of *Wolbachia*, sampling from conservation land in eastern central Florida. This list includes mosquito species that are implicated in pathogen transmission as well as highly abundant nuisance biters. We used a custom qPCR assay to assess *Wolbachia* infection frequencies and titers and Sanger sequencing to assess *Wolbachia* diversity. Our results will facilitate the examination of the role of native *Wolbachia* in pathogen transmission for those species.

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VERTICAL AND HORIZONTAL TRANSMISSION OF *MICROSPORIDIA MB* IN *ANOPHELES ARABIENSIS* OCCURS THROUGH GERMLINE INFECTIONS

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Microsporidia MB is a promising candidate for developing a symbiont-based strategy for malaria control because it disrupts *An. arabiensis*' ability to transmit the *Plasmodium* parasite. The symbiont is predominantly localized in the host's reproductive organs as it is vertically transmitted from mother to offspring and horizontally (sexually) transmitted during mating. Due to efficient transmission by both routes, *Microsporidia MB* has the potential to invade and spread in target vector populations to establish high prevalence rates. The stability and efficiency of *Microsporidia MB* transmission in *An. arabiensis* is important for its sustainable use for malaria control. In this study, we investigated the mechanistic basis of vertical and horizontal transmission of *Microsporidia MB* in *An. arabiensis* by establishing the localization patterns of this symbiont in the reproductive organs. We found that the germline stem cell niche, the primary and secondary follicles of newly emerged female *An. arabiensis* mosquitoes were infected with different stages of *Microsporidia MB* in high intensities. These infections were consistent across the pre and vitellogenic stages of egg development. Furthermore, *Microsporidia MB* replicated and increased intensities in the oocyte of developing eggs when mosquitoes were given a blood meal. Additionally, we investigated the *Microsporidia MB* infection rates of developing eggs and adult F1 offspring of infected female mothers. The adult-to-adult vertical transmission rate of *Microsporidia MB* was lower than the primary follicle infection rate indicating a significant impact of symbiont clearing during mosquito development. In males, *Microsporidia MB* also was localized in the stem cell niche. The symbiont replicated in infected cells and formed cyst-like structures within the testis and migrated into the ejaculatory duct with the sperms for transfer to females during mating. The ability of *Microsporidia MB* to consistently maintain infections in the germline stem cell niche and developing eggs in *An. arabiensis* provide evidence of an intimate association of this symbiont and its mosquito host.

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ZOONOTIC AND HUMAN MALARIA TRANSMISSION BY VECTOR SPECIES AND LANDSCAPES IN INDONESIA

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Zoonotic malaria infections in humans, particularly *Plasmodium knowlesi*, are increasing across Southeast Asia, notably in rural areas of Malaysia and Indonesia, and have been associated with changes in land use patterns. Nine species of the *Anopheles leucosphyrus* and *Anopheles dirus* species complexes are vectors of zoonotic malarias to humans in Southeast Asia but, little is known about their bionomics. The bionomics of zoonotic (*An leucosphyrus* group) and malaria (*An maculatus* group) vectors were studied in three land-use types: an oil palm plantation, a residential area, and a mixed-crop agriculture area in northern Sumatra, Indonesia. All night human landing collections characterised vector distributions, abundance (biting rates), endophily, seasonality and sporozoite rates and behaviours. Larval surveys characterised the anopheline immature habitats. The members of the *An leucosphyrus* group mosquitoes collected in Sumatra belonged to the *An dirus* complex. Distributions of anophelines varied significantly by land use within a limited geographic area with larvae of both *An dirus* and *An maculatus* complex species being found in both natural and man-made habitats. Biting rates of the *An dirus* complex was highest in a mixed-crop agriculture area while *An maculatus* group biting rates were highest in the oil palm plantation. Albeit significantly less in the village, *Ans dirus* complex biting rates in the village were greater than *An. maculatus.* The *An dirus* complex bit throughout the night and was highly exophagic in Sumatra. PCR analyses detected *Plasmodium vivax, P. inui, P. fieldi* and *P. coatneyi* in areas where *P. knowlesi* infections in humans were detected. Indoor interventions such as insecticide treated nets and indoor residual spraying are likely not as effective against the *An dirus* complex species in northern Sumatra given their exophagic habit and their lesser abundance in residential areas. The risk of both being bitten by *An dirus* complex mosquitoes and transmission of zoonotic malarias to humans will depend on human movement patterns among the different landscapes present in Sumatra.

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ADVANCING MOSQUITO SURVEILLANCE USING MALDI-TOF-MS

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Vector surveillance is pillar of malaria control however it is hindered by the cost and time needed to process the numerous mosquitoes collected during surveys. Current methods require multiple laboratory assays to gather species, bloodmeal source, and infection data. This project investigates a single spectroscopic approach using MALDI-TOF MS (matrix-assisted laser desorption/ionization time-of-flight) reducing costs and processing time, maximizing information from entomological collections. Sampling of malaria vectors was done in different sites across Mozambique and Kenya using CDC light traps. The collected samples were morphologically identified to species, preserved in silica gel, and transported to the lab for further analysis. The cephalothorax mosquitoes of were aseptically dissected into two halves - one half for gold standard molecular assays and the other half for MALDI-TOF MS spectra acquisition. The malaria vectors were processed using PCR and bidirectional Sanger sequencing for species. A subset (a minimum of 10 per species) of the samples with quality spectra were selected were for unsupervised clustering using dendrograms and database build-up and the rest for validation. MALDI-TOF MS was able to identify primary and secondary malaria vectors including members of the An. gambiae s.s, An. arabiensis, An. merus, An. quadriannulatus, An. funestus s.s, An. rivulorum, An. leesoni, An. parensis, An. rivulorum, An. coustani, An. cf. coustani, An. cf. rivulorum, An. rufipes and An. pretoriensis. Additional species are continuously being added to the database. The development of a comprehensive database is anticipated, providing valuable insights into lesser-known vectors, and potentially aiding our understanding of the role of different primary and secondary vector species in transmission leading to improved surveillance and control. The ease of performance, the rapid turn-around time to results, and the minimal cost per sample make it a novel methodology that could bring about a paradigm shift in routine entomological surveillance.

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FACTORS AND EXTENT OF DISCORDANCE BETWEEN HOUSEHOLD DECLARATIONS OF INSECTICIDE TREATED BED NET USE AND CONFIRMATORY DIRECT OBSERVATIONS OF NETS HANGING ON OR LYING NEAR THE BED

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Five triennial mass distribution campaigns and annual ancillary continuous distribution of insecticide treated-bed nets (ITNs) occurred in Benin from 2011 to 2023 with malaria incidence (cases/1000 population) ranging between about 294 in 2011 to 270 in 2022 (peak: 340 in 2016); previous studies report ITN use rates after net distribution based on household-declaration of net use, but there is uncertainty on the reliability of these self-reports. This study compares household declaration of ITN use with confirmatory direct ITN observation in houses to determine the factors and the extent of discordance between declared and observed use rates. The study took place 4-months after the 2023 ITN distribution campaign. To capture the variation in cultural and socio-economic characteristics of the country, in this study, 1567 households were visited in 24 randomly selected villages along a south-north Benin transect. ITN use rates were calculated by 1) obtaining a declaration of having slept under a net last night by the head of the household and 2) confirmatory direct observations of nets in the household. Any net found hanging on a bed was considered in use; nets not hanging but found over the bed or laid on or near the bed were also considered in use when the heads of households confirmed it. Survey data was recorded using the Open Data Kit (ODK) software loaded on tablets. Most ITNs directly observed were campaign nets 77% (3,223/4,210) and for campaign nets and other nets found in households, the coverage rate was 46% [44% - 48%] (1 ITN for every 2 people). Of 1567 households visited, 1492 (95%) declared sleeping under a net the night before; however, only 82% (3434/4210) of all nets, and 82% (2653/3223) of the 2023 campaign nets were observed hanging over the bed or lying on or near the bed where use was confirmed by the heads of the households. One of the reasons for the absence of hanging nets is the lack of space; some rooms serve as a place for sleeping and resting. While the declared ITN use rate seemed high (~95%), confirmatory direct observation suggested rates may be lower.

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COMPREHENSIVE ASSESSMENT OF SOCIODEMOGRAPHIC PROFILE, MALARIA EPIDEMIOLOGY AND VECTOR BIONOMICS IN NORTHEASTERN TANZANIA: A PRE-INTERVENTION BASELINE SURVEY FOR A PROSPECTIVE CLUSTER RANDOMIZED CONTROLLED TRIAL ASSESSING THE EFFICACY OF A NOVEL 3D-WINDOW DOUBLE SCREENS (3D-WDS) FOR SUSTAINABLE MALARIA VECTOR CONTROL

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The emergence of insecticide-resistant malaria vectors has necessitated the development of alternative methods that are non-reliant on these chemicals. In response, a novel window screen, the 3D-Screen, has been developed in Finland. Prior to implementing a cluster-randomized controlled trial (cRCT) to assess its efficacy in reducing malaria at the community level, a cross-sectional survey was conducted to establish the sociodemographic profile, malaria prevalence, and vector bionomics in 20 villages across the Muheza district in northeastern Tanzania. Blood samples were collected from 778 children aged 6 months to 14 years to detect *Plasmodium* parasite using malaria RDTs and to measure hemoglobin concentration for anemia. Adult mosquitoes were captured indoors using CDC light traps followed by morphological identification and molecular analyses to establish sibling species, *Plasmodium* infection, and blood meal sources. Insecticide resistance to common pyrethroids was evaluated using WHO cylinder test, recording knockdown time and mortality rate, followed by the genotyping of L1014F kdrE mutation using TaqMan assay. A total of 1203 households (HH) from 20 villages were enumerated during the study. The average LLINs per HH was 1.7 with universal coverage in 54.53% HH. The average malaria prevalence in the study area was 40.23%. *An. gambiae* and *An. funestus* were the two major malaria vectors at an overall proportion of 29.78% and 70.21%, respectively. The average bites per person per night were 5.219, and the overall *Plasmodium* infection rate in *Anopheles* was 2.15%. High levels of resistance to pyrethroids were observed with mortality of 56.50% and 52.77% against permethrin and deltamethrin, respectively, and the average occurrence of kdrE resistant and susceptible alleles in *An. gambiae* s.s. across the study area was 0.49 and 0.41, respectively. The study reported high prevalence of malaria and widespread resistance to common pyrethroids, underscoring the necessity for a non-insecticidal approach in the study area. These findings also guided the selection of study clusters for the cRCT of the 3D-WDS conducted from 2019 and 2021.

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THERMAL ADAPTATION IN *AEDES ALBOPICTUS*

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Ectotherms depend on environmental temperature to support their physiology and use several physiological (e.g., synthesis of heat shock proteins) and behavioral (e.g., shift in microhabitat selection) strategies to avoid the risk of thermal stress when exposed to rapid changes in temperature. Long-term exposure to a thermal challenge can have profound and lasting physiological changes. In *Drosophila* these changes include both plastic responses and genetic adaptations. How arboviral vectors respond to a long-term thermal challenge like that imposed by global warming is still not fully understood. To address this knowledge gap, we used an experimental evolution approach on *Aedes albopictus*, the primary vector of arboviruses in temperate areas of the world. We have been rearing mosquitoes through 13 generations under tropical (32°C for 14 h and 26°C for 10 h) and control (28°C for 14 h and 26°C for 10 h) conditions. We compared mosquito fitness at G_1, G_5 and G_{10} with respect to G_0 and observed significant fitness differences between G_0 and G_1 mosquitoes, indicating acclimation, as well as among G_0 and $G_{5\text{-}10}$, suggesting adaptation. Importantly, we observed 14.93% mortality one day after emergence in G_1 females, which reached 31.21% in G_5 and 27.54% in G_{10} for the mosquitoes under tropical conditions. This result suggests that this condition represents a strong selective force. We further took a batch of G_{13} eggs and reared them under control condition (28°C). We observed that the fitness of these mosquitoes is different from the fitness of mosquitoes at G_0, $G_{1\text{-}5\text{-}10}$. Overall, these result support thermal adaptation includes more than plasticity in *Ae. albopictus*.

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THE EFFECT OF VARIATION IN MICROCLIMATE AND LAND USE ON THE DISTRIBUTION OF THE *AEDES ALBOPICTUS* AT THE INVASION EDGE

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In recent decades, there has been a significant rise in vector-borne disease incidence, posing a significant public health threat. The increase in vector-borne disease risk can partially be attributed to the increased distribution of several vector species. Furthermore, with invasion often occurring in environments with high densities of susceptible people (many urban centers), another principal concern is being able to use vector distribution information to identify populations most at risk. Mosquito surveillance data is often lacking for recently invading species, so it is important to understand the extent at which surveillance data can be extrapolated into new, often heterogenous, landscapes to predict species distribution. In this study, we use long-term (2004 to 2023) mosquito surveillance data collected in Suffolk County, Long Island, NY, to explore the environmental drivers of spatial variation in *Aedes albopictus* populations, a recently arrived invasive species, across a heterogenous landscape using a variety of Species Distribution Modeling methods. We use cross-validation and field collections to validate model results and to compare accuracy between methods. Additionally, we sample outside the Suffolk County to evaluate each model's ability to spatially extrapolate mosquito distributions. Finally, we combine predicted species distributions with human census data to identify populations of people most likely to experience greater mosquito population burdens. We specifically explore correlation of income status and access to medical care with predicted mosquito distributions. Ultimately, this study will help improve the deployment of targeted vector control efforts for invasive vector species in new environments.

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PREDICTION MODELING OF THE GEOGRAPHICAL DISTRIBUTION OF *AEDES ALBOPICTUS* IN TUNISIA

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The Asian tiger mosquito, *Aedes (Stegomyia) albopictus* (Skuse), was first reported in Tunisia in 2018, at an archeological site, located in the northern part of the country. The Tunisian strain of *A. albopictus* has been shown experimentally to be competent for transmission of Chikungunya, Dengue, and Zika viruses; thus, the country is facing increased risk of Asian tiger mosquito-borne viruses—serious threats to public health. Currently there is limited information concerning the geographical distribution of *A. albopictus* in Tunisia, and the absence of comprehensive data and accurate modeling to predict geographical distribution hinders vector control efforts. To address this gap, we collected larval and adult mosquitoes from nine Tunisian governorates between October 2022 and January 2024, gathering a total of 52 positive occurrence points. We developed a Maximum Entropy (MaxEnt) model incorporating one vegetation, two topographic, and 19 bioclimatic variables as potential predictors for the habitat distribution of *A. albopictus*. These variables were selected based on their biological relevance to the target species distribution. The model predicts that the most suitable areas for *A. albopictus* are located in northern and northeastern Tunisia. Key factors contributing to the distribution of *A. albopictus* in Tunisia include elevation, temperature seasonality, precipitation during the warmest quarter, annual precipitation, and mean temperature during the wettest quarter. The phenology of *A. albopictus* showed a major peak during the month of October. Since 2018, and driven by climate changes and urbanization, *A. albopictus* has extended its reach in the country. Our findings offer crucial insights for monitoring the spread of this invasive mosquito species and provide guidance for decision-makers aiming to implement comprehensive surveillance and control programs in Tunisia.

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FIRST RECORD OF *AEDES ALBOPICTUS* IN YEMEN

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Aedes albopictus was recorded for the first time in Yemen in September 2023, during routine surveillance in Al Mahara Governorate. This invasive mosquito species is considered a public health threat due to its ability to transmit viral diseases such as dengue and chikungunya, its wide range of hosts and its ecological plasticity. Five villages, namely Rahn, Al Fatk, Damqout, Jadheb and Houf, were screened for the presence of mosquitoes. We surveyed water bodies and containers, and deployed Communicable Disease Control traps (CDC), Biogents Sentinel (BG) traps, spray catches and aspiration for adult collection. Adults and immature stages of *Ae. albopictus* were identified in Houf, a city 17 m above sea level in the easternmost part of the Governorate of Al Mahara, which is located less than 8 km from the border with Oman. Our findings show that *Ae. albopictus* was coexisting with both *Ae. aegypti* and *Anopheles stephensi* and co-inhabiting the same container with *Ae. aegypti* with a ratio of 1:2. The role of continuous human movement and transportation in facilitating cross-border dispersal of *Ae. albopictus* between Al Mahara and Oman, will be addressed. Intensive efforts should be undertaken to monitor and manage *Ae. albopictus* spread in the country The presence of both Aedes vectors together highlights the need for surveillance for associated diseases and consideration of countermeasures.

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THE USE OF EDNA AS A METHOD TO DETECT PRESENCE OF *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* IN INTERSPECIFIC LARVAL HABITAT

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Environmental DNA (eDNA) analysis is an emerging technology that could be utilized as a novel tool to test for the presence of *Ae. aegypti* and *Ae. albopictus* in areas suspected of recent invasions. To investigate the utility of eDNA for detection of *Ae. aegypti* and *Ae. albopictus,* we first validated detection of these species from single-species larval rearing containers using species-specific qPCR assays targeting the ribosomal internal transcribed spacer 1 region. We then designed a series of experiments to: (i) test the sensitivity of real-time qPCR to detect eDNA of *Ae. aegypti* and *Ae. albopictus* in mixed species containers at different ratios, and (ii) detect eDNA as a proxy for the presence of *Ae. aegypti* and *Ae. albopictus* in containers treated with varying concentrations of larvicides. Experiments were performed in three replicates under controlled laboratory conditions using sterilized containers, distilled water, and nutrient sources including appropriate controls. Larvae rearing water in each container was vacuum-filtered using 1.2 µm membrane filters before eDNA extraction using the CTAB-chloroform method. After extraction, quantification of *Ae. aegypti* and *Ae. albopictus* eDNA was performed using qPCR. Our preliminary results suggest that, *Ae. aegypti* and *Ae. albopictus* can be accurately detected in mixed species larval habitats. Experiments are currently ongoing to test possible detection of *Ae. aegypti* and *Ae. albopictus* eDNA in containers treated with larvicides. Our findings will provide important preliminary data to assess the potential of using eDNA approaches to enhance surveillance of *Ae. aegypti* and *Ae. albopictus* in the High Plains and Mountain West regions of the US, where invasion of these medically important species is suspected.

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IMPACT OF SUGARCANE IRRIGATION SCHEME ON ANOPHELINE MOSQUITO ECOLOGY, BEHAVIOR, MALARIA TRANSMISSION RISK AND INSECTICIDE RESISTANCE IN SOUTHWESTERN ETHIOPIA

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Ethiopia is expanding extensive irrigation developments to meet food demands and alleviate poverty in the country. However, the effect of such water development projects on malaria transmission risk is not well investigated. Moreover, agrochemicals used in irrigation activities are blamed to drive resistance selection in malaria vectors. Studies evaluating the impact of these agrochemicals on malaria vector's resistance are lacking. This study investigated impact of sugarcane irrigation on vector dynamics, behavior, transmission risk and insecticide resistance of malaria vectors in Southwestern Ethiopia. Adult *Anopheles* mosquitoes were collected using CDC light traps and human landing catches from irrigated and non-irrigated clusters of Arjo-Didessa sugarcane irrigation scheme in wet and dry seasons, between 2018 to 2021. Mosquito species composition, abundance, seasonality, behavior (biting & blood feeding) and *Plasmodium* infection rates were compared. Mosquitoes were identified to species morphologically and using molecular techniques. Mosquito host blood meal sources were determined by polymerase chain reaction (PCR). *Plasmodium* sporozoite infections were analyzed using CSP ELISA. Adult *Anopheles gambiae* s.l. were tested for their susceptibility to insecticides using WHO tube test. Among 6,058 female *Anopheles* mosquitoes collected, 72.3% (n= 4379) were from irrigated and 27.7% (n= 1679) from non-irrigated clusters. Mosquito composition, abundance and density was significantly higher in the irrigated than non-irrigated clusters during the wet and dry seasons. Anophelines in the irrigated clusters were more anthropophagic and showed overnight as well as outdoor biting activity. A 2-fold higher *Plasmodium* infection rates were recorded in the irrigated than non-irrigated areas. *Anopheles gambiae* s.l. was resistant to deltamethrin and alphacypermethrin insecticides. Thus, malaria vector interventions should be strengthened in Arjo-Didessa sugarcane irrigation scheme to reduce malaria transmission risk during wet and dry seasons. Integrated resistance management strategies should also be implemented.

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CONTRIBUTION OF *ANOPHELES FUNESTUS* IN MALARIA ENDEMIC TRANSMISSION ON THE EAST COAST OF MADAGASCAR

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An. funestus group is an important malaria vector in Madagascar. This species thrives in endemic areas and caused increase malaria cases during dry season. *n*evertheless A*n. funestus* has been understudied. To assess entomological indicators of *Anopheles funestus* in malaria endemic villages, Vangaindrano district, Madagascar, from August to November 2023. So Human Landing Catch (HLC), Outdoor Resting Catch (ODC) and Indoor Resting Catch (IDC) were used to collect mosquitoes. All the anopheline collected were assessed for species identify . The entomological indicators such as density, Human Bating rating (HBR), the entomological inoculation rate (EIR), human blood index (HBI) and vectorial (Cv) was used to obtain intensity of malaria transmission.A total of 453 females were identify as *An. funestus,* it was confirmed as *An. funestus s.s*. The highest densities were observed in August (42.6%). Interestingly, 75.5% of the collected *An. funestus s.s.* were captured from HLC, with biting behavior exophagic (mean exophagic rate 62.6%). The peak biting activity was between 12:00 - 03:00 hours in outdoor and indoor during the survey. Detection sporozoites showed *P. falciparum* and *P. vivax* positif on this species. According to the mean HBR and the mean sporozoite index, EIR of *An. funestus* s.s. was 0.13 to 0.22 and 0.44 infectious bites/person/night (ib/p/N) for *P. falciparum* and *P. vivax* respectively. The longest longevity recorded for *An. funestus s.s.* was six days from August. The IDC proved that *An. funestus s.s* is exophilic (mean endophilic rate under 50%), high HBI values (0.83 to 0.50), indicating that these vectors are anthropophilic .The recorded blood meals were mainly from humans (50%). The Cv of *An. funestus s.s*. for P. *falciparum, P. vivax was* decreasing to the beginning of rainy season. The ODC showed this species has a strong preference resting on cattle dwellings. The results showed that *An. funestus s.s.* maintaining the transmission of malaria in dry season in this area, the trophic and resting behavior suggests that using long-lasting insecticidal nets alone is insufficient as a vector control strategy in this area.

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COST COMPARISON ANALYSIS OF DIFFERENT WORKFLOWS FOR ENTOMOLOGICAL SURVEILLANCE USING A DECISION-TREE APPROACH

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MALDI-TOF MS is increasingly applied for entomological surveillance. However, the potential for cost savings using MALDI-TOF MS in routine entomological surveillance has never been evaluated. This study compares the costs of current diagnostic methods used in entomological malaria surveillance in Kenya to the expected costs when using MALDI-TOF MS. To perform a cost comparison analysis of the conventional methods currently used for entomological malaria surveillance in Kenya to the use of MALDI-TOF MS, a decision tree analytic model to provide a systematic process for calculating the costs associated with materials, labour and direct costs, and time-to-results for the two workflows was developed. The analysis compared the costs of the current methods used in entomological malaria surveillance by the NMCP in Kenya to the expenses expected if MALDI-TOF MS was used instead, assuming a sample size of 15,000 mosquitoes and accounting for time-to-results and direct costs (materials and labour). Using MALDI-TOF MS for mosquito surveillance would result in a total direct cost savings of 83% (6 times cheaper) compared to the current workflow. It would also result into a 94.31% net time savings (17.6 times faster) compared to the current workflow. MALDI-TOF MS represents a platform that significantly reduces costs for the laboratory's sample processing, materials, and labour. Despite the initial high capital cost of the instrument, the ease of performance, the rapid turn-around time to results, and the modest cost of testing for each sample make this novel methodology a paradigm shift for entomological surveillance.

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DEVELOPMENT OF A SYSTEM TO SUPPORT COMMUNITY-BASED SURVEILLANCE OF DISEASE-TRANSMITTING MOSQUITOES IN RESOURCE-CONSTRAINED SETTINGS

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The identification and tracking of disease-transmitting mosquito populations are crucial for understanding their geographical distribution, behavior,

and species composition. Furthermore, understanding the dynamics of these mosquito populations is essential for guiding vector control interventions to improve their effectiveness and identify areas that require attention. Given the high burden of mosquito-borne diseases, particularly in resource-limited settings, and the limitations of traditional surveillance methods, there is a need for an innovative solution. To address this, we have developed a system to facilitate community-based surveillance of disease-transmitting mosquitoes. The system architecture comprises three main components: the user interface layer, the data processing layer, and the feedback and reporting layer. The user interface layer includes a mobile and web application that serves as the primary point of contact for users, allowing community members to submit mosquito data. The data processing layer manages the secure transmission, storage, validation, and trust assessment of the data, ensuring its integrity and reliability. The feedback and reporting layer provides necessary feedback to community members, generates comprehensive reports based on validated data, and manages compensation, thereby fostering wider community engagement. This system allows for the timely and efficient tracking of mosquito populations, significantly improving public health response capabilities across diverse geographic settings. By streamlining data collection and making it accessible to a wider audience, the system enhances the quality of surveillance data and enables targeted public health interventions. This system supports the tracking of disease-transmitting mosquito populations while simultaneously enhancing healthcare quality over the long term by informing public health practices. .

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INTEGRATION OF VECTOR AND HUMAN BEHAVIOR IN RESIDUAL MALARIA IN RURAL COMMUNITIES IN THE PERUVIAN AMAZON

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Malaria remains a significant public health concern in Peru where 22,349 cases were reported in 2023, mainly in Loreto in the Peruvian Amazonian Region. The national malaria control plans (NMCP) rely primarily on Long-lasting insecticidal nets (LLIN) and Indoor Residual Spraying (IRS) for vector intervention. This study investigates residual malaria exposure among LLIN users in Loreto, in three riverine communities from the Mazan district: Gamitanacocha (GAM) and Libertad (LIB) in the Mazán river basin; and Urcomiraño (UM) in the Napo basin. We assessed exposure levels across dry and wet seasons to identify gaps in protection to help guide Peruvian health authorities in developing NMCP. We integrated entomological and epidemiological data to adjust for mosquito exposure by human behavioral data. Our analysis reveals inter-seasonal variation in *Ny. darlingi*, with a peak of Human Biting Rates (HBR) during the wet season predominantly outdoors, ~18:00, diminishing overnight, and resurging in the morning. Previous studies in LIB and UM showed peak activity ~21:00. Additionally, Mazan watershed communities exhibited higher HBR than Napo across all seasons. Behavior-corrected exposure indices allowed us to determine that most of the main sources for remaining exposure are indoors awake and unmitigated bites, despite LLIN usage across seasons; and higher levels of outdoor remaining exposure in the wet season especially during early evening hours. We examined the malaria diagnosis associated with various potential risk factors, including socio-demographic characteristics and human behavior (age, gender, primary job), entomological indices and indoor/outdoor exposure during the early evening. Applying logistic regression with mixed effects showed that there is slight statistical evidence (p=0.123) for individuals who work outside to have a greater chance of contracting malaria. We suggest enhancing indoor protection measures for effective malaria control, particularly during early evening hours. Additionally, extra precautions should be taken with individuals outdoors in the early morning, particularly during the wet season.

6192

EFFECT OF *MICROSPORIDIA MB* INFECTION ON THE DEVELOPMENT AND FITNESS OF *ANOPHELES ARABIENSIS* UNDER DIFFERENT DIET REGIMES

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The symbiont *Microsporidia MB (MB)* found in *Anopheles arabiensis* tested in Kenya has shown malaria blocking potency against the transmission of the *Plasmodium* parasite. *MB* density is high in mosquito gonads, which is linked to horizontal (sexual) and vertically (transovarial) transmission from one mosquito to another. We have investigated how environmental factors such as diet affect the *MB An. arabiensis* symbiosis phenotype. F1 larvae of G_0 females confirmed to be *An. arabiensis* and infected with *MB* were either combined (Isogroup lines (IGLs)) or reared separately (Isofemale lines (IMLs)) depending on the experiments. Four diet regimes, Tetramin 0.07, Tetramin 0.3, Gocat 0.3 and Cerelac 0.3 mg/larva were tested on F1 IGLs for larva diet. IGLs reared on Tetramin 0.3 mg/larva were fed on either 1% or 6% glucose diet to determine adult survival. Larva of IMLs were fed on Tetramin 0.07mg and Tetramin 0.3mg for larva experiment. The adult experiment on IMLs were reared on 1% and 6% respectively. We found that amongst the four larval diet regimes tested on *An. arabiensis* development in the presence of *MB,* Tetramin 0.3 mg/larva gave the fastest larva development, highest adult emergence, largest body size mosquitoes, greatest prevalence, and density of *MB*. Also, adult *MB* mosquitoes fed on 6% glucose survived longer than negatives whilst with 1% glucose diet there was no significant difference between *MB*+ & -. However, development time and wing size, and the survival of adult were not significantly different between *MB* infected and uninfected *An. arabiensis* under the Tetramin 0.07 and 1% glucose diet respectively, suggesting that the *MB* conferred fitness advantage was diet dependent. *Microsporidia MB* does not adversely impact the development of *An. arabiensis*, even under limited dietary conditions. Optimal larval and adult diet regimes have been determined for mass rearing of *An. arabiensis* mosquitoes infected with *MB* for future trial releases for Malaria control and elimination. Knowledge on the effect of diet is important for understanding *MB* spread in *An. arabiensis* in the field.

6193

CLIMATE-SENSITIVE VECTOR-BORNE DISEASES: INTEGRATION OF TEMPERATURE, PRECIPITATION AND RELATIVE HUMIDITY IN A DYNAMIC PROCESS-BASED MODELLING APPROACH FOR IMPROVED SURVEILLANCE AND OUTBREAK PREPAREDNESS

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The global burden of climate-sensitive vector-borne diseases to public health system has increased significantly. Changing climatic conditions tend to support the environmental suitability for vector population establishment, pathogen replication and transmission at known or previously unknown locations. Public health agencies rely on surveillance and early warning systems for information on spatial and temporal patterns of vector population and pathogen transmission. Accurate and timely information are important for effective interventions and control programs. Laboratory experiments has shown that vector population density and pathogen transmission suitability are driven by temperature. However, in the natural environment, complex interactions exist where several factors play significant roles in the overall processes. We developed a series of dynamic process-based models that represent a simplified replication of the complex interactions that exists in nature. The models were forced with precipitation and relative humidity in addition to frequently used temperature variables. They can serve as the backend of an early warning system. The

epidemiological model simulates *Aedes aegypti* population, dengue and chikungunya outbreaks in different spatial and temporal scales. We applied the model to different geographical locations (Mexico, Germany, Kenya). In addition, a population model was developed to simulate population of *Culex torretium* mosquito population in Germany, Sweden and UK. Results were validated with vector occurrences and cases of outbreaks with high accuracy levels. Our research was able to demonstrate that a model forced with temperature, precipitation and relative humidity can replicate vector population and pathogen transmission in several geographical location with accurate seasonal variation better than classical models forced with temperature alone. We conclude that dynamic process-based models which can be automated, scaled and transferred between geographical areas serve as important tools for early warning systems of climate-sensitive vector-borne diseases.

6194

MODELLING WOLBACHIA REPLACEMENT FOR DENGUE CONTROL: A SCOPING REVIEW

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Aedes aegypti mosquitoes, the primary vector for dengue, Chikungunya, and Zika virus, have been shown to have reduced vector competence when deliberately infected by strains of the bacterium *Wolbachia*[1]. Utilising this novel technology for dengue control, the release of *Wolbachia*-infected *Ae. aegypti* mosquitoes into wild populations, where they naturally proliferate, is known as *Wolbachia* replacement. *Wolbachia* replacement has the potential to be an effective tool for dengue control, demonstrated by a successful randomised controlled field trial in 2021 which reduced dengue incidence by 77% in intervention areas[2]. While a 2018 review of *Wolbachia* replacement considered takeaways from modelling[3], computational literature which explores this technology is rapidly growing, thus, the need for a review specifically addressing modelling of *Wolbachia* replacement is pressing. This scoping review will examine novel findings in the field of modelling *Wolbachia* replacement since 2018, as well as evaluating how recent developments could be incorporated into and improve future models.

6195

FIGHTING MALARIA WITH THE MOSQUITO SYMBIONT BACTERIA SECRETED BIOACTIVE CELL-FREE SUPERNATANT

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Malaria control is critical in reducing the disease burden caused by mosquitoes, and insecticides are an effective tool to control vector. Resistance to common insecticides is now widespread, and novel classes of insecticides or tools are needed. In previous work, we described the mosquitocidal activities of *Chromobacterium anophelis sp.nov.*, a bacterium found in association with wild mosquitoes. In this current work, we further explored the effects of bacterium cell free supernatant on *An. cuoluzzii* mosquito fitness, mosquito physiology and *P. falciparum* infection development. We found that cell free supernatant from *C. anophelis sp.nov.,* has mosquitocidal activity against a broad range of malaria mosquito. Mosquitocidal activity of *C. anophelis sp.nov*., was retained after removal of live cells from M9 medium, suggesting the bacteria secrete mosquitocidal compound(s) into the M9. 100% of mosquito fed to chromobacterium cell-free supernatant (80-100 %) die less than 5 days and 10 days post exposition respectively in lab and semi field condition. Mosquito exposure to *C. anophelis sp.nov*., cell free supernatant reduces significantly its susceptibility to *Plasmodium falciparum* infection, thereby compromising the mosquito's vector competence. Parasite inhibition rate was 72.06% when the mosquitoes took solution (20 %) through a cotton ball before taking *P. falciparum*-infected blood, and 40.24% when solution was mixed with gametocytes. Our findings suggest that *C. anophelis sp.nov.,* cell free supernatant has factor(s) with strong effects on mosquito longevity, fitness and decrease significantly *P. falciparum* infection, which may be of interest for mosquitocidal, anti-Plasmodial tools development and is promissing for malaria elimination.

6196

ASSESSMENT OF THE EFFICACY OF FLUDORA FUSION ON SPRAYED SURFACES IN THE GAMBIA

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The use of insecticide for indoor residual spraying has significantly reduced malaria cases in The Gambia. However, this efficacy is jeopardized by a variety of factors such as mode of application method, insecticide type, and spray surface nature. In this study, we examined how different wall surfaces found in Gambia affect insecticide efficacy. The efficacy of the spraying is evaluated after a month. Different sprayed walls were randomly chosen from Gambisara village in the Upper River Region. Trained regional Vector control officers and field biologists collected mosquito larvae from various natural breeding sites. The collected larvae and pupae were separated. The anopheles pupae are reared into adults, Female anopheles mosquitos aged 2-5 days were exposed to sprayed walls for 30 minutes and the mortality rate is monitored after 24 hours. A total of 2160 female anopheles mosquitoes were exposed to different levels on sprayed walls. Dead after 24 hours exposure were, 331 (92%) mud wall, 324 (90%) mud wall plastered, 321 (89%) mud wall plastered and painted, 320 (89%) cement wall, 290 (81%) cement wall plastered 275 (76%) cement wall plastered and painted. Overall 1861 dead mosquitoes were recorded which result to 86% mortality rate. While in the control, 120 mosquitoes were exposed, 20 mosquitoes for each wall type. At the end of the test, 10 dead mosquitoes were recorded in the control representing 3% mortality rate. This short survey indicated that insecticide efficacy last longer on mud walls compared to other types. However, since factors like mode of spraying, volume of water and sprayed surfaces affect insecticide efficacy on sprayed wall make it difficult to conclude. All the walls tested were sprayed by different people who may have different mode of application speed, make it difficult to draw line on these findings

6197

SPATIOTEMPORAL CO-DISTRIBUTION AND TIME LAGGED CROSS CORRELATION OF MALARIA AND DENGUE IN LORETO, PERU

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Malaria and dengue account for most vector-borne disease-related cases and deaths worldwide, disproportionately affecting tropical regions such as Peru. Previously identified social, environmental, and climate determinants for both diseases are similar despite differences in vector ecologies. Control strategies for both rely on interventions such as removal of breeding sites or insecticide-based strategies, which could be integrated. We assessed synchrony (temporal correlations, temporal order, lagged relationships) and spatial correlations between malaria and dengue in the Loreto region of Peru. We conducted a time-lagged cross-correlation (TLCC) analysis between district-level dengue and malaria time series in Loreto between 2000-2021. We identified temporal patterns of dengue that could precede malaria patterns or vice versa. We categorized districts based on dengue/malaria spatio-temporal patterns and conducted Moran's tests for spatial autocorrelation of maximum TLCC coefficients and optimal lag times. The number of districts reporting both diseases has increased. Maximum TLCC coefficients varied in magnitude and direction between districts, as did corresponding lag times. In the Northwest, increases in malaria often preceded increases in dengue, while in the Northeast increases in malaria preceded decreases in dengue cases. We found spatial correlation

between coefficients in some regions in the Northwest, suggesting that characteristics of a geographic area may influence the observed associations. The identification of districts with strong associations between dengue and malaria incidence can inform implementation of targeted integrated interventions, while identification of distinct patterns of association can inform future studies assessing drivers of both diseases in different settings.

6198

DIET AFFECTS THE LONGEVITY AND THE RESPONSE TO INSECTICIDE OF *ANOPHELES GAMBIAE*

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The longevity of mosquitoes is a key parameter underlying the epidemiology of malaria, and it is the main target of insecticides in malaria control. The evolution of resistance is therefore threatening the success of control. While several genes underlie a mosquito's longevity and resistance, it is often overlooked that both can be influenced by the mosquito's environment, and in particular its diet, i.e. the combination of sugar obtained from plants and the blood obtained from its hosts. Within this context we aimed to determine with a series of experiments (i) how nectar influences a mosquito's longevity, (ii) how the type of sugar obtained in nectar affects a mosquito's response to insecticide, and (iii) how sugar and blood meal interact to influence resistance. First, we fed mosquitoes for five days with four types of sugar diluted to either 1.97 or 19.7 kcal per 100 ml of water and then measured their resistance with a WHO bioassay test. While the mosquitoes fed on the lower concentration were 2 times more likely to die within 24 hours of being exposed to the insecticide than those fed on the higher concentration, the type of sugar did not influence mortality. Second, we let mosquitoes feed throughout their lives on one of five species of local plants - *Thevetia nerifolia*, *Mandalium coromandelianum*, *Ixora coccinea*, *Tabernanthe iboga* or *Carica papaya* - and linked their longevity to the types and concentrations of sugar in the plants' nectar. The mean longevity ranged from 9 days with *C. papaya* to 22 days with *T. nerifolia*, but was not linked to the concentration of any of the sugars in the nectar. Third, we fed mosquitoes on one of three plant species for four days, then gave half of them a blood meal and measured the resistance of all of the mosquitoes. The blood-fed mosquitoes were less likely to be killed by the insecticide than those that had fed only on plants - Plant species not influence their response to insecticide. Our studies reveal that other compounds of nectar have an important impact on mosquito - there is a close link between blood meal and the detoxification of insecticide. These concepts will lead to improve attractive toxic sugar baits.

6199

ABUNDANCE & CHARACTERIZATION OF MALARIA VECTORS IN SAKASSOU, CENTRAL IVORY COAST

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In preparation of an indoor residual spraying programme to control malaria in Sakassou, Central Côte d'Ivoire, we assessed whether insecticide-treated nets and indoor residual spraying are potentially suitable vector control strategies. From November 2018 to July 2020, we collected mosquitoes using human landing catches, pyrethrum spray catches and CDC light traps. We identified all mosquitoes morphologically and further determined members of the *Anopheles gambiae* species complex using molecular PCR diagnostics. In addition, we estimated sporozoite rates using enzyme-linked immunosorbent assays. We collected 98,314 mosquitoes with higher numbers in months with increased rainfall*. Anopheles coluzzii* was the most prevalent species (90%), showing a *Plasmodium* infection rate of 0.017 and biting throughout the night with a peak around 1.00 am. In the houses selected for human landing catches, an individual was exposed to 516 infective bites per year. As *An. coluzzii* is resting indoors and is the main vector biting indoors at night, both insecticide-treated nets and indoor residual spraying are potentially effective malaria control interventions in Sakassou. However, as biting was also observed earlier in the night and outdoors, additional interventions should be considered.

6200

OPTIMIZING AND VALIDATING THE HOST-FREE TUNNEL TEST: A MORE AFFORDABLE, PRACTICAL, AND ETHICAL TOOL FOR THE EVALUATION OF INSECTICIDE-TREATED NETS

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The tunnel test is recommended by the World Health Organization (WHO) to investigate the biological activity of an insecticide-treated net (ITN) surface by observing relevant effects on mosquitoes subjected to exposure that is more representative of interaction while host seeking. Data generated using the tunnel test is routinely used by ITN manufacturers as part of the dossier generation for applications for listings by the WHO Prequalification (PQ) team to demonstrate efficacy and/or quality, and by implementers to monitor chemical durability and ongoing efficacy post-deployment. The tunnel test involves a series of chambers where mosquitoes must pass through a holed ITN sample to reach a live animal bait to blood feed. It is necessary to have a bait in the test to provide cues that stimulate mosquitoes to be attracted towards, and through, the holed ITN sample. Mosquitoes are scored for their passage through the net as well as blood feeding and mortality. Currently, the WHO tunnel test is the best available method for testing the bioefficacy of chlorfenapyr nets at the laboratory scale. However, the reliance on live animal hosts raises ethical concerns and logistical challenges if suitable hosts aren't available. To address this iiDiagnostics, with support from IVCC and Syngenta, developed an alternative method that eliminates the need for live hosts. Preliminary data shows that there is evidence that this method is appropriate with mosquito feeding rate over 50% in control arms and mortality above 80% for treatment arms. Innovation to Impact (I2) are utilising a method validation framework to establish an optimised, validated, and accessible alternative to the standard tunnel test. It is imperative that a robust and validated bioassay is available for conducting durability monitoring for those dual-AI ITNs already on the market and those in development. Following engagement with the WHO PQ/VCT team our aim is for a version of the final Standard Operating Procedure (SOP) for the host-free tunnel test to be incorporated as an Implementation Document supporting the WHO Guideline for Prequalification Assessment of ITNs.

6201

RESIDUAL EFFICACY OF WALL CONTACT BIOASSAYS AND FUMIGANTS EFFECTS INDUCED BY ACTELLIC®300CS AND FLUDORA®FUSION WP-SB 56.25 INSECTICIDES USED FOR INDOOR RESIDUAL SPRAYING AGAINST SUSCEPTIBLE *ANOPHELES GAMBIAE* S.S.

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From 2020 to 2022, the study area of Nyagatare District located in Eastern Province of Rwanda rotated two insecticides for Indoor residual spraying (IRS), Fludora® Fusion WP-SB 56.25 and Actellic® 300CS**.** This assessed the residual efficacy of wall contact and non-contact (fumigant effect) bioassays induced by the two new insecticides sprayed during the IRS. The residual efficacy tests used WHO standard protocol and was performed in two sites. The surveys were conducted September 2020 to July 2021 for Fludora® Fusion WP-SB 56.25 and August 2021 to June 2022 for Actellic®CS300. Six houses per month were tested for fumigant effect while the direct wall contact bioassays were carried out in 12 houses. At 10-months, Fludora® Fusion WP-SB 56.25 provided a residual efficacy of five months for direct mortality (24h) and 6 months to 10 months for

the delayed mortality (96 hours) while Actellic® 300CS provided a residual efficacy for more than 10 months period with mortality only counted at 24 hours. The fumigant effect was four months and five months of delayed mosquito mortality for Fludora® Fusion WP-SB 56.25 and Actellic® 300CS respectively. This study showed the efficacy of 10 months for both insecticides using wall cone bioassay tests and complemented by a fumigant effect of four months for Fludora® Fusion WP-SB 56.25 and five months for Actellic® 300CS. These results show that the application of one IRS round per year is sufficient to ensure adequate annual prevention against malaria (month to month) in Rwanda. More research is needed to evaluate the effects of fumigant effects on mosquito control for reductions in malaria cases and anything about sustaining this intervention.

6202

IMPACT OF FOCAL MALARIA CONTROL USING TARGETED INDOOR RESIDUAL SPRAYING (IRS), 4 YEARS RESULTS FROM RUSIZI DISTRICT, WESTERN PROVINCE OF RWANDA

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After facing its highest malaria incidence rate of 409 per 1000 population in 2016, Rwanda developed a malaria contingency plan (MCP) that focused on high malaria burden districts. In Rusizi, a district with heterogeneous malaria transmission, the MCP recommended focal indoor residual spraying (IRS), targeting 9 out of 18 sectors within the district. The goal of focal IRS is to cover epidemiological hotspots in geographic areas that experience regular seasonal increases in confirmed malaria cases with high transmission activity in comparison to surrounding areas. This assessment evaluated the impact of IRS focal spraying in Rusizi district comparing 2019 and 2023, after four years (2020-2023) with focal IRS. Monthly uncomplicated and severe malaria cases and deaths were retrospectively extracted from the Health Management Information System (HMIS) for 2019-2023. Monthly entomological data were collected using Human Landing Catches from the same period in three villages of Mashesha entomological sentinel site in Rusizi. The sporozoite rate (SR) derived from *Plasmodium* sporozoite positive ELISAs by the total vector mosquitoes tested. The entomological inoculation rate (EIR) was calculated as the product of the human biting rate (HBR) and the SR.A substantial decrease of 95.7% ($W = 305$, $p < 0.001$), in uncomplicated cases was observed, from 256,271 in 2019 to 10,918 in 2023. Severe malaria cases and deaths were reduced by 92.3% (from 689 to 53 cases), and 100% (from 15 to 0 cases) for the same period. An 86% reduction of HBR for *Anopheles gambiae s.l,* the main malaria vector, (from 69.95 to 9.63 bites/person/night) for the same period. The EIR decreased by 93%, from 97.93 to 6.74 infectious bites per person per year. These findings from Rusizi District demonstrate the sustained success of a focal IRS intervention for controlling hot spots of malaria transmission, ultimately advancing progress towards sustainable elimination objectives while optimizing resource allocation for IRS.

6203

BUILDING AN EVIDENCE BASE TO SUPPORT INSECTICIDE-TREATED NET DISTRIBUTION IN TWO HIGH-BURDEN TO HIGH-IMPACT COUNTRIES

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Insecticide-treated nets (ITNs) are a key tool for preventing malaria. The World Health Organization (WHO) recommends delivering ITNs through mass campaigns and continuous distribution channels, such as antenatal clinics and the expanded programme on immunisation. These mechanisms, and how they are operationalised vary between countries and at present the information that underpins decision-making at different administrative levels for distribution is not well documented. Building an evidence base of the factors that influence decisions on ITN distribution is critical to optimise this intervention. This qualitative study investigates planning and delivery experiences with ITN distribution at national and subnational levels in two high-burden countries - Cameroon and Tanzania. Participants are selected through purposive sampling, in consultation with the National Malaria Control Programme (NMCP). At national level, we conduct semi-structured interviews with the NMCP, other relevant government departments and external partners. Focus group discussions are also carried out at two sub-national sites and four delivery-points in each country with operational-level NMP staff, community focal points and individuals overseeing net distribution. Topic guides are informed by the WHO Health Systems Building Blocks. Thematic data analysis is used to understand the planning and delivery experiences of individuals involved in ITN distribution at different administrative levels and across countries. We present our results under the key themes of leadership and governance, financing, access to essential commodities, service delivery, health workforce, and information, learning and accountability. Findings across administrative levels allow for comparison of influencing factors within countries as well as across different national contexts. Our results highlight key commonalities, differences, barriers, and enablers associated with ITN distribution mechanisms used in these contexts.

6204

COMBINING HOUSE-SCREENING AND ODOUR BAITED MOSQUITO TRAPS FOR SUSTAINABLE CONTROL OF MALARIA TRANSMISSION IN LOW INCOME COMMUNITIES DOMINATED BY *ANOPHELES FUNESTUS*

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Tanzania is making tremendous progress against malaria by scaling up long-lasting insecticide-treated nets (LLINs), indoor residual spraying (IRS), and effective treatments. There's a greater need for new complimentary tools to monitor the persistent malaria transmission. Two simple interventions that fit this target profile are house screening and odor-baited mosquito traps which have not previously been tested jointly. This current study, therefore, investigated the impact of combining house-screening and odor-baited traps in reducing malaria vector density by; a)identifying an effective trap for *Anopheles arabiensis*, b)measuring the impact of house-screening with and without an odor-baited trap, c)testing the personal/household and community level of protection of users (either or both interventions) and non-users(control), and d)conducting a small-scale field experiment on testing the combination of house-screening (eaves and windows) and outdoor baited traps in rural setting in Tanzania. This

study aimed to assess the impact of house-screening and odour-baited traps on reducing mosquito vector density and biting risks. Semi-field and field experiments were conducted in rural Tanzania, focusing on *Anopheles arabiensis* mosquitoes, a dominant malaria vector. In semi-field experiments, the Suna trap exhibited higher mosquito recapture rates than the BGM trap in both non-competitive and competitive evaluations of odor-baited traps revealing it as an effective outdoor trap for mosquito collection. House screening, whether alone or combined with traps, demonstrated substantial reductions in indoor biting risk, offering protection efficacies of 80% and 93%, respectively. Also, in the field experiments, a total of 38,281 mosquitoes were collected both by CDC light trap and Suna trap. House screening whether alone or combined with traps provided more than 80% protection indoors whereas there was a clear diversion and recapture of mosquitoes from the odor-baited Suna traps outdoors. It is evident that house screening can potentially reduce indoor mosquito-biting risk.

6205

THE EFFECT OF REPEATED WASHING OF THE ROYAL GUARD, INTERCEPTOR G1 AND G2 NETS ON BLOOD FEEDING BEHAVIOR AND SURVIVAL OF *ANOPHELES* MOSQUITOES

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Long-lasting insecticidal nets offer longer time of protection because they are wash resistant. Whether the new LLINs (Interceptor IG2 and Royal guard) are wash resistant compared to the conventional nets are unknown. This study assessed the wash resistance of two nets, Interceptor G2 (IG2) and Royal guard (RG) compared to the mono-treated version of InterceptorG1 and a negative control (untreated net). Blood feeding behavior and mortality were measured against Anopheles mosquitoes. WHO cone bioassays were conducted using 2-3 days *An. gambiae* Kisumu and *An.gambiae s.l*. A total of 1,400 mosquitoes were exposed to untreated net and 0-20th washed IG1,IG2 and RG nets for 3minutes. Each test had 10 replicates and 50 mosquitoes per replicate. Knockdown was observed from 5 minutes to 60 minutes after which mosquitoes were provided with blood to check the feeding behavior after exposure. Final mortality was observed from 24hrsto 72 hours for each net. High mortality (>80%) of mosquitoes and high blood feeding inhibition (100%) was observed across the washes for all the three treated nets and test mosquitoes. Time to knock down increased with number of washes for IG1. There was a significant difference in knock down mortality for *An. gambiae s.l* between untreated vs RG (95% CI -98.26 to -92.54, p=<0.001). The difference was not significant in IG1 and IG2 (95% CI -5.737 to 2.137, p=0.6317). No difference was observed in blood feeding inhibition and mortality due to repeated washing of the two new nets, Interceptor IG2 and Royal guard nets which shows that the distribution of these nets in Malawi may have a positive impact in reducing malaria vectors.

6206

DISTRIBUTION OF ANOPHELES VECTORS AND THEIR ROLE IN MALARIA TRANSMISSION ACROSS HIGH MALARIA BURDEN AREAS IN MALAWI INCLUDING CHIKWAWA, KARONGA AND NKHATA BAY DISTRICTS

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A comprehensive understanding of vector distribution and malaria transmission dynamics at a local scale is essential for implementing and evaluating effectiveness of vector control strategies. In Malawi, *Anopheles funestus* s.l. and *An. gambiae* s.l. are the main malaria vectors. To assess the intersection between vector distribution and malaria transmission dynamics, we collected vector bionomics and malaria case data from July 2022 to June 2023 in three high malaria burden districts: Chikwawa, Karonga and Nkhata Bay. Monthly malaria case data were obtained from the National Malaria Control Program database from health facilities affiliated with the entomological sentinel sites. Monthly mosquito collections were carried out using pyrethrum spray catches (PSCs) and Center for Disease Control light traps (CDC-LTs). Sporozoite rate (SR) and entomological inoculation rates (EIR) were calculated from mosquitoes collected using CDC-LTs. The total number of *An. funestus* s.l. and An. gambiae s.l. mosquitoes collected were 1,745 and 8,979, respectively. *An. funestus* s.l. was predominant in Nkhata Bay and the densities were high throughout the year with a peak in May. An. gambiae s.l. were more abundant in Karonga and densities were highest between August and September. In Chikwawa both Anopheles species were almost evenly distributed. The SRs were higher for *An. funestus* s.l. ranging from 1.4 to 8.3% than for An. gambiae s.l. with a range from 0 to 0.8%, among the three areas. The EIR of *An. funestus* s.l. was higher in Nkhata Bay [26.0 infective bites/person/month (ib/p/m)], followed by Chikwawa (7.0 ib/p/m). *An. gambiae* s.l. infective bite rate was highest in Karonga (6.5 ib/p/m. Malaria cases were high in all three districts during and immediately after the rainy season from January 2023 to June 2023 ranging from 160 to 370 malaria cases per 1,000 population per month with highest cases reported from Nkhata Bay. EIR and malaria burden were highest in Nkhata Bay where *An. funestus* s.l. is dominant. Species composition, spatial and temporal distribution of vectors should be considered when planning targeted vector control interventions.

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EFFECTS OF SAMPLE PRESERVATION METHODS AND DURATION OF STORAGE ON THE PERFORMANCE OF MID-INFRARED SPECTROSCOPY FOR PREDICTING THE AGE OF MALARIA VECTORS

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Monitoring the biological attributes of mosquitoes is critical for understanding pathogen transmission and estimating the impacts of vector control interventions on the survival of vector species. Infrared spectroscopy and machine learning techniques are increasingly being tested for this purpose and have been proven to accurately predict the age, species, blood-meal sources, and pathogen infections in *Anopheles* and *Aedes* mosquitoes. However, as these techniques are still in early-stage implementation, there are no standardized procedures for handling samples prior to the infrared scanning. This study investigated the effects of different preservation methods and storage duration on the performance of mid-infrared spectroscopy for age-grading female *Anopheles arabiensis.* Laboratory-reared *An. arabiensis* (N=3,681) were collected at 5 and 17 days post-emergence, killed with ethanol, and preserved using either silica desiccant at 5°C, freezing at - 20°C, or absolute ethanol at room temperature. For each preservation method, the mosquitoes were divided into three groups and stored for 1, 4 or 8 weeks, then scanned using a mid-infrared spectrometer. The best performing classifier for age-grading mosquitoes was the support vector machine (SVM). The classification of mosquito ages (as 5 or 17-day-olds) was most accurate when the samples used to train the SVM model (training samples) and samples being tested (test samples) were preserved the same way or stored for equal durations.

However, when the test and training samples were handled differently, the classification accuracies declined significantly. When using mid-infrared spectroscopy and supervised machine learning to age-grade mosquitoes, the highest accuracies were achieved when the training and test samples are preserved in the same way and stored for similar durations. This underscores the critical need for standardized sample-handling protocols for infrared-based entomological studies. These protocols not only enhance accuracy but also holds significant implications for advancing malaria vector control strategies.

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EXPLORING THE INFLUENCE OF MOSQUITO FEEDING BEHAVIOR AND EXISTING VECTOR CONTROL INTERVENTIONS ON THE IMPACT OF ENDECTOCIDES FOR MALARIA CONTROL

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Endectocides are mosquito-killing drugs; upon taking a bloodmeal on a treated host, the mosquito ingests the drug and is killed. If approved for malaria control, endectocides will be distributed in areas with different mosquito species, feeding behaviours and on top of existing vector control interventions, predominantly LLINs. The aim of this study focuses on using a malaria transmission model to predict the impact of an ivermectin-like endectocide (3x300 µg/kg, 80% coverage) in settings differing in LLIN usage, mosquito species, pyrethroid resistance and LLIN age. In one model version, endectocide uptake was determined by the LLIN-mediated human biting rate and endectocide coverage, whereas in another, uptake was independent of the impact of LLINs. Model-specific intervention dynamics and efficacy were explored by comparing prevalence in under 5-year-olds and the annual entomological inoculation rate (EIR), across a range of entomological contexts, between settings with LLINs or LLINs and endectocide. Model-derived trends in mosquito life expectancy and time between human bloodmeals, across LLIN usage and resistance profiles, were explored. Both models predicted a reduction in EIR and slide prevalence when endectocides were added to settings with historic LLIN usage, compared to when only LLINs were used, across a range of insecticide resistance profiles. Both models predicted similar dynamics and reductions in the EIR and slide prevalence in under 5-year-olds, indicating a marginal impact of LLINs on endectocide uptake. Endectocides in humans were predicted least impactful in settings with *Anopheles stephensi*-like zoophilic vectors. Across a range of settings, the differences in the average time between human bloodmeals were relatively small compared to the differences in the average mosquito life expectancy. This work suggests that as the LLIN-induced delays in human bloodmeals are relatively small compared to respective reductions in mosquito life expectancy (as assumed by the model) across these LLIN usage and entomological settings, LLINs have a negligible impact on endectocide uptake.

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EVALUATION OF THE CHAIN OF CUSTODY OF THE RESIDUAL INSECTICIDE USED IN MALARIA VECTOR CONTROL IN THE AMAZON REGION OF BRAZIL

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In Brazil, malaria remains a significant public health issue, particularly in the Amazon region where 99% of malaria cases are concentrated, primarily affecting the most vulnerable populations. The primary method for controlling the main malaria vector, the *Anopheles* darlingi mosquito, continues to be the use of various residual chemical insecticides. However, there is no complete overview of the chain of custody of these products in Brazil. The objective of this research is to evaluate the cost-effectiveness of the insecticide supply chain utilized for malaria control in three municipalities with a high disease incidence in the Brazilian Amazon region from 2017 to 2023. The study involved a statistical analysis that included proportions, frequencies, and Pearson correlations. Data on costs from the National Program for the Prevention and Control of Malaria (PNCM) over the past six years, details on the supply chain process, and epidemiological information from São Gabriel da Cachoeira, Tefé, and Barcelos in Amazonas state were examined. Preliminary results indicate that the total expenditure on national purchases of Vectron and Lankron insecticides over the last six years amounted to US$ 6,690,358.16. Comparing the period from 2017 to 2023, there was a 39% decrease in purchases of these products by the municipalities under review. However, these inputs still represent a considerable cost for the PNCM. During the same timeframe, there were variation in reported malaria incidence, with a 6% increase in São Gabriel da Cachoeira, 43% reduction in Tefé and 24% decrease in Barcelos. Although there was a decline in the distribution of insecticides in the municipalities, the expenses still total US$ 514,430.33. The analyses indicate a variation in the quantity of insecticides procured alongside variation in the incidence of malaria cases in the studied areas. This study aims to contribute to enhancing the cost-effectiveness assessments of chemical insecticides employed by the PNCM for malaria control in Brazil.

6210

THE INTERSPECIFIC COMPETITION BETWEEN LARVAE OF *AEDES AEGYPTI* AND MAJOR AFRICAN MALARIA VECTORS IN A SEMI-FIELD SYSTEM IN TANZANIA

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The interspecific competition between larvae of *Ae. aegypti* and *Anopheles* species may influence adult life history traits such as body size, fecundity, pathogen susceptibility, longevity, vector competence, flight capacity and overall vectorial capacity of both species and affect their ability to transmit diseases. We examined the effects of intra and interspecific competition on individual fitness between *Ae. aegypti* and *An. arabiensis, Ae. aegypti* and *An. gambiae,* as well as *Ae. aegypti* and *An. funestus* at the larvae stage in a semi field system. We designed the experiment with intra and interspecific competition under three species combinations, with and without food; 100:100, 200:0, 0:200. Two habitat sizes were utilized, small (0.5 liter of water) and medium (1 liter of water). Tetramin fish food (0.02g) was provided on daily basis to the food assigned group. Interspecific competition had significant effects on developmental time, larval survival to adulthood, and adult body size via wing size. However, these effects were more prominent in *Anopheles* species in interspecific than *Ae. aegypti*. Cannibalism and predation were observed in both experiments, with and without food, for both species. In the absence of food, *Ae. aegypti* exhibited prolonged survival compared to *Anopheles* species, although no larvae survived to adulthood for the two species. Our results suggest that the interspecific competition significantly impacted malaria vectors than *Ae. aegypti*. Owing to the epidemiological importance of the two species in diseases transmission, it is crucial to understand the outcomes of competition between these two species on species distribution and individual fitness and performance for effective vector control strategies especially in urban and suburban settings.

6211

ESTIMATING SPATIAL DISTRIBUTIONS OF *AEDES AEGYPTI*, *AEDES ALBOPICTUS* AND *CULEX QUINQUEFASCIATUS* IN HAITI

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Here we modelled the geographic distributions of three arbovirus vectors, *Aedes aegypti*, *Ae. albopictus* and *Culex quinquefasciatus* across Haiti. All three of these mosquito species are known to occur across Haiti; however, determining their most likely distributions is crucial for tailoring vector-borne disease control strategies. Idiosyncratic presence points for all three species were obtained from the VectorMap and Global Biodiversity Information Facility databases and were supplemented by a recent mosquito collection project within Haiti. An ecological niche model experiment using maximum entropy (MaxEnt) was used to estimate the probability of presence across the landscape for each of the three target species. The model incorporated several predictor variables: human population, nighttime lights, distance to roadways, distance from inland waterways, distance from the coast, elevation, mean annual temperature, maximum temperature, minimum temperature, annual precipitation, wind speed, normalized difference vegetation index and built surface extents. All covariates were obtained in raster format from publicly available databases. The MaxEnt-based prediction elucidated several key patterns for the three mosquito species, with the highest probability of presence for all species being found at and around urban and highly populated areas, especially around the capital of Port-au-Prince and other cities such as Léogâne, Jacmel, Gonaïves and Cap-Haitien. This trend persists for all three mosquito species, with significant overlap between the predicted distributions for *Ae. aegypti* and *Ae. albopictus*, with *C. quinquefasciatus* having a wider distribution than the others. These models corroborate existing research that depicts the frequent co-existence of these three species and their synanthropy. While additional count modelling approaches may elucidate additional species-specific preferences, these presence/absence models provide first pass, actionable spatial data for public health policy and tailored vector management strategies in Haiti.

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ALARMINGLY EXPANDING GEOGRAPHIC DISTRIBUTION OF *ANOPHELES STEPHENSI* IN ETHIOPIA

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Anopheles stephensi is a primary vector of urban malaria in India and the Middle East. It has been introduced to Africa in the last decade. Its expansion into new geographical regions has posed a threat to malaria control and elimination efforts in the region. Strengthening surveillance and targeted vector control have been advocated to limit its spread. This study sought to determine the geographic distribution of *An. stephensi* in Ethiopia. A targeted entomological survey, both larvae and adult, was conducted in three major cities in southern Ethiopia; Hawassa, Dilla, and Arba Minch, between 2023 and 2024. *Anopheles* larvae collected from the field were reared to adults for species identification. Adult *Anopheles* mosquitoes were also collected using BG pro traps and Prokopack aspirators. Species identification was made using morphological keys. Mosquito blood meal sources was examined using qPCR. A high larval positivity rate was recorded for *An. stephensi* in Hawassa (16.6%), Arba Minch (14.1%) and Dilla (9.0%). Out of 1284 adult female *Anopheles* mosquitoes reared from larvae, 514 (40.0%) were identified as *An*. *stephensi*. This is the highest proportion of *An. stephenis* ever documented in Ethiopia or any Eastern African countries. Blood meal analysis indicated that a zoophagic tendency of *An. stephensi*. The study, for the first time, confirmed the wide range spread of *An. stephensi* with high larval positivity rates in Ethiopia. The presence of both larval and adult stages of *An. stephensi* proves that the species has established in southern Ethiopia. The findings suggest the need for further investigations into the ecology, behavior, population genetics, and the role of *An. stephensi* malaria transmission in Ethiopia.

6213

A SYSTEMATIC REVIEW OF ENTOMOLOGICAL INDICATORS AND SAMPLING APPROACHES USED IN THE EVALUATION OF CLUSTER RANDOMIZED TRIALS FOR MALARIA VECTOR CONTROL PRODUCTS

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Vector control plays a crucial role in the fight against malaria and other vector-borne diseases. Recommendations for designing vector control trials in assessing vector control products emphasize the importance of well-designed epidemiological trials, particularly cluster Randomized Controlled Trials (cRCT), to demonstrate public health value. Entomological indicators as secondary outcomes complement epidemiological outcomes by providing valuable insights into the effectiveness of vector control interventions and aiding in the interpretation of epidemiological trial outcomes. There remains ambiguity regarding the selection of these parameters, their relationship with epidemiological indicators and the approach taken to collect entomological data in trials is not standardized. This study aims to assess the methodological variability and constraints in cRCTs evaluating vector control interventions by analysing how entomological outcomes are incorporated into epidemiological trials, study designs for entomological monitoring, and the value of resultant data for interpreting epidemiological impacts. Through a systematic review of existing methodologies focusing on malaria, we will determine the frequency with which entomological outcomes are measured, assess variability in the types of entomological indicators collected and study designs used to measure them. This study underscores the importance of robust trial methodologies in vector control research and highlights the need for standardized approaches to the selection of entomological indicators and associated study designs. By clarifying the variability in trial methodologies and its impact on trial outcomes, this research aims to inform the development of guidelines for conducting high-quality vector control trials, ultimately enhancing the effectiveness of vector control interventions, and reducing the burden of malaria and other vector-borne diseases worldwide.

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MALARIA VECTOR CONTROL IN SUB-SAHARAN AFRICA; COMPLEX TRADE-OFFS TO COMBAT THE GROWING THREAT OF INSECTICIDE RESISTANCE

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Mass distribution of insecticide-treated nets (ITNs) has been a key factor in reducing malaria cases and deaths in sub-Saharan Africa. A shortcoming has been overreliance on pyrethroid (PY) insecticides, with more than 2.1 billion PY ITNs distributed in the past two decades, leading to widespread PY resistance. Progressive changes are occurring, with increased deployment of more effective PY-chlorfenapyr or PY-piperonyl butoxide (PBO) ITNs in areas of PY resistance. We performed a critical review of contemporaneous trends in the malaria vector control landscape in sub-Saharan Africa and cost implications associated with use of new chemical classes for improved malaria vector control and resistance management. In 2023, PY-PBO ITNs accounted for 58% of all ITNs shipped to sub-Saharan Africa. Pyrethroid-PBO and PY-chlorfenapyr ITNs are 30-37% more expensive than standard PY ITNs, equating to an additional $132-159 million required per year in sub-Saharan Africa to fund the shift to more effective ITNs. Several countries are withdrawing or scaling back indoor residual spraying (IRS) programs to fund the shortfall. This is reflected by the number of structures sprayed by the US-President's Malaria Initiative decreasing by 30% from 5.67 million (2021) to 3.96 million (2023). Benin is a prime example of a country which ceased IRS in 2021 after fourteen

years of annual spraying. Our economic evaluation indicates that IRS in Benin cost $3.50 per person protected per year, around five times more per person protected per year compared to PY-PBO ($0.73) or PY-chlorfenapyr ITNs ($0.76). While relatively costly to implement, a major advantage of IRS is the portfolio of at least three chemical classes for prospective resistance management. With loss of synergy to PBO developing rapidly, there is a grave danger of overreliance on PY-chlorfenapyr ITNs. Based on current projections, the WHO estimates that key 2030 malaria incidence milestones will be missed by a staggering 89%; in order to enhance the prospects for malaria control and elimination in sub-Saharan Africa, it is imperative to urgently develop a diverse range of insecticide classes for ITNs.

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IVERMECTIN AND *ANOPHELES* GLUTAMATE-GATED CHLORIDE ION CHANNEL INTERACTIONS

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Ivermectin is a novel vector control tool for malaria as ivermectin-treated humans or animals are lethal to blood-feeding *Anopheles* mosquitoes, the vectors of malaria. In fruit flies and nematodes, the target for ivermectin is the Glutamate-Gated Chloride (GluCl) ion channel. However, *Anopheles* GluCl channel and ivermectin interactions have not been well characterized. We have been working with the primary Southeast Asian malaria vectors, *Anopheles dirus* and *Anopheles minimus*, which are the most ivermectin-tolerant and -susceptible *Anopheles* found worldwide. Interestingly, compared to ivermectin parent compound, ivermectin monosaccharide (missing second sugar ring) and ivermectin aglycone (missing both sugar rings) structures impart only partial and no mosquito-lethal effect, respectively. This suggests that there are important binding interactions with the second ivermectin sugar ring and *Anopheles* GluCl. Genomic and cDNA sequencing were used to determine the GluCl sequence and primary splice isoforms present in *An. dirus* and *An. minimus*. New AI techniques utilizing AlphaFold 2.0 software, Schrodinger software, and the A*Star CLICK method were applied to build 3-D *in silico* docking models of *Anopheles* GluCl-ivermectin, -monosaccharide, -aglycone interactions to characterize how ivermectin binds to the GluCl channel of *An. dirus* and *An. minimus*. Indeed, the *in silico* docking models indicate novel *Anopheles* GluCl-ivermectin binding interactions not observed previously during protein crystallography investigation of nematode GluCl-ivermectin interactions. This work will benefit the research community working to advance ivermectin use for malaria control as it will improve our understanding of: 1) the binding and mode of action of ivermectin and *Anopheles* GluCl, and 2) potential mechanisms for ivermectin resistance development in *Anopheles*.

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EFFECTIVENESS OF ECO BIOTRAPS - AN INNOVATIVE LARVAL SOURCE MANAGEMENT VECTOR CONTROL TOOL IN DHARAVI, MUMBAI, INDIA

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In recent years mosquito-borne diseases especially arboviral diseases such as dengue, chikungunya, Japanese Encephalitis, and Zika virus disease are surging leading to an escalating mortality rate. Many efforts are being made to vector control. Innovations in vector control is utmost necessary. The present study presented an eighteen-month of longitudinal investigation of the effectiveness of an eco-friendly EcoBio Trap for vector control tool in two urban slum areas Kumbharwada and Rajiv Gandhi Nagar covering approximately 500,000 population in 8,000 households of Asia's largest slum Dharavi, Mumbai, India. Dharavi is endemic for dengue for several years. A set of one trial EcoBio Trap (with mosquito attractant and anti-larval IGR compound (Pyriproxyfen) and control (without attractant and IGR) was placed 6 to 8 meter apart in the study sites following the World Health Organization (WHO) guideline for mosquito larvicides. The field team comprising of two trained health staff conducted the study with a weekly follow-up period on day 7, day 14, day 21 and day 28 intervals, respectively. One senior staff supervised for quality assurance. Breading instances and larval density (hatching) data was recorded in Microsoft Excel Worksheet and frequency with proportion was tabulated for each follow-up week. The periodic change in breeding and hatching proportions in EcoBio Trap and control has been recorded and compared. Significant higher proportion of breeding instances (OR: 2.0; 95% CI: 1.7 - 2.4; $p<0.0001$) and lower rate of hatching (OR: 0.04; 95% CI: 0.01 - 0.06; $p<0.0001$) in the EcoBio Trap was reported compared with the control arm. The result of survey to assess the people perception on acceptability of EcoBio Trap as a vector control method had showed a positive responses in reduction of mosquitoes biting experience in the community. Alongside, a WHO-recommended silicone-based monomolecular film-based larvicide plus attractant showed comparable results with Pyriproxyfen. A large-scale trial in six locations in Mumbai city including the existing Dharavi sites is underway.

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ANOPHELES ARABIENSIS, A POTENTIAL THREAT TO MALARIA ELIMINATION IN HWEDZA DISTRICT, ZIMBABWE 2023

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In Zimbabwe most malaria cases are reported in rural areas, mainly transmitted by *Anopheles arabiensis, An. gambiae s.s.* and *An. funestus s.s.* In 2018, Hwedza transitioned to malaria elimination phase and 36,044 Deltamethrin-treated nets were distributed to 4,658 households in 5 targeted wards to achieve 100% coverage. Subsequently, Hwedza recorded 737 malaria cases in 2019, 118 in 2021, 105 in 2022, and 64 in 2023. To conduct surveillance against the residual transmission, from August – November 2023, 102 larval and 268 adult mosquitoes were collected around Garaba, Chikurumadziva, Makarara, and Zvidhuri health centers in Hwedza District. Of the 370 mosquitoes morphologically identified and confirmed by PCR, 22.4% were *An. gambiae s.l.,* 19.4% *An. rufipes,* 18% *An. coustani*, 13.5% *An. pretoriensis,* 8.9% *An. demeilloni*, 6.8% *An. funestus s.l.,* 5.7% *An. marshallii,* 1.3% *An. maculipalpis*, 0.003% *An. squamosus,* and 4% remained unidentified. Two *An. gambiae* complex species were identified by PCR, namely *An. arabiensis* (7.8% of the total samples) and *An. quadriannulatus* (9.5%). 5.1% of the *An. gambiae* complex did not amplify using the PCR protocol, requiring sequencing for identification. Pf-ELISA showed that none of the adult-collected mosquitoes were infected. Insecticide resistance tests against Deltamethrin were done on the 64 larval-collected adult specimens, among which 18 (28%) were *An. arabiensis.* These 18 were tested for Kdr and ACE-1 resistance PCR assays and showed no markers of resistance. This study showed a 7.8% relative abundance of *An. arabiensis* after a period of scarcity (median 1.2%) from 2019 – 2022. Although none of *An. arabiensis* caught as adults (11), among which 5 were caught outdoors, were found Pf-infected. As an efficient malaria vector in Zimbabwe, *An. arabiensis* needs monitoring because its escalating abundance amid residual cases may threaten the malaria elimination status of Hwedza. Its exophagic trait can pose challenges for indoor-based vector control interventions. Supplementary vector control tools could potentially complement indoor-based interventions to maintain the malaria elimination status of Hwedza.

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TAILORING MALARIA CONTROL IN ETHIOPIA: HUMAN AND VECTOR BEHAVIOR CREATE DIFFERENT EXPOSURE PROFILES IN HIGHLANDS AND LOWLANDS

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Malaria elimination in Ethiopia is challenged by seasonal worker movement between highlands and lowlands, transmitting parasites and requiring targeted interventions. To understand the effectiveness and limitations of vector interventions, this study evaluated mosquito and human behavior in migrant workers, residents, and highland populations during peak and minor malaria seasons. Hourly CDC light trap collections coupled with human behavior observations were conducted in four highland and four lowland villages (eight households/farm structures per village). Sampling/observations occurred between 18:00 and 06:00 hrs. Exposure was estimated by multiplying mosquito catches inside/outside by the proportion of individuals exhibiting different behaviors during each hour. Adult mosquitoes were morphologically identified (subset confirmed by DNA sequencing). In the highlands, 4,697 *Anopheles* (13 species) were identified. *Anopheles gambiae* s.l. (41.9%), *An. demeilloni* (24.1%) and *An. cinereus* (11.0%) were the dominant species. While lowlands had less mosquito catches (3,220 *Anopheles*) but higher diversity (20 species groups). *Anopheles gambiae* s.l. (36.9%), *An. pretoriensis* (27.9%) and *An. demeilloni* (17.5%) were predominant. Indoor biting rate was highest in highlands (2.5x outdoor), while outdoor biting dominated lowlands. Human behavior data suggested the peak biting risk in early evening (18.00-20.00 hrs.) for both settings. In highlands, 87.3% of exposure occurred indoors in individuals not using bed nets. In lowlands, exposure mostly occurred outdoors, among migrants, outdoor exposure accounted for 74.5% of total exposure, while residents had 65.5% outdoor exposure. High diversity among mosquito vectors, coupled with the variability of human and mosquito behaviors, presents a significant challenge for malaria control. These factors create gaps in preventative measures, allowing malaria to persist. Thus, to achieve optimal control, the limitations of one-size-fits-all strategies must be recognized, and interventions need to be tailored to the diverse spatiotemporal behaviors of mosquito and human.

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COMPARATIVE SUSCEPTIBILITY OF WILD-DERIVED AND LABORATORY-REARED *AEDES* AND *ANOPHELES* LARVAE TO IVERMECTIN: A PRELIMINARY STUDY TOWARD EXPERIMENTAL SELECTION OF LARVAL IVERMECTIN RESISTANCE MECHANISMS

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Administering ivermectin to humans and livestock renders their blood toxic for mosquitoes like *Anopheles* and *Aedes*, offering a promising approach for controlling these vectors. However, the impact of such treatment on larval stages exposed to the drug through contaminated breeding sites is not fully understood. This study looked at how ivermectin affects the development of *Aedes* and *Anopheles* larvae. We exposed laboratory-reared (*An. gambiae* Kisumu and *Ae. aegypti* Bora Bora) and wild-derived (*An. coluzzii* VK5 and *Ae. aegypti* Bobo) larvae to ivermectin concentrations ranging from 1 to 100 ng/ml for 24h, and transferred surviving larvae into free-ivermectin medium to monitor development until adult stage. Parameters measured were: survival, pupation dynamics, emergence rates, and fecundity of the adult females. Four independent replicates were performed. Ivermectin effects were characterized by comparison with larvae raised in control medium. Results indicated that highest ivermectin concentrations (100, 75, and 50 ng/ml) reduced larval survival by over 50% within 24 to 48 hours post-exposure, with varying effects across different strains. Wild-derived larvae showed lower susceptibility to ivermectin compared to laboratory larvae for both *Anopheles* and *Aedes* species. The concentrations leading to 50% larval mortality (4-day-LC50) were 3.65 and 1.86 ng/ml for *Anopheles* VK5 and Kisumu strains, and 15.60 and 2.56 ng/ml for *Aedes* Bobo and Bora Bora strains, respectively. The transition from larval to adult stage was significantly affected, particularly in the Kisumu strain ($p = 0.001$). No significant effects on the number of laid eggs were observed across different strains. Overall, these data showed how lab-raised and wild-derived *Anopheles* and *Aedes* larvae and females are affected differently by ivermectin, highlighting potential implications for vector control strategies. Further investigations are planned to understand potential existing mechanisms allowing wild-derived larvae to better survive than laboratory ones despite the presence of ivermectin in their breeding environment.

6220

UPDATES ON COMMUNITY-BASED BIOLARVICIDING FOR MALARIA CONTROL IN TANGA REGION, TANZANIA

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Malaria remains a disease of great public health importance. Globally in 2022, there were an estimated 249 million cases and 608,000 deaths. Tanzania accounted for approximately 4% of all malaria deaths globally. In addition to mainstream vector control interventions, the country has deployed recently community-based biolarviciding to enhance its efforts toward malaria control and elimination. Biolarviciding is implemented routinely in three councils in Tanga Region: Handeni DC, Tanga CC, and Lushoto DC, representing 'high', 'moderate', and 'low' malaria risk strata/councils respectively, as well as both rural and urban settings. Implementation started in June 2022 following a community-based approach using trained community-owned resource persons (CORPs) to monitor breeding habitats and apply biolarvicide. CORPs are supervised using existing local government structures. Two biolarvicide products produced in-country are used: *Bacillus thuringiensis var. israelensis* (Bti) and *Bacillus sphaericus* (Bs). Application of biolarvicide follows a discontinuous temporal pattern based on rainfall, with three rounds conducted per year. Each round comprises eight weeks of larvae monitoring and biolarvicide application. All three councils have now completed six rounds of biolarvicide application. Programmatic monitoring shows that biolarviciding reduces significantly mosquito larvae abundance and larvae occupancy. Larvae occupancy within breeding habitats across eight weeks of implementation decreased by 66% in round two, 93% in round three, 95% in round four, and 90% in round five. The analysis of the extensive entomological, epidemiological, and costing evaluation to determine the impact and cost-effectiveness of the intervention is ongoing, and will be reported at the conference. These results from an extensive real-world program will inform the decision for future scale-up of larviciding to other councils across the country, and represent an important piece of global evidence, especially with regard to larviciding in endemic rural areas.

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INVESTIGATING THE MOSQUITO MYCOBIOTA: FROM BASIC KNOWLEDGE TO POTENTIAL APPLICATIONS FOR MOSQUITO CONTROL

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Mosquito control is a crucial aspect of public health, especially in regions where mosquitoes pose a threat for disease transmission. Traditional vector control methods such as insecticides have proven effective but are often associated with environmental concerns and the development of insecticide resistance. In recent years, there has been growing interest in alternative approaches. Understanding composition and function of mosquito microbial communities could have profound implications for new vector control strategies. While the bacterial community has been deeply studied, the fungal component is still little appreciated. It is reported that budding yeasts associated with larvae and/or adult mosquitoes are involved in symbiotic associations, but extensive investigations of the fungal community in mosquito breeding sites is still lacking. The present work represents an in-depth characterization of the larval mycobiota in wild mosquitoes. NGS analysis has unveiled a diverse fungal community including Ascomycota (budding yeasts) and Basidiomycota in vector mosquitoes including *Aedes albopictus*, *Culex pipiens* and *Aedes koreicus*. Fungi such as *Wickerhamomyces anomalus*, *Metschnikowia pulcherrima*, and *Candida parapsilosis* were detected across all analysed species, whereas *Hyaloraphidium* and *Microidium* were associated with *Cx. pipiens* and *Ae. koreicus*, respectively. Metagenomic outcomes were confirmed using culture-dependent methods and the isolated fungal strains were processed by headspace solid-phase microextraction combined with gas chromatography-mass spectrometry to extract and analyse the yeast volatile organic compounds (VOCs). Results provide the base for next functional tests of selected fungi, that are aimed at the evaluation of attractant properties towards gravid mosquitoes or entomopathogenic activity against larvae. Fungal blends might be used for the implementation of 'lure and kill' formulations to be released in artificial or natural breeding sites of mosquitoes. Such innovative fungal-based products might contribute to mosquito control through a sustainable 'ready to use' technology.

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BACTERIAL SYMBIONTS IMPACTING THE BIOLOGY AND VECTORIAL COMPETENCE OF MOSQUITOES

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The role of symbiotic microbes of mosquito vectors in the processes of environmental adaptation and resistance to insecticides has been proposed, however the mechanisms by which these processes occur are still unclear. Our group at the University of Camerino, in recent years has focused predominantly on the characterization of the contribution that symbionts offer to thermal adaptation and insecticide resistance to the host mosquito, thus identifying symbiotic bacteria of different mosquito species which seem to reveal a role in both mechanisms. In fact, the exposure of mosquitoes of the *Aedes* (*Ae. albopictus, Ae. koreicus, Ae. japonicus*), Culex (*Cx. pipiens*) and Anopheles (*An. stephensi*) genera to different temperatures has made it possible to identify some bacterial species that seem to allow tolerance to low or high temperatures. Similarly, the analysis of mosquitoes resistant or sensitive to pyrethroids has allowed us to identify potential bacteria that play a role in resistance mechanisms. We have identified a pyrethroid hydrolase potentially underlying these mechanisms. The relevant research in progress will be presented in detail.

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MICROBIAL COMPETITION IN MOSQUITO: POSSIBLE APPLICATION IN MONITORING AND CONTROL

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Wolbachia is an obligate intracellular bacterium naturally found in 60% of all arthropod's species. There are discrepancies in Wolbachia detection, with some studies revealing it in 14% of species while others report negative results, indicating regional variability in infection rates and potential limitations in detection methods. Wolbachia can influence host fitness and vector competence thus a series of application has been developed to decline viral transmission within mosquito host. Recently we have identified Wolbachia in the sylvatic African vector Aedes africanus, a mosquito vector widely distributed throughout sub-Saharan Africa, except Madagascar, where it acts as one of the major vectors of yellow fever arboviruses. We have characterised Wolbachia of Ae. africanus and its relationships with members of the mosquito microbiota, highlighting competition dynamics between Wolbachia and Pantoea.Wolbachia was found in nearly all the specimens of Ae. africanus examined, displaying varying quantities. The phylogenetic analysis via multi-locus sequence typing revealed that this Wolbachia strain belonged to Supergroup B yet exhibited closer resemblance to Wolbachia strains observed in Lepidoptera and Hymenoptera rather than mosquitoes. Fluorescence in situ hybridization analysis revealed Wolbachia localization in both male and female reproductive organs. Moreover, microbiota analysis suggested a potential competition among highlighting competition dynamics between Wolbachia and Pantoea.Whole genome sequencing of the two bacteria is ongoing to better define the dynamics of this competition.

6224

BIOMARKERS FOR MOSQUITO AGE GRADING AND PARITY STATUS OF *ANOPHELES DIRUS*

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Malaria transmission predominantly occurs through the bites of infected *Anopheles* mosquitoes. Female mosquitoes necessitate blood for egg development to initiate oogenesis and vitellogenesis. Recent research has focused on mosquito population age structure, given the consideration of microbial agents targeting mosquito lifespan in disease mitigation strategies. Mosquito age is linked to blood feeding behavior, significantly influences malaria transmission dynamics. Age grading methods rely on changes in insect morphology by the ovary tracheation method, differentiating nulliparous and parous mosquitoes based on the presence or absence of tracheole skeins. Beyond the limitation of conventional morphological techniques, transcriptome profiling of blood-fed and non-blood-fed female mosquitoes offers insights into molecular processes triggered by blood meals, aiding in characterizing mosquito aging and feeding behavior. In this study, lab reared *Anopheles dirus* was utilized for transcriptomic analysis in which several genes have been found to be regulated differently by age and parity status as candidate biomarkers. The candidate genes were validated by RT-qPCR with the controlled age mosquito under laboratory settings. Analyzing age-dependent gene expression in the changes of mosquito biological structure, including the process of completing the gonotrophic cycle, as biomarkers to be implemented for the field validation using wild-caught mosquitoes, eventually serving as indicators for effective vector control and intervention.

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MEMBRIN GENE IDENTIFICATION AND JUVENILE HORMONE PRODUCTION AND MATING EFFICIENCY IN ADULT MALE *CULEX PIPIENS* MOSQUITOES

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In order to successfully implement various vector control programs, such as the sterile insect technique (SIT), on *Culex* mosquito disease vectors, it is crucial to identify the specific genes that can be targeted for male sterilization. Additionally, it is important to determine the locations where these reproductively relevant genes are most concentrated in males. In our previous study, we conducted an RNA-seq and qRT-PCR analysis on the complete genome of the male accessory gland (MAG) of *Cx. pipiens*. This gland is widely recognized as a significant, albeit understudied, reproductive organ. The objective of our investigation was to identify genes that may be elevated and potentially beneficial for adult male sterilization. Subsequently, we selected the gene membrin (CPIJ006096) that is linked to increased expression in young and, consequently, reproductively viable MAGs, for a subsequent functional examination. The initial step involves conducting RNA interference (RNAi) knockdown of membrin (CPIJ006096) to assess the phenotype of *Cx. pipiens* MAG tissue between the wild type and the knockdown. To evaluate the reproductive capacity of male *Cx. pipiens* individuals with knockdown compared to those with wild type, a small cage fertility assay is conducted after analyzing variations in knockdown tissue using a light microscopy. In the test, wild type and knockdown males are segregated in distinct enclosures and given a period of 2-3 days to engage in mating. Subsequently, females are gathered and dissected to measure the rate of sperm insemination in their spermatheca. The spermatheca is monitored to determine the presence or lack of sperm. Ultimately, the MAG tissue of both wild type and knockdown males is analyzed using mass spectroscopy to ascertain the presence or absence of the potentially crucial JH hormone. This analysis aims to establish a connection between membrin activity and the sufficient production of JH hormone in the MAG.

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A RAPID, COST-EFFECTIVE, COLORIMETRIC LAMP ASSAY (CLASS) FOR DETECTING INVASIVE MALARIA VECTOR, *ANOPHELES STEPHENSI*

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Anopheles stephensi, an invasive malaria vector in Africa, threatens to put an additional 126 million people per year at risk of malaria. To accelerate the early detection and rapid response to *An. stephens*i, it is critical to confirm its presence and geographic extent. However, morphological identification may be easily misinterpreted, and existing molecular species assays require specialized laboratory equipment and training to interpret, requiring sequencing confirmation. A colorimetric rapid loop-mediated isothermal amplification (LAMP) assay for molecular *An. stephens*i species identification was developed and optimized. The CLASS assay requires only a heat source and reagents and can be used with or without DNA extraction resulting in positive color change in 30-35 minutes. To determine analytical sensitivity, a 1:10 dilution series of the DNA extract was conducted showing 100% assay sensitivity down to 0.0003 nanograms. To determine specificity, 3 different *An. stephens*i laboratory strains (STE2, SDA 500, UCI), 8 other *Anopheles* mosquito species, and *Aedes aegypti* were compared, and the results indicated 100% specificity across these species. To determine use without the need for DNA extraction, samples included a single mosquito leg, whole adult or larval mosquitoes, and pooled DNA extract from several mosquito species. A total of 1687 individual reactions were tested, and all LAMP assay results were compared against the conventional PCR assay and confirmed through Sanger sequencing. To validate the assay on wild caught specimens, DNA extracted from 12 wild caught, sequence-confirmed *An. stephensi* from Marsabit, Kenya, were tested and the assay was accurate in identifying all the specimens as *An. stephensi.* The assay presents an opportunity to accelerate *An. stephensi* molecular identification and offers a simple, rapid, alternative to existing PCR -based *An. stephensi* species identification strategies. The CLASS assay provides, an opportunity to better understand the spread of the species in Africa and other recently invaded areas, thus accelerating a response to mitigate its impacts on malaria on the continent.

6227

EFFECTS OF TEMPERATURE ON *AEDES* HEAT SHOCK PROTEIN EXPRESSION

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In the last 50 years, increased urbanization, and climate change are believed to have contributed significantly to the increased prevalence of vector-borne diseases such as West Nile, Zika, and dengue. As global temperatures rise, vector-borne diseases are uniquely responsive as insects are ectothermic organisms, meaning that the surrounding environmental temperature modulates the host's body temperature. As mosquitoes adapt to a warming climate, it is paramount to understand what genetic determinants play a role in mosquito thermal tolerance. Thermal stress can initiate a suite of responses that mitigate the effects of extreme heat on mosquito life history traits. One such response, the heat shock response, is facilitated by a family of proteins, known as heat shock proteins, that are well conserved across *Aedes* species. Those genes associated with thermal stress include *hsp70*, *hsp26* and *hsp83*. Understanding how heat shock protein expression varies within and among populations from different thermal ranges is important in assessing the future effects of climate change on mosquito-borne disease transmission. Here, we investigated the effect of temperature on heat shock protein expression by utilizing *Aedes sierrensis*, the western tree hole mosquito, which is the primary vector of dog heartworm. *Aedes sierrensis,* a close relative of the major vector *Aedes aegypti*, is found across a wide swath of the West Coast of North America spanning different thermal regimes. We utilized samples from a common garden experiment where *Aedes sierrensis* mosquitoes collected from across a temperature gradient spanning over 1200 km were reared at various temperatures, RNA was extracted from whole mosquitoes, and heat shock protein expression was quantified via qRT-PCR. The results of this work found variability in heat shock protein expression and determined the role of source thermal environment and rearing temperature on thermal tolerance. Elucidating species-wide targets for future vector control measures is pertinent as public health officials prepare to limit vector-borne disease risk in a warming climate.

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CHARACTERIZATION OF *AEDES AEGYPTI* INFECTION WITH THE NATURALLY ATTENUATED DENV-2D30-7169 VIRUS

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Several dengue virus (DENV) challenge human infection models (CHIMs) have been used to assess the safety and efficacy of dengue vaccines and therapies. However, these have used needle inoculation of the virus, bypassing the natural mosquito vector. Prior research has shown that mosquito saliva can potentiate viral infections and may promote distinct DENV infection outcomes in mouse models. Here, we propose a "natural CHIM" where DENV infected *Aedes aegypti* will be used for human challenge. For safety and feasibility, we chose a cGMP-grade, naturally

attenuated DENV-2Δ30-7169 virus, that was tested in prior FDA-approved CHIMs. DENV-2Δ30-7169 infection was shown to cause mild symptoms (rash) and viremia, but no severe dengue outcomes in humans. An additional benefit of using DENV-2Δ30-7169 is its poor transmissibility back into *Aedes aegypti* by blood feeding. To overcome this paradox for our "natural CHIM", we injected *Aedes aegypti* intrathoracically with 100 DENV-2Δ30-7169 plaque forming units and evaluated viral dissemination by PCR of dissected mosquito salivary glands, heads, abdomen, legs, Malpighian tubules and midgut at days 1, 3, 5, 7, 10, 14, 18, 21, 25, and 30 post-infections. We found that all tissues had detectable virus at day 3 post-infection. Viral titers increased over time, leveling off at day 18 post-infection. Salivary glands accumulated significantly higher viral titers versus midguts and Malpighian tubules from day 7 post-infection onwards. Finally, we detected virus in mosquito saliva by PCR and confirmed its infectivity by salivary gland titration in Vero cell. In summary, we show that DENV-2Δ30-7169 can infect and disseminate within *Aedes aegypti* mosquitoes following intrathoracic inoculation, making this a suitable model to develop a "natural CHIM" using dengue infected mosquitoes.

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OPEN QUESTIONS IN *ANOPHELES* DOSAGE COMPENSATION

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Two recent studies (PMIDs: 37769784, 37774706) provide insights into the process of X chromosome dosage compensation in *Anopheles* mosquitoes. These results confirm that dosage compensation is a process present across multiple Dipteran species and that the mechanism used involves a variation of the evolutionarily conserved male X chromosome upregulation approach. Important findings and limitations of this study, along with deeper analysis of the data and comparisons to dosage compensation in other species, suggest multiple lines of inquiry for future studies. In this work, we interrogate the amino acid structure of SOA/007 for clues to its molecular function, provide a more complete understanding of why binding and gene expression regulation were observed at many sites not located on the male X chromosome, highlight an updated view of the relationship between dosage compensation and sex determination in *Anopheles*, and describe follow-up experiments important for considerations in the creation of vector control strategies that rely upon male mosquitoes. Our aim is to inform future studies that intersect with *Anopheles* dosage compensation.

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NATURALLY OCCURRING RECESSIVE LETHAL ALLELES (RLAS) AND SEX-RATIO DISTORTION IN THE YELLOW FEVER MOSQUITO, *AEDES AEGYPTI*

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Aedes aegypti female mosquitoes are critical public health issues on a global scale, as they are vectors of many arboviral diseases like Zika, yellow fever, dengue, and chikungunya viruses. Currently, prevention relies on effective vector control, which is hindered by rising insecticide resistance. There have been several research efforts, such as using genetic tools for population suppression and population modification—by reducing the female population or making the females resistant to virus transmission, respectively. Studies have reported the presence of recessive lethal alleles (RLAs) on the Y-like chromosome of *A. aegypti*, resulting in sex ratio distortion. Here, we report the discovery of naturally-occurring RLAs on the X-like chromosome. To map these novel RLAs, we generated several genetic strains that will enable rapid identification of the RLA loci through marker-assisted mapping. Upon successful completion, this study will provide insights into the evolutionary forces that led to the occurrence and persistence of sex-linked RLAs. It could also help remove the biting females so only males are released in the previously described genetic control programs.

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REDUCED GENETIC DIVERSITY OF KEY FERTILITY AND VECTOR COMPETENCY RELATED GENES IN *ANOPHELES GAMBIAE* S.L. ACROSS SUB SAHARAN AFRICA (SSA)

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Targeting crucial fertility and susceptibility to *Plasmodium* genes of malaria mosquito with small molecule inhibitors is a promising alternative approach to curb the vector population and transmission down. We identified 4 key potential genes associated both in *Anopheles* reproductive success and ability to transmit *Plasmodium*: *MISO*, *HPX15*, *VG* and *LP*. However, the successful application of this approach would require a comprehensive knowledge of the genes' diversity in natural vector populations to ensure its large implementation. Using whole-genomic SNPs data of the Ag1000G project, we extracted each gene from 2784 wild-caught *Anopheles gambiae* s.l across 19 SSA countries. We performed a population structure-based analysis and estimated the differentiation level and genetic diversity. We also computed neutrality tests and evaluated nsSNPs linkage. We found a significant conservation of the 4 genes in SSA *Anopheles gambiae* s.l. populations. Fst values between species were globally low (<0.051, <0.146, <0.022 and <0.048 for *MISO*, *Vg*, *Lp* and *HPX15* respectively) with the highest divergence consistently observed in *An. arabiensis* populations, reinforcing the principal component analysis where genes in *An. arabiensis* slightly diverged from genes in *An. gambiae*, *An. coluzzii* and their intermediates. Among genes, *MISO* showed less structuration. The low nucleotide diversity within populations (>0.10) and negative Tajima's D values suggest a purifying selection. The observed heterozygosity did not significantly deviate from expectation and provided insights into the low genetic diversity within populations. No associated nsSNPs were found across *MISO* gene, while few low linked nsSNPs with ambiguous haplotyping were found in the other genes. Our results provide rare integrated findings on major malaria vectors' biological factors with their genetic features in natural populations and offer new insights for sustainable malaria control tools development. As reasonably conserved, *MISO*, *VG*, *LP* and *HPX15* could be good targets of small molecule inhibitors for controlling vector populations and lowering global malaria transmission.

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SPATIALLY-EXPLICIT SAMPLING OF *ANOPHELES GAMBIAE S.L* REVEALS FINE-SCALE POPULATION STRUCTURE AND MECHANISMS OF INSECTICIDE RESISTANCE

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Progress in malaria control in sub-Saharan Africa is stalling, partly due to the spread of insecticide resistance in the Anopheline vector. Monitoring the evolution of insecticide resistance alleles and their spatial heterogeneity is important for malaria control programmes, and genomic surveillance has emerged as a pivotal tool for this purpose. Earlier genomics research has typically employed convenience-based sampling, and research has yet to be performed to optimise sampling regimens for malaria vector genomics. In this study, we developed a spatially explicit sampling framework that

considers the underlying ecology to enable sampling mosquitoes with reduced bias. We applied this framework to sample An. gambiae s.l mosquitoes in Obuasi, central Ghana, and performed whole-genome sequencing on 485 individual specimens. In this region, An. gambiae s.l have been documented as highly resistant to pyrethroid insecticides, with emergent resistance to other classes. Our sampling framework allowed us to explore fine-scale population structure at high resolution, detecting isolation-by-distance in An. coluzzii in Obuasi, and finding that at this scale, geographic distance, rather than the underlying ecology, drives population structure. We develop methods to estimate kinship between mosquitoes, finding that polymorphic chromosomal inversions impede the accuracy of established tools. We perform genome-wide selection scans and discover novel mutations in detoxification enzymes that are driving selective sweeps and look to be important for resistance, Gste2-F120L, and Cyp9K1-N225I. We also elucidate the continued evolution of the target of pyrethroid insecticides, the Voltage-gated sodium channel. Overall, we demonstrate that by sampling vectors strategically we can enhance our ability to perform effective genomic surveillance.

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MITOCHONDRIAL SEQUENCES OF *HAEMAOGOGUS* MOSQUITOES FROM TRINIDAD REVEAL PHYLOGEOGRAPHIC RELATIONSHIPS WITH SPECIES ENDEMIC TO THE AMAZON

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Haemagogus species are the primary vectors in the sylvatic cycle for yellow fever and the emerging Mayaro virus. Mosquitoes belonging to this genus are divided into two subgenera (*Haemagogus* and *Conopostegus*), with their distribution geographically restricted to forests of Central and South America and the Caribbean. While one primary vector *Haemagogus janthinomys* is well-studied, most other *Haemagogus* species are understudied. Likewise, there exists limited molecular data which can be used to better understand the taxonomy and evolutionary phylogenetics of this genus. Mitochondrial genomes (mitogenomes) have proved useful in determining phylogeographic associations, constructing phylogenies and taxonomic classification of an increasing number of Culicidae. Here we report the complete mitochondrial sequence of a putative new *Heamagogus* species from Trinidad. This mitogenome is 16, 615 bp long with 78% A-T content and 37 genomic features which is comparable to five *Haemagogus* mitogenomes available in NCBI's GenBank database. Bayesian inference and maximum likelihood using the concatenated 13 protein coding genes from all mitogenomes were analyzed to construct phylogenies and molecular dating estimations. Phylogenetic analyses revealed that the putative new Trinidad *Haemagogus* species diverged from *Hg. tropicalis*, a species restricted to the Brazilian Amazon region ~74 million years ago (MYA) and ~102 MYA from the albomaculatus section of the *Haemagogus* subgenera. This further supports previous taxonomic studies that placed mosquitoes in the subdivision of the *Haemagogus* subgenera into 3 sections (albomaculatus, spledens, tropicalis), with the putative new species being placed into the tropicalis section. These findings highlight the need for future investigations into the phylogenetics and evolutionary studies by encompassing more taxa from the endemic geographic regions where this mosquito genus is found.

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CHANGES IN *ANOPHELES STEPHENSI* DIVERSITY IN MAJOR HUB OF GENOMIC CONNECTIVITY IN ETHIOPIA

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Anopheles stephensi has been established in eastern Ethiopia since 2018, and evidence has shown that the *An. stephensi* in Dire Dawa, Ethiopia is a hub of genetic diversity for the Horn of Africa. *An. stephensi* has been implicated as the cause of a major malaria outbreak in 2021-2022 in Dire Dawa as well. The goal of this study is to elucidate regions of the genome that are changing over time, identify regions of the genome under selective pressure, and to understand what this means for malaria transmission in Dire Dawa. To do this, ten *An. stephensi* from Dire Dawa from 2018 and 2022 will be sequenced via Illumina short read sequencing. Single nucleotide polymorphisms (SNPs) will be identified in each dataset and compared via paired F_{ST} and Tajima's D, as well as principal component analysis. Preliminary data indicates 7.8 million SNPs across the genome in the 2022 dataset. There are 3.5 million SNPs concentrated to the second chromosome and 3.9 million concentrated to the third chromosome. Preliminary principal component analysis indicates that the 2022 population is significantly differentiated from the 2018 population. Ultimately, this data will provide a key look into the *An. stephensi* of Dire Dawa and what is happening to this population over time that could be responsible for increased cases of malaria.

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WHOLE GENOME SEQUENCE DATA REVEALS SELECTIVE SWEEP SIGNALS AROUND MAJOR INSECTICIDE RESISTANCE LOCI IN *ANOPHELES FUNESTUS* POPULATIONS FROM UGANDA

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Insecticide resistance threatens malaria control and elimination in Sub-Saharan Africa. To combat this, novel products, active ingredients and delivery methods are now coming to market and being evaluated in large cluster randomized trials (cRCTs). To maximize the efficacy and longevity of all vector control tools, early detection of resistance mutations in the *Anopheles* vector is crucial. The LLINEUP trial in Uganda (2017–2019), covering 40% of the country in 104 health sub-districts, evaluated the effectiveness of combined pyrethroid and synergist long-lasting insecticidal (PBO) nets. During LLINEUP, a shift in species composition was observed, with *An. funestus* becoming predominant in some regions. We embedded genomic surveillance within the trial with the aim of detecting and tracking insecticide resistance variants. We collected *An. funestus* mosquitoes using Prokopack aspirators and performed whole-genome sequencing on 1149 specimens, obtaining high-quality SNP and haplotype data. Genetic diversity and kinship analyses were indicative of a large and stable population throughout the intervention, this corroborated *An. funestus* density data collected during the trial. Standard approaches for describing genetic diversity e.g. F_{ST}, PCA revealed little genetic differentiation across Uganda. Genome-wide selection scans revealed strong signals of positive selection at a Cyp9k1 gene cluster (8 Mb-X chromosome) and CypP6a (8 Mb-2RL chromosome), both loci previously implicated in pyrethroid resistance. At both loci, haplotype clustering analyses showed a single haplotype shared across the entirety of Uganda. Weak signals of selection corresponding to the eye diacylglycerol kinase and Gste-2 were detected at approximately 13.5Mb on the X chromosome and 76Mb on the 2RL

chromosome respectively. The known in DDT and permethrin resistance associated variants in the *Gste2* locus, L119F and L119V, were identified. Embedding genomic surveillance in cRCTs enables the vector control community to discover putative resistance variants in a timely fashion and also can provide evidence of their impact on vector control tool efficacy.

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CONTINUOUS VITAL SIGN MONITORING OF INDIVIDUALS WITH ACUTE LASSA FEVER USING WEARABLE BIOSENSOR DEVICES

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Lassa fever is a fulminant viral illness associated with high in-hospital mortality. In Sierra Leone, continuous monitoring of critically ill patients is hindered by a lack of equipment and personnel. In this study, we used wearable biosensor devices to remotely monitor hospitalized individuals with confirmed acute Lassa fever (n=30) in order to describe vital sign trends that may be associated with clinical outcome and to evaluate the feasibility of this approach in such a setting. A substantial amount of physiological data had to be discarded for low quality, yielding 8 patients with 558.4 hours of waveform data to be analyzed, with an average of 69.8 hours (12.6 - 133.3 hours) per patient. The median age of participants included in the analysis was 6.5 years (0.4-40 years), 50% were female, the median time from onset of symptoms to admission was 7 days (2-21 days), and rapid malaria test was positive in 50% of participants. The in-hospital mortality rate was 62.5%. Our results show that individuals who died (n=5) had higher mean heart rate (HR; 126 beats per minute) and respiratory rate (RR; 29 breaths per minute), as well as lower mean heart rate variability (HRV; 10 ms), compared to those that survived (63 beats per minute, 22 breaths per minute, and 59 ms, respectively). These findings are align with prior data regarding the relationship between HR, RR, HRV, and mortality in bacterial sepsis. Some interesting physiological phenomena were captured by the biosensors, including an episode of rapid atrial fibrillation that repeatedly was broken by cough-induced increase in vagal tone. Periods of clinical decompensation were able to be identified by captured vital sign changes. Although real-time monitoring of vital signs using wearable biosensors may have the potential to identify decompensations earlier than traditional bedside vital sign collection in a resource-limited setting, we encountered issues with device's data quality. Namely, there were issues with adhesion, connectivity, and rare spurious vital sign readings.

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STANDARDIZED BRIGHTON COLLABORATION CASE DEFINITIONS AND COMPANION GUIDES ON ADVERSE EVENTS OF SPECIAL INTEREST FOR HARMONIZED SAFETY MONITORING OF LASSA FEVER VACCINES

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Lassa virus (LASV) is a zoonotic pathogen causing Lassa fever, a severe hemorrhagic disease endemic in West Africa. The WHO lists LASV as a priority pathogen needing new countermeasures. The Brighton Collaboration has advanced the science of vaccine safety since 2000. The Coalition for Epidemic Preparedness Innovations has funded Brighton's Safety Platform for Emergency vACcines (SPEAC) project to facilitate harmonized safety assessment of novel vaccine candidates for LASV and other priority pathogens with epidemic or pandemic potential. SPEAC conducted landscape literature reviews to generate a list of adverse events of special interest (AESIs) to be monitored for LASV vaccines, including those relevant for maternal immunization studies. These AESIs (https://speacsafety.net/tools/aesi-lists/lassa-fever/) are selected based on their association with immunization or vaccine platforms, theoretical links from animal models, or possible occurrences due to wild virus replication or virus-host immunopathogenesis. A prioritization of AESIs was conducted for the development of standardized case definitions, along with companion guides containing references on risk factors and background rates of these events; diagnostic codes; and structured data collection forms with algorithms to determine level of diagnostic certainty. Currently, 14 case definitions and 12 companion guides, including one for sensorineural hearing loss (SNHL), have been published. SPEAC is digitalizing the data collection forms and case logic algorithms into REDCAP forms and online Automated Brighton Classification (ABC) tools. Six case definitions, covering conditions such as anaphylaxis, generalized convulsion, Guillain-Barré syndrome and Fisher syndrome, myocarditis and pericarditis, SNHL, and thrombocytopenia, will be prioritized for this digitalization process. SPEAC is transforming knowledge and literature into practical tools that support harmonized safety assessment of LASV vaccines from clinical trials to postmarketing studies. All resources are publicly accessible on speacsafety.net and brightoncollaboration.org.

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SEROLOGIC EVIDENCE OF DENGUE AND CHIKUNGUNYA AMONG PATIENTS WITH ACUTE FEBRILE ILLNESS IN GHANA 2016 - 2018

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Dengue and Chikungunya Virus diseases are mosquito-borne tropical diseases, that has globally appreciated. These infections are characterized by febrile illness and a rash in most cases. Patients presenting with symptoms due to these infections in Ghana are usually screened for malaria, typhoid, or Yellow Fever virus. However, screening is rarely done for other possible causative agents such as Dengue fever and Chikungunya virus. A study was conducted in health facilities in seven selected regions in Ghana: namely, Ashanti, Greater Accra, Northern, Upper West, Volta, Western, and Western North regions. Patients who met the case definition were enrolled in the study. A total of 1105 blood samples were collected from patients from 2016 to 2018 and serological analysis of Dengue and Chikungunya viruses were performed with ELISA IgM and IgG commercial kits (Abcam, Cambridge, UK). However, for Chikungunya, only 1053 samples were tested. Analyzed results indicated that the Dengue fever virus and Chikungunya virus showed positivity rates of 61.63% and 40.27% respectively. Indicating the percentage of the study participants exposed to dengue fever virus and chikungunya virus. Greater Accra and Ashanti regions recorded the highest positivity for Chikungunya and Dengue fever viruses respectively. This study sought to establish a differential diagnostic system for Dengue and Chikungunya Viruses and to identify these viruses if they were in circulation in selected health facilities in Ghana.

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MAPPING THE GLOBAL BURDEN OF CHIKUNGUNYA

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Chikungunya is a re-emerging arbovirus that presents a significant global health risk due to its potential to cause severe epidemics, including a recent outbreak in Paraguay. Harmonization of Chikungunya virus (CHIKV) surveillance and reporting systems is needed to improve prioritization of disease control interventions, including recently-approved vaccines. This study aimed to improve understanding of global Chikungunya risk and the burden of disease. Geospatial mapping of the global burden of CHIKV was performed utilizing surveillance data extracted from government and international health agency sources. A novel disease severity grading scale, including three additional high-risk classifications, was developed and applied to evaluate global and sub-national risk. This scale enabled high resolution geospatial modeling of CHIKV and was critical for modeling

subnational trends in Brazil, Paraguay, and India. Disability-adjusted life years (DALYs) were calculated for WHO regions and Americas subregions. An open-source risk map was produced showcasing the global distribution of CHIKV. Available data indicate that over 425,000 cases of Chikungunya occurred globally in 2022, a figure that is 17% higher than presented by recent international reports. CHIKV caused an estimated loss of at least 130,000 annualized global DALYs, with a greater proportion occurring in the WHO South-East Asia Region (SEARO) than previously suggested by the literature. Despite this, vaccine prioritization was low, even in high-burden countries. These estimates confirm CHIKV as an arbovirus that causes significant morbidity in the WHO Region of the Americas and SEARO regions. Disease distribution is spatially and temporally heterogeneous, with a shift in disease burden from the Caribbean to South America over the last decade. A Chikungunya vaccine is likely better targeted towards outbreak response compared to routine immunization.

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NOVEL RT-QPCR ASSAY FOR THE DETECTION AND QUANTIFICATION OF GROUP C ORTHOBUNYAVIRUS

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Group C orthobunyaviruses (GRCVs) are an emerging group of arboviruses transmitted primarily by mosquitoes of the genus *Culex*. Infection with the GRCV causes malaise, fatigue, and loss of capacity for working; symptoms usually last about a week. For military forces deployed in endemic areas, particularly in tropical and subtropical areas of South and Central America, GRCV infections can reduce operational effectiveness and impact the ability to accomplish a mission. In recent years, climate change and demographic factors have been shown to foster the adaptation and proliferation of vector mosquitoes in urban areas, increasing the risk of arbovirus transmission. Hence, the transmission of emerging viruses that have the potential to cause outbreaks and epidemics in these regions, like GRCV, has increased. In previous years, GRCV detections were made by classical tools such as virus culture and serologic tests, which are expensive and time consuming. Currently, there is still lack of molecular tools to detect rapidly GRCV infections in human samples and vectors. Here, we describe a new TaqMan-based reverse transcription quantitative PCR (RT-qPCR) assay for the rapid detection of GRCV by using primers and probe targeting the S genome segment. The real-time PCR assay specificity was confirmed using five GRCV references and eighteen non-GRCV arboviruses. The limit of detection of GRCV was between 0.005 to 0.05 PFU/reaction. The effectiveness of this real-time PCR assay was determined by its ability to detect GRCV positives in acute-phase clinical samples from Iquitos, Peru. The results demonstrate that this newly established RT-qPCR assay may be useful for rapid detection of GRCV infections, allowing better management of the illness and investigation of the epidemiological factors of this emerging tropical pathogen.

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USE OF A NEW WORLD HANTAVIRUS RT-QPCR ASSAY TO DETECT MULTIPLE HANTAVIRUS IN HUMAN AND RODENT SAMPLES IN THE AMERICAS

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Hantavirus pulmonary syndrome (HPS) cases and non-HPS hantavirus infections are often overlooked in South and Central America. Multiple New World hantaviruses have been reported, however, hantaviruses remain underdiagnosed likely due to lack of awareness and testing in some endemic areas. Serological assays and end-point RT-PCR have been previously used to diagnose hantavirus infections. Since the COVID-19 pandemic, the capacity for laboratories in South and Central America to perform molecular diagnostic testing has significantly increased. The Pan American Health Organization and WHO Collaborating Centers in the US, Argentina, Panama and Bolivia, have identified a necessity to validate hantavirus molecular assays that could be implemented in the region. A New World hantavirus RT-qPCR assay (targeting the N gene) developed at the CDC, was tested using multiple New World hantavirus species in the US Centers for Disease Control and Prevention collection including Andes, Black Creek Canal, Convict Creek, Lechiguanas, Laguna Negra, Maciel and Sin Nombre virus, as well as the Old World hantaviruses, Seoul, Hantaan and Puumala viruses. The RT-qPCR detected all New World hantaviruses, while not detecting Old World hantaviruses. The exclusivity of the assay was confirmed by testing with other pathogens: arenaviruses, leptospira, rickettsia and malaria This assay detected hantavirus RNA in human samples collected from acutely ill individuals in Bolivia in 2018 and 2019. Of 14 patients with available clinical data, IgM and IgG antibodies were identified in 12 (86%) and 7 (50%) blood specimens, respectively; 11 (79%)were RT-qPCR positive. Metagenomic next generation sequencing identified Oran, Tunari, Alto Paraguay-like, Laguna Negra, and Lechiguanas hantaviruses from various geographic locations in Bolivia. We report here the New World hantavirus RT-qPCR results and the phylogenetic tree from Bolivia as well as recent data generated in Argentina and Panama with this assay. This work will help improve monitoring of hantavirus circulation in the Americas.

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SEROPREVALENCE OF LASSA AND OTHER EMERGING AND RE-EMERGING VIRUSES CIRCULATING IN HUMANS AND ANIMALS (DOGS AND RODENTS) IN LIBERIA

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Liberia is among the low and middle-income countries that remain the home to Lassa Fever (LF). Like most emerging and re-emerging viral diseases, LF remains a problem due to the limited healthcare infrastructure and poor laboratory-based surveillance system necessary for proper management and control of diseases. Over 70 % of these emerging and re-emerging viral diseases have a zoonotic origin, with more than three-quarters of the emerging zoonosis pathogens originating from wildlife, constituting an ongoing threat to human and animal health, worldwide livelihoods, and economies. The objective of our study was to estimate the prevalence of LF and other emerging and re-emerging infectious diseases among people living in communities known as the Lassa belt in Liberia, their dogs, and rodents that live in close contact with them for seroreactivity. Approximately 6000 serum samples (200 healthy individuals with consent, 200 rodents, and 200 dogs) were collected between January and July 2021 from four regions/counties (Bong, Lofa, Nimba, and Grand Bassa counties), known as the Lassa fever belts. analyzed using a multiplexed MAGPIX assay to detect humans, dogs, and rodents IgG antibodies against a panel of virus antigens. The overall prevalence for LASV and other emerging and re-emerging diseases in the four regions was estimated at LASV, followed by SARS-CoV-2 S, CHIKV E2, and PUUV. The filoviruses, including EBOV, MARV, and SUDV, were extremely low in humans. A similar pattern was observed in the rodents. In the dogs, we observed low reactivity to all the antigens. There was a correlation between LASV GP & NP and SARS-CoV-2 S & NP. Interestingly, we see a correlation between LASV and

humans and rodents, clearly highlighting that there is an interlink between human and rodent transmissible diseases. This shows the importance of using the One Health approach in disease surveillance.

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EVIDENCE OF CO-TRANSMISSION OF ZIKA VIRUS DURING THE 2023 DENGUE OUTBREAK IN BANGLADESH

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Bangladesh saw its worst dengue outbreak in its history in 2023 when more than three hundred thousand people were hospitalized with a case fatality rate of 0.5% the highest in the world of that year. While Zika is a mosquito-borne virus transmitted by Aedes mosquitoes like dengue, it is primarily known for causing severe birth defects, including microcephaly, in babies born to infected mothers. Zika typically causes dengue like mild symptoms in adults. However, it can also lead to serious neurological complications like Guillain-Barré syndrome. Despite detecting the indirect evidence of the Zika virus in archived samples on rare occasions, the absence of a functional surveillance system prevented confirming its presence in any concurrent circulation. We identified a cluster of Zika cases during a diagnostic evaluation study for dengue. We enrolled 185 individuals coming at icddr,b diagnostic unit at Mohakhali, Dhaka from October 15 to December 31, 2023 with dengue-like symptoms including fever for 2-5 days coming for a confirmatory diagnosis. An NS1-based rapid diagnostic test (RDT) was performed as a routine test according to national guidelines. Regardless of their RDT test status, 152 samples were tested later with a commercial RT-PCR kit for the presence of dengue, Chikungunya and Zika viruses. Among them, 32.9% (50/152) were positive for dengue. However, among the negative samples, four were positive for Zika and one dengue-positive sample was found to be co-infected for a total of 3.3% (5/152) being positive for Zika. All of the identified cases were male, living within a kilometre radius of each other and without prior travel history outside of the country in the past two years indicating a local Zika virus transmission in the community. The identification of Zika virus co-circulating with dengue in an outbreak suggested a serious threat to public health in the coming years in Bangladesh. It is urgently needed to conduct emergency sero-surveillance to identify the spatiotemporal clusters of Zika virus and perform effective control measures to prevent the further spreading of Zika virus in Bangladesh.

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ASSOCIATION BETWEEN ANGIOTENSIN-CONVERTING ENZYME 2 SINGLE-NUCLEOTIDE POLYMORPHISMS AND RISK OF SARS-COV-2 INFECTION IN A GHANAIAN POPULATION

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Angiotensin-converting enzyme 2 plays a pivotal role in the development of COVID-19, caused by the novel severe acute respiratory coronavirus 2. Individual susceptibility to COVID-19 has been strongly linked to single-nucleotide polymorphisms in the angiotensin-converting enzyme 2, which may alter its expression or binding affinity to the virus. This study examined a total of 749 SARS-CoV-2-specific IgG seronegative and 890 SARS-CoV-2-specific IgG seropositive individuals obtained from a population-based SARS-CoV-2-specific IgG seroprevalence study conducted between February 2021 and February 2022, using a highly specific and approved Enzyme-Linked Immunosorbent Assay to investigate the association between two important angiotensin-converting enzyme 2 single-nucleotide changes, hypothesized to downregulate angiotensin-converting enzyme 2 levels, (rs2285666-C>T and rs2106809- A>G) and the risk of COVID-19 infection among a Ghanaian population. Extracted host DNA from collected blood samples was genotyped using the Allele-Specific Oligonucleotide Polymerase Chain Reaction technique, with melting curve analysis. Associations between the single-nucleotide polymorphisms and COVID-19 were assessed using logistic regression models. Participants did not differ in terms of demographics and the distribution of allele and genotype frequencies, except for rs2106809 among males. The T-allele of rs2285666 was observed to significantly reduce SARS-CoV-2 infection risk among Ghanaian females. However, having two copies of the T-allele did not offer additional benefits. Interestingly, no association was observed for rs2106809. These findings provide preliminary evidence that suggests that variations in the angiotensin-converting enzyme 2 might influence COVID-19 infection among Ghanaians, aiding ongoing discussions on the COVID-19 genetic basis, which is important to inform strategies and policies for treatment, prevention, risk assessment, and diagnosis.

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CRYPTIC CIRCULATION, PERSISTENCE, AND POSITIVE SELECTION OF YELLOW FEVER VIRUS IN COLOMBIA

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Yellow fever virus (YFV) is a cause of acute febrile illness (AFI) endemic to tropical areas of South America and Africa and transmitted by *Aedes* mosquitoes. In Colombia, YFV causes periodic outbreaks, during 2020 to 2023, we conducted health facility based AFI surveillance in Leticia. The study enrolled 1,460 individuals with AFI of unknown etiology, from which 120 specimens were randomly selected for metagenomic next generation sequencing (mNGS). Complete genome coverage of YFV was obtained from the serum of a 23-year-old male presenting with fever, vomiting, chills, headache and body/muscle pain. It is unknown if the individual received prior yellow fever vaccination. Maximum likelihood tree of all YFV references indicated this strain (LET1450) branched with Bolivian sequences and formed a monophyletic clade within South American genotype II (SamII). This strain's ancestor emerged around 1989 and Skygrid analysis shows that despite a decline in YFV genetic diversity in 1951 coinciding with the beginning of global vaccination efforts, a slight rebound was observed between 1978 and 1985 which corresponded with the emergence of SamII. The subsequent formation of the Peru/Bolivia/Colombia cluster within SamII resulted from positive episodic selection. Examination of the envelope protein identified an A343S mutation under positive selection found exclusively in this SamII cluster. This mutation, situated in an exposed loop of domain III, suggests evasion of vaccine-mediated immunity. Discrete phylogeographic analysis undertaken to identify the putative origin and assess the geographic circulation of the LET1450 strain revealed two major importation events of YFV to Colombia from Peru and Bolivia, but it also revealed that Colombian strains were being transmitted back to Bolivia. Markov jump reconstruction further confirmed that the prevalence of YFV in Colombia is not due to repeated external introductions, but rather results from continuous, cryptic internal circulation. Our study highlights the value of mNGS for determining causes of AFI and for surveilling the emergence of potential vaccine evading strains.

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PERFORMANCE OF THE NG-TEST® IGG/IGM COVID-19 RAPID TEST FOR THE DIAGNOSIS OF SARSCOV2 INFECTION AMONGST HEALTHCARE WORKERS IN BAMAKO, MALI

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Coronavirus 2019(COVID19) represents a worldwide public health emergency with an impact on economic and socio-cultural development. Although the PCR technique remains the gold standard of COVID-19 diagnosis, rapid diagnostic tests (RDTs) are an alternative in resource-limited countries such as Mali. However, adhesion of health care workers to the use of these RDTs still a problem due to the low performance. This study aimed to assess the performance diagnostic of NG-Test® IgG/IgM COVID19 rapid test to reinforce COVID19 case management in Mali. As part of a cohort study amongst health workers (HW), a cross-sectional survey was conducted in May 2022 amongst HW in six health centers and deux university hospitals of Bamako. Sociodemographic and clinical data, Nasopharyngeal swabs and blood sample were collected to determine SARS-CoV-2 infection by RT-qPCR and RDT (NG-Test® IgG/IgM). REDCap application was used for data management, Stata 14 software for data analysis and. KAPPA was used to determine the concordance between the results RT-qPCR (gold standard) and RDT with a significant level at 5%. A total of 917 health workers were included. The prevalence of SARS-CoV-2 infection was 1.3%. The sensitivity was 25%, specificity 76%, Predictive values of positive test 1,4%, Predictive values of negative test 98,7%, with a Kappa of 0.001 for RDT (IgM) compared to PCR. The sensitivity was 25%, specificity 75%, Predictive values of positive tests 1,3%, Predictive values of negative tests 99% with a Kappa of -0.0002 for RDT (IgG) compared to PCR. The NG-TEST® IgG-IgM COVID-19 test performance in the diagnosis of SARSCoV2 infection was very low compared to PCR.

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DETECTION OF NEUTRALIZING ANTIBODIES AGAINST ARBOVIRUSES FROM LIVER HOMOGENATES

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Yellow fever virus (YFV) circulates in a sylvatic cycle between non-human primates (NHPs) and arboreal mosquitoes in Brazil. Passive monitoring of ill or deceased NHPs is a key component of the Brazilian YF surveillance program. Samples from NHP carcasses are usually suitable for molecular tests but not for serological assays. As an alternative to the conventional plaque reduction neutralization test (PRNT) based on sera, we tested the utility of liver homogenates from experimentally infected (with YFV, Mayaro virus [MAYV], chikungunya virus [CHIKV], or mock) mice to quantify PRNTs. Although homogenates from mock-infected mice showed a low level of nonspecific virus neutralization against YFV, MAYV or CHIVK, homogenates from YFV-, MAYV- and CHIKV- infected mice demonstrated significantly higher levels of virus neutralization compared to controls. Receiver operating characteristic (ROC) curves analyses were performed using the median neutralization values of three technical replicates for each infected group separately or collectively. Results showed scores above equal or higher than 0.97 (95% CI equal or higher than 0.89-1.0) for the area under the curve at dilutions 1:20 to 1:80, suggesting that median virus neutralization values effectively differentiated YFV-, MAYV-, or CHIKV-infected groups from controls. Liver homogenates obtained from 25 NHP carcasses (collected during the 2017 YFV outbreak in Brazil) were also tested using both the adapted PRNT as well as rapid anti-YFV IgM immunochromatographic tests. Neutralization activity was detected in 6 NHP samples that were also positive by PCR and anti-YFV IgM tests and one sample that tested negative by PCR and IgM test. Our results demonstrate the feasibility of using liver homogenates as an alternative approach for serological investigation in viral epidemiologic surveillance. Carcasses are convenient samples that can be used for outbreak investigations, and the potential use of liver homogenates in serological tests expands the possibilities for the investigation of outbreaks and epizootics.

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A HIGH-THROUGHPUT LIVE-IMAGE REPORTER FLAVIVIRUS NEUTRALIZATION ASSAY PLATFORM FOR SEROSURVEILLANCE AND VACCINE EVALUATION

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Virus neutralization tests, such as plaque (or viral focus) reduction neutralization tests (PRNT/FRNT), used to measure neutralizing antibodies elicited by virus infection or vaccination are critical tests for diagnostics, vaccine evaluation, and serosurveillance. To significantly improve the time/labor-intensive gold-standard PRNT for many medically important flaviviruses, we have engineered a panel of live-reporter flaviviruses to develop a high-throughput reporter-based micro-focus reduction neutralization test (R-mFRNT). The reporter flaviviruses express a strong tetrameric ZsGreen fluorescent protein within 24-28 hours post cell infection, and the intensive fluorescent viral foci can be accurately measured through a live-image cell cytometry plate reader. All reporter viruses were optimized for reporter stability after multiple cell passages, and validated by genome sequence, reporter RT-PCR, and dual-color (viral antigen and reporter) flow cytometry to be qualified for use in R-mFRNT. We have made more than 12 different reporter-flaviviruses for the R-mFRNT and verified that the neutralization antibody titers obtained from the R-mFRNT using the reporter viruses were equivalent to titers obtained by PRNT using wild-type viruses. The reporter WNV-based chimeric platform used to derive the reporter flaviviruses affords an identical high-throughput R-mFRNT workflow for multiple flaviviruses. So far, we have validated and used the assay for Zika vaccine studies, neutralizing IgM evaluation of dengue and Zika viruses, neutralizing antibody profiling after sequential flavivirus infections, and a serosurveillance of Powassan virus that required processing a large number of samples. We will report an update of the reporter flavivirus panel, including validation and characterization of several newly generated reporter viruses, the workflow of the R-mFRNT, and summary of study outcomes using the assay.

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PREDICTING THE IMPACT OF A POTENTIAL CHIKUNGUNYA OUTBREAK IN MIAMI AND THE IMPACT OF A CHIKUNGUNYA VACCINE

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The chikungunya virus (CHIKV), an alphavirus transmitted primarily by *Aedes* mosquitoes, poses a significant global health threat. In the past two decades, we have seen a notable expansion of CHIKV's geographic reach due to climate changes and increased human mobility amongst others. In the United States (US), a total of 3,941 travel-acquired cases were reported between 2014 and 2016, and in June 2014, the first locally acquired CHIKV case was reported in Florida. A CHIKV outbreak in a big city such as Miami could have detrimental consequences, however, the potential impact has

not been studied so far. With this study, we aim to prepare public health authorities by quantifying both the potential size of an outbreak and the effectiveness of a reactive vaccination program. We developed a dynamic transmission model with a host-vector structure calibrated to incidence data from Puerto Rico using the Generalized Reduced Gradient (GRG) algorithm. The mosquito parameters within the model were climate-dependent and were derived from daily temperature, precipitation level, and relative humidity data specific to Miami. Model outputs suggest that with current routine vector control and climate conditions, approximately 10% of the local population of Miami could become infected with CHIKV in the first year after a potential outbreak. Implementing an emergency response vaccination program with 20% vaccine coverage would reduce the number of infections by 83%. Our model results show that an emergency response vaccination program can be effective during a CHIKV outbreak, especially if the outbreak is detected early on and the program is initiated promptly after detection. Future research should explore the applicability of these findings in other locations where *Aedes* mosquitoes are present.

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CHIKUNGUNYA INFECTION IN PERUVIAN PATIENTS WITH ACUTE FEBRILE ILLNESS: PREVALENCE AND CLINICAL CHARACTERISTICS

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Chikungunya fever (CHIKF) is an emerging zoonotic disease that presents as an acute febrile illness (AFI), classically associated with arthralgia. Due to limitations regarding availability of diagnostic tests and health system access, cases may be underreported. Therefore, we performed a study to evaluate in the northern coast of Peru to measure its prevalence and describe their clinical manifestations. We conducted a 2-year cross-sectional study in Piura region, Peru, located in the north coast of Peru, neighboring Ecuador, and Colombia. Patients presenting with AFI to primary care clinics were included. Serum plasma collection was performed in all participants and evaluated for chikungunya virus (CHIKV) serology and molecular diagnosis with RT-PCR. Our study location was also endemic for Dengue virus (DENV); thus, IgM was also analyzed for coinfection evaluation. A total of 688 samples were collected and 669 were analyzed. CHIKV was detected in 60 (8.89%) samples through serology. Only 5% of the cases were identified with RT-PCR. CHIKV cases were most reported among participants aged 18-29 years old (30.0%) and the most common symptoms reported were headaches (68.0%), myalgias (54.4%) and arthralgias (50.8%). Coinfection with DENV was also reported (5.0%) among CHIKV samples. We report a significant prevalence of CHIKV in a northern coast of Peru and a considerable prevalence of CHIKV-DENV coinfection. These results highlight the need for improved surveillance of CHIKV, as it is a continuously transmitted pathogen in various parts of Peru. To accurately detect CHIKV, epidemiological surveillance should be strengthened using reliable diagnostic methods, as clinical symptoms may be unspecific.

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A COMPARISON OF THREE DIAGNOSTIC TESTS TO DETECT HUMAN PAPILLOMAVIRUS IN ASYMPTOMATIC WOMEN'S ENDOCERVICAL SAMPLES FROM 2022 TO 2023 IN A NORTHERN PERUVIAN REGION

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Infection with the Human papillomavirus (HPV) is one of the causes of cervical carcinoma, which is on the rise. There has been no improvement in the development of research tools or testing methods. The Pap smear is the only method used to detect dysplasia and cervical cancer in developing countries. Therefore, we compared the concordance and reliability of three HPV tests and the Papanicolaou smear as primary cervical cancer screening methods. This study included 135 patients co-tested with HPV test and Pap smear simultaneously. The results of sensitivity, specificity, Positive predictive value (PPV) and Negative predictive value (NPV) and Cohen's Kappa index (agreement) were compared with the Gold standard. The tests were coded for statistical analysis (Sequencing "Test1", a commercial DNA_Flow kit "Test2", Multiplex PCR "Test3") and the Pap smear "Test4". We detect that 66.67% (90/135) were positive for HPV and 33.33% (45/135) were negative for HPV. The 17% (24/135) were positive PAP results with high-grade lesions, of which 25% (6/24) of women were HPV positive (6/24) and 75% (18/24) negative for HPV. The Test1, Test2 and Test3 detected; 82(60.74%), 97(71.85%) 91(67.41%), respectively. The sensitivity of Test2 (96.67%) was higher, and the specificity (77.78%) and NPV (89.69%) were lower compared to the other methods. Test1 presented greater specificity (100%) and NPV (100%) compared to the other methods. The Test1 showed one k=0.87, very good agreement, and the Test2 and Test3 showed k=0.78 and k=0.75, respectively, one moderate agreement. Also, we observed that higher rates of multiple infection (71.13%) and (70.33%) were obtained through Test2 and Test3, respectively. Infection rates were high in Test1. There is a difference between the Pap test and the HPV test. These tests must be accompanied by HPV tests. All HPV tests showed different sensitivities greater than 90% when compared. It is important to take these data into consideration to avoid false positives and negatives.

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PREVALENCE OF HEPATITIS D VIRUS INFECTION AND ASSOCIATED FACTORS AMONG HEPATITIS B VIRUS PATIENTS FROM SELECTED HOSPITALS IN ACCRA

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The most severe form of viral hepatitis infection is caused by co-infection of hepatitis B and D viruses (HBV and HDV) simultaneously or superinfection of hepatitis D virus on B infected patients. In 2021, total global estimate for HBV infections was 262,240000; out of which 1,994000 were newly diagnosed infections. However, in the same year, an estimated total of 69,512000 HBV infections was reported for Africa, and 187,000 were new infections. Magnitude of HDV infection is the fast progression of disease to liver cirrhosis, hepatocellular carcinoma (HCC) and high mortality rate, and no information known in our hospitals. Aim of the study was to determine the prevalence of HDV and its associated risk factors among HBV patients from selected hospitals in Accra. It was a cross sectional purposive study in four selected hospitals in Accra, Ghana. A total of 152 eligible participants were enrolled. Serum marker HBsAg was confirmed for each blood sample and the nucleic acid was extracted and purified from the positives. Molecular amplification assays were used on the positives and high yielding

nucleic acid positives were sequenced, and the phylogeny determined. Prevalence of HDV in the total number of participants screened was 1.4% (2/144). Out of the eligible participants who enrolled (152), 8 tested negative for serum marker, HBsAg. Genotype of the sequenced HDV positive was HDV-1. There was association between age, HBV and HDV infections with their p-values 0.022 and 0.037 respectively. An association was established between multiple sexual partners and HDV infection with a p-value 0.039. Males were mostly infected with the HBV; 9 of them having HCC. Among the age groups, 30 to 39 years were the most infected with HBV (28.3%). The 2 male HDV positives were within this age group; and had multiple sexual partners. The 1.4% prevalence of the HDV infection suggest the presence of the virus among the participants and presents a public health threat in the study communities which are endemic for HBV. We advocate awareness creation through education, HBV screening and vaccination for all, especially, young adults in HBV hyperendemic countries.

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ACCURACY OF PHYSICIANS' CLINICAL DIAGNOSIS OF DENGUE AMONG PATIENTS PRESENTING TO EMERGENCY ROOMS — PUERTO RICO, 2012-2022

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Clinically diagnosing dengue is challenging due to overlapping symptoms with other febrile illnesses. Warning signs predict progression to severe disease & warrant admission for treatment with protocolized therapy. The Sentinel Enhanced Dengue Surveillance System enrolls patients presenting with fever or respiratory symptoms to 3 emergency departments & urgent care clinics in Puerto Rico, collecting clinical data & samples for pathogen identification. We compared the accuracy of physicians' clinical diagnosis to laboratory-confirmed dengue, defined as a positive RT-PCR ≤7 days or a positive IgM, with concurrent negative Zika testing, ≥4 days after symptoms onset. We considered "dengue" a correct diagnosis. Non-dengue or nonspecific diagnoses were considered incorrect. Among 43,608 participants, 1,432 (3.3%) had laboratory-confirmed dengue. Clinical dengue diagnosis had a sensitivity, specificity, positive predictive value, & negative predictive value of 40.7%, 98.2%, 43.9%, & 98.0%, respectively. Sensitivity was highest among children 10-19 yr (53.5%) & lowest among children 1-4 yr (17.2%) & adults ≥50 yr (20.9%). More dengue warning signs correlated with higher clinical diagnosis sensitivity ($p<0.001$), reaching a maximum sensitivity of 64.0% with ≥5 warning signs. Sensitivity did not vary by specific warning signs, comorbidities, or seasonality. Sensitivity was similar during dengue epidemic years (2012-2013, 44.8%) compared to non-epidemic years with dengue transmission (2019-2022, 37.9%, $p = 0.06$). Among participants with dengue & ≥1 warning sign, hospitalization rates were higher in participants with correct diagnoses vs. incorrect (77.8% vs. 23.5%, $p <0.001$). Among 849 participants with dengue & incorrect diagnoses, the most common misdiagnoses were "viral syndrome" (n = 438, 51.6%), "fever not otherwise specified" (n = 227, 26.7%), & "pneumonia" (n = 75, 8.8%). Limited sensitivity in physicians' clinical diagnosis compared to laboratory testing resulted in inappropriate triage. Clinical training & dengue rapid diagnostic testing could improve diagnosis & increase rates of appropriate care.

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GENETIC CHARACTERIZATION OF INFLUENZA AND SARS-COV-2 IN THE DEPARTMENT OF DEFENSE BENEFICIARIES DURING THE 2023-2024 SEASON

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The Department of Defense (DoD) Global Respiratory Pathogen Surveillance Program conducts testing on respiratory specimens from a worldwide network of sentinel sites using PCR-based assays and next-generation sequencing (NGS) to detect and characterize respiratory pathogens. Analyses aid in the annual selection of influenza vaccine strains and help define the impact of influenza and SARS-CoV-2 in the DoD. The program collects respiratory specimens and metadata from DoD active duty and beneficiaries with influenza-like or COVID-19-like illness symptoms across 100+ global sentinel sites. PCR confirmed influenza and SARS-CoV-2 positive specimens are further characterized by NGS. In combination with partner laboratory data, phylogenetic analyses and lineage determinations are performed to assess the genetic changes occurring in these viruses. 487 influenza viruses were analyzed, including 257 A(H1N1)pdm09, 151 A(H3N2), and 79 B/Victoria. Among A(H1N1)pdm09 viruses, 70 were clade 5a.2a and 187 were 5a.2a.1. For A(H3N2), one was clade 2a.3a and the remaining 150 were 2a.3a.1. All B/Victoria viruses were clade V1A.3a.2. For SARS-CoV-2, 685 specimens were sequenced; lineages identified included one BA.2, 36 BA.2.86, two CH.1.1, 125 EG.5, 120 HV.1, 195 JN.1, 74 XBB.1.16, 57 XBB.1.5, 38 XBB.1.9, 24 XBB.2.3, and 13 other recombinant viruses. Influenza activity was moderate for the 2023-2024 season. Circulating strains for A(H1N1)pdm09 and B/Victoria closely matched the vaccine strains genetically and antigenically, however the A(H3N2) strains drifted slightly therefore the influenza vaccine A(H3N2) strain was changed from a clade 2a virus to a 2a.3a.1 virus. SARS-CoV-2 activity was also moderate with lineage diversity remaining high throughout the season. Lineage EG.5 predominated early in the season while JN.1 predominated later in the season.

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RECONCILING HETEROGENEOUS DENGUE VIRUS INFECTION RISK ESTIMATES FROM DIFFERENT STUDY DESIGNS

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Revealing rates at which susceptible individuals contract a pathogen, known as the force of infection (FOI), is crucial for evaluating transmission risk and reconstructing the distribution of immunity within populations. For dengue virus (DENV), reconstructing exposure statuses is particularly important due to the strong association between prior exposure and severe disease risk, and potential detrimental effects from vaccinating DENV-naive individuals. Various study designs can be employed to measure FOI. Longitudinal cohort studies are considered the gold standard, directly tracking the transition of individuals from seronegative to seropositive states due to incident infections (seroincidence). Cross-sectional studies can provide FOI estimates by comparing seroprevalence

across different age groups, while FOI can be inferred from the ages of reported cases. However, agreement between these methods has not been adequately assessed. Drawing from 26 years of data obtained from cohort studies and hospital-attended cases in Kamphaeng Phet province, Thailand, we estimated annual FOI between 1994 and 2019 of the same population. We observed highly inconsistent FOI estimates from the three sources (seroincidence, seroprevalence, and case counts). Annual FOI estimates derived from seroincidence were 1.94 to 3.77 times higher than those derived from reported cases. Although the correlation between seroprevalence-derived and case-derived FOI was low (correlation coefficient=0.20), no systematic bias was detected. Through comprehensive simulations and theoretical analyses, we demonstrate that discrepancies between the estimates can arise from failing to account for complexity in anti-DENV antibody kinetics, assay noise, and variations in infection risk across ages. Extending standard inference models to incorporate these factors reconciled the FOI and susceptibility estimates. Our findings underscore the value of comparing inferences across multiple data types to uncover additional insights that may not be attainable through single data type analyses alone.

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EXPANSION FACTOR ESTIMATES OF DENGUE UNDERREPORTING IN ENDEMIC COUNTRIES: A SYSTEMATIC REVIEW

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There is a substantial burden of dengue, with the 3 largest annual epidemics globally reported since 2019. Dengue is commonly underreported in passive surveillance systems, and expansion factors (EF) are often used to correct for this. An expansion factor of 10 means that for every 1 reported case there are a total of 10 cases, including 9 unreported cases. We conducted a systematic literature review of the dengue literature to identify references calculating EF or reporting unique EF or the data needed to derive EF. We searched Embase, MEDLINE, Cochrane Library, Latin American and Caribbean Health Sciences Literature from 1995-2022, and the gray literature to identify dengue EF for endemic countries using pre-defined search terms and inclusion/exclusion criteria. We identified 31 references from 22 countries (Latin America [LATAM], n=9; Asia Pacific [AP], n=13). In total, 290 EF were identified (LATAM, n=106; AP, n=185), 87% (n=252) of all EF were calculated using country-specific empirical data, whereas 13% (n=39) were derived using expert opinion or by extrapolation. The most EF identified were for Thailand (n=45), Cambodia (n=32), and the Philippines (n=28). Of identified EF, 48% (n=140) pertained to symptomatic cases (EF range: 0-265), 21% (n=61) to hospitalized cases (EF range: 0.3-10.6), 13% (n=37) to combinations of hospitalized and outpatient cases (EF range: 2-288), 10% (n=29) to asymptomatic infections (EF range: 3-318), and 7% (n=20) to outpatient cases only (EF range: 3.7-178.8). Just 1% (n=3) of EF pertained to fatal cases. Only 3 studies (2 involving expert opinion) stratified results by a public or private facility, and all reported higher EF in private settings. In summary, we identified EF for only 22 of >100 dengue endemic countries and observed variability with how EF are derived across studies.

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HIGH PREVALENCE OF HEPATITIS B VIRUS AMONG PREGNANCY WOMEN IN GUINEA

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Hepatitis B virus (HBV) infection poses a significant global challenge, particularly in developing countries. While efforts to control HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases progress, hepatitis B emerges as a major public health issue. HBV infection during pregnancy carries a high risk of vertical transmission, negatively affecting both mother and child. Our study aimed to assess the prevalence of HBV in pregnant women and identify associated risk factors. We conducted a cross-sectional observational study from 1 July 2020 to 30 August 2021, involving a random sample of 5,000 pregnant women attending antenatal clinics across the country, encompassing rural and urban areas. The study, funded by a World Bank health project, collected capillary whole blood (50 µL) from the fingertip using a pipette for serum testing. The Elisa test served as a confirmatory method. We gathered data on socio-demographic characteristics and risk factors via a questionnaire developed with the Open Data Kits (ODK) application, analyzing samples using chemiluminescence. Statistical analysis utilized Pearson's chi-square or Fisher's exact test, with a significance level set at $p < 0.05$. We employed stepwise multiple logistic regression to identify HBV risk factors in pregnant women. The surveyed pregnant women, predominantly under 35 years old (90.2%), with 30.7% under 21 and 59.5% between 21 and 34, were mainly illiterate (61.8%) and married (95.8%). The study revealed HBsAg prevalence at 19.64% (95% CI [18.53%, 20.80%]) and HBeAg prevalence at 2.49% (95% CI [2.08%, 2.97%]). Significant risk factors for HBV infection included place of residence, education level, hepatitis B vaccination history, number of parities, and history of endoscopic examinations. The study indicates a high prevalence of HBsAg among pregnant women in Guinea, underscoring the need for the PMTCT programme to enhance systematic screening and vaccination against HBV during antenatal visits.

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INFORMING AN INVESTMENT CASE FOR JAPANESE ENCEPHALITIS VACCINE INTRODUCTION IN BANGLADESH

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Japanese encephalitis virus (JEV) circulates endemically in Bangladesh and the country is set to introduce JEV vaccine. However, knowing how best to deploy the vaccine has been hampered by an insufficient understanding of key aspects of JEV ecology, including the spatial heterogeneity in risk, and risk factors for infection. We conducted a national seroprevalence study where we visited 57 communities around the country and collected blood from randomly selected individuals (N=2,938). The blood was tested for anti-JEV IgG antibodies using a novel Luminex platform assay that

limits cross-reactivity with dengue virus. We found 3.4% (95%CI: 2.8-4.1) of participants had antibodies against JEV. We used spatially explicit mathematical models to predict risk for infection and estimated that on average 215,000 (95% CI:160,000-300,000) people get infected each year. Infection risk was greatest around pig-raising communities. For each 10 additional pigs within a 5km radius we found an increase of 1.02 in the odds of being seropositive (95%CrI:1.01-1.03). This study provides the basis to identify regions in the country where vaccine deployment would be most beneficial and, will allow us to assess the impact of different approaches in terms of health outcomes (infections, cases, deaths, and disability life-years averted) per doses used.

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DENGUE IN AMAZONAS: UNDERSTANDING SPATIOTEMPORAL DYNAMICS AND SEROTYPE CIRCULATION

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Peru is currently facing its worst dengue outbreak on record, with Amazonas among one of the most severely affected regions, reporting 3195 cases in five of its seven provinces in 2023. This study analyzed the spatiotemporal dynamics of dengue and climate effects in Amazonas from 2000 to 2023 and identified the circulating serotypes utilizing 420 serum samples. Climate data was acquired from NASA MERRA-2, a global high-resolution dataset. Serotype detection was performed using multiplex reverse transcription polymerase chain reaction (RT-PCR). Statistical analysis was executed with R software v.4.3.1. According to the data, major dengue outbreaks were reported in Bagua, Utcubamba, and Condorcanqui provinces between 2008 and 2011. In 2020, after the introduction of Cosmopolitan DENV-2, cases increased dramatically and expanded to Bongará (Jazán) and Chachapoyas (Balsas). By 2021, DENV-1 (46.19%) and DENV-2 (53.81%) were co-circulating across all five provinces, and the latter serotype was associated with complex clinical manifestations of the disease ($p = 0.004$). Although Bagua, Condorcanqui, and Utcubamba showed no significant correlation between incidence and climatic variables, principal component analysis (PCA) revealed these endemic regions have favorable conditions for year-round transmission. On the other hand, Chachapoyas showed a weak association between incidence and minimum temperature ($rho = 0.17$, $p = 0.03$), relative humidity ($rho = 0.15$, $p = 0.05$), and precipitation ($rho = 0.18$, $p = 0.01$) at 0-1-month lag, this implies that factors beyond climate, disrupting sanitation and facilitating population movement, played a more significant role in dengue dynamics. In conclusion, the increase in incidence and cases with warning signs were associated with the DENV-2 serotype and other factors such as hydrogeological events could have contributed to the expansion of the disease. This underscores the need for local control and prevention programs to grasp the extent of the disease and factors influencing vector establishment and arbovirus transmission.

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NEURODEVELOPMENTAL OUTCOMES IN CHILDREN WITH AND WITHOUT ZIKA, DENGUE, AND OTHER FLAVIVIRUS EXPOSURE, ZIKA EN EMBARAZADAS Y NIÑOS, COHORT, COLOMBIA

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Congenital Zika virus (ZIKV) infection is associated with severe birth defects and adverse neurodevelopmental outcomes; there is less evidence for these outcomes for dengue virus (DENV) and other flaviviruses. We aim to describe neurodevelopmental outcomes up to 18 months of age among children in Colombia by confirmed ZIKV, DENV and other flavivirus exposure *in utero* and by reported microcephaly or any brain or eye abnormality. Data are from the prospective cohort study Zika en Embarazadas y Niños, in which pregnant women were enrolled 2017-2018 and their children followed until 2020. Pregnant women were tested for ZIKV, DENV, and other flaviviruses using the Trioplex Real-time RT-PCR Assay, ZIKV *Detect* 1.0 or 2.0 IgM Capture ELISA Kit assays, and/or the Panbio Dengue IgM Capture ELISA assay. Child development in cognitive, language, and motor areas was assessed at four timepoints (6, 9, 12, 18 months) using the Bayley Scales of Infant and Toddler Development (BSID-III). Confirmed developmental delay was defined as BSID-III scores > 2SD below the mean in one area or > 1.5SD below the mean in two or more areas; "at risk" was defined as >1.5 - <= 2SD below the mean in one area. Of 732 children enrolled with at least one follow-up visit and a BSID-III result, 67 (9%) were exposed to ZIKV *in utero,* 11 (2%) were exposed to DENV or other flavivirus infections. Among ZIKV-exposed children, 19% had a confirmed delay and 39% were at risk for delay. Among DENV- or other flavivirus-exposed children, 9% had a confirmed delay and 45% were at risk. Among unexposed children, 19% had a confirmed delay and 43% were at risk for delay. Among 35 children with microcephaly or any brain or eye abnormality, 37% had a confirmed delay. Among 697 children without these birth defects, 18% had a confirmed delay. Similar proportions of developmental delay were observed between children who were exposed vs. unexposed to flaviviruses. There was a higher prevalence of developmental delays among children with certain birth defects. All young children, including those with infectious disease exposure in utero, should receive recommended screenings and prompt referrals for developmental delays.

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QUANTIFYING THE IMPACT OF MASS DOG VACCINATION ON PUBLIC HEALTH OUTCOMES IN TANZANIA

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Dog-mediated rabies causes ~59,000 human deaths annually, mostly children, with the highest disease burden in Africa and Asia. Rabies is fatal upon onset of symptoms, but disease progression can be halted with prompt use of post-exposure prophylaxis (PEP) following a high risk bite. 'Zero by 30' is a global strategic plan that aims to end human deaths from dog-mediated rabies by 2030 using a One Health approach, and encompasses the use of PEP for human bite victims and mass dog vaccination (MDV) to interrupt dog-to-dog transmission. The strategy also advocates for the use of integrated bite case management (IBCM) as a One Health surveillance approach that promotes inter-sectoral collaboration between human and animal health workers. IBCM has been implemented across four regions in Tanzania since 2018, and using this data we describe the epidemiology of rabies in Tanzania over a six-year period, with detailed information on high risk bites, PEP use and animal investigations. In addition, the implementation of a large MDV trial across Mara region offers the opportunity to explore the impact of MDV on public health outcomes such as PEP use and human rabies deaths, by comparing MDV trial districts prior to and post MDV implementation and by comparing regions with and without sustained MDV. Specifically, in Mara region the human rabies mortality rate is significantly lower at 0.14 (0.06 - 0.21) per 1,000 dogs compared with other regions [Morogoro: 0.49 (0.32 - 0.65); Lindi 0.98 (0.52 - 1.42) ; Mtwara 0.74 (0.40 - 1.08)], and demonstrates the impact of MDV on reducing human rabies deaths. MDV is known to interrupt dog-to-dog rabies transmission, however, the impact of MDV on public health outcomes has rarely been demonstrated at scale in African settings. As we approach 2030, robust evidence on the effectiveness of MDV is required if countries are to implement rabies elimination strategies to achieve this

goal. Public health policies often focus on interventions to prevent rabies onset in bite victims through PEP, however, ending human deaths from dog-mediated rabies will only be achieved by a One Health approach to eliminate the disease in the source population.

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CHARACTERIZING DENGUE SEROPREVALENCE AND HETEROGENEITIES IN TRANSMISSION INTENSITY IN GHANA

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There has been no confirmed case of dengue in Ghana to-date, and the risk of infection is unknown. This is largely on account of limited dengue surveillance in the country. To determine the historical circulation of dengue and reconstruct the immunity profile of the population, we conducted an age-stratified seroprevalence study using archival samples obtained from a representative SARS-CoV-2 serosurvey in three major cities.
An Enzyme-Linked Immunosorbent Assay (ELISA) was used to measure IgG antibody levels against purified dengue particles (ELISA-1). A subset of samples was also tested by ELISA to detect IgG against the recombinant nonstructural protein (NS1) of dengue (ELISA-2) (n=200) and Plaque Reduction Neutralization Test (PRNT) for all 4 dengue serotypes (n=69). We used a Bayesian approach to reconstruct all results obtained in the study and estimate the force of infection of dengue assuming a time-constant transmission.
1486 plasma samples were tested from Kumasi (n= 477), Accra (n= 490), and Tamale (n= 519). The estimated sensitivity and specificity of the IgG ELISA -1 assay compared to the PRNT were respectively 83% (95% CrI 78-88) and 89% (95% CrI 80-97), while the IgG ELISA-2 assay had a sensitivity of 20% (95% CrI 12-30), and a specificity of 99% (95% CrI 94-1). We estimated large heterogeneities in dengue transmission intensity across locations. A higher average annual per-capita risk of dengue infection was estimated in Tamale [0.071 (95% CrI 0.056-0.096)] compared to Accra [0.026 (95% CrI 0.021-0.033)] and Kumasi [0.005 (95% CrI 0.001-0.008)]. On average, we estimated that respectively 43%, 11%, and 70% of the Accra, Kumasi, and Tamale populations have been exposed to dengue. This study provides evidence that dengue has been circulating at different endemic levels across Ghana, with higher circulation in locations close to Burkina Faso, which has recorded Africa's largest dengue outbreaks to date. There is hence the need for enhanced passive and active surveillance to monitor the circulation and potential emergence of dengue outbreaks in the country.

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LESSONS LEARNED FROM GEOGRAPHIC INFORMATION SYSTEMS FOR INFECTIOUS DISEASES RESEARCH AND SURVEILLANCE

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WRAIR-Armed Forces Research Institute of Medical Sciences (WRAIR-AFRIMS) collaborates closely with public health partners in Nepal, the Philippines, Thailand and other areas in Southeast Asia, forming an infectious disease research and surveillance network. Medical research and surveillance often entail the collection of vast amounts of data, which are then analyzed for clinical and statistical significance, as well as for generating hypotheses. Geographic Information Systems (GIS) technology emerges as a valuable tool for researchers and epidemiologists, facilitating the graphical representation of infectious disease outbreak results in a universally understandable manner, displaying both temporal and spatial aspects. WRAIR-AFRIMS utilizes GIS-based procedural visualization for conducting infectious disease research and surveillance, generating crucial insights necessary for decision-making at local, national, and international levels. WRAIR-AFRIMS' Virology department integrates clinical and laboratory data related to respiratory illnesses, SAR-CoV2, febrile and vector-borne infections (FVBI) including geolocation data on thousands of samples collected annually. Employing GIS software such as ArcGIS and QGIS, they create visual maps illustrating the spread of infectious diseases over time and surveillance areas such as FVBI and respiratory surveillance. These maps facilitate the analysis of spatial patterns encompassing disease incidence, prevalence, and distribution. The resulting data enables authorities to monitor disease trends, detect anomalies, and allocate resources effectively for targeted interventions. Through collaborations facilitated by WRAIR-AFRIMS, GIS technology has advanced in monitoring infectious diseases in real-time, enhancing the accuracy of disease risk assessments, and supporting decision-making processes. These efforts contribute to improved communication of surveillance findings to stakeholders and the public, ultimately bolstering public health responses and outcomes.

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THE IMPACTS OF COVID-19 ON THE TREND OF MEASLES OUTBREAK IN NIGERIA

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The COVID-19 pandemic that started in 2019 is one of the worst pandemics that affected both developing and developed countries. Measles is a vaccine-preventable disease caused by a virus. It occurs more in children. This study aims to look at the implications of the COVID-19 pandemic on the reportage of Measles and on the uptake of the Measles vaccine in Nigeria. Data was extracted from the Nigeria Centre for Disease Control (NCDC) Measles situation report. Measles situation reports from 2018-2023 and COVID-19 reports for 2020-2022 were extracted and used in this study. The total number of confirmed cases of Measles in Nigeria was 5,067 in 2018, 28,440 in 2019, 9,316 in 2020, 10,096 in 2021, 11,433 in 2023. There was a 67.3% decrease in the number of confirmed cases in 2020 with a subsequent gradual increase of up to 19% as of 2023. The percentage of confirmed cases that were not vaccinated was 53.3% in 2020 with a significant rise to 82.2% in 2021 and a subsequent decline to 73% in 2023. The percentage of children between age of 9-59 months that were confirmed with measles was 58.7% in 2020 with an increase to 75% in 2021 and a decline to 64% in 2023. In 2020, a total of 88,414 cases of COVID-19 had been recorded. In 2021, there was a rise in the figure by 168.7% to 237,561 and in 2022, the number of confirmed cases rose by only 12% to 266,415. While COVID-19 was on the rise, there was a decrease in the number of confirmed cases of Measles. This could be due to the under-reportage of the incidence of measles at this period among other reasons. There was also a significant increase in the percentage of unvaccinated Children who were affected by the disease. This could be due to decrease in the uptake of vaccines during the lockdown in Nigeria at the time of the COVID-19 pandemic. The gradual increase to 73% in

2023 could be because of the gradual increase in access to vaccines after the lockdown. The concurrent incidence of COVID-19 and Measles greatly reduced the reportage and the vaccine uptake for Measles. Health agencies should be equipped to manage both infections concurrently; making vaccines accessible and also putting up measures to ensure adequate reportage of other tropical diseases.

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PREVALENCE OF PREVIOUS DENGUE INFECTION AMONG SCHOOL CHILDREN IN GRADES 3-10— AMERICAN SAMOA, SEPTEMBER-OCTOBER 2023

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Dengue has caused multiple outbreaks in American Samoa, with >660 reported cases during 2016-2018. In the U.S., the Dengvaxia dengue vaccine is recommended for children aged 9-16 years with a previous dengue infection and living in areas where dengue is endemic, including American Samoa. Since previous infection must be confirmed with laboratory testing to determine eligibility, seroprevalence estimates in the vaccine age-eligible population are critical to inform resource planning and ensure safe vaccine implementation. To determine dengue seroprevalence in this population, we conducted a serosurvey with a single-stage cluster sampling strategy, stratified by elementary and high schools. Among a total of 36 schools in American Samoa, we selected 7 and invited all children in grades 3-10 with parental permission to participate. We tested participants with the CTK Onsite Dengue IgG rapid test with a sensitivity and specificity of 89.6% and 95.7%, respectively. We computed estimates of seroprevalence and 95% confidence intervals (CIs) using design weights. Among 2267 children invited to participate, we tested 887 (39%). Median age was 11 (range: 7-16) years, 492 (56%) were positive, 371 (42%) were negative, and 24 (3%) had uninterpretable results. The estimated seroprevalence for all ages tested was 59% (95% CI: 47-71) and 60% (95% CI: 48-72) for individuals aged 9-16 years. The seroprevalence was lowest for children aged 10 years (53%; 95% CI: 25-81) and highest among children aged 13 years (72%; 95% CI: 56-88). Dengue seroprevalence among vaccine age eligible children in American Samoa exceeded the 20% seroprevalence threshold in vaccine recommendations for use. Dengue vaccination could be safely implemented as part of a comprehensive dengue control and prevention strategy in American Samoa.

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INTERACTIONS AMONG ACUTE RESPIRATORY VIRUSES IN PUERTO RICO, 2013-2023

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Respiratory viral infections can modify immune responses to subsequent unrelated respiratory viral infections via non-specific immunity or increased immunopathology. Limited data exist on how infection with one virus affects the immediate course of another at the population level, especially in the tropics. We analyzed 2013–2023 data from the Sentinel Enhanced Dengue Surveillance System in Puerto Rico, which enrolls patients with fever or respiratory symptoms at 3 emergency departments or urgent care clinics and collects nasopharyngeal samples for pathogen identification using a panel of 7 acute respiratory viruses: influenza A (IAV) and B (IBV); respiratory syncytial virus (RSV); human parainfluenza virus 1 (HPIV-1) and 3 (HPIV-3), adenovirus (HAdV), and metapneumovirus (HMPV). We used a multivariate Bayesian hierarchical model to evaluate correlations in monthly infection prevalence between virus pairs, adjusting for demographics, temporal autocorrelations, seasonality, long-term trends, and multiple comparisons. Among 43,385 enrolled participants, 13,315 (30.7%) tested positive for any acute respiratory virus and 223 (0.5%) were coinfected with >1 virus. Our model identified zero virus pairs with negative correlations and five with positive correlations, indicating increased likelihood of detection when one is present, with 0 and 1 indicating no and perfect correlation: HMPV/HPIV-1 (ρ = 0.51), RSV/HPIV-3 (ρ = 0.45), IBV/HAdV (ρ = 0.39), IBV/HMPV (ρ = 0.35), and IAV/IBV (ρ = 0.31). These interactions can influence disease severity, transmission, immune response, and vaccine effectiveness. Identifying correlations between respiratory viruses can inform public health strategies. For example, a positive correlation of 0.51 between HMPV and HPIV-1 means that when HMPV prevalence deviates from its expected seasonal trend, HPIV-1 prevalence tends to deviate in the same direction and by a moderate degree. A surge in HMPV cases might signal a coming increase in HPIV-1 cases, allowing hospitals to prepare for a potential rise in patients with croup and bronchiolitis, both complications associated with HPIV-1 infection.

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HUMAN SEROPREVALENCE OF ANTIBODIES TO FILOVIRUSES CAUSING OUTBREAKS IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Recent outbreaks of Ebola virus disease and Marburg virus disease in sub-Saharan Africa illustrate the urgent need to better understand animal reservoirs, natural causes, burden of disease, and human transmission of filoviruses. We conducted a systematic literature review to assess the seroprevalence of antibodies against filoviruses that cause human outbreaks in sub-Saharan Africa. Titles, abstracts, and full texts resulting from a search of PubMed, Embase, and Web of Science were reviewed for inclusion by a primary reviewer and a team of three secondary reviewers. Data were extracted using a pre-specified and piloted data extraction form. The review included human cross-sectional studies, cohort studies, and randomized controlled trials conducted in sub-Saharan Africa and published before March 13, 2024. We stratified seroprevalence by virus species and sample population, and presented seroprevalence in forest plots with 95% confidence intervals. For strata containing five or more studies, data with an I^2 value ≤75% were pooled. All included studies were assessed for risk of bias using the JBI Prevalence Critical Appraisal Tool. We identified 4,870 records, from which 74 studies were included. Ebola virus (species *Orthoebolavirus zairense*) seroprevalence in 31 studies ranged broadly from 1%-18% in the general population, 1.4%-15.3% in asymptomatic individuals, and 2.6%-32% in close contacts. For Marburg virus (species *Orthomarburgvirus marburgense*), seroprevalence in 13 studies ranged from 0%-2.4% in the general population and 0%-18.6% in symptomatic individuals. In the risk of bias appraisal, five studies were rated very low risk of bias, 47 low, and 22 moderate. This systematic review identifies gaps in filovirus clinical research, such as an apparent lack of knowledge about asymptomatic infection and the lack of a gold standard assay or processes to establish cutoff for relevant assays used for diagnosis of exposure in humans. Thus, this work provides comprehensive literature research information that may contribute to the improvement of clinical trial design and standardized cross-sectional seroprevalence studies.

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OUTBREAK OF MONKEYPOX IN BENIDORM, ALICANTE (SPAIN)

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Spain has been one of the countries with the highest reported cases of mpox. Benidorm City in the East Coast of Spain is a tourist area attracting numerous visitors. From June 2022, up to date, we reviewed the cases of mpox diagnosed in our area. Mpox infection was confirmed in samples of skin exudates or mucosal lesions by RT-PCR (RealStar Orthopoxvirus PCR kit 1.0 Altona Diagnostics GmbH, Hamburg). We diagnosed 35 cases in males (100%) with a mean age of 41 +/- 11 years, of whom 26 were European Caucasian and 9 Latin American, none of them with a history of travel to Central Africa. A total of 15 patients had HIV infection (CD4 range 212-1542 cells/mm3) and 7 were receiving PrEP. Syphilis was detected in 14 (40%), and RT-PCR screening for other STIs was negative. Patients presented with fever (48%), malaise or fatigue (94%), and odinophagia 22%. All patients showed skin lesions in vesicles or pustules distributed over the pubic region, genitals extremities, face and body. Three patients required admission to the hospital due to the severity of symptoms, with high fever, proctitis, and odinophagia. There were no cases of encephalitis, pneumonia, or corneal involvement. All patients evolved favorably with symptomatic treatment. Cases peaked in the summer 2022 and rapidly decreased in the following months. The outbreak was controlled before the routine availability of mpox vaccine programs and antivirals like tecovirimat. The infection control program and the information on preventive measures for people at risk were important factors in controlling the outbreak.

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SPATIO-TEMPORAL DISTRIBUTION OF CRIMEAN CONGO HEMORRHAGIC FEVER AND ITS RELATIONSHIP WITH CLIMATE FACTORS IN PAKISTAN: A DECADE-LONG EXPERIENCE FROM TERTIARY CARE LABORATORY NETWORK

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Crimean Congo Hemorrhagic Fever (CCHF) has a case fatality rate as high as 80%. Pakistan shares borders with high incidence countries for CCHF, placing Pakistan at risk for outbreaks. There is limited knowledge about the total burden and spatio-temporal distribution of CCHF in Pakistan. We aim to study the spatio-temporal distribution of CCHF, using laboratory data from over 100 cities across Pakistan from 2012 to 2023 and observe correlation of CCHF cases with seasonal variation and climatic factors. Data was extracted of test requests generated for CCHF at country-wide patient sample collection points (n=307) across Pakistan from January 1st, 2012 to May 31st, 2023. Average monthly temperature and precipitation data was used in the Poisson regression method to examine the effect on the number of cases. Total 2,559 patients were clinically suspected with 547 samples confirmed positive for CCHF using real-time PCR assay, with a positivity rate of 21.37% and a male predominance (84.6%). A linear increase in cases was noted year-wise. More than half the cases (57.6%, n=315) were detected between 2016 and 2019 while 97.4% (n=533) were detected in 3 cities. Highest number of cases were reported during summer ($p < 0.001$) with 41.13% confirmed cases reported in the months of August and September. A positive correlation of suspected cases was observed with temperature of zero-month lag (p=0.000), and a negative correlation was observed with precipitation with a 2-month lag (p=0.000). Case fatality rate for CCHF patients admitted at Aga Khan University Hospital was 45.8%. CCHF is on the rise in Pakistan. Positive cases are concentrated within 3 big cities where human and animal migration rates are high. Number of cases in these cities positively correlate with summer season and temperature, and negatively correlate with precipitation. Outbreak situations occur when multiple factors coincide. Seasonal and climatic patterns can be used as predictors of disease by policymakers for strict implementation on animal regulation, transport, and surveillance of animal migration to curtail outbreak situations in Pakistan.

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SPATIAL DRIVERS OF DENGUE TRANSMISSION INTENSITY IN COASTAL ECUADOR, 2015-2016

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Dengue, predominantly associated with urban areas, has also emerged in rural settings. This challenges the historical perception and underscores a knowledge gap regarding the influence of rural and urban spatial characteristics on dengue virus (DENV) transmission dynamics. This study examines spatial drivers of dengue dynamics at a parish-level in coastal Ecuador, aiming to identify the most influential aspects of urbanicity for characterizing dengue risk. We employ a spatial generalized linear mixed model (GLMM) to compare how four metrics of urbanicity influence our model's ability to explain fine-scale spatial patterns of dengue force of infection (FOI). These four urbanicity predictors are i) population density, ii) a binary urban census assignment, iii) an EU Organization for Economic Co-Operation and Development's Functional Urban Areas (FUA) assignment, and iv) a composite urbanicity index. This composite index is constructed from Ecuador's 2010 census variables, chosen for their variation across parishes and their relevance to dengue risk, including percentage of households with modern roofs, piped water inside home, access to public water, paved roads, and trash collection services. Between January 2015 and December 2016, Ecuador's passive surveillance system reported 1609 severe dengue and dengue with warning signs (DwWS) cases with associated ages across 266 coastal parishes within El Oro, Esmeraldas, Guayas, Manabí, and Santa Elena provinces. FOI increased geometrically as a function of our urbanicity metric. In comparison with the politically defined dichotomous urban/rural variable, we found that 4% of urban parishes were classified with low dengue risk and 21% of the rural parishes were classified with high dengue risk. Our findings highlight a need for a more nuanced characterization of spatial and conceptual aspects of urbanicity as they apply to DENV transmission — beyond an urban/rural dichotomy — to enhance the identification and management of existing and emerging high burden areas in other dengue-endemic countries with resource-limited surveillance systems.

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THE BURDEN OF DENGUE IN LATIN AMERICA AND ASIA: EPIDEMIOLOGICAL DATA OVER 57 MONTHS OF FOLLOW-UP IN A PHASE 3 TRIAL

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The placebo arm data from Takeda's phase 3 trial, DEN-301 (NCT02747927), offer a rare opportunity to assess the standardized burden

of febrile illness, serotype-specific virologically confirmed dengue (VCD), dengue hemorrhagic fever, dengue shock syndrome, and severe dengue across time, countries, and regions. The trial enrolled 20,099 participants aged 4-16 years in Asia (the Philippines, Sri Lanka, Thailand) and Latin America (Brazil, Colombia, Dominican Republic, Nicaragua, Panama), of which 6,687 were randomized to placebo. Of these, 91% completed the study follow-up of ~57 months (30,620.6 person-years [p-y]). A total of 9,698 febrile illnesses were recorded through active surveillance, of which 98% were tested for dengue virus (DENV) using RT-PCR, and 5.8% (560 cases) were confirmed as dengue. This proportion increased with age (among those 4-5 years: 4.7%, 6-11 years: 5.8%, 12-16 years: 6.9%). By region, the incidence of dengue was more than twice as high in Asia (incidence rate [IR]=2.7/100 p-y) than Latin America (IR=1.2/100 p-y). Over 25% of VCD cases were hospitalized (IR=0.5/100 p-y). The decision to hospitalize was per local standard of care and rates of hospitalized VCD ranged widely by country (eg, 4.4% in Panama, 8.3% in Brazil, 68.0% in Sri Lanka). From December 2018 (study month 28) through ~57 months of follow-up, there was a decrease in VCD incidence/100 p-ys (months 28-39: 3.0, months 40-51: 0.7, months 52-57: 0.4). Of the 560 VCD cases over 57 months, DENV-1 was the most predominant serotype detected (41.1%), followed by DENV-2 (34.5%), DENV-3 (20.4%), and DENV-4 (4.1%). These data allow a standardized comparison across populations and time (2016-2022). The burden of dengue in children aged 4-16 years was higher in Asia than in Latin America. Different local standards of care may explain the variable hospitalization rates. The observed decrease in dengue incidence may reflect epidemiological trends or more probably the impact of social restrictions during the COVID-19 pandemic. These findings may help validate assumptions needed to design public health interventions such as vaccination programs.

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SEROPREVALENCE AND SEROINCIDENCE OF LASSA FEVER VIRUS INFECTION IN A POPULATION-BASED COHORT STUDY IN SIERRA LEONE (IAVI X100)

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An improved understanding of Lassa fever virus (LASV) epidemiology is needed to inform the design of efficacy trials and delivery strategies for LF vaccines. Investigators at Kenema Government Hospital (KGH) in Sierra Leone, Tulane University, and IAVI implemented a prospective study (X100) to obtain the seroprevalence and seroincidence of LASV. Three districts were selected based on confirmed case frequencies presenting at the KGH National Viral Hemorrhagic Fever Ward: high (Kenema District), emerging (Tonkolili District), and low (Port Loko District). Residents of 26 villages across the 3 districts were enrolled. Demographic data, medical history, and blood were collected using finger sticks and dried blood spots at two time points (baseline and 18-24 months later). Dried blood spots were tested by pan-LASV-NP IgG ELISA (Zalgen Labs, MD, USA). Between April 2021 and May 2022, 8,237 residents aged ≥2 years were enrolled; baseline and follow-up data were available for analysis for 6,447 (78.3%) participants from 803 total households across all 26 villages. Of the 6,447 participants, 3,255 (50.5%) were female, 1,634 (25.4%) were children aged 2-10 years, and 1,532 (23.8%) were adolescents aged 10-19 years. Baseline LASV seroprevalence was 1,832/6,447 (28.4%). Among 4,615 seronegative participants we observed 528 cases of incident infection for an incidence of seroconversion of 6.9 cases/100 person years (95% CI: 6.3-7.5). The incidence of reinfection among seroprevalent participants, defined as a 4-fold increase in ELISA antibody titres from baseline to follow up, was significantly lower, at 4.2 cases/100PY (3.5-4.9, p<0.001). We observed high rates of seroincidence in this rural, population-based cohort of Sierra Leonians at risk of LASV infection. These data are crucial for understanding the populations most at risk for incident LF disease, which will inform efficacy trial designs and future vaccine delivery strategies.

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CHARACTERIZING THE INTRA-HOST PLAQUE VARIANTS AND GROWTH KINETICS OF GLOBAL ZIKA VIRUS STRAINS

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Zika virus (ZIKV), originally isolated from Zika forest in Uganda has two primary lineages: African and Asian. The ZIKV strains that circulate in the Americas, Pacific, and Southeast Asia compose the Asian lineage while the African lineage is associated with the strains that circulate in Africa. The Asian lineage is responsible for all human outbreaks caused by ZIKV strains while the African lineage has not been associated with any epidemic transmission. We hypothesize that intra-host viral mutations exist, within each ZIKV strain, and these variants drive the geographical disparities in pathology of disease resulting from infection with ZIKV. To address our hypothesis, we characterized the plaque morphology and growth kinetics of the Dakar, Uganda, Nigeria, Honduras, and Thailand ZIKV isolates, purified single plaques of Dakar and Honduras isolates, and assessed their growth kinetics. The global ZIKV isolates demonstrated unique plaque variants associated with distinct plaque morphology in the parental population. Dakar isolate had plaque morphologies different from the other isolates belonging to the African lineage (Nigeria and Uganda) but were identical to the isolates in the Asian lineage (Honduras and Thailand). Further, the Dakar isolate displayed the most significant cytopathic effect on the cell monolayers. Interestingly, Honduras and Thailand isolates did not clear the cell monolayer at the point of infection as the African strains did. The Dakar strain manifested dual host tropism compared to the other isolates. Purification of single plaques resulted in a significant reduction in growth kinetics compared to the parental wild type, suggesting a cooperative behavior of swarm mutants to achieve virulence. Our results provide important information on lineage-specific viral biological characteristics. The observation of intra-host plaque variants suggests that the virus could evade immune system response and make it more difficult to develop vaccines that can effectively target all ZIKV strains.

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MAPPING RESPIRATORY VIRUS EVOLUTION AND OUTBREAKS IN CAMBODIA USING PATHOGEN GENOMICS

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Genomic surveillance can guide early detection and response to emerging epidemics. We applied metagenomic sequencing to investigate respiratory virus outbreaks in Cambodia. Nasopharyngeal swabs were collected from subjects aged 6 months to 65 years with respiratory symptoms and fever in 4 Cambodian hospitals. Geographic coordinates for subject home villages were recorded. We performed shotgun short-read RNA sequencing and aligned sequences of Influenza A virus H3N2, human parainfluenzavirus 3 (PIV3), and human respiratory syncytial virus (RSV) strains A and B. We performed Bayesian inference of phylogenetic trees for each pathogen, where branch lengths were measured in calendar time, which allowed us to compute posterior medians and highest posterior density (HPD) intervals for all divergence times, including time to most recent common ancestor (TMRCA). From December 2020 to August 2023, 1,118 subjects with acute respiratory febrile illness were enrolled. Sequencing detected 25 distinct respiratory virus species among 502 (44.9%), most commonly within genus

Enterovirus (N=189), Betacoronavirus (N=94), Orthopneumovirus (N=65), Respirovirus (N=47), and Alphainfluenzavirus (N=41). Discrete time-clusters were noted of H3N2 (September 2022), PIV3 (March 2021 and July 2022), RSV-A (November 2021), and RSV-B (August 2022). The posterior median of TMRCA ranged from 1.5 years (95% HPD 0.8-2.7) for H3N2 HA segment and 2.6 years (1.8-3.7) for RSV-A, to 5.5 years (1.6-18.3) for RSV-B and 12.9 years (7.5-21.9) for PIV3. Within time-clusters, pairwise genetic and physical distances at strain (for all 4 viruses) and clade (for RSV-B and PIV3) levels were not correlated. Sequencing detected diverse respiratory viruses among Cambodians with febrile respiratory illness during the COVID-19 pandemic. Peaks in RSV-B and PIV3 cases initially suggested discrete outbreaks in summer 2022, but genomic data revealed co-circulation of several clades, potentially arising due to lifting pandemic restrictions. While H3N2 and RSV-A outbreaks may have resulted from single introductions, sampling was insufficient to map transmission networks.

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ANALYSIS OF SARS COV2 VARIANTS IN WASTEWATER OF THE METROPOLITAN DISTRICT OF QUITO USING A PASSIVE SAMPLING 3D PRINTED DEVICE

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SARS CoV2 infection in humans produces viral RNA elimination mainly through respiratory droplets but also actively through fecal matter. Wastewater surveillance of pathogens has become an essential tool for epidemic preparedness. It has allowed tracking of the SARS CoV2 emerging variants in populations with low clinical diagnosis rates. For this reason, we implemented a passive sampling approach to determine SARS CoV2 variants in Quito, Ecuador, during 2023 and 2024 and to correlate it with the results from the national genomic surveillance performed in patients in hospitals in Quito. A passive torpedo-type sampling equipment was used to collect the samples, which contained a nylon membrane, gauze, and a swab; the device was placed in wastewater collectors for 24 hours weekly. This method is a more straightforward approach to wastewater sampling than the conventional one that requires several liters of collection and spin-down/PEG concentration. RNA was concentrated with PEG. RNA viral extraction was performed, followed by real-time PCR for virus detection and multiplex PCR for sequencing with Oxford Nanopore Technology. Bioinformatics data was analyzed in Freyja. A predominance of omicron variant with lineages HN.1, EG.5.1.6, XBB.1.5.1.5, and HV.1 were encountered during the infection peaks in Quito on August 2023 and January 2024. The same variants and in similar proportions were encountered in our genomic surveillance in infected humans during both peaks. Strikingly variant JN.1 was not the leading cause of infections during this time compared with its northern hemisphere predominance. SARS CoV2 wastewater epidemiological surveillance is a straightforward approach for genomic characterization of circulating variants and viral abundance quantification.

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DENGUE VIRUS SEROTYPE 3 ORIGINS AND GENETIC DYNAMICS, JAMAICA

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Dengue is hyperendemic in Jamaica with increasingly frequent epidemics. Due to the limited number of whole or near whole genome sequences it remains unclear as to the temporal origin of dengue viruses introduced into Jamaica and their subsequent transmission to other countries. In this study we examined the molecular epidemiology of dengue virus serotype 3 (DENV3) in Jamaica during 2016-2020, a time period inclusive of the 2016 and 2019 epidemics. Residual dengue virus NS1 positive serum samples collected from patients seeking care for dengue during 2019-2020 at the University Hospital of the West Indies were sequenced with a target enrichment approach using the Comprehensive Viral Research Panel probe set. Five whole genome (100% coverage), 7 near whole genome (91-99% coverage), and 3 partial genome (28-65% coverage) sequences were obtained. Ten additional publicly available dengue virus sequences from 2016-2019 were also included for analysis. Sequences were aligned to reference DENV sequences obtained from Nextstrain using MAFFT. Phylogenomic and phylogeographic analyses of the sequences were completed using IQTREE2 and BEAST, respectively. All 25 samples analyzed were identified as DENV3 genotype III, with a *skygrid* reconstruction showing a stable evolutionary rate of 1.78×10^{-3} substitutions/site/year. Positive selection of mutations within the E gene accumulated over time after introduction of DENV3 genotype III, allowing for continuous circulation of this genotype in Jamaica. Phylogeographic analysis indicated that DENV3 most likely originated from India and China in 2014, two years prior to the initial detection of DENV3 during the 2016 dengue epidemic. DENV3 genotype III circulating in Jamaica was subsequently transmitted to Saint Lucia and potentially other unsampled countries. Our investigation yielded a wealth of information about the molecular epidemiology of dengue virus in Jamaica, previously not available to local public health officials and providing a greater understanding of the circulation of dengue worldwide.

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RECOVERY OF COMPLETE GENOME SEQUENCES OF CRIMEAN-CONGO HAEMORRHAGIC FEVER VIRUS THROUGH TARGETED NEXT-GENERATION SEQUENCING APPROACHES: A COMPARATIVE STUDY BETWEEN MULTIPLEX TILING PCR AND PROBE HYBRIDIZATION CAPTURE

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Crimean-Congo haemorrhagic fever (CCHF) is the most prevalent human tick-borne viral disease, with a reported case fatality rate of 30% or higher. The disease is caused by the CCHFV virus (CCHFV), an orthonairovirus within the *Nairoviridae* family (order *Bunyavirales*), and is endemic to vast geographical areas spanning Africa, Europe, Middle East and Asia. There are currently no licensed vaccines or effective therapeutics against CCHF. The geographical expansion of tick vectors coupled with the fast mutation rate of RNA viruses has made the investigation of tick-borne pathogens a public health priority. Although modelling data from Türkiye has shown that anthropogenic factors such as fragmentation of agricultural land interspersed with forest and shrub-type vegetation play a role in increased CCHFV transmission, other studies have shown that climatic factors such as reduced rainfall and increases in temperature will cause a northward expansion of the suitable habitat for several tick species including *Hyalomma marginatum*, the most common CCHFV vector. With the predicted expansion of the habitat for many tick species including CCHFV vectors, the development of enrichment strategies to recover CCHFV genomic sequences from genetically diverse viruses will be of paramount importance to not only detect the presence of the virus in potentially new areas, but also for public health laboratories actively involved in CCHFV molecular surveillance to rapidly detect/diagnose and characterize currently circulating strains. We have developed a novel probe hybridisation capture method and successfully recovered near complete genome sequences for different CCHFV genetic lineages including Europe 1, Europe 2, Africa 2 and Africa 3. The presented methodology could be valuable in CCHFV endemic regions in which circulating viruses have not yet been characterised or their presence is still unknown.

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MULTIPLE GENOTYPES AND CLADES OF DENGUE VIRUS IDENTIFIED DURING 2022 AND 2023 IN CENTRAL NEPAL

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Dengue virus (DENV), a virus of the *Flaviviridae* lineage, causes one of the most widespread arboviral diseases with 100-400 million cases occurring each year. DENV exists in four antigenically distinct serotypes which can be further subclassified into 3-6 genotypes and numerous clades. In Nepal, Dengue has been a disease of public health concern since its first case in 2004. Originally limited to the lowland "Terai" regions of Nepal, the at-risk region for DENV has been steadily expanding into higher elevation regions, with the last two years each recording over 50,000 cases. We analyzed 90 NS1-seropositive serum samples with qPCR from patients presenting with dengue-like illness at Dhulikhel Hospital, a tertiary care hospital, in 2022 and 2023. Among 90 seropositive samples, 80 were positive by qPCR. We utilized the iSeq100 to perform amplicon-based whole genome sequencing on DENV from qPCR-positive serum (Ct<35.00). Of the 41 complete genomes obtained, 9 were identified as DENV-1, 15 as DENV-2 and 17 as DENV-3. Phylogenetic analysis revealed a clade of DENV-1 sequences within genotype III clustering with 2019 Indian strains and 2022 Nepali strains. This represents a shift in the predominant genotype of DENV-1 in Nepal from genotype V since 2017. All DENV-2 sequences fell into the Cosmopolitan genotype. DENV-2 sequences did not cluster into discrete clades, but were related to sequences from India, Singapore, Bangladesh, and China from 2018-2022, Nepali sequences from 2017, and recent isolates from the US. Though historically outbreaks have been dominated by DENV-1 and -2 in Nepal, we identified numerous DENV-3 sequences. These were related to Indian strains from 2019 and Nepali strains from 2022 and were identified as genotype III. Our study showed a dominance of Indian DENV populations on Nepali DENV-1 and -3. Moreover, the findings have demonstrated the shift of DENV-1 genotype from V to III with notable genetic diversity within the cosmopolitan genotype of DENV-2 in Nepal, linking cases to those in South and Southeast Asian countries and North America.

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PHYLOGENETIC ANALYSIS OF CRIMEAN CONGO HEMORRHAGIC FEVER VIRUS STRAINS CIRCULATING IN PAKISTAN DURING 2022-2023

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Crimean-Congo haemorrhagic fever (CCHF) is a tickborne viral disease endemic in regions of Asia, Africa, and Europe, with case fatality rate of 10-40%. Pakistan is considered endemic region for CCHFV, while limited studies have been conducted in the country to provide insights into the genetic diversity and evolution of CCHFV. In this study we aimed to perform whole-genome sequencing of CCHFV strains and its phylogenetic analysis for better understanding of epidemiology and evolutionary relationship of indigenous strains during 2022-2023. Thirty-one CCHFV positive serum samples were collected from the Aga Khan University Hospital laboratory during 2022 to 2023. RNA was isolated and sequencing was performed on Illumina MiniSeq platform. Raw reads were aligned to reference genome using BWA tool followed by variant calling and generating consensus sequence using iVar tool. Inclusion criteria for phylogenetics analysis was set at a depth of equal to or greater than 10X and more than 95% coverage. Phylogenetic trees of all segments were constructed using Fasttree, visualization and annotation of trees was done in iTOL. A total of eight samples were sequenced successfully. All three segments (S, M, and L) were clustered in Clade-IV (Asia-1), along with other regional strains from Afghanistan, India, and Iran, as well as reported sequences from Pakistan. Detailed mutation analysis was conducted, and samples were compared with publicly available whole genome sequences in BV-BRC database. We found that all segments contain unique mutations 1, 10 and 30 in S, M and L segments, respectively. The study provides valuable insight into the genomic diversity and evolutionary history of CCHF strains circulating in Pakistan during 2022-2023. While similarities with neighboring country strains show that climatic conditions of the region play a role in disease transmission, as vector proliferation is dependent on climate and animal movement between borders.

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WEST NILE VIRUS INFECTIOUS UNITS CONTAIN MULTIPLE VIRUS PARTICLES

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A virus infectious unit is widely considered to consist of a single virus particle that enters a cell to initiate the infectious cycle. However, a growing body of research suggests multiple alternate mechanisms through which viruses may initiate infection. For example, Zika virus plaques tend to be initiated by aggregates containing a mean of 10 virus particles, with single-particle infections occurring only very infrequently. To define the extent to which West Nile virus (WNV) infections are similarly initiated by infectious units consisting of multiple aggregated virus particles, we assessed the genomic content of single WNV plaques using a molecularly barcoded WNV. Multiple vertebrate cell lines were infected at a low multiplicity of infection and well-isolated plaques were allowed to develop. From these plaques, we extracted RNA and analyzed viral barcode diversity using next-generation sequencing. Our results suggested that 3 to 8 WNV virus genomes comprise a typical WNV plaque-forming unit. However, some plaque-forming units were highly diverse, containing more than 20 discrete input genomes. We plan to identify the virus genome numbers associated with a single-cell infection and compare them with the results in a plaque-forming unit. We are also investigating the mechanism of polyinfection, which we hypothesize occurs through the aggregation of multiple, individually packaged, virus particles. To visualize WNV virus aggregation, we are developing a "flow virometry" assay that will allow us to precisely quantify the number of virus particles in virus aggregates.

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GENOMIC CHARACTERIZATION OF DENGUE VIRUS CIRCULATION IN ETHIOPIA

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Dengue virus is becoming more prevalent in tropical and subtropical regions of the world, including Ethiopia. In Ethiopia, dengue fever cases have been reported in five regions, however, the circulating serotypes and genotypes are not well known. This study investigated the circulating serotypes and genotypes of dengue virus using phylogenetic analysis. The study also compared these patterns to previous studies conducted in African countries and in a global context. A cross-sectional study was conducted in three hospitals to collect blood samples from patients with acute febrile illnesses. The samples were screened for three arboviral pathogens (DENV, CHIKV, and ZIKV) using RT-PCR. For dengue isolates, serotyping was performed using a CDC kit. Phylogenetic analysis was conducted using sequenced data, and the results were compared with previous studies conducted in Africa and other dengue-endemic countries. Seasonality and human mobility were taken into account to predict and understand the viral introduction. In this study, two serotypes (DENV1 and DENV3) were isolated from Dire Dawa, and DENV3 was isolated from the Afar region. The DENV1 serotype belongs to genotype III of the major lineage A, while the DENV3 serotype showed two transmission clusters and belongs to genotype III and

major lineage B. This study contributes to a deeper understanding of the circulating serotype and genotype in Ethiopia, which could inform decision-makers and help plan national and public health strategies to manage the emergence of dengue.

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MOLECULAR CHARACTERIZATION OF SARS-COV-2 VARIANTS IN PATIENTS LIVING IN DIFFERENT PROVINCES OF BURKINA FASO

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The initial strain of SARS-CoV-2 that appeared at the end of 2019 and has since spread around the world mutates regularly. Since the start of the epidemic, the SARS-CoV-2 genome has changed and evolved as a result of the many mutations that have occurred. Like all viruses, SARS-CoV-2 mutates constantly during multiplication, copying its genetic material and sometimes making mistakes or mutations in the process. Whole-genome sequencing of SARS-CoV-2 using next-generation sequencing (NGS) has shown to be a powerful tool for studying coronavirus 2019 (COVID-19) and tracking the evolution and spread of the virus. The aim of this study was to identify the different SARS-COV-2 variants circulating in different zones in Burkina Faso. Samples were collected at health facilities located in different second level towns (Kaya, Ouahigouya and Tenkodogo) in Burkina Faso during the period of the SARS-CoV-2 pandemic. 156 SARS-CoV-2 genomes obtained from RtPCR-positive collected were analyzed. The analyses were carried out using the MinION (Oxford Nanopores Technology). Genomic sequences were assigned to phylogenetic clades using NextClade and to Pango lineages using pangolin. After analysis of the results, the SARS-CoV-2 genomes obtained in this study can be classified into 15 phylogenetic clades and 36 existing Pango lineages. Five distinct variants were identified: Omicron (46.15%), Delta (35.90%), Eta (7.69%), Iota (7.69%) and Alpha (2.56%). The Delta variant (56.25%) was most common in subjects living in rural areas. The Omicron variant was not only most common among those living in urban areas (48.39%), but also among subjects who presented as suspected cases (54.05%) of the disease. As in many other countries around the world, several variants of concern of SARS-CoV-2 virus were present during the COVID-19 pandemic in Burkina Faso. This study provides additional data on SARS-CoV-2 variants in the country.

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ELUCIDATING THE MOLECULAR EPIDEMIOLOGY OF WEST NILE VIRUS IN SOUTHERN NEVADA

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West Nile Virus (WNV) is a positive-sense single-stranded RNA virus transmitted by
Culex mosquitos (*Cx. quinquefasciatus, Cx. tarsalis, Cx. pipiens*). The disease caused by this arbovirus can be benign or associated with poor prognoses including encephalitis, meningitis, or meningoencephalitis in humans. WNV first appeared in the United States in 1999 and rapidly spread westward reaching Nevada in 2004. Subsequently, WNV has been found annually in the state, including Las Vegas in Southern Nevada. Due to recent El Niño events, Las Vegas has seen unusual amounts of precipitation. Ongoing local climate change is likely to result in increases in mosquito-human contact. Despite ample knowledge of WNV in general, little is known about its origins in Nevada. A WNV surveillance program is in place in Southern Nevada, spearheaded by the Southern Nevada Health District (SNHD). The SNHD collect mosquitoes during the peak mosquito breeding months of April through October using encephalitis vector surveillance (EVS), Gravid, and BG Sentinel traps. Between March 2023-April 2024, over 3000 *Culex* mosquitoes were collected, with 30 pools positive for WNV. While this provides information about local WNV prevalence, there is still a paucity of data regarding the source of WNV in Southern Nevada. In this study, we aimed to elucidate the genetic origins of WNV using next-generation whole-genome sequencing techniques. cDNA was synthesized from forty-two unique WNV RNA samples, derived from pooled *Culex* spp. collected from 2020-2023, identified by positive qPCR results (Ct value range: 16-31). A hemi-nested PCR approach, based on 12 published primer sets was used to amplify across the entire WNV genome. Library preparation and sequencing is ongoing using the Oxford Nanopore Technologies MinION™ platform. Bioinformatic analysis will be used to reveal the genetic diversity of WNV in Clark County and to determine whether WNV strains are endemic or are reintroduced from other geographical disease foci annually.

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ROTAVIRUS AND STRAIN DIVERSITY: DISENTANGLING THE REASSORTMENT RATES OF PAIRWISE SEGMENT COMBINATIONS

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Rotavirus is an RNA virus with 11 segments and is the main cause of severe gastroenteritis in infants and young children. This virus exhibits significant diversity in strains globally, with multiple strains co-circulating in the population. To better understand the population dynamics of this highly diverse pathogen, it is imperative to study the mechanisms that generate and maintain diversity at the population level. One such mechanism is reassortment, which refers to the ability of segmented viruses to exchange their segments during coinfection, thereby producing hybrid progeny. Although reassorted viruses have been previously characterized, the rate at which these reassortment events occur and are observed at the population level is an open question. In this study, we reconstructed the reassortment networks and inferred reassortment rates by implementing a Bayesian phylogenetic method. We analyzed 142 publicly available human rotavirus A whole-genome sequences from the virus variation database and the GenBank collected globally during 1974-2019. We inferred co-reassortment rates for all pairs of segments, showing that these rates vary drastically between segment pairs, with values ranging from 0.03 to 0.11 reassortment events per lineage per year. The highest rates were observed in events reassorting the antigenic segments, VP4 or VP7. In contrast, the lowest reassortment rates were seen in pairs with VP2 and VP3, which play roles in core assembly and genome replication. Notably, each segment has a wide range of co-reassortment rates with its different pairs. These findings suggest that reassortment is not only influenced by the type of segment (antigenic or non-antigenic) but also by the combination of segments in the rotavirus strain. We conclude that different reassortment rates of both antigenic and non-antigenic segments of rotavirus could lead to shifts in diversity patterns, with unknown consequences for vaccine efficacy, which is known to be very low in low- and middle-income countries.

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CLINICAL AND GENOMIC CHARACTERIZATION OF DENGUE VIRUS OUTBREAK IN MALI

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An outbreak of dengue fever transpired in November and December 2023, resulting in roughly 30 reported deaths and 700 cases by December 19.[1] Aedes aegypti, the mosquito from which dengue virus and other diseases are spread, has been the cause of a number of arboviral outbreaks in the West African region, and climate changes may further result in these outbreaks becoming more severe and frequent.[2] We employed the pan-viral

sequencing assay known as VirCapSeq-VERT[3] at the University Clinical Research Center (UCRC) in Bamako, Mali to identify dengue prevalence, discover potential co-infections, and recover complete genomes to better characterize the spread of dengue virus. Of 23 identified cases of dengue virus, 61% were male and the mean age of cases was 43. 83% experienced fever and 57% reported headache. Several cases displayed symptoms of gingival bleeding, anemia, jaundice, and myalgia. Roughly 65% of detected dengue virus cases were identified as serotype 3 (DENV-3), falling within the phylogenetic clade nearest genotype 3 sequences. Bayesian analysis via Monte Carlo chain method[4] further explored the temporal evolution of the genomic sequences detected by VirCapSeq-VERT, and revealed the need for better arboviral genomic surveillance in West Africa.

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DENGUE VIRUS DETECTION AND GENOMIC ANALYSIS IN A HIGH JUNGLE REGION OF NORTHERN PERU IN 2020 AND 2023

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In Peru, more than 50% of arbovirus cases are caused by dengue (DENV), a disease transmitted by arthropods (arbovirus). Our study assessed the prevalence and circulating DENV genotypes among febrile patients. Between June 2020 and July 2023, 4413 serum samples were collected from patients with acute febrile illness (AFE) in the province of Jaén, department of Cajamarca, located in the high jungle of northern Peru. The diagnosis of DENV was made by real-time RT-PCR and NS1 and IgM ELISAs. ILUMINA technology was used to sequence and assemble the genome. The phylogenies were constructed using maximum likelihood phylogenetic inference (ML). DENV was confirmed in 2131 cases (48.29%), where 249 (11.68%) were diagnosed by RT-PCR, 961 (45.10) by RT-PCR and Elisa NS1, 58 (2.72%) by RT-PCR and IgM ELISA, 130 (6.10) by NS1 ELISA, 146 (6.85%) by NS1 ELISA and IgM, 389 (18.25%) by IgM and 198 (9.29%) by essays. Infected patients were mostly aged 18 to 39 years (53.01%), followed by those aged 40 to 59 years (18.91%) and those aged 12 to 17 years (10.65%). Female patients (56.78%) also had a higher incidence of DENV. Among the infected population, headaches (89.32%), arthralgia (77.56%), myalgia (76.93%) and fever (76.35%) were the most common clinical symptoms. Based on phylogenetic analysis of nine complete DENV genomes, the South American lineage of DENV-1 genotype V has circulated in Peru since 2021, and lineage 5 of the cosmopolitan DENV-2 genotype has circulated since 2019. They were also found cocirculating in Jaén between 2022 and 2023. As a result of the recent co-circulation of two DENV genotypes in the high jungle of northern Peru, we report a high incidence of DENV in the high jungle. In Peru, DENV is showing a divergent pattern of distribution and diversity compared to other outbreaks in Peru and South America, so we emphasize the importance of powerful genomic surveillance to understand its distribution.

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DETECTION AND WHOLE GENOMIC CHARACTERIZATION OF TWO UNUSUAL REASSORTANT DS-1-LIKE ROTAVIRUS A STRAINS CO-CIRCULATING IN BOLIVIA IN 2023

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Group-A rotavirus (RVA) is the most common cause of acute gastroenteritis (AGE) in young children. Following the introduction of the rotavirus vaccine, a significant decline in the burden of the RVA-associated disease was observed. In the last few years, the emergence and spread of unusual DS-1-like intergenogroup reassortant rotavirus strains have been reported across different countries around the world.The objective of this study was to report the detection and full genome characterization of unusual intergenogroup reassortant RVA circulating strains using an NGS-based approach. To this end, 317 fecal samples collected from hospitalized children with AGE across different regions of the country during seasonal and non-seasonal outbreaks were analyzed by ELISA and real-time PCR. A total of 136 (43%) episodes of AGE were associated with RVA, and 34 samples were further selected for genomic analysis. Viral dsRNA was extracted from feces using a QIAamp Viral RNA Mini Kit (Qiagen). The cDNA libraries constructed using the NEBNext Ultra RNA Library Prep Kit were sequenced on an ISeq100 platform (Illumina). The genotype of each of the 11 RVA genes was determined using Rotavirus A Genotyping online tool (versión 0.1). For each gene multiple alignments were carried out using MAFFT 7.0, and phylogenetic trees were constructed using neighbor-joining in MEGA-X. Fifteen samples were found to have a complete genome; eight and seven of those were categorized as belonging to equine-like G3P[8] and G12P[6], respectively. Based on the genomic analysis, RVA strains of both genotypes displayed the segment constellations of G3P[8]-I2-R2-C2-M2-A2-N1/N2-T2-E2-H2 and G12-P[6]-I2-R2-C2-M2-A2-N2-T2-E2-H2. To our knowledge, this is the first description of DS-1-like intergenogroup reassortant strains displaying two different co-circulating genotypes in Bolivia. This data supports the need for continued RVA surveillance of circulating strains in the country.

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ASSESSMENT OF SARS-COV-2 GENOMIC SURVEILLANCE IN THE DEMOCRATIC REPUBLIC OF CONGO, CHALLENGES AND PERSPECTIVES

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December 2019, the world has been turned upside down by the emergence of SARS-CoV-2 which spread across the entire planet. The publication of the first sequence made it possible to characterize the strain and develop vaccines and therapies. In the DRC, the first case was confirmed on March 10, 2020, and the first sequence made public 2 weeks later. In the course of the Covid-19 pandemic, the emergence of variants of interest made it necessary to continue and intensify genomic surveillance. This work enabled us to discuss the role of whole-genome sequencing whole genome sequencing to support the pandemic response and describe the emergence of variants of concern/interest in SARS-CoV2. The positive samples were sent to the sequencing laboratory. We then proceeded with extraction, Amplification, the various library preparations were carried

out respectively by two kits, Midnight for the Nanopore platform and Coviseq for the Illumina platform. integrated the fasta consensus pipeline and GeVarLi for Illumina and Artic for Nanopore. Lineage assignment was performed using Pangolin and Nextclade software, genomes with over 80% coverage were submitted to Gisaid**.** Genomic monitoring has made it possible to detect the introduction and circulation of various variants of interest. Variants of interest: In 2021, we note that the Delta variant circulated throughout the year before predominating during the 3rd wave. It then gave way to the B.1.640 and Omicron variants. In 2022, the majority of variants were Omicron with its sub-variants BA.1, BA.2, BA.3, BA.4, BA.5, BE.1, BF, BN.1, BQ.1, XBB. We also note the presence of B.1.640, Beta and Delta. In 2023, the Omicron variant was predominantly detected in the samples analyzed. To date, the DRC has shared 2233 sequences on Gisaid. We cannot predict where the new variants of concern will appear, but we should count on their early detection and characterization in places where genomic genomic surveillance is advanced.

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ENHANCED IFN-Γ, BUT NOT IL-2, RESPONSE TO *MYCOBACTERIUM TUBERCULOSIS* ANTIGENS IN HIV/ LATENT TB CO-INFECTED PATIENTS ON LONG-TERM HAART

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HIV-infected individuals with latent TB infection are at increased risk of developing active TB. HAART greatly reduces the incidence rate of TB in HIV-infected patients and reconstitutes MTB-specific immune response in the first 12 months of therapy. Evaluation of M.TB-specific functional immune responses in HIV/latent TB co-infected patients who were on HAART for at least 1.5 up to 9 years as compared to HAART-naïve patients were done. Three-hundred sixteen HIV-infected patients without active TB were screened by tuberculin skin testing for M. tuberculosis infection and peripheral blood mononuclear cells (PBMCs) were isolated from 61 HIV/ latent TB co-infected patients (30 HAART-naïve and 31 HAART-treated). IFN-γ and IL-2 ELISPOT as well as CFSE cell proliferation assays were performed after stimulation with M. tuberculosis antigens PPD and ESAT-6. The median frequency of PPD and ESAT-6 specific IFN-γ secreting cells was significantly higher in HAART-treated patients compared to HAART-naïve patients, p=0.0021 and p=0.0081 respectively. However, there was no significant difference in the median frequency of IL-2 secreting cells responding to PPD (p=0.5981) and ESAT-6 (p=0.3943) antigens between HAART-naïve and-treated groups. Both IFN-γ and IL-2 responses were independent of CD4+ T cell count regardless of the HAART status. Notably, the frequency of PPD and ESAT-6 specific IL-2 secreting cells was positively associated with CD4+ T cell proliferation while inversely correlated with duration of HAART, raising the possibility that M. tuberculosis-specific IL-2 response that promote the antigen-specific CD4+ T cell proliferation diminish with time on antiretroviral therapy in HIV/latent TB co-infected patients. This study shows an increased M. tuberculosis-specific IFN-γ, but not IL-2, response in HIV/latent TB co-infected patients with long-term HAART, consistent with only partial immune restoration. Future studies should, therefore, be done to prospectively define the rate and extent to which functional immune responses to M. tuberculosis are restored after long-term HAART.

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COMPUTATIONAL STRUCTURE-BASED DESIGN OF THE SPIKE RBD IMPROVES SARS-COV-2 VACCINES

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SARS-CoV-2 vaccines, almost all of which contain the spike protein, have dramatically reduced morbidity and mortality due to COVID-19. However, vaccine efficacy wanes as protective antibody titers decrease and escape variants emerge. Improved SARS-CoV-2 vaccines that elicit higher neutralizing antibody titers could counteract such decreases in titer. We have created a computational structure-based design method named SPEEDesign to identify amino acid changes that increase neutralizing antibody titers, focus the immune response to desired epitopes, and improve antigen production and stability. Nine amino acid changes to the receptor-binding domain (RBD) of the spike protein increase the neutralizing antibody titers elicited by monomeric WA1 RBD approximately 10-fold. Production yields also increase approximately 10-fold for all variants tested, including WA-1, XBB.1.5, and B.1.351. These same amino acid changes enable the production of a BA.5 RBD nanoparticle vaccine that elicits potent and broadly neutralizing antibody titers in mice. Finally, incorporation of these amino acid changes into the full-length spike protein significantly increases neutralizing antibody titers elicited in mice and monkeys. These results suggest that the efficacy of most SARS-CoV-2 vaccines, regardless of platform and strain, could be improved by incorporating the nine amino acid changes identified by SPEEDesign. Additionally, we note that the SPEEDesign method is modular and generalizable and thus could be applied to diverse pathogens and antigens.

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CORRELATION BETWEEN CLINICAL BIOMARKERS AND LUNG PATHOLOGY OVER THE COURSE OF ACUTE COVID-19

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COVID-19 is characterized by a broad range of symptoms and disease trajectories. Understanding the correlation between clinical biomarkers and lung pathology over the course of acute COVID-19 is necessary to understand its diverse pathogenesis and inform more precise and effective treatments. Here, we present an integrated analysis of longitudinal clinical parameters, peripheral blood biomarkers, and lung pathology in COVID-19 patients from the Brazilian Amazon. We identified core clinical and peripheral blood signatures differentiating disease progression between recovered patients from severe disease and fatal cases. Signatures were heterogenous among fatal cases yet clustered into two patient groups: “early death” (< 15 days of disease until death) and “late death” (> 15

days). Progression to early death was characterized systemically and in lung histopathology by rapid, intense endothelial and myeloid activation/chemoattraction and presence of thrombi, associated with SARS-CoV-2$^+$ macrophages. In contrast, progression to late death was associated with fibrosis, apoptosis and abundant SARS-CoV-2$^+$ epithelial cells in post-mortem lung, with cytotoxicity, interferon and Th17 signatures only detectable in the peripheral blood 2 weeks into hospitalization. Progression to recovery was associated with higher lymphocyte counts, Th2 and anti-inflammatory-mediated responses. By integrating ante-mortem longitudinal systemic and spatial single-cell lung signatures, we defined an enhanced set of prognostic clinical parameters predicting disease outcome for guiding more precise and optimal treatments. Finally, this study represents a major advance in the investigation of acute respiratory infections by integrating serial clinical data and peripheral blood samples with histopathological and spatially-resolved single-cell analyses of post-mortem lung samples.

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DISENTANGLING DIFFERENCES IN DENGUE VIRUS INFECTION RISK ACROSS SEX IN A LONGITUDINAL COHORT IN KAMPHAENG PHET, THAILAND

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Dengue virus (DENV) infection is a significant public health concern, with incidence increasing across the globe. To determine the impact of sex on infection risk we analyze data from an ongoing multigenerational longitudinal cohort that began enrollment in 2015 with 3020 participants across 494 households in Kamphaeng Phet, Thailand. Yearly serological sampling of participants yielded 12,161 intervals with 12.1% of intervals having an inferred DENV infection, allowing us to study infection risks across age and sex. At the population scale, females are as likely as males to be infected (OR 0.91; 95% CI 0.81-1.02). However, for individuals of child-bearing age (defined by the 95% of mothers who gave birth between 16-38 in this cohort) we find that sex is a significant risk factor for DENV infection, with females more likely to be infected than males in both univariate (OR 1.37; 95% CI 1.06-1.77) and multivariate logistic regression analyses (aOR 1.44; 95% CI 1.09-1.89) when accounting for prior immunity, seasonality, and household random effects. We incorporated information on if an individual had given birth in the previous year to explore whether risk can be attributed to pregnancy and associated biological changes. We found no significant impact of pregnancy on infection risk (aOR 1.18; 95% CI 0.86-1.61) when also controlling for sex, prior immunity, seasonality, and household random effects. We hypothesize that the observed differences by sex are driven by behavior, e.g., extended exposure to an environment with a susceptible newborn. Using generalized additive models we further explore these results by incorporating age, sex, and household composition to disentangle the behavioral and biological risk factors for DENV infection in the cohort. This work sheds light on the biological, social, and behavioral determinants of dengue virus infection risk and should help to guide efforts to mitigate virus transmission in endemic settings.

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VACCINE-INDUCED T CELL RESPONSES CONTROL FLAVIVIRAL CHALLENGE INFECTION WITHOUT NEUTRALIZING ANTIBODIES

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A significant impediment to viral vaccine development has been the lack of well-defined immune correlates of protection. Increasing evidence suggests a crucial role for T cells, but the level of vaccine-induced T cells needed, and the extent to which they alone can control acute viral infection in humans remains uncertain. To address this knowledge gap, we conducted a randomized double-blind vaccination and challenge study in human volunteers, using the live-attenuated yellow fever (YF17D) and chimeric Japanese encephalitis (JE/YF17D) vaccines. Study volunteers were randomized to receive either YF17D vaccination followed by JE/YF17D challenge 28 days later, or JE/YF17D vaccination followed by YF17D challenge. Viremia, humoral and T cell responses pre- and post-vaccination, as well as pre- and post-challenge infection were longitudinally assessed in all study volunteers. Both YF17D and JE/YF17D induced T cell responses against their shared capsid and non-structural proteins, without inducing cross-neutralizing antibody responses. YF17D induced a greater magnitude of antigen-specific T cell responses compared to JE/YF17D, and vaccination with YF17D was able to reduce mean viremia levels, antibody titers and symptom rates after JE/YF17D challenge. Importantly, even without neutralizing antibodies, viral control after challenge infection was achievable to the extent of undetectable viremia and absence of seroconversion in some vaccinees. Indeed, high vaccine-induced T cell responses, specifically against the capsid protein, correlated with the level of viral control. Our findings further validate the importance of T cell immunity in controlling acute viral infection, and suggests a potential correlate of protection for flaviviral infections and vaccines.

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DELETIONS IN THE 3' UNTRANSLATED REGION COMPROMISED TRANSLATION INITIATION TO ATTENUATE A DENGUE VIRUS 3 VACCINE STRAIN

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Phases I-III clinical trials of TV003, a live attenuated dengue vaccine, have demonstrated favorable safety, immunogenicity, and efficacy profiles. TV003 consist of four DENVs, components attenuated via nucleotide deletions in the 3′ untranslated region (3'UTR). The mechanism behind the attenuation of these vaccine strains remains unknown. To address this knowledge gap, we began by focusing on the DENV-3 component of TV003, which was developed using wild-type DENV-3 Sleman/78. Two mutants were generated, both with 30 nucleotide deletions (Δ30) in dumbbell (DB) II, one additionally with 31 nucleotide deletions (Δ30/31) in DBI of the 3'UTR, alongside Sleman/78, Sleman/78Δ30 (insufficiently attenuated), and Sleman/78Δ30/31 (vaccine strain), offer a unique opportunity to discern the attenuation mechanism from other 3'UTR interactions, evident through a progressive loss of function in these DENV variants. Using Gibson assembly, we constructed infectious clones of these 3 DENV-3. Sleman/78Δ30/31 showed slower replication in Huh-7 cells and primary MoDC, with smaller plaque sizes in BHK-21 monolayers than Sleman/78 and Sleman/78Δ30. To identify binding partners of wild type and mutant DENV-3 3'UTR, we utilized total protein extract from Huh-7 cells in RNA-affinity chromatography coupled with mass spectrometry. We found enrichment of ribosomal proteins (RPs) and translation initiation factors

(TIFs) in wild-type 3'UTR, which were deficient in the Δ30 and Δ30/31 3'UTRs; Δ30/31 3'UTR bound the fewest RPs and TIFs. Consistent with the loss of binding findings, the expression kinetics of prM, NS3 and NS5 proteins of Sleman/78Δ30/31 was the slowest, compared to Sleman/78 and Sleman/78Δ30. Similarly, replacement of the DENV-3 open reading frame with enhanced green fluorescent protein (eGFP) showed lowest eGFP expression with Sleman/78Δ30/31, compared to the other two DENV-3s. Our results suggest that, beyond forming the pan-handle structure of the DENV genome, the 3'UTR through the DBI and DBII secondary structures contribute to recruiting factors involved in translation, reduced efficiency of which attenuated Sleman/78Δ30/31.

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CROSS-NEUTRALIZING ANTIBODY RESPONSES ELICITED BY THE CHIKUNGUNYA VACCINE VLA1553

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In November 2023, the first vaccine against chikungunya virus (CHIKV) was approved by the U.S. Food and Drug Administration (brand IXCHIQ®, referred to as VLA1553). Approval came after decades of burden of chikungunya fever in South America, Southeast Asia, and Africa. CHIKV has cocirculated with other pathogenic alphaviruses for decades and as the vaccine rolls out, questions remain regarding the cross-reactive immunity elicited by VLA1553 and potential cross-protection for populations susceptible to multiple alphaviruses. Here, we quantified cross-neutralizing antibody (nAb) responses against arthritogenic alphaviruses in 30 individuals that received VLA1553 in trials NCT04546724 (301) and NCT04838444 (303) conducted in non-endemic settings at one month, six months, and one year post-vaccination. We quantified nAbs against CHIKV strains LR2006 (ESCA), 181/25 (Asian) and 2021 isolate of Tocantins, Brazil (Brazil7124/ESCA). We found the potency of nAbs against the CHIKV strains in vaccinees was nearly identical for the CHIKV strains, with geometric mean 50% plaque reduction neutralization titers ($PRNT_{50}$) ranging ~3000-5000 at one year post-vaccination. We also quantified cross-nAb $PRNT_{50}$ against o'nyong-nyong (ONNV), Mayaro (MAYV) and Ross River (RRV) viruses which were 1156, 650, and 39, respectively. We compared the vaccinee's responses to cross-nAbs elicited by CHIKV infection in 9 individuals in the endemic setting of Puerto Rico at 8-9 years post-infection. We found no significant differences when comparing cross-nAbs between vaccinees at one year post-vaccination and participants at 8 years post-infection for CHIKV-LR2006, MAYV, and RRV, but the $PRNT_{50}$ for CHIKV-181/25, CHIKV-Brazil7124 and ONNV trended slightly significantly higher following infection. Finally, we used antigenic cartography to demonstrate vaccinee and infection sera cluster antigenically. These data imply that VLA1553 elicits a cross-nAb breadth that extends to related alphaviruses to a similar potency of CHIKV infection, which may have important cross-protective implications for individuals susceptible to alphavirus cocirculation.

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DENGUE NS1 ANTIBODIES ARE ASSOCIATED WITH CLEARANCE OF VIRAL NS1

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Dengue vascular permeability syndrome, the syndrome whereby dengue infection leads to plasma leakage and shock, is the primary cause of death in severe dengue infections. The protective versus potentially pathogenic role of dengue NS1 antibodies is not well understood. The main goal of our analysis was to characterize the relationship between free NS1 concentration and NS1 antibody titers in primary and secondary dengue infection in order to better understand the presence and duration of NS1 antibody complexes in clinical dengue infections. Participants with acute dengue infection were recruited from Atlántico and Magdalena Departments in Northern Colombia from 2018 to 2020. Symptom assessment including dengue signs and symptoms, chart review and blood collection was performed. Primary versus secondary Dengue was assessed serologically. NS1 titers and anti-NS1 antibodies were measured daily. We observe that patients with secondary infection have higher antibody titers than those in primary infection, and we find a negative correlation between anti-NS1 antibody titer and NS1 protein. We demonstrate that in a subset of secondary infection, there are indeed NS1 antibody-antigen complexes at the admission day during the febrile phase that are not detectable by the recovery phase. Furthermore, dengue infection status is associated with higher circulating sialidases. The negative correlation between antibody and protein suggests that antibodies play a role in clearing this viral protein.

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CHARTING THE IMPACT OF MATERNAL ANTIBODIES AND EXPOSURES ON SAPOVIRUS IMMUNITY IN EARLY CHILDHOOD FROM A NICARAGUAN BIRTH COHORT

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Sapovirus was recognized as the second leading cause of acute gastroenteritis (AGE) in children under 24 months of age in the multi-site MAL-ED cohort study. While vaccines against sapovirus may reduce AGE burden, a major challenge to their development is a lack of information about natural immunity to sapovirus. We characterized the development of humoral immunity to sapovirus over the first 3 years of life in a Nicaraguan birth cohort. We measured sapovirus-specific IgG responses in serum collected between 2017 and 2020 from mothers soon after delivery and at 6 time points in children (6 weeks to 3 years of age, n=112 dyads), using virus-like particles representing three sapovirus genotypes (GI.1, GI.2, GV.1). Sixteen (14.3%) of the 112 children experienced at least one sapovirus AGE episode, of which GI.1 was the most common genotype. Seroconversion to GI.1 and GI.2 was most common between 5 and 12 months of age, while seroconversion to GV.1 peaked at 18 to 24 months of age. Most seroconversions were not accompanied by AGE symptoms. All children who experienced sapovirus GI.1 AGE seroconverted and developed genotype-specific IgG responses. In summary, Infants are born with broad

sapovirus-specific IgG, similar to their mothers, that declines to its lowest levels in mid-infancy. After this age, genotype-specific seroconversions occur, and by 24 to 36 months of age, seropositivity patterns of children resemble that of their mothers. By tracking humoral immunity to sapovirus over the first 3 years of life, this study provides important insights for the design of future pediatric sapovirus vaccines.

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SIGNALING CIRCUITS INVOLVED IN THE SELECTION OF HIGH-AFFINITY ANTIGEN-SPECIFIC B CELLS IN THE GERMINAL CENTER

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The germinal center (GC) functions as the site where somatic hypermutation, affinity maturation, and the selection of high-affinity B cells occur. Two selection models are proposed within the GC: a death-limited model and a birth-limited model. In the simplified death-limited model, low-affinity GC B cells undergo apoptosis, while high-affinity B cells do not. In the more practical birth-limited model, selection signals are conveyed through increased upregulation of metabolic factors in high-affinity cells, leading to accelerated proliferation compared to low-affinity GC B cells. Despite the selection model, high-affinity B cells consistently outperform low-affinity B cells in the GC. However, the exact signaling pathways governing this selection are not yet fully elucidated. An experimental approach involving the use of a 4-hydroxy-3-nitrophenyl (NP) antibody mouse model combined with a non-responsive NP recipient mouse model was employed. High and low-affinity B cells from donors were competitively transferred into the recipient mice. Recipient mice were sacrificed on days 6 and 9 of the GC response, and the GC response was assessed. RNA was extracted from donor B cells, followed by bulk RNA sequencing and analysis of differential gene expression to identify potential genes involved in GC selection. High-affinity B cells consistently outperformed low-affinity B cells, even when the initial ratio of high-affinity to low-affinity B cells was 1:138. Differential expression analysis of low and high-affinity GC B cells revealed a set of genes. Initially, focus was placed on a single gene with significant biological function. Through multiple subsequent experiments, it was observed that high-affinity B cells downregulated the expression of the candidate gene not only at the transcriptome level but also at the protein level. This project identified a novel gene that seems to play a role in regulating the GC selection process and the differentiation into antibody-secreting cells. Valuable insights were gained through the potential identification of a new signaling pathway within GC selection, mediated by the novel gene.

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PRIMARY ZIKA VIRUS INFECTION INCREASES HETEROTYPIC DENGUE VIRUS SERUM NEUTRALIZATION UPON SECONDARY DENV-3 INFECTION IN RHESUS MACAQUES

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Zika (ZIKV) and dengue (DENV) viruses co-circulate in the equatorial tropics. Due to genetic and structural similarities, antibody (Ab) cross-reactivity between ZIKV and DENV is common, and pre-existing ZIKV immunity can be protective, pathogenic, or neutral on successive DENV infections. Assessing the effect of prior infections on Ab responses in observational human studies is complicated by the heterogeneity in infection histories and the ability of both viruses to cause paucisymptomatic and asymptomatic infections. Here, we used rhesus macaques (RM) to model the effect of a prior ZIKV infection on the specificity and neutralizing activity of serum Ab elicited by subsequent DENV-3 infection. Flavivirus-naïve (n=8) or ZIKV-immune RMs (n=10) were subcutaneously inoculated with 10^4 PFU DENV-3 strain 6629, originally isolated from a human in Nicaragua in 2013. Plasma vRNA burden, serum Ab binding and neutralization titers were assessed over 90 days post-DENV-3 infection. RMs were productively infected with DENV-3 and all resolved infection by 15d post-inoculation. Prior ZIKV infection did not affect DENV-3 viral load peak or viremia duration. Primary DENV-3 infection yielded minimal, non-neutralizing ZIKV-cross-reactive binding Ab (geometric mean [GM] peak EC_{50} Ab titers = 89) whereas ZIKV-immune RMs developed high ZIKV-cross-neutralizing Ab titers (GM peak reporter viral particle neutralization titer $[RVPNT]_{50}$ = 2492), consistent with recall of pre-existing cross-reactive Ab. Prior ZIKV infection did not affect DENV-3 binding or neutralizing Ab titers. However, compared to RMs with primary DENV-3 infection, ZIKV-immune RMs developed significantly higher peak neutralizing serum Ab titers against other DENV serotypes (GM $RVPNT_{50}$ peak values: DENV-1 = 540 vs <100, DENV-2 = 1307 vs 135, and DENV-4 = 606 vs <100). In conclusion, pre-existing ZIKV immunity did not have a detrimental impact on the course of secondary DENV-3 infections. Instead, prior ZIKV immunity engaged Ab specificities that cross-neutralize heterotypic DENVs and skewed Ab recall responses toward epitopes that are present and accessible on all DENV serotypes.

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LIFESTYLE SCORES ARE ASSOCIATED WITH CELLULAR IMMUNE PROFILES IN HEALTHY TANZANIAN ADULTS

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Different immune profiles have been associated with responses to vaccines in high-income regions of the world. Importantly, immune system and vaccine responses can vary across geographical locations worldwide. Not only are responses different between high and low-middle-income countries (LMICs) but also between rural and urban populations within LMICs. Lifestyle factors such as housing conditions, exposures to microorganisms, parasites and diet are variables associated with rural-/urban-living. However, the relationships between lifestyle factors and immune profiles have not

been mapped in detail. Here, a lifestyle score was developed based on household assets, housing conditions and recent dietary history of an individual and its association with cellular immune profiles was studied. Immune profiling of healthy Tanzanians adults across four rural-/urban areas was performed using mass cytometry. Seventeen of *80* clusters were associated with location or lifestyle score, with eight identifiable only when using lifestyle scores. Rural residents with low lifestyle scores showed higher frequencies of $CD56^+$ NK cells, plasmablasts, atypical memory B cells, T helper 2 cells, Regulatory T cells, and activated $CD4^+$ T effector memory cells expressing CD38, HLA-DR, and CTLA-4. In contrast, those with high lifestyle scores, most of whom living in urban areas, showed a less activated state of the immune system and were enriched for naïve $CD8^+$ T cells. Using an elastic net machine learning model, we identified 'cellular immune signatures' by assessing the association between cell clusters and lifestyle scores. Assuming a link between these immune signature and vaccine responses, these signatures may inform us the cellular mechanisms underlying vaccine hyporesponsiveness, reduced autoimmunity, and allergies in low- and middle-income countries.

6301

APPLYING A ELECTROCHEMILUMINESCENCE MULTIPLEX SEROLOGIC ASSAY TO DETECT AND DIFFERENTIATE ZIKA AND DENGUE VIRUS EXPOSURES DURING LONG-TERM FOLLOW UP OF A COMMUNITY COHORT IN BRAZIL

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The cross-reactivity between flavivirus has been a major barrier to performing epidemiological investigations that address fundamental questions on how many people were exposed to the Zika virus (ZIKV) in the Americas and whether immunity persists for extended periods after exposure. These questions are critical for suspected cases continue to be detected in regions where population immunity is presumably high. To address this challenge, we developed an electrochemiluminescence assay and evaluated its performance for the serological detection of ZIKV and DENV infections in a cohort from Salvador, Brazil, which was followed from 2014 to 2024. We previously found that 70% of the cohort were exposed to ZIKV in 2015. In this pilot evaluation, we evaluated samples obtained before and after the epidemic for evaluation in a multiplex electrochemiluminescence assay (MesoScale Discovery, MSD) that detects ZIKV and DENV NS1-specific IgG antibodies. We determined the sensitivity and specificity of fold changes in ZIKV IgG antibodies as compared to DENV IgG antibodies. Among the 1453-member cohort, we selected 106 participants among which 58% (61) had serologic evidence of a DENV exposure prior to the ZIKV epidemic. Of the 61 and 45 participants with and without prior DENV exposure, respectively, 66% (40) and 67% (30) demonstrated MSD seroconversion to ZIKV after the epidemic. The MSD assay demonstrated 95% sensitivity and 93% specificity for detecting ZIKV infection among individuals previously exposed to DENV, and 97% sensitivity and 98% specificity among individuals without prior DENV exposure. These findings provide preliminary evidence the multiplex electrochemiluminescence assay is sensitive and specific for detecting ZIKV infection in a population with high background DENV exposure. We are extending these analyses to address whether ZIKV antibodies persist during a ten-year follow-up of our cohort and whether there is continued circulation of ZIKV. If validated, the assay may hold promise as a tool in detecting ZIKV transmission in populations where infections may be underrecognized and in screening pregnant women during prenatal care.

6302

UNDERSTANDING IMMUNITY TO MPOX AND SMALLPOX VACCINATION TO INFORM ON SEROSURVEILLANCE, DIAGNOSTIC DEVELOPMENT, AND NEXT-GENERATION VACCINES

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In early 2022, a cluster of Monkeypox virus (MPXV) cases were identified within the UK with no prior travel history, suggesting localised transmission of MPXV within the UK, particularly affecting gay, bisexual, & other men who have sex with men. Subsequently, a global outbreak occurred & Mpox continues to spread, with outbreaks in South-East Asia. Public health agencies worldwide have offered the Smallpox vaccination (IMVANEX/JYNNEOS) as a means to provide protection & limit the spread of MPXV. Through the development of a comprehensive set of multi-antigen ELISA & Luminex assays, we have been able to assess the serological responses to ~27 different Orthopoxvirus antigens in individuals with one, two, or three doses of Smallpox vaccination, & those with prior infection with MPXV. Furthermore, a subset of these have been tested for their neutralisation capacity against MPXV & VACV, as well as epitope mapping using a 15-mer peptide library against 33 MPXV-specific proteins. Using diverse Orthopoxvirus antigen ELISAs & Luminex assays, we observe differential trends in antigen-specific antibody dynamics after Smallpox vaccination, with variable waning by antigen. Prior MPXV infection induces similar responses to vaccination, in addition to an infection-specific response to A27. We observe trends in neutralisation against MPXV & VACV consistent with previous findings, whilst epitope mapping also shows similar yet distinctive antibody binding between both Smallpox-vaccinated & those with prior Mpox infection. Here, we show that both MPXV-infected & Smallpox-vaccinated individuals mount immune responses to a diverse yet core set of poxvirus antigens, with previous infection inducing a similar response. Neutralisation & epitope mapping varied by infection & vaccination, with core yet distinctive responses between infected & vaccinated individuals. We have since used these data together to develop next-generation serological tools for serosurveillance, and diagnostic development, & aid in future vaccine or therapeutic development to support the ongoing response to Mpox.

6303

ROBUST T CELL RESPONSES IN ADULT MICE PROVIDE INSIGHTS INTO PROTECTION AGAINST LA CROSSE VIRUS ENCEPHALITIS

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La Crosse virus (LACV), a negative-sense RNA bunyavirus, is a causative agent of pediatric encephalitis, often leading to severe clinical outcomes, including fatalities. LACV encephalitis predominantly affects individuals aged 16 years or younger, indicating an age-associated vulnerability. This susceptibility is recapitulated in murine models, with weanling mice (≤3 weeks old) exhibiting LACV-induced neuropathology, while adult mice (≥6 weeks old) display resistance. Despite the severity of LACV infections, approved vaccines or therapies are lacking, and the immunological mechanisms safeguarding adult mice from severe disease remain elusive. This study aimed to characterize the cellular response in adult and weanling mice following LACV infection. Leveraging in silico analysis, we identified peptides across the LACV proteome predicted to induce T cell responses in both mice and humans. Subsequently, through the use of ELISPOT assays, flow cytometry, and intracellular cytokine staining, we assessed the quantity and functionality of $CD4^+$ and $CD8^+$ T cells in LACV-infected adult and weanling mice. Our findings demonstrated that as early as 6 days post-infection, adult mice mount significantly more robust and polyfunctional cellular responses directed against both structural and non-structural proteins of LACV compared to weanling mice. Notably, $CD4^+$ and $CD8^+$

T cells derived from both spleens and brains of LACV-infected adult mice displayed heightened magnitude and polyfunctionality, characterized by significantly increased intracellular expression of key cytokines including IFN-γ, TNF-α, IL-2, and granzyme B. Furthermore, adoptive transfer of immune splenocytes to weanling mice 1 day prior to infection conferred protective effects. These data shed light on the role of robust, polyfunctional T cell responses in conferring disease resistance in adult mice against LACV infection. A comprehensive understanding of the cellular correlates of immunity following LACV infection is essential for the development of effective vaccines aimed at protecting children from LACV-induced disease.

6304

ZIKA VIRUS DNA VACCINES INCORPORATING DISULFIDE-BOND STABILIZATION OF ENVELOPE PROTEIN DIMERS

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The introduction of Zika virus (ZIKV) to South America in 2015 prompted the rapid advancement of vaccine candidates through preclinical and clinical studies, many of which were designed to express the two structural proteins premembrane (prM) and envelope (E). Expression of these two flavivirus proteins is sufficient for the production of noninfectious subviral particles (SVPs). SVPs represent a favorable approach to immunization due to their incorporation and display of the antiparallel E dimers that comprise the surface of an infectious virion and have been shown to be the target of neutralizing antibodies. Because protection from ZIKV infection has been correlated with an ability to neutralize mature forms of the virus, we hypothesized that locking these dimers in place via the introduction of engineered cysteine mutations may favor the induction of E dimer-specific antibodies, while limiting the elicitation of antibodies against less desirable targets. To investigate this, we designed multiple SVP vaccine constructs incorporating various combinations of cysteine mutations previously shown to promote disulfide bond formation between neighboring E proteins within a dimer. Transient transfection studies demonstrated that not all constructs were efficiently released from cells and that temperature could impact particle formation. Western Blot analysis confirmed the presence of disulfide-bonded E dimers in a subset of constructs. Neutralization assays will be performed on sera collected from mice immunized with our panel of DNA vaccine constructs to determine if the incorporation of cysteine mutations improves the antibody response in comparison to parental constructs that lack cysteine mutations.

6305

INVESTIGATING THE ROLE OF VACCINE INDUCED HUMORAL IMMUNE RESPONSES IN PROTECTION AGAINST MARBURG VIRUS AND SUDAN VIRUS DISEASES

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Filoviruses cause severe disease and different members of the family have led to outbreaks in humans. Currently, two vaccines have been approved to protect against Ebola virus (EBOV) infection, but there are no vaccines licensed to protect against other filoviruses. Specifically, Sudan virus (SUDV) and Marburg virus (MARV) have demonstrated the capability of causing deadly outbreaks of disease necessitating the need for additional effective filovirus vaccines. The EBOV glycoprotein (GP) shares limited homology with SUDV and MARV glycoproteins which eliminates the chance for cross-protection of EBOV specific vaccines. To address this problem, our group developed adjuvanted recombinant glycoprotein subunit vaccines for EBOV, MARV, and SUDV. Monovalent SUDV and MARV vaccines as well as bivalent formulations containing EBOV GP and either SUDV or MARV GP were tested for efficacy in cynomolgus macaques showing full protection against lethal infection with live MARV and SUDV. Our current work further investigates the role of humoral immune responses in protection against these diseases. Specifically, we analyze high avidity, neutralizing antibodies. Neutralizing antibody titers were determined using an rVSV-GFP reporter based microneutralization assay and antigen specific binding IgG concentrations and avidity was measured using a multiplex immunoassay. Two or three doses of the both SUDV vaccine formulations induced high titers of antigen binding IgG, antigen-specific virus neutralization and increasing IgG avidity which suggests continuing B-cell maturation. Interestingly, despite increasing MARV GP specific IgG concentrations and avidity, and full protection against challenge, neither MARV GP vaccine elicited high MARV neutralizing antibody titers suggesting that neutralizing antibodies may play a limited role in protection against that virus. Overall, these results reveal important information regarding the role of the humoral immune response in protection against filovirus disease which will help to direct future vaccine development efforts as well as a better understanding of natural immunity to filoviruses.

6306

FLAVIVIRUS TOOLS FOR VACCINE RESEARCH

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To help characterize the immune response to flavivirus infection and vaccines we have generated tools to analyze monoclonal antibodies (MAbs) and sera. We identify the binding sites (epitopes) for MAbs (>300 to date) at amino acid-resolution, using comprehensive alanine-scan mutation libraries (each >660 single mutations) of prM/E envelope proteins for dengue virus (DENV) serotypes 1-4, and Zika virus (ZIKV). Libraries were transfected into human cells for native expression and folding, with MAb binding to individual prM/E variants quantified by high-throughput flow cytometry. The epitopes have expanded our understanding of the immune response to prM/E and individual MAb neutralizing capabilities. Epitopes were both conformational (including quaternary) and non-conformational, were spread across prM and E domains I-III, and many have been correlated with their protective abilities against DENV or ZIKV infection. Epitope locations can give insights into MAb mechanism of action, such as MAbs that bind across adjacent E proteins, preventing rearrangements necessary for infectivity. Mapping also revealed epitopes common to DENV and ZIKV, information that can help create better vaccines and therapeutics. For vaccine development and research, we have produced reporter virus particles (RVPs) for DENV 1-4, ZIKV, West Nile and Yellow Fever viruses. RVPs are produced by expressing virus structural genes - C/prM/E - in trans with full-length replicon from which these genes were removed and replaced with a luciferase reporter gene. RVPs are safe and convenient for infectivity neutralization studies, including high-throughput analyses. RVPs are antigenically highly similar to wild type virus, and their maturation state can be readily manipulated, but are capable of only one round of infectivity, detected by luminescent readout. RVPs provide reproducible neutralization data across different production lots, volumes, time frames, laboratories, and are stable over long-term storage. DENV and ZIKV RVPs are used in studies to determine neutralization titers of sera from animals and humans immunized with candidate vaccines.

6307

THE ANGIOPOIETIN-TIE-2 AXIS IN CHILDREN AND YOUNG ADULTS WITH DENGUE VIRUS INFECTION IN THE PHILIPPINES

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Dengue virus (DENV) infection is associated with plasma leakage, which may progress to shock. The Angiopoietin (Ang)-Tie-2 axis regulates endothelial permeability. We examined the clinical utility of Ang-1, Ang-2

and the Ang-2:Ang-1 ratio for prediction of progression to severe DENV in a prospective cohort study of children and young adults (age 1 to <26 years) with DENV infection presenting to an outpatient clinic in the Philippines. Ang-1, Ang-2, and Tie-2 were measured from stored plasma by multiplex Luminex® assay. Patients were followed prospectively to document the clinical course (hospitalization, length of stay, intravenous fluid resuscitation, and transfer to a higher-level facility). We included 244 patients (median age 9 years, 40% female). At presentation, 63 patients (26%) had uncomplicated dengue, 179 (73%) had dengue with warning signs, and 2 (0.82%) had severe dengue. 181 patients (74%) were hospitalized. Ang-1 levels were lower and Ang-2 higher in patients who required hospitalization. Ang-2:Ang-1 ratio > 1 was associated with a relative risk of hospitalization of 1.20 (95% 1.03-1.36, p=0.016). A higher Ang-2:Ang-1 ratio was associated with longer length of hospital stay, higher frequency of transfer to a higher-level facility, larger intravenous fluid requirement, hemoconcentration, and thrombocytopenia. Ang-2 was correlated with procalcitonin (Kendall's τ =0.17, p=0.00012), a marker of systemic inflammation, as well as sVCAM-1 (τ =0.22, p<0.0001) and Endoglin (τ =0.14, p=0.0017), markers of endothelial activation. In conclusion, altered Ang-2:Ang-1 ratio can be detected early in the course of DENV infection and predicts clinically meaningful events (hospitalization, length of stay, and fluid resuscitation).

6308

IDENTIFICATION OF THE FLAVIVIRUS CONSERVED E-L295 RESIDUE AS A TARGET FOR THE RATIONAL DESIGN OF CANDIDATE WEST NILE LIVE-ATTENUATED VACCINES

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West Nile virus (WNV) is a flavivirus endemic in the United States. There is no licensed WN vaccine. Development of a candidate WN live-attenuated vaccine (LAV) that can elicit protective immunity after a single immunization is a research priority. In the 21st century, LAVs are expected to encode multigenic mutations underlying a defined molecular basis of attenuation. The envelope (E) protein governs viral entry and is a major target for neutralizing antibodies, making it a critical component for WN LAV development. Each E protein monomer has three domains (EDI, EDII, and EDIII). Two neighboring E monomers form the dimer parallel to the virion. As a class II fusion protein, the conformational change of the E protein from dimer to trimer induces the membrane fusion for releasing viral genome into the cytoplasm. Formation of the E protein trimer is irreversible due to the relative movement between EDI and EDIII that creates a stable structure. EDI and EDIII are connected by a single EDI-EDIII linker. Five of 11 residues within the EDI-EDIII linker are conserved among flaviviruses, indicating a common mechanism for the EDI-EDIII interdomain movement. Mutations of the flavivirus conserved residues in the EDI-EDIII linker exhibit attenuating effects for yellow fever and dengue -2 viruses. However, no study has systematically examined the utility of these mutations for the rational design of candidate LAVs. As a proof-of-concept, we demonstrate that the WNV E-L295 residue in the EDI-EDIII linker is a potential target for attenuating mutation. Eight alternative amino acid substitutions of the E-L295 residue were retained in the consensus sequence of WNV mutants rescued from a cDNA infectious clone of the NY99 strain. The E-L295S mutant exhibited infectivity exceeding 6 log10PFU/ml in transfected Vero cells and yet fully attenuated WNV-NY99ic without compromising the neutralizing antibody response in 4-week-old outbred Swiss mice. Further, the genome-PFU ratio suggests that the E-L295S mutation did not significantly compromise virion assembly. Our results indicate that the E-L295 residue is a target for the rational design of candidate WN LAVs.

6309

IL-1β MEDIATES POWASSAN VIRUS INFECTION AND ESTABLISHMENT AT THE SKIN INTERFACE

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Powassan virus Lineage I (POWV) and Lineage II (DTV) are tick-borne flaviviruses endemic to the United States and Canada that can cause severe encephalitis and meningitis and are primarily transmitted by *Ixodes scapularis and Ixodes cookei* ticks. During blood feeding, a variety of pharmacologically active proteins and other molecules are transmitted via salivary gland secretion that acts in ways that disrupt the homeostasis of the bite-site microenvironment. The mechanisms of blood feeding and tick salivary factors have been demonstrated to facilitate virus transmission. However, a significant gap exists in our current knowledge of how the immunomodulation at the tick-host-virus interface enhances POWV transmission, establishment, and dissemination to the target organs. We have demonstrated the activation of IL-1β during POWV-infected tick feeding at the transmission interface. Here, we describe the activation and secretion of IL-1β via the NLRP3 inflammasome pathway during POWV infection. We show that infection with POWV in THP-1^{PMA} cells results in the secretion of IL-1β into the supernatant, in line with LPS positive control. However, the mechanism of this secretion during POWV infection is poorly understood. We aim to utilize NLRP3-KO-THP1 cells alongside CASPdef-THP1 cells to assess the lack of NLRP3 and Caspase-1 on the cleavage/secretion mechanisms. Next, we will infect these cells with POWV with and without *Ixodes scapularis* salivary gland extract (SGE) to assess the role of salivary gland factors in activating IL-1β via the inflammasome pathway. Additionally, to fully validate our findings on a relevant model, we will utilize an *ex vivo* human skin model that utilizes whole dermal tissue to assess the impacts of tick-borne virus infection. Our proposed studies will lead to a better understanding of immunomodulation at the tick-virus-host interface during POWV transmission.

6310

SUSCEPTIBILITY AND TRANSMISSION POTENTIAL OF ECTOTHERMS AND HOUSE SPARROWS TO JAPANESE ENCEPHALITIS VIRUS

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Japanese encephalitis virus (JEV) is a vector-borne flavivirus that is known to be maintained in an enzootic lifecycle between mosquitoes, pigs and wading birds. An estimated 68,000 human cases are reported annually, and symptoms in humans can range from a mild fever to severe neurological complications. Arboviral diseases are spreading to new areas at alarming rates secondary to increases in global trade and travel, climate change and migration of both animal reservoirs and vectors. Although JEV is currently only endemic in Asia, concerns for the spread of JEV into new areas are rising as indicated by a recent outbreak on the mainland of Australia. This outbreak is causing significant public health impacts by inflicting illness in humans and creating notable economic losses to the pig industry. Given that other closely related arboviruses such as West Nile virus have spread to the U.S. over the past several decades, JEV holds high potential to become established in the U.S. However, little is known about what animal reservoirs, particularly wildlife inhabiting mosquito-dense locales, could contribute to JEV ecology in the U.S. Here we report that ball pythons, garter snakes, and house sparrows are susceptible to JEV genotypes I and III, but not to JEV genotypes II and IV. Frogs exhibited susceptibility to JEV genotype I. Meanwhile, toads, alligators and green anoles were not susceptible to any of the four genotypes of JEV. Our results expand upon the knowledge base of susceptible species and provide evidence that domestic wildlife species could play a role in the introduction or maintenance of JEV within the U.S.

6311

EVALUATION OF 41 BIOMARKERS FOR PREDICTION OF MORE SEVERE DENGUE OUTCOMES

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Dengue continues to be a major public health burden globally. While most dengue cases resolve after one week, 1-5% of hospitalized patients develop severe manifestations during the critical phase (day 4-6 from fever onset), allowing a window of opportunity to identify patients at risk of progression. This nested case-control study assessed 41 biomarkers using stored blood samples from 2 previous studies performed between 2010 and 2015 in Vietnam. One study enrolled children and the other enrolled adults, all presenting within 3 days after fever onset. The biomarkers were selected from the vascular, immunological, and inflammatory pathways in dengue. Six biomarkers were analysed using the Elecsys system, and 35 were analysed using a Luminex panel. Clinical endpoints were severe dengue (based on the WHO 2009 classification) for children and moderate-to-severe plasma leakage for adults. We used logistic regression to analyse the relation of each biomarker with outcome separately, and used multivariable lasso logistic regression to select which biomarkers best predict the outcome. We found that for most biomarkers elevated values in children associated with severe dengue (the most notable were ESM-1, syndecan-1, osteopontin, ferritin, GDF-15, and angiopoietin-2), whereas for 10 markers, typically vWFA-2 and PDGFCC, the association was reversed. In adults, for almost all biomarkers elevated values associated with moderate-to-severe plasma leakage, with the most notable being IL-6, GDF-15, angiopoietin-2, procalcitonin, and IL-8. From the lasso models, 17 biomarkers were identified as promising for children, with ESM-1, syndecan-1, IL-1ra, procalcitonin, FDGFCC, and sFLT-1 having the strongest association with severe dengue. For adults, four biomarkers were identified as promising, including procalcitonin, IL-6, IL-1ra, and GDF-15. These suggested biomarkers may play a role for future biomarker based prognostic tests for dengue disease progression.

6312

NEUTROPHIL MEDIATORS LINKED TO TIGHT JUNCTION DISRUPTION AND INCREASED INTESTINAL PERMEABILITY IN SEVERE DENGUE

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In both pediatric and adult dengue cases, there is a correlation between disease severity and increased intestinal permeability. Notably, in dengue mouse models, infection activates monocytes and tissue macrophages that result in viral dissemination and heightened neutrophil infiltration within the gastrointestinal tract. While the breakdown of tight junctions due to neutrophil mediators has been observed in inflammatory bowel conditions, this phenomenon has not yet been reported in the context of dengue. Plasma samples from 97 adult dengue patients; 39 dengue fever (DF), 45 dengue with warning signs (DWS) and 13 severe dengue (SD) were collected in the febrile, critical and recovery phases. Samples were assayed for markers of intestinal injury; Trefoil factor 3 (TFF3), microbial translocation; lipopolysaccharide binding protein (LBP) and CD14, tight junction integrity; zona occludens-1 (ZO1) and claudin-5; and neutrophil mediators; matrix metalloprotease-8 (MMP8), myeloperoxidase, and elastase. Thirty healthy controls were included. In the febrile and critical phases, all measured proteins were elevated in dengue samples compared to controls and proteins returned to baseline at recovery phases. In the febrile phase, SD subjects had higher ZO1, myeloperoxidase and elastase levels compared to DWS and DF. In the critical phase, TFF3, CD14 and myeloperoxidase were increased in SD vs DWS and DF. In the febrile phase, LBP was significantly associated with ZO1 (r=0.43, P<0.001) and CD14 was associated with claudin-5 (r=0.41, P<0.001), indicating intestinal injury and microbial translocation. Additionally, in the febrile phase, ZO1 was associated with MMP8 (r=0.67 P<0.01), myeloperoxidase (r=0.23, P=0.03) and elastase (r=0.38, P<0.01), and claudin-5 with myeloperoxidase (r=0.01. P<0.01) and elastase (r=0.22, P=0.03), suggesting neutrophil mediators to disrupt tight junctions in the gut. In adults with dengue, increased intestinal permeability and microbial translocation in severe disease were associated with disruption of the tight junctions mediated by neutrophil mediators.

6313

DIFFERENTIAL EFFECT OF MOSQUITO SALIVA FROM DISTINCT SPECIES ON HUMAN DERMAL ENDOTHELIAL CELL FUNCTION *IN VITRO* AND WEST NILE VIRUS PATHOGENESIS *IN VIVO*

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During probing and feeding, an infected mosquito injects both virus and saliva into the skin of the host. The presence of mosquito saliva in the skin increases arbovirus pathogenesis in the bitten host, however the exact mechanism behind this remains to be determined. It is hypothesized that disease enhancement is dependent on the function of the dermal endothelium, where an increased permeability aids in the influx of virus-susceptible cells to the bite site and therefore more cells for the virus to replicate in. The effect of mosquito saliva on the human dermal endothelium has been studied primarily for *Aedes aegypti*. Here, we investigate and compare the effects of saliva from *Culex* and *Aedes* species on the human dermal endothelial cell function *in vitro*. Furthermore, we investigate the effect of *Culex* saliva on West Nile virus (WNV) pathogenesis in a mouse model. We found that salivary gland extract from anthropophilic mosquito species (*Aedes* and *Cx. pipiens molestus*) induce permeability of the human dermal endothelium, while an ornithophilic mosquito species (*Cx. pip. pipiens*) does not. We identified that this effect is due to the presence of protease(s) in *Cx. pipiens molestus* saliva. In addition, we show that the presence of *Cx.* saliva at the WNV inoculation site *in vivo* leads to an increased mortality rate, more consistent weight loss and slightly higher viremia compared to inoculation of WNV alone. Moving forward, identification and characterization of novel salivary proteins from distinct mosquito species will advance the development of intervention methods to combat potential transmission risks and disease severity of emerging mosquito-borne pathogens.

6314

DETECTION OF WEST NILE VIRUS IN FORMALIN-FIXED, PARAFFIN-EMBEDDED TISSUES FROM FATAL CASES BY USING RT-PCR AND *IN SITU* HYBRIDIZATION: INSIGHTS INTO PATHOGENESIS

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West Nile Virus (WNV) is a flavivirus transmitted through infected birds by mosquitos to humans, and the leading cause of mosquito-borne disease in the continental United States. Although most people do not develop symptoms or develop only minor symptoms, about 1 in 150 people infected with WNV develop serious central nervous system (CNS) illness, such as encephalitis or meningitis, and 1 in 10 with serious illness die. The risk of serious illness increases for individuals over the age of 60 and those with comorbidities such as cancer, hypertension, kidney disease, and organ transplant associated risk factors. Due to the low incidence of serious illness and death, little information is available on the pathogenesis in humans. The

goal of our study was to compare the results of RT-PCR assay targeting the NS1 gene to the results of other tissue-based assays for the detection of WNV in formalin-fixed, paraffin-embedded (FFPE) autopsy tissues, and to better understand the tissue tropism and pathogenesis of the virus through *in situ* hybridization (ISH). RNAscope ISH probes were designed and a WNV ISH assay was developed. FFPE autopsy tissues from the CNS from 29 cases positive for WNV by RT-PCR were tested by immunohistochemistry (IHC) and ISH. WNV genomic/replicative RNA was detected by ISH in 24/29 (83%) cases and viral antigens were detected by IHC in 14/29 (48%) cases. The median age of infected individuals was 64 years old, and the median duration of illness was 19 days. Fifteen of 29 (52%) cases had at least one known comorbidity. WNV RNA was localized in neurons and glial cells of various parts of the CNS, including cerebellum, cerebral cortex, medulla, pons, thalamus, and spinal cord. Tissue-based molecular assays expand diagnostic opportunities, particularly when conventional specimens are unavailable, and provide deeper insights into viral tissue tropism, sites of replication, and pathogenesis.

6315

EXPLORING THE ROLE OF HOST GLYCOSAMINOGLYCANS ON FLAVIVIRUS NS1-MEDIATED ENDOTHELIAL DYSFUNCTION

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The mosquito-borne flaviviruses cause diverse disease presentations, often involving endothelial barrier dysfunction that is driven by vasoactive cytokines and viral factors, such as nonstructural protein 1 (NS1). NS1 induces tissue-specific endothelial dysfunction and leakage by disrupting the endothelial glycocalyx layer (EGL) and intercellular junctions upon binding and internalization into endothelial cells (ECs). Glycan/NS1 interactions are a key determinant of NS1 binding to ECs. Heparan sulfate (HS) is a ubiquitous glycan component of the EGL of ECs and is present in diverse forms with variability in extent and linkages of sulfation in addition to chain length. While HS is known to be critical for NS1 cell binding, it is unclear what species of HS mediate NS1 interactions with ECs and what species are present on ECs from distinct tissues. To address this gap in knowledge, we used a glycosaminoglycan (GAG) array to determine what species of HS bound dengue virus (DENV) NS1. We found that NS1 bound well to diverse HS linkages, including 2-O-S, 3-O-S, and 6-O-S, and that the strength of DENV NS1 binding correlated with the extent of sulfation. We then tested the capacity of synthetic GAGs with these HS linkages to bind to DENV NS1 and protect against NS1-mediated endothelial hyperpermeability in human pulmonary microvascular endothelial cells (HPMEC). Using an ELISA, we found that NS1 bound strongly to certain synthetic GAGs, confirming the GAG array data. Interestingly, we found that only GAGs containing 3-O-S, and to a lesser extent 6-O-S, blocked NS1 from inducing endothelial hyperpermeability. Further, we found that a 3-O-S binding peptide abrogated the capacity of DENV NS1 to bind to ECs and trigger endothelial hyperpermeability, in contrast to a control peptide. We then confirmed the expression of multiple 3-O-S sulfotransferases on the surface of HPMEC, suggesting their expression in lung ECs, and are currently knocking out individual genes via CRISPR-Cas9. Together, these data indicate that while NS1 can bind to multiple HS species, only specific species of HS, like 3-O-S, may be important for NS1-mediated endothelial dysfunction.

6316

HETEROLOGOUS PROTECTION OF RECENT O'NYONG-NYONG VIRUS STRAIN UVRI0804 BY AN INACTIVATED CHIKUNGUNYA VIRUS VACCINE

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O'nyong-nyong virus (ONNV) is a mosquito-transmitted alphavirus identified in Uganda in 1959. The virus has potential for enzootic and urban transmission cycles, and in humans, ONNV infection manifests as fever, rash, and joint/muscle pain lasting months. There are currently no specific vaccines or antiviral treatments for ONNV. Since highly passaged alphaviruses often lose pathogenic features, we constructed an infectious clone for ONNV-UVRI0804 ($ONNV_{0804}$), a 2017 isolate from a febrile patient in Uganda (Ledermann, 2022). The recovered recombinant virus was passaged in mosquito cells and sequenced to ensure genome integrity. Viral replication for $ONNV_{0804}$ was compared to the highly passaged strain $ONNV_{UgMP30}$, and $ONNV_{UgMP30}$ replicates to higher levels in fibroblasts and Vero cells, but performed similarly in C6/36 cells. We performed a head-to-head comparison in both C57BL/6 mice and AG129 interferon-deficient mice. In both types of mice, $ONNV_{0804}$ dramatically outperformed $ONNV_{UgMP30}$. Specifically, in AG129 mice, $ONNV_{0804}$ caused a quicker onset of disease (footpad swelling/weight loss) and much higher viremia at 3 dpi. In WT mice, $ONNV_{0804}$ caused footpad swelling beginning at 5dpi, and the virus demonstrated much broader tissue distribution and higher vRNA loads at both 5 and 43 dpi relative to $ONNV_{UgMP30}$. This finding indicates that ONNV can persist in joint and muscle tissues for long periods of time, which has been associated with chronic arthritogenic disease. Mice were vaccinated with HydroVax-CHIKV using prime-only and prime/boost approaches. Neutralizing antibody titers against $ONNV_{0804}$ and CHIKV were slightly higher in the prime/boost group. At 4 weeks post-vaccination, animals were challenged with $ONNV_{0804}$ and only control animals developed viremia. Both vaccine groups had increased survival and were protected against weight loss. Significant footpad swelling occurred in the control and prime-only groups but not in the animals receiving the prime-boost CHIKV vaccine. These data imply that vaccination against CHIKV can protect against ONNV infection and disease even for a contemporary, highly pathogenic strain.

6317

GENETIC ANCESTRY-ASSOCIATED DIFFERENCES IN DENGUE VIRUS INFECTION OF PRIMARY HUMAN SKIN CELLS

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Host genetic ancestry is a risk factor for severe dengue; however, the lack of translatable models has hindered studying this relationship. We acquire discarded human skin specimens from elective cosmetic surgeries to use for *ex vivo* skin explants or digestion into single cell suspensions to study dengue virus (DENV)-host interactions. Genetic ancestry is determined for all donors through a panel of 128 ancestry informative markers specific for European ancestry (EA) and African ancestry (AA). Skin explants were inoculated with DENV-2 (strain 16681) and analyzed with confocal microscopy at 24 hours post-infection (hpi). This revealed a striking correlation between infection in the epidermal and dermal layers with an increase in proportion of EA. EA donors also had a three-fold increase in recruitment of CD163+ macrophages to the site of infection and a two-fold increase in infection of those cells. AA donors had significantly higher levels of interferon-α while EA donors had a marked inflammatory response with significantly higher levels of interleukin-1β. To identify mechanistically what is responsible for these observed differences, we separated epidermal and

dermal layers of human skin and digested them into single cell suspensions. Cells were infected with DENV-2 and analyzed by flow cytometry at 24hpi. Preliminary data indicate that epidermal cells, most notably keratinocytes, from EA donors have significantly higher levels of infection than AA donors. Contrary to *ex vivo* explant data, there was no significant ancestry-associated difference in infection of isolated dermal cells. These initial findings suggest that epidermal keratinocytes are potentially the driving force behind ancestral differences observed in intact tissue. This work provides biologic evidence of ancestry-associated differences in cutaneous responses to DENV. Identification of cells or innate proteins responsible for protection will provide potential targets for therapeutic development against severe disease.

6318

ARBOVIRUS DISEASE PATHOGENESIS IN OBESE AND TYPE-II DIABETIC-LIKE MICE

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Mosquito-borne viruses are important public health threats, and Mayaro virus (MAYV) is an arbovirus with epidemic potential. Also, underlying chronic diseases like diabetes, cardiovascular disease, and cancer, affect more than 40 million individuals who live in arbovirus-endemic areas. Clinical data indicate that arbovirus infections in diabetic patients lead to more severe outcomes and higher mortality compared to the non-diabetic. We hypothesized that individuals with preexisting diabetes could have increased MAYV replication, resulting in severe disease outcomes and mosquito transmission alterations. We employed murine model of insulin resistance/obesity as proxy for Type II diabetes mellitus (T2DM). Leptin receptor mutant $LEPR^{db/db}$, $LEPR^{db/WT}$, and wild type (WT) C57BL/6J mice were pretreated with IFNAR blocking antibodies to render them permissive to MAYV infection via infected mosquito bite. Acute viremia, viral load, pathogenesis, and immune responses were quantified. The model demonstrated a predictable pattern of viremia with titers starting to increase at 2 days post infection (dpi) (7.6, 5.2 and 4.77 $\log_{10}$ ffu/mL, respectively), and with highest titers (9.2 and 8.5$\log_{10}$ ffu/mL) at 4 dpi. No significant differences in viremia were observed between T2DM genotypes on any day. MAYV was detected in all tissues analyzed, with highest viral loads detected in liver and spleen of WT (8.7 - 8.9 $\log_{10}$ffu/mL), and $LEPR^{db/db}$ (8.82 - 9.33 $\log_{10}$ ffu/mL) mice, and spleen of $LEPR^{db/WT}$ (9.1 $\log_{10}$ ffu/mL). Although higher titers were detected in $LEPR^{db/db}$ mice tissues, no significant differences in viral load were observed compared to $LEPR^{db/WT}$ or WT controls. Histopathological analysis showed necrotic foci in some $LEPR^{db/db}$ livers of infected animals, which was not detected in the controls. In summary, MAYV infection of $LEPR^{db/db}$, $LEPR^{db/WT}$, and WT C57BL/6J yielded no genotype dependent difference in serum viremia, and no significant association of peak viremia with tissue viral burden suggesting that these observations were driven by host-intrinsic factors (e.g. cytokines, clotting factors) as opposed to direct viral action.

6319

PRM AND E SEQUENCE VARIATION ALTERS THE STRUCTURE ENSEMBLE OF ZIKV TO INFLUENCE ANTIBODY EPITOPE ACCESSIBILITY

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Zika virus (ZIKV) is a mosquito-borne flavivirus discovered in 1947 in Uganda. ZIKV has been responsible for multiple outbreaks in humans, including the 2015 epidemic of the Americas. Flavivirus virions are characterized by the presence of 180 envelope (E) structural proteins on the surface, arranged as antiparallel dimers, that represent the major target of neutralizing antibodies. Virions also incorporate an equal number of a second structural protein, premembrane (prM), that is cleaved by the host protease furin during viral egress. In the mature form of the virus, 90 E homodimers lie flat on the viral membrane, with short membrane-bound M peptides located beneath the E protein herringbone lattice. This complex and dense arrangement of E proteins results in limited accessibility of many surfaces to binding by neutralizing antibodies. Antibodies may access cryptic epitopes that are variably accessible amongst the ensemble of states sampled by flaviviruses. To investigate the effect of amino acid variation on the accessibility of cryptic E protein epitopes, we produced a library of ZIKV reporter virus particles using structural proteins of 174 genetically diverse strains that possess naturally occurring variation in the structural proteins prM and E. We performed neutralization studies using E protein-specific monoclonal antibodies that poorly neutralized a reference strain H/PF/2013 to identify strains that display unexpected neutralization sensitivity. These studies revealed distinct clusters of genetically related strains that facilitate the rapid identification of single amino acid substitutions in prM and E proteins that influence epitope accessibility of distal sites on the E protein. These studies will provide a high-resolution understanding of how amino acid variation contributes to the antigenic structure of ZIKV and will inform antigen design and vaccine development.

6320

BEYOND THE ROOST: EXPLORING THE IMPACTS OF A MODIFIED DIET ON MERS-COV INFECTION IN THE JAMAICAN FRUIT BAT (*ARTIBEUS JAMAICENSIS*)

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Bats harbor a wide range of high-consequence zoonotic viruses, yet many ecological and biological mechanisms underlying the risk of spillover remain understudied. Several field studies have shown that the loss of food sources, often caused by climate change and anthropogenic disturbance, alters bat behavior and potentially increases the risk of viral spillover. Middle East Respiratory Syndrome coronavirus (MERS-CoV) is a zoonotic bat-borne virus endemic to the Arabian Peninsula, where evidence of spillover to dromedary camels and humans has been recorded. To interrogate physiologic processes that influence viral shedding and cross-species transmission, we sought to determine how an altered diet, mimicking natural periods of low-quality forage, impacts infection dynamics and immune responses in bats. Our preliminary work examining immune responses of Jamaican fruit bats (*Artibeus jamaicensis,* Aj's) following immunization with a virus-like particle expressing Nipah virus glycoprotein suggest that bats fed a diet restricted in protein content develop a more robust neutralizing antibody response than those provided standard diet. To determine whether similar immunologic patterns hold true in bats experimentally inoculated with MERS-CoV, we altered the diet composition of Aj's infected with MERS-CoV. Aj's were fed a protein-restricted diet, with one group inoculated with MERS-CoV (n=12) and a second group mock-

inoculated with sterile PBS (n=12). A third group of uninfected bats (n=3) were cohoused with experimentally infected bats (n=3) to assess potential bat-to-bat transmission. Results will be presented that compare protein-restricted Aj's to those fed their standard diet to compare viral shedding rates and serological, immunological, and histopathological analyses between the diet groups.

6321

INVESTIGATION OF VIRUS-HOST INTERACTIONS IN SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS INFECTION USING A TRANSCRIPTOMICS APPROACH

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Severe fever with thrombocytopenia syndrome virus (SFTSV) is an emerging tick-borne bunyavirus that can cause severe disease in human with a mortality rate of more than 10%. Local transmission of SFTSV has been reported in a number of Asian countries, including China, Japan, South Korea, Vietnam, and Thailand. Symptomatic SFTSV infection usually presents as an acute febrile illness with high fever, thrombocytopenia, and hemorrhage. To provide novel insights into the virus-host interactions in SFTSV infection, we investigated the transcriptomics profile of SFTSV-infected Huh-7 (human hepatoma) cells using RNA-Seq. Our transcriptomics analysis identified 164 (33 down- and 131 up-regulated) differentially expressed genes (DEGs) between mock and SFTSV infection groups at 8 hours post-infection (hpi). Compared to 8 hpi, the expression profile at 48 hpi was largely altered with more than 2900 DEGs. Among these DEGs, 113 out of 164 (68.9%) DEGs at 8 hpi were also differentially expressed at 48 hpi. Gene ontology and pathway enrichment analyses showed that most of the perturbations were related to the host immune response, particularly those related to the cytokine and chemokine response. Protein-protein interaction network of DEGs identified three clusters. In the largest cluster (cluster 1), there were 80 nodes and 647 edges in Cluster 1 with average node degree 16.2, suggesting that the DEGs in this cluster were highly connected. The DEGs in Cluster 1 are mainly involved in neutrophil apoptotic process, neutrophil chemotaxis, and T-helper 17 cell differentiation. The top 5 hub genes with high connectivity in the network regarded as key regulators in cluster 1 were IL-6, IL-1B, CXCL-8, ICAM-1 and PTGS-2. In summary, our study characterized the SFTSV-induced host transcriptomics perturbations and may facilitate the identification of host factors as potential antiviral targets for SFTSV infection.

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MYELOID CELL REPLICATION PHENOTYPES UNDERLIE EPIZOOTIC POTENTIAL OF ALPHAVIRUSES

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Alphaviruses are globally distributed +ssRNA viruses which are transmitted by mosquito vectors. Viral determinants which impact the transmission and pathogenesis of numerous alphaviruses have been identified, including amino acid coding changes in the viral attachment protein (E2). However, the role of viral RNA secondary structure in viral emergence is still poorly defined. We have developed a computational approach to compare RNA structures across the alphavirus genus in order to identify RNA structure signatures associated with specific viral properties (e.g. RNA structures unique to epizootic viruses). Using this approach we have identified several regions in the Venezuelan equine encephalitis virus and Sindbis virus genomes that are predicted to contain RNA structures relevant for emergence and pathogenesis of these viruses. Surprisingly, despite encoding distinct viral RNA structures, pathogenic/epizootic strains of these different viral species were all observed to replicate differentially in myeloid cells, suggesting that myeloid cell replication fitness may be a hallmark of viral emergence for alphaviruses. Changes in myeloid cell replication fitness were also associated with changes in pathogenesis in a small animal model. Using molecular approaches, we have identified several RNA binding proteins which differentially interact with these viral RNA structures, indicating that distinct molecular mechanisms underlie this shared replication phenotype across different alphaviruses. Presently we are investigating the mechanism by which altered myeloid cell replication contributes to transmission and pathogenesis in other relevant species.

6323

THERAPEUTIC EFFICACY OF ARTEMETHER LUMEFANTRINE PLUS SINGLE DOSE PRIMAQUINE FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN IRRIGATED AGRO INDUSTRIAL METAHARA SUGAR FACTORY, CENTRAL ETHIOPIA

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Artemether-lumefantrine (AL) plus a single dose of primaquine is recommended as the first-line treatment of uncomplicated *P*lasmodium *falciparum* malaria in Ethiopia. WHO recommends regular monitoring of the therapeutic efficacy of frontline drugs. Anti malaria drug resistance is now a threat to malaria control programs. This study was conducted to assess the therapeutic efficacy of AL with a single dose of primaquine for the treatment of uncomplicated *P. falciparum* malaria in Central Ethiopia. A one arm prospective study was conducted at the Metahara Sugar Factory site from December 2022 to February 2023 following the WHO protocol. Eighty-seven patients were enrolled and each patient was treated with a standard, 6 doses of AL given twice daily for 3 days under partial supervision, Moreover, each patient was given a single dose of primaquine on Day 0. Clinical and parasitological responses were assessed during the 28 day follow-up period. Outcomes of treatment were defined according to the standard WHO classification. Recurrent parasitemia was genotyped. The outcome of the present study revealed that PCR uncorrected and corrected cure rates at day 28 were 97.7% (95% CI: 91.8-99.8%, and 98.8% (95%CI: 91.0-99.4%), respectively. The high parasite and gametocyte clearance rate (100%) was recorded on day 3. Fever was resolved in all patients on day 2. Hemoglobin level was significantly improved on day 28 compared to both day 0 and day 14. There was no evidence of severe adverse events during the study period. The results of this study revealed that AL with single does PQ treatment recommended by the National Malaria Elimination Program is highly efficacious with a high parasite clearance rate and fast resolution of fever in the study setting. Regular monitoring of AL plus PQ efficacy, including molecular markers of drug resistance studies is suggested in this and another malarious area of the country.

6324

LOW LEVEL OF ANTIMALARIAL DRUG RESISTANCE IN 2014-15: INTEGRATION OF PRIMAQUINE INTO INDIA'S ANTIMALARIAL DRUG POLICY 2013

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The surveillance and containment of antimalarial drug resistance play a pivotal role in the efforts of countries striving to eliminate malaria. It is imperative to monitor the evolution of resistance through studies conducted before and after changes in treatment policies. Between 2014 and 2015, a thorough study collected 939 P. falciparum-positive blood samples from ten sites in India, organized into four clusters. Sequencing amplified PCR products identified point mutations in genes linked to drug resistance: Pfdhfr, Pfdhps, Pfmdr1, and Pfk13. Triple Pfdhfr mutants were exclusive to northeast India near the Myanmar border, contrasting with the central region dominated by wildtype. Pfdhps wildtypes prevailed nationwide, lacking double mutants. Pfmdr1 wildtype dominated, except in Northwest India with nonsynonymous double mutations. Pfk13 exhibited synonymous mutations, primarily in Central India. Low drug resistance pressure and

geographic cluster heterogeneity were indicated by linkage disequilibrium and principal component analysis. India displayed low drug resistance levels during the transition from CQ to SP to ACTs, surpassing global endemic countries. India's unique treatment policy included gametocidal primaquine (PQ), potentially slowing resistance spread. The study underscores India's comparatively low drug resistance, possibly due to gametocidal and schizonticidal drug use, limiting parasite transmission. Conducted nationwide from 2014-2015, the study establishes a baseline for monitoring and understanding ACT resistance emergence and dissemination in India. Highest resistance occurred in Northeast India near Myanmar, a region prone to resistance. Primaquine's broad use, with gametocidal and schizonticidal properties, likely crucially sustains low resistance, averting strong selection pressures.

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MOLECULAR SURVEILLANCE OF *PLASMODIUM FALCIPARUM* DRUG RESISTANCE MARKERS IN GHANA

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Antimalarial drug resistance looms as a threat to malaria control. Artemisinin-based combination therapy (ACT) remains the standard treatment for uncomplicated malaria. However, the emergence of artemisinin partial resistance and increasing tolerance of *Plsodium falciparum* to ACT partner drugs in Africa cast a shadow on the efficacy of ACTs. Therefore, necessitating genomic surveillance of *P. falciparum* to monitor known antimalarial drug resistance markers in *Pfcrt, Pfmdr1, Pfkelch13, Pfdhfr, and Pfdhps* genes and to look for novel markers of resistance. We demonstrated the utility of amplicon sequencing of longitudinal cross-sectional samples collected from clinical sources in an ongoing study across Ghana for surveillance using Oxford Nanopore Technologies (ONT). We sequenced 285 samples and analyzed the presence of haplotypes in known antimalarial drug resistance genes for *P. falciparum.* We found no evidence of mutations in the *kelch13* gene known to mediate artemisinin partial resistance. The *Pfmdr1*-N86Y and YI84F mutations associated with multi-drug resistance were identified at a prevalence of 1.4% and 73.3% respectively. The combination of PfcrtK76T, found at a prevalence of 7.0% with Pfmdr1 N86Y is characterized to mediate LUM resistance. Our study revealed a high prevalence (83.9%) of triple mutation (IRNI) in *Pfdhfr*, across all sites. A quadruple mutant (IRNL) known to confer high grade SP treatment failure was observed at a low prevalence of 2.1% in six isolates. The predominant *Pfdhps* haplotypes were single mutants (SGKAA) and double mutant (AGKAA) occurring in 55.4% and 34.6% respectively. Analysis of combined haplotypes of *Pfdhfr-Pfdhps* revealed 23 unique haplotypes, with the quadruple mutant SGKAA-IRNI (47.2%) and quintuple mutant AGKAA-IRNI (29.9%) being the most prevalent. These findings highlight the absence of artemisinin resistance in Ghana but, raises concern about high prevalence of markers of ACT partner drug and sulfadoxine-pyrimethamine (SP) resistance, which are key interventions for malaria prevention during pregnancy and seasonal malaria chemoprevention among young children.

6326

INVESTIGATING THE PRESENCE OF FALSIFIED AND POOR QUALITY FIXED-DOSE COMBINATION ARTEMETHER-LUMEFANTRINE PHARMACEUTICAL DOSAGE FORMS IN KUMASI, GHANA

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Artemether-Lumefantrine (AL) is a highly effective and commonly used Artemisinin-based Combination Therapy (ACT) for treating uncomplicated malaria caused by *Plasmodium falciparum*, including drug-resistant strains. However, ineffective regulatory systems in resource-limited settings can lead to the infiltration of poor-quality and counterfeit anti-malarial medicines into the pharmaceutical supply chain, causing treatment failures, prolonged illness, and disease progression. The objective of the study was to assess the quality of selected brands of fixed-dose combination (FDC) AL tablets and suspensions marketed in Kumasi, Ghana. A total of fourteen brands of FDC AL medicines, comprising eight tablets and six suspensions were purchased from various retail pharmacy outlets in Kumasi, Ghana. All samples were subjected to thorough visual inspection as a quick means of checking quality through meticulous observation of the packaging or dosage form. The quality parameters of the tablets were determined using uniformity of weight, hardness, friability, and disintegration tests. Suspensions were assessed based on pH and compared with the British Pharmacopeia (BP) standard. The samples were then analyzed for drug content (assay) using Reverse-Phase High Performance Liquid Chromatography. All the tablet samples conformed to BP specification limits for uniformity of weight, hardness friability, and disintegration time. The drug assay analysis demonstrated that all the tablets met the BP specifications. The results of the pH studies showed that out of the six brands of suspension investigated, five (83.3%) were compliant with the official specification for pH, while one (16.7%) failed the requirement. Unlike the tablet brands, drug content analysis of the six suspensions showed that two (33.3%) were substandard. The artemether and lumefantrine content in these failed suspensions were variable (artemether: 81.31% - 116.76%; lumefantrine: 80.35% - 99.71%). The presence of substandard drugs underscores the necessity for robust pharmacovigilance and surveillance systems to eliminate counterfeit and substandard drugs.

6327

RECRUDESCENCE OF *PLASMODIUM FALCIPARUM* AFTER QUININE THERAPY: A CASE REPORT

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The recurring bouts of malaria caused by the parasites' persistence in red blood cells are the fundamental cause of recrudescence. This can be attributed to a variety of factors, including inadequate drug exposure, drug resistance, suboptimal dosage, noncompliance, or subpar medications. This is the case of a returning traveler to the Philippines, a forester from the Republic of Congo, where malaria *Plasmodium falciparum* is endemic. Presenting with fever prior to and upon return to Philippines. He was previously treated with IV quinine once a day for 3 days, multiple times since 2010 until 2023, without previous malarial smears or polymerase chain reaction. The patient presented with febrile episodes; the physical examination was unremarkable; however, the patient smear revealed malaria P. falciparum trophozoites. The patient was admitted and treated with artemether-lumefantrine 20/120 mg tablets for 3 days, followed by primaquine 15 mg/tablet on the 4th day, and was discharged. He was prescribed mefloquine 250 mg/tab, 1 tab weekly, as prophylaxis. Since then until present date, patient remains to be asymptomatic despite being in an endemic area. Recurrent malarial exposure, in the absence of malarial prophylaxis, and with inadequate treatment, the risk for recrudescent malaria increases.

6328

FIRST EVALUATION OF MOLECULAR AND PATHOGEN GENOMIC IMPACT ON *PLASMODIUM FALCIPARUM* POPULATION FOLLOWING SEASONAL MASS DRUG ADMINISTRATION WITH DIHYDROARTEMISININ-PIPERAQUINE IN A HIGH TRANSMISSION HIGHLY SEASONAL SETTING IN WEST AFRICA

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The World Health Organisation conditionally recommends the use of mass drug administration (MDA) for burden reduction in moderate to high transmission settings. *P. falciparum* is endemic to the Bijagos Archipelago, a remote collection of islands off the coast of West Africa. In November 2019, Soga Island had the highest estimated peak malaria season prevalence with 48% (95%CI: 39.8-56.3%) by qPCR. The MATAMAL trial (NCT04844905) delivered six rounds of MDA with dihydroartemisinin-piperaquine (DP) across the archipelago in 2021 and 2022. Nested within MATAMAL, this study delivered DP MDA to Soga in August, September, and October 2022. MDA coverage was over 80% for each round. One month after the final MDA round the estimated prevalence was 5.6% (95% CI: 3.3-8.8%). Nine and 12 months following the final MDA round the estimated prevalence was respectively 1.7% (August 2023, 95% CI: 0.54-3.8%) and 2.6% (December 2023, 95% CI: 1.1-5.1%). Therapeutic efficacy studies for DP and the first-line anti-malarial agent artemether-lumefantrine (AL) were also conducted across the MATAMAL trial site. The impact of multiple rounds of DP MDA on drug resistance of the *P. falciparum* parasite population is a significant knowledge gap and a potential significant threat to malaria control and elimination. I recruited 111 patients presenting with uncomplicated *P. falciparum* infection diagnosed by rapid diagnostic test and treated with AL. *P. falciparum* parasitemia 28 days since commencing AL was 81% (20/105) when assessed by PCR. The impact of MDA on the parasite phylogenomic structure and transmission using identity by descent (IBD) and multiplicity of infection (MOI) was investigated. The prevalence of molecular markers of drug resistance between MDA rounds was also examined. For the first time, this study investigates close monitoring of the efficacy of first-line therapy with molecular approaches during and shortly after MDA. This study provides an approach which may be invaluable to rapidly identify an emergent threat of parasite drug resistance in the context of future scale up of mass preventive chemotherapy strategies across endemic areas.

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PHENOTYPIC ASSESSMENT OF MOLECULAR MARKERS ASSOCIATED WITH SULFADOXINE-PYRIMETHAMINE RESISTANCE IN SENEGAL

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Sulfadoxine-pyrimethamine (SP) is used for chemoprevention in Senegal for intermittent preventive treatment in pregnancy (since 2004) and seasonal malaria chemoprevention (since 2013). SP resistance occurs via the accumulation of *Pfdhfr* and *Pfdhps* mutations. Using whole genome sequence data from samples collected (2000 - 2022) from malaria patients at health facilities across Senegal, we observed near fixation of *Pfdhfr* triple mutant (N51I, C59R, S108N) and fluctuation in *Pfdhps* A437G and S436A mutation frequencies over time. It is unclear how these mutations influence drug resistance and fitness phenotypes in natural isolates. To test this, we classified natural parasite isolates into groups based on their *Pfdhps* ('double'; S436A, A437G) and *Pfdhfr* ('triple') alleles. Parasites were culture-adapted and phenotyped for antimalarial drug susceptibility (EC_{50}) and fitness. Preliminary data show that all parasites with the *Pfdhfr* triple allele were significantly more resistant to pyrimethamine (PYR) compared to *Pfdhfr* wildtype parasites (p<0.0001-0.0445). Moreover, we observed a range of phenotypes among PYR resistant parasites according to their *Pfdhps* status: the *Pfdhfr* triple + *Pfdhps* double mutant parasite was significantly more PYR resistant than the *Pfdhfr* triple in combination with either *Pfdhps* single mutation S436A (p=0.0126) or A437G (p=0.0001-0.05). We found *Pfdhfr* triple parasites were significantly more resistant to PYR + 100uM sulfadoxine compared to *Pfdhfr* wildtype parasites (p<0.0001), but there was no statistical difference between *Pfdhfr* triple parasites. Pairwise competitive growth assays revealed the *Pfdhfr* triple + *Pfdhps* double mutant parasite as the most competitively fit of all parasites tested; interestingly, this parasite was also the most PYR resistant. Assessment of these mutations in an isogenic Senegalese background will help determine the causal role of *Pfdhps* mutations in drug resistance and fitness, predict the evolutionary trajectory of SP resistance in Senegalese parasites, and provide molecular markers for ongoing surveillance to monitor and guide the use of SP-based interventions.

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KNOWLEDGE OF ANTIMALARIALS BY PATIENT LEAVING HEALTH FACILITIES IN THE DEMOCRATIC REPUBLIC OF CONGO

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Malaria remains one of the leading causes of death in the DRC, particularly among children under five, with thousands of deaths each year. Despite the availability of safe and effective medicines, the DRC accounts for over 12% of global malaria deaths. One possible factor contributing to this situation is the inappropriate use of antimalarials by patients, which may be due to a lack of understanding of the correct dosage. As part of a national survey on rational use of antimalarials, we assessed patients' knowledge of prescribed antimalarials in 33 health facilities in all 11 former provinces of the DRC. Methods.This was a descriptive cross-sectional study conducted in 2018. All patients leaving the pharmacies of the selected 33 health facilities were invited to participate by answering a questionnaire on the course of dispensing and knowledge of the antimalarials they had just received. Data were analysed using SPSS version 25 software. Results.A total of 845 participants were interviewed; 68.6% knew the name of the antimalarials they had just received. However, 74% did not know the number of intakes per day and 61% did not know the dose. 72% did not know the duration of treatment. 90% had not been informed about possible side effects. 60% reported that dispensers did not specify storage conditions and 94% did not know how to store antimalarial drugs. Only a small percentage of participants knew all the relevant information about their antimalarial drug. ConclusionMalaria patients are discharged from hospital without receiving relevant information about their medication. This lack of information may lead to inappropriate use of medicines, which could have a negative impact on the fight against this deadly disease. It is important to develop effective interventions to address this situation.

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EFFICACY AND SAFETY OF ARTEMETHER-LUMEFANTRINE FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA AMONG CHILDREN UNDER FIVE IN BENIN, 2022

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In Benin, artemether-lumefantrine (AL) is the first-line treatment for uncomplicated *Plasmodium falciparum* malaria. In accordance with World Health Organization recommendations to routinely test antimalarial efficacy, a study was conducted between June and December 2022 in three sentinel sites: Bohicon in the south, Allada in the south-central department, and Parakou in the north. Participants (children 6 to 59 months old) were monitored for 28 days to assess their clinical and parasitological responses. Molecular correction was performed using PCR fragment-length analysis of *msp1* and *msp2* genes and the poly alpha microsatellite to differentiate recrudescence from new infection. Molecular markers of resistance were assessed using targeted amplicon deep sequencing.

In Allada and Parakou, 115 patients received AL per site. The Bohicon arm had 70 participants. Uncorrected 28-day Kaplan-Meier efficacy was 94% (95% confidence interval (CI):89-100) in Bohicon, 95.6% (92-99) in Allada, and 89.6% (84-95) in Parakou. PCR-corrected efficacy was 98.5% (96-100) in Bohicon, 97.4% (94-100) in Allada, and 94.8% (91-99) in Parakou. The proportion of patients with parasitemia on day three of follow-up was 3% in Bohicon, 1% in Allada, and 2% in Parakou.

A total of 284 non-failure samples and 30 late treatment failure samples were sequenced for *pfk13, pfmdr1, pfcrt, pfdhfr,* and *pfdhps* genes. No *pfk13* mutations were found. Low rates of *pfmdr1* N86Y (3.7-8.8%), moderate to high rates of Y184F (41-74%), and low rates of the *pfcrt* K76T (2-38%) allele suggest a circulating parasite population that may be predisposed to reduced lumefantrine susceptibility. The *pfdhps* A437G mutation was found in 98% of Bohicon samples, 100% of Allada samples, and 94% of Parakou samples. The *pfdhps* haplotype of interest VAGKGS, which has been observed to be moving westward across the Sahel region, was detected in one sample in Allada.

Results from this study indicate that both components of AL, the current first-line treatment for malaria in Benin, remain effective.

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MONITORING INTERMITTENT PREVENTIVE TREATMENT ON PREGNANT WOMEN EFFICACY THROUGH ANTENATALS CLINICS IN SENEGAL

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Intermittent Preventive Treatment in pregnant woman (IPTp) and Seasonal Malaria Chemoprevention (SMC) are two strategies recommended for the prevention of malaria among the most vulnerable groups. These strategies using Sulfadoxine Pyrimethamine (SP) have been implemented in Senegal and have coexisted in some areas for six years. This could increase the pressure on the parasite and lead to resistance. It is therefore necessary to assess this resistance by monitoring molecular markers. Monitoring SP resistance among pregnant women attending the antenatal clinics (ANC) could be a cost-effective approach. This study was conducted during the high malaria transmission period of 2019 among women attending ANC in Senegal to determine the prevalence of SP resistance markers. After consent obtained, Rapid Diagnostic Test performed, three dry blood spots on Whatmann paper were collected. All samples were analysed by real-time PCR (VarATS gene testing) to determine parasite carriage. Positive samples were genotyped by High Resolution Melting for mutations in the dihydrofolate reductase and dihydropteroate synthase genes. A total of 1050 pregnant women were included and the parasite prevalence was 57.14%. The prevalence of the I164L mutation was 11.67% and there was no association with gravidity (10.81% in primigravida; 11.95% in multigravida; p=0.40) or SP intake (12.92% in SP- group; 10.64% in SP+; p=0.44). The prevalence of A581G was 12.16% in primigravida and 16.15 % in multigravida (p=0.20). This mutation was no associated with SP intake (p=0.50). In primigravida before the first dose of SP, the prevalence was 14.29% for I164L and 15.58 % for A581G. Among those who had taken at least one dose of SP, the prevalence was 7.04 % for the I164L and 8.45% for A581G. The differences were not statistically significant. The quintuple mutation was not found then SP is still effective for IPTp in Senegal, however, regular surveillance of molecular markers of resistance in pregnant women is necessary for informed decision-making. This monitoring could be carried out in pregnant women who come to ANC, providing an alternative to cross-sectional surveys.

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MOLECULAR SURVEILLANCE OF ARTEMISININ-RESISTANT *PLASMODIUM FALCIPARUM* PARASITES IN MINING AREAS OF THE RORAIMA INDIGENOUS TERRITORY IN BRAZIL

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Multidrug Artemisin-resistant (ART-R) *Plasmodium falciparum* parasites represent a challenge for malaria elimination worldwide. Molecular monitoring in the Kelch domain region (*pfk13*) gene allows tracking mutations in parasite resistance to artemisinin. The increase of illegal miners in Roraima Yanomami indigenous land (IYL) could favor ART-R parasites. Thus, the study aimed to investigate ART-R in patients from illegal gold mining in the YIL of Roraima, Brazil. A questionnaire was applied and blood was collected from 48 patients diagnosed with *P. falciparum* (*Pf*) or mixed malaria (*Pf +P. vivax*). The DNA was extracted and the *pfk13* gene was amplified by PCR. The amplicons were subjected to DNA Sangers sequenced; the entire amplified fragment was analyzed. Among patients, 96% (46) were from illegal mining areas of the YIL. All parasite samples carried the wild-type genotypes / ART-sensitive phenotypes. These data reinforce the continued use of ACTs in Roraima as well as the maintenance of systematic monitoring for early detection of parasite populations resistant

to ART, mainly in areas exposed to the individual's influx from mining areas, such as the YIL. This is especially true when the achievement of falciparum malaria elimination in Brazil is planned and expected by 2030.

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IN VITRO SENSITIVITY TO ANTIMALARIALS AND GENETIC MARKERS OF RESISTANCE OF KENYAN *PLASMODIUM FALCIPARUM*

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Resistance to antimalarial drugs poses a challenge to malaria eradication. This study aimed to analyze both the in vitro sensitivity and genetic markers of resistance of 30 Kenyan clones of *Plasmodium falciparum* collected from Lake Victoria area in 2014-2015 to eight antimalarial drugs. Only five clones were resistant to chloroquine with a resistance-associated CRT triple mutation haplotype(I_{74}-E_{75}-T_{76}), indicating the resistance is lessening. We found a novel mutation I859 in MDR1 potentially associated with increasing the half maximal inhibitory concentration (IC_{50}) of chloroquine resistant clone and is now under further investigation. All clones were resistant to pyrimethamine, and showed resistance-associated DHFR haplotypes (29 I_{51}-R_{59}-N_{108}, 1 I_{51}-N_{108}-L_{164}, and 1 I_{51}-R_{59}-N_{108}-L_{164}). All showed DHPS E_{540} mutation associated with sulfadoxine resistance, indicating the quadruple mutant of DHFR(I_{51}-R_{59}-N_{108})-DHPS(E_{540}) against Fandidar® are dominant. Five clones were resistant to mefloquine, and no association was observed with any known genetic marker, including copy number variation of the mdr1 gene locus. One clone was resistant to lumefantrine, but we found no association with MDR1 F184 mutation. The remaining clones were susceptible to dihydroartemisinin, piperaquine, amodiaquine, and quinine; no mutations associated with resistance were observed in k13.

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QUALITY OF MALARIA TREATMENT AND COUNSELING FOR CHILDREN YOUNGER THAN FIVE YEARS IN OUTPATIENT DEPARTMENTS IN TANZANIA, 2020-2023

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High quality malaria case management reduces malaria morbidity and mortality and prevents the emergence of antimalarial resistance. To assess malaria case management quality in outpatient departments (OPD) in Tanzania, we analyzed OPD Malaria Service and Data Quality Improvement (MSDQI) supportive supervision (SS) data for children younger than five years. MSDQI OPD data were collected using standard SS visit checklists. Quality of treatment and counseling were assessed using parasitological confirmation of malaria diagnosis, adherence to weight-based dosing and dosing frequency, satisfactory treatment adherence counseling, client demonstration of understanding of prescription, and health care worker (HCW) solicitation of caregiver questions. Exit interviews were conducted for caregivers who completed treatment (observed and not observed during SS) to measure HCW service quality. From 2020–2023, 5,030 SS visits were conducted for children under five years old with suspected malaria. Malaria tests were ordered for 4,755 (94.5%), not ordered for 127 (2.5%), and 148 (2.9%) had missing testing information. Of children tested for malaria, 4,630 (97.4%) had test results with 2,414 (52.1%) testing positive. Of those testing positive, 2,343 (97.1%) were prescribed artemisinin-based combination therapy (ACT). Of 2,616 with negative or missing tests, 152 (5.8%) received ACTs. Of the 2,495 children given ACTs, the dose was correct for 98.8%, dosing frequency correct for 98.7%, treatment administration counseling sufficient for 97.8%, treatment understanding confirmed for 72.2%, and questions solicited for 59.0%. Exit interviews were conducted for 4,479 caregivers; 85.0% could explain how to give medicine at home and 82.9% reported receiving instructions on when to return. The quality of malaria testing and treatment among children under five is high. While patients demonstrated a good understanding and recall of anticipatory guidance, data suggest some providers might not sufficiently engage their patients in two-way communication. Interventions designed to address this might improve the quality and outcome of services.

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ASSESSING ANTIMALARIAL *EX-VIVO* DRUG EFFICACY IN WEST AND CENTRAL AFRICA FROM IMPORTED *PLASMODIUM FALCIPARUM* MALARIA CASES IN FRANCE BETWEEN 2016 AND 2023: A GENOTYPE-PHENOTYPE ASSOCIATION STUDY

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Malaria continues to pose a persistent global health threat. Artemisinin-based combination therapies (ACTs) are pivotal, yet emerging resistance threats their efficacy in several regions. Monitoring drug resistance, especially in Africa, is crucial due to limited therapeutic alternatives. We retrospectively analyzed 805 *Plasmodium falciparum* isolates (2016-2023) from travellers returning to France from mainly West and Central Africa by assessing the *ex-vivo* susceptibility of six antimalarials (chloroquine, amodiaquine, lumefantrine, piperaquine, mefloquine, dihydroartemisinine; growth inhibition assays) and sequencing key resistance markers across *P. falciparum* genome by molecular inversion probes (MIPs). Over 90% of isolates carried the *pfdhfr* IRN mutations (codons 51-59-108), over half harboured *pfdhps* S436A and A437G mutations, whereas *pfdhps* A613S prevalence was at 15%. *Pfmdr1* exhibited the NFD haplotype (codons 86-184-1246) in 54.8% of isolates. *Pfcrt* mutations were present in 20-30%, and *pfkelch13* mutations occurred in 0.3% (Y493H, I543T and A675V). IC_{50} values revealed reduced susceptibility to mefloquine (49% of isolates with IC_{50}>30nM), chloroquine (10% with IC_{50}>100nM), and amodiaquine (3% with IC_{50}>80nM). Less than 1% showed high IC_{50} for dihydroartemisinin, piperaquine, and lumefantrine. Genotype-phenotype analysis emphasized *pfcrt* and *pfmdr1* associations, with haplotypes influencing *ex-vivo* susceptibility to several drugs. *Pfcrt* K76T-mutant haplotypes IETSENTI and IETSENII (codons 74-75-76-220-271-326-356-371) were associated with decreased susceptibility to chloroquine and amodiaquine and increased susceptibility to dihydroartemisinin, lumefantrine and piperaquine. *Pfmdr1* NFD haplotype correlated with reduced susceptibility to dihydroartemisinin, lumefantrine, mefloquine, and piperaquine. Our longitudinal study shows a low prevalence of artemisinin resistance markers and of *ex-vivo* resistance to the main partner drugs in contemporary isolates from West and Central African countries. This suggests that ACTs are not immediately threatened in these regions of Africa.

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IRRESISTIBLE β-CARBOLINE DERIVATIVE ACTIVE AGAINST PROLIFERATING AND QUIESCENT RING STAGES OF ARTEMISININ-RESISTANT *PLASMODIUM FALCIPARUM*

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Malaria remains a serious parasitic disease in the world, with over 240 million new infections and over 600,000 deaths each year, mostly caused by *Plasmodium falciparum*. Due to the rising resistance to current antimalarial drugs, there is an urgent need to develop new chemotherapeutic agents that engage new targets in the malaria parasite. Antimalarial drugs targeting the *P. falciparum* ring stage are highly attractive as they can prevent the development of the trophozoite and schizont stages that are sequestered by the cytoadherence of infected erythrocytes to the endothelial cells of deep vascular beds in vital organs. The ring stage also precedes gametocytogenesis, the intraerythrocytic sexual development stage required for transmission of the parasite to the *Anopheles* mosquito vector, thus reducing or blocking transmission of the disease. It is known that exposure to dihydroartemisinin (DHA) induces a quiescent state in the Plasmodium *falciparum* ring stage. Quiescence is a survival mechanism of *Plasmodium* following drug treatment. This phenomenon increases the risk of clinical failure following artemisinin-based combination therapies by slowing parasite clearance and allowing the selection of parasites resistant to partner drugs. We have discovered a novel β-carboline class of antimalarials that has demonstrated an inability to select resistant parasites in vitro, kills both the proliferating and the DHA-quiescent ring stages of sensitive and DHA-resistant strains of *P. falciparum*, and has a promising oral PK profile. In addition to extensive medicinal chemistry, we are characterizing the mechanism of action of this novel antimalarial class using an array of approaches, including chemoproteomics and fluorescent and electron microscopy. Our studies revealed that this β-carboline class displays a fast-killing profile and that it may act through a novel mechanism of action affecting hemoglobin uptake and digestion.

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ARTEMISININ RESISTANCE MUTATIONS IN *PFCORONIN* IMPEDE HEMOGLOBIN UPTAKE

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Mutations in *Pfcoronin* (*Pfcrn*), including R100K/E107V, drive *in vitro* evolved artemisinin (ART) resistance in Senegalese *Plasmodium falciparum* isolates. However, the mechanisms underlying *Pfcrn*-mediated ART resistance remain unknown. Immunofluorescence microscopy in late-stage asexual parasites showed no difference in *Pf*CRN localization between mutant and wildtype (WT) parasites. Ultrastructure-expansion microscopy (U-ExM) was then used to examine ring-stage parasites, the stage at which ART resistance occurs. In WT rings, *Pf*CRN localized to the parasite plasma membrane, the digestive vacuole (DV) membrane, and a newly identified preDV compartment. By contrast, in mutant ring stage parasites, *Pf*CRN was not observed at the PPM, DV, or preDV, and mutant *Pf*CRN protein expression was 30% lower compared to WT *Pf*CRN, as quantified by western blot. The preDV compartment, visible in WT parasites as an invagination in early rings, and a fully-contained compartment in older rings, was aberrant in *Pfcrn* mutant parasites. In U-ExM images, a preDV was visible in all WT parasites, but 76% of *Pfcrn* mutant parasites lacked a preDV. When present, preDVs in mutants were 21% smaller than in WT parasites. These observations led us to hypothesize that *Pfcrn* mutations might impair hemoglobin uptake, possibly via abnormal development of the preDV. Endocytosis assays showed a significant reduction ($p < 0.0001$) in uptake of hemoglobin contents (45% decrease) in mutant *Pfcrn* parasites, compared to WT, similar to a 36% decrease observed in *Pfk13-C580Y* parasites. These data suggest that mutations in *Pfk13* and *Pfcrn* both confer reduced hemoglobin uptake in early rings and may similarly mediate ART resistance by reducing heme-dependent ART activation. However, *Pf*CRN localization differs from that of *Pf*K13, which is localized at the cytostomal collar, implying that *Pf*CRN and *Pf*K13 might facilitate hemoglobin uptake through different pathways. Ongoing studies will determine whether *Pf*K13- and *Pf*CRN-coated structures share a common pathway for hemoglobin uptake or if multiple pathways are involved.

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INTERVENTION STRATEGIES FOR ENHANCING PRIMAQUINE ADHERENCE ON *PLASMODIUM VIVAX* MALARIA: RESULTS FROM A CLUSTER RANDOMIZED CONTROLLED TRIAL IN MYANMAR

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Plasmodium vivax malaria remains a concern for malaria elimination. The completion of a 14-day primaquine (PQ) regimen is essential for the radical cure of *P. vivax* malaria by clearing liver hypnozoites. Adherence to treatment is an important issue in malaria management. This study was carried out from August 2022 to March 2023 to develop an intervention for enhancing patients' adherence to PQ treatment and evaluate the effectiveness of this intervention in a malaria-endemic area in Myanmar. Based on a previous qualitative study, an intervention package emphasizing the family-orientated, directly observed treatment (family DOT), was developed. This package included training provided to Integrated Community Malaria Volunteers (ICMVs) on the importance of radical cure, managing adverse effects, and the role of family members in administering family DOT. Trained ICMV gave on-site training to family members of *P. vivax* patients on the first day of diagnosis and standardized pamphlets were distributed to reinforce key messages on primaquine treatment adherence. Patients diagnosed with *P. vivax* were administered the prescribed drugs under supervision of trained family members. A cluster randomized controlled trial was conducted to evaluate this intervention in 10 study villages from Waingmaw township, Kachin State, Myanmar. The proportion of treatment adherence was 98.8% and 77.6% in the intervention and control groups, respectively. Parasite recurrences were assessed in both groups on days 14, 28, and 42. Although the overall malaria trend did not sharply decline, the incidence in the intervention group showed reduction over time. In malaria-endemic areas with limited human resources, interventions to improve treatment adherence should be initiated to enhance the radical cure of *P. vivax*. The National Malaria Control Program should prioritize the research areas addressing malaria recurrences, cost-effectiveness of implementing family-based DOT, and treatment adherence in the specific context of Myanmar.

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PREVALENCE OF DRUG RESISTANCE MOLECULAR MARKERS IN *PLASMODIUM VIVAX* CLINICAL ISOLATES FROM SOUTHERN PAKISTAN

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Despite the implementation of various malaria control strategies, malaria continues to persist as an endemic disease in Pakistan. *Plasmodium vivax* and *P. falciparum* are common species and P. vivax is prevalent across

Sindh and Baluchistan region. Due to the rise in Chloroquine resistance until 2007, the National Malaria Control Programme (MCP) guidelines in 2008 recommended Chloroquine along with sulphadoxine pyrimethamine (SP) as the first-line treatment for *P. falciparum* infection. However, rise in resistance to sulphadoxine pyrimethamine in *P. vivax* has been observed due to mutations in *pvdhfr* and *pvdhps* genes. In this study we present the frequency of drug resistance-associated mutations in *pvdhfr* and *pvdhps* genes in clinical isolates of *P. vivax* from Southern Pakistan.From 2015-2018, a total of 650 samples were collected from clinical laboratories of Aga Khan University Hospital and its outreach laboratories located across Pakistan. Blood samples of patients with malaria positive microscopy results were amplified by nested PCR using *pvdhfr* and *pvdhps* specific primers and amplified products were purified and sequenced. The results were further analyzed using Mega 6 software in comparison to Wild Type reference strains. In *pvdhfr*, non-synonymous mutations were observed at codons N50I (6.154%), F57L (1.23%), S58R (44%), S93H (0.76%), D105N (8.92%), S117N (53.38%) and G469A (4.4%) while synonymous mutation was observed at codon 69Y. One hundred and eighty-seven (28.7%) were wild type strains. Mutations in *pvdhps* gene were observed at codons A383G (0.92%), G419C (0.65%), D459A (2.92%), R491K (0.65%) and six hundred and twenty-two (95.7%) were wild type.We report sulfadoxine-pyrimethamine (SP) resistance in clinical isolates of P. vivax originating from Southern regions of Pakistan, providing valuable insights into the prevalence of drug-resistant alleles in these malaria-endemic areas. The heightened occurrence of mutations in pvdhfr genes is particularly alarming for healthcare professionals, signaling a potential challenge in combating SP resistance within the population.

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OPTIMIZING NOVEL CLASS OF ANTIMALARIAL DRUG AND PYRONARIDINE COMBINATION TO GUIDE CLINICAL DOSING AND PREVENT DRUG RESISTANCE

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The emergence and fast spread of drug resistance calls for the development of effective antimalarial combinations. However, the selection and combination of drug dose regimens involve a complex set of considerations, and there are various complications and limits to be considered such as pharmacokinetic and pharmacodynamic interactions. To ensure adequate translation of data from bench to bedside we sought to use immediate *ex vivo Plasmodium falciparum* field isolates employed for the *in vitro* testing of mono and combination effects of novel class of antimalarial drug and pyronaridine. These data are then fed into our model to generate an interaction map that later is used to simulate meaningful clinical dose ratios. First, we demonstrated that the pharmacometric model of parasite growth and killing under monotherapy as well as combination therapy provided a well-defined description of parasite kinetics *ex vivo* against susceptible and novel class of antimalarial drug-resistant parasites. Then, the model was used for clinical trial simulations translating the *ex vivo* data into human doses for the combination of novel class of antimalarial drug and pyronaridine. While monotherapy of pyronaridine was found to provide suboptimal killing rates, even at the highest studied dose, the combination of a lower single dose of novel class of antimalarial drug and pyronaridine provided a killing rate of 90% in more than 99% of the simulated conditions until 96 h. We have established a rapid, 3R-compliant *in vitro* method allying field isolate data and modelling to help guiding clinical drug development to set meaningful doses for antimalarials in clinical development.

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PREVALENCE OF HAPLOTYPES ASSOCIATED WITH RESISTANCE OF *PLASMODIUM FALCIPARUM* TO DIHYDROARTEMISININ-PIPERAQUINE, SULFADOXINE-PYRIMETHAMINE AND AMODIAQUINE DURING SEASONAL MALARIA CHEMO-PREVENTION CAMPAIGNS AMONG CHILDREN AGED 6-15 YEARS IN MALI

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The World Health Organization recently recommended extending the age of seasonal malaria chemoprevention (SMC) and the use of other molecules effective against malaria. One of the factors that could threaten the effectiveness of this strategy is resistance to the drugs used. Following a study to evaluate the tolerance and effectiveness of Dihydroartemisinin-Piperaquine (DP) used in SMC, we measured the prevalence of haplotypes associated with the resistance of *Plasmodium falciparum* to DP, to Sulfadoxine-Pyrimethamine (SP) and Amodiaquine (AQ). From September 2020 to August 2021, we carried out a randomized controlled trial in Bandiagara, Mali including 345 children aged 6 to 15 years. Participants were assigned to three treatment regimens (DP vs SP-AQ vs Albendazole) for 4 consecutive months during malaria transmission season. Sanger-Sequencing of the *dhfr, dhps* and *crt* genes was performed on 90 *P. falciparum* PCR-positive samples randomly selected on study days 1, 7, 31, 61, 91, 180. The molecular prevalence of *P. falciparum* varied from 38.9% (35/90) on day1 to 7.8% (7/89) on days 61, 91 and 180. The *CVIET* prevalence (*C72S, V73, M74I, N75E, K76T*) of the crt gene was 12.5% on day 1 and 28.6% on day 61. The prevalence of *dhfr IRN* haplotypes (*N51I C59R S108N*) varied from 78.5% to 50% respectively on day1 and day 91. The wild NCS allele was dominant at day31 (56.5%). The *dhps* haplotype *SGKAA* was dominant (50% at day1 and 57% at day61) followed by *AGKAA* (35.7–40%) respectively from day1-91 (*S436A G437A K540E A581G A613S).* A reduction in the parasite load was observed from day61. The prevalence of *dhps* and *crt* mutant haplotypes was low compared to *dhfr* and remained stable during the SMC campaigns.

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EFFICACY AND SAFETY OF ARTESUNATE-AMODIAQUINE (ASAQ) AND ARTEMETHER-LUMEFANTRINE (AL) FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA IN TWO COUNTIES IN LIBERIA, 2022-2023

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Artemether-lumefantrine (AL) is currently the first line treatment for uncomplicated *Plasmodium falciparum* (*Pf*) malaria in Liberia. In order to ensure antimalarial treatments continue working, the WHO recommends routinely testing the efficacy of antimalarials using therapeutic efficacy studies (TES) every two years. As a result of the TES conducted in 2018, artesunate-amodiaquine (ASAQ) was withdrawn as a first-line therapeutic option in Liberia. The 2018 TES reported PCR-corrected adequate parasitological and clinical response (APCR) rates of 90.2% in Bensonville and 92.7% in Saclepea for ASAQ, and 100% in Kakata and Sinje for AL.

Given other countries in West Africa continue to report high efficacy of ASAQ, and per WHO recommendations to routinely conduct TESs, the therapeutic efficacy of ASAQ and AL was evaluated using the standard WHO protocol in Saclepea and Sinje, Liberia from August 2022 to July 2023. Eligible children aged 6 months to 5 years old with uncomplicated *Pf* malaria infection (2,000 - 200,000 asexual parasites/μL of blood) were recruited, treated with either ASAQ or AL at each site, and monitored clinically and parasitologically for 28 days. A total of 1,639 children were screened for eligibility and 305 were enrolled. Among enrolled children, 153 were treated with ASAQ (77 in Sacleapea and 76 in Sinje) and 152 were treated with AL (78 in Sacleapea and 74 in Sinje). Of the enrolled children, 299 (98%) completed the 28 days of follow up. No adverse events were reported for either ASAQ or AL during the study period. The proportion of participants with parasitemia on day 3 of follow up was 1.3% (2/153) for ASAQ, none were detected among those treated with AL. Both fall below the WHO threshold of 10%. The uncorrected APCR at day 28 was 100% (95% CI: 96.2%-100%) in Saclepea and 90.1% (95% CI: 82.6%-95.8%) in Sinje for ASAQ, and 100% (95% CI: 96.2%-100%) in Saclepea and 93.2% (95% CI: 85.6%-97.5%) in Sinje for AL. The day 3 slide positivity and uncorrected efficacy results greater than the 90% WHO threshold suggest that AL and ASAQ are likely still effective treatments for uncomplicated *Pf* malaria infections in Liberia.

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WIDESPREAD *PFHRP2/3* DELETIONS AND HRP2-BASED FALSE-NEGATIVE RESULTS IN SOUTHERN ETHIOPIA

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Rapid diagnostic tests (RDTs) are vital for malaria case management in peripheral healthcare systems, with Histidine-rich protein-2 (HRP2) antigen detection RDTs being widely used for *Plasmodium falciparum* diagnosis. However, the emergence of *P. falciparum* strains with deleted hrp2/3 genes causing false-negative results raises concerns. This study assessed HRP2-detecting RDTs' diagnostic performance and *pfhrp2/3* deletions prevalence among symptomatic patients in southern Ethiopia. A cross-sectional study (July-September 2022) enrolled febrile patients with microscopically confirmed P. falciparum infections. Blood samples underwent microscopy, RDT (SD BiolineTM Malaria Pf/Pv Test), and molecular analysis via nested PCR for *hrp2/3* gene deletions confirmation. Among 279 PCR-confirmed *P. falciparum* cases, 89.2% had successful *msp-2* amplification, revealing common *pfhrp2/3* deletions in all health centers (57.8% prevalence). Deletions in *hrp2 exon 2*, *hrp3 exon 2*, and double deletions (*hrp2/3*) accounted for 27.3%, 30.5%, and 13.2% of cases, respectively, with variations across study sites. The SD Bioline PfHRP2-RDT test sensitivity was 76.5% compared to PCR. The study confirmed widespread *pfhrp2/3* deletions exceeding the WHO-recommended threshold (> 5%), impacting malaria control and elimination efforts in Ethiopia and beyond. The adoption of non-HRP2-based RDTs is crucial to mitigate false-negative results' consequences.

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PREVALENCE OF AND CHALLENGES IN DIAGNOSING SUBCLINICAL *PLASMODIUM FALCIPARUM* INFECTIONS: IMPLICATIONS FOR MALARIA CONTROL AND ELIMINATION IN GHANA

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Many national malaria elimination programmes (NMEP) are intensifying campaigns for malaria control and elimination. The high prevalence of subclinical infections may hamper control efforts. The detection of subclinical and low-density infection is crucial in monitoring progress towards malaria control. This study sought to determine the prevalence of subclinical infections in three districts of Ghana, the proportion that could be detected by a novel rapid diagnostic test (RDT) developed by Rapigen, and the occurrence of *hrp2/hrp3* deletions which may impede diagnosis by HRP2-based RDTs. A community-based cross-sectional study was conducted in Nkwanta South, Sekyere South and Ga South districts in Ghana. A total of 1134 whole blood samples were screened by rapid diagnostic test (RDT), expert microscopy, and *var*ATS qPCR. 304 *Plasmodium falciparum* positive samples were typed for *hrp2/hrp3* deletions by digital PCR (dPCR). Malaria prevalence was 57.1% by qPCR, 40.9% by RDT, and 8.4% by microscopy. 33.8% (219/647) of infections were sub-patent. Compared to qPCR, the sensitivity of RDT was 65.7%, and specificity of 91.9% and thus substantially higher than microscopy (sensitivity 14.4%, specificity 99.4%). The prevalence was highest in children aged 5-15 years (68.2%), followed by adults >15 years (51.2%) and children < 5 years (45.3%). Prevalence also differed across the three districts, ranging from 44.0% (183/416) in Sekyere South, 55.8% (143/253) in Ga South, to 68.8% (321/466) in Nkwanta South. No *hrp2* deletions were observed, and one sample (1/304) carried *hrp3* deletion. The high prevalence of subclinical malaria infections is likely to be a potential reservoir in sustaining malaria transmission. HRP2-based RDTs detected two thirds of the subclinical infections. Thus, community test and treat programs using highly sensitive RDTs could be a valuable strategy to reduce the reservoir and accelerate progress towards malaria control and elimination in Ghana.

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REMOSCOPE: A LABEL-FREE IMAGING CYTOMETER FOR MALARIA DIAGNOSTICS

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Malaria diagnostic testing in high transmission settings is a challenge to global healthcare systems. Here we present remoscope, an automated imaging cytometer that scans fresh, unstained whole blood using a custom neural network on low-cost hardware. By screening up to two million red blood cells, remoscope performs quantitative stage-specific detection of *Plasmodium falciparum* in 1-12 minutes without sample fixation, staining, or slide scanning. Flow is used to achieve high cellular throughput, with blood confined to a 5 μm monolayer in low-cost disposable flow chambers. We tested remoscope performance *in vitro* by titration of cultured parasites into uninfected whole blood at concentrations of 710,000-21.7 parasites/μL. Counts generated by the remoscope demonstrated a linear response across the entire range. The potential for using remoscope in drug susceptibility assays and evaluation of clinical treatment efficacy was tested by measuring the half-maximal effective concentration (EC50) of chloroquine in a cultured W2 *P. falciparum* strain, which resulted in an EC50 value of 224 nM, vs 191 nM for flow cytometry. We next studied remoscope's diagnostic accuracy in a cohort of 500 individuals in eastern Uganda, comprising 629 unique clinic visits. Parallel measurements of parasitemia were performed using remoscope, qPCR targeting the multicopy conserved *var* gene acidic terminal sequence, and traditional Giemsa microscopy of thick blood smears. Remoscope's limit of detection with respect to qPCR was 156 parasites/μL. At this threshold, the system had a sensitivity of 86%, specificity of 95%, Positive Predictive Value (PPV) of 87%, and a Negative Predictive Value (NPV) of 94% compared to qPCR. Remoscope's speed and ease of use address practical challenges in malaria diagnostic settings

around the world. The system can also inform development of recognition models for the diagnosis of other infectious or non-communicable blood disorders.

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COMPARATIVE STUDIES OF MALARIA PARASITE NONINVASIVE AND INVASIVE DIAGNOSTIC TESTS AMONG PREGNANT WOMEN IN NIGERIA

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The gold standard for malaria parasite diagnostic methods requires blood collection. This may be associated with pain, the risk of transmitting blood-borne pathogens and poor compliance when repeated sampling is needed. Pregnant women who live in the tropics who regularly attend antenatal clinics for routine checks are at risk. Hence, the potential use of non-invasive methods (saliva and urine specimens) as alternative sources of malaria parasite (DNA) in the diagnosis of malaria infection using real-time polymerase Chain Reaction (qPCR) was studied. The participants (628 pregnant women) were randomly selected patients at the Ante Natal Care (ANC) Department in Nnamdi Azikiwe University Teaching Hospital, Nigeria. The biomarkers (18S rRNA) were captured and concentrated from the samples using the magnetic bead-based. DNA recovered from these samples was evaluated by qPCR. The prevalence of malaria based on saliva specimens was 430 (68.5%). Out of this, 373 (86.7%) were true positive (TP) and 57 (13.3%) false positive (FP). The prevalence based on urine specimens was 411 (65.4%), where 365 (88.8%) were true positive (TP) and 46 (11.2%) false positive (FP). A significant association was observed between the saliva, urine qPCR and blood microscopy ($P = 0.0002$, $P < 0.05$). The malaria microscopic prevalence was 60.0%. Urine qPCR was found to have a higher Kappa coefficient agreement (0.80308) with microscopy than saliva qPCR (0.76094). When the qPCR method was compared to thick blood film-microscopy as reference standard, saliva qPCR had sensitivity of 98.94%, specificity of 77.29%, positive predictive value (PPV) of 86.73%, and negative predictive value (NPV) of 97.98%; while urine qPCR had sensitivity of 96.82%, specificity of 81.67%, PPV of 88.79%, and NPV of 94.48%. This further confirmed that qPCR of saliva and urine is a promising non-invasive approach for malaria diagnosis as their sensitivity is comparable to that of blood microscopy. It is essential to continue research to facilitate the development of a tool that will aid the control and elimination of malaria. More research that will focus on pregnant women in Nigeria is needed**.**

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COMPARISON OF PREVALENCE ESTIMATES OF *PFHRP2* AND *PFHRP3* DELETIONS IN *PLASMODIUM FALCIPARUM* DETERMINED BY CONVENTIONAL PCR AND MULTIPLEX QPCR AND IMPLICATIONS FOR SURVEILLANCE AND MONITORING

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Accuracy of malaria rapid diagnostic tests is threatened by *Plasmodium falciparum* with *pfhrp2/3* deletions. This study compares gene deletion prevalence determined by multiplex qPCR and conventional PCR (cPCR) using existing samples with clonality previously determined by microsatellite genotyping. Multiplex qPCR was performed to estimate prevalence of *pfhrp2/3* deletions in three sets of previously collected patient samples from Eritrea and Peru. The qPCR was validated by multiplex digital PCR. Sample classification was compared with cPCR, and ROC analysis used to determine the optimal ΔCq threshold that aligned results of the two assays. qPCR classified 75% (637/849) of samples as single, and 212 as mixed-*pfhrp2/3* genotypes, with a positive association between clonality and proportion of mixed-*pfhrp2/3* genotype samples. Sample classification agreement between cPCR and qPCR was 75.1% (95% CI 68.6-80.7%) and 47.8% (95% CI 38.9-56.9%) for monoclonal and polyclonal infections. qPCR prevalence estimates of *pfhrp2/3* deletions showed almost perfect (κ=0.804; 95% CI 0.714-0.895) and substantial agreement (κ=0.717; 95% CI 0.562-0.872) with cPCR for Peru and 2016 Eritrean samples, respectively. For 2019 Eritrean samples the prevalence of double *pfhrp2/3* deletions was approximately two-fold higher using qPCR. The optimal threshold for matching assay results was ΔCq=3. In conclusion, multiplex qPCR and cPCR produce comparable estimates of gene deletion prevalence when monoclonal infections dominate, but qPCR provides higher estimates where multiclonal infections are common.

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ACUTE UNDIFFERENTIATED FEBRILE ILLNESSES SURVEILLANCE IN TWO MILITARY HEALTH FACILITIES IN ABUJA, NIGERIA

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The distribution of etiologies causing acute undifferentiated febrile illnesses (AUF) in Nigeria has limited study due to the high malaria burden. We investigated the prevalence of etiologies causing AUF using malaria microscopy, PfHRP2 rapid diagnostic test (RDT), and qPCR targeting 16 pathogens. From February 2023 to February 2024, 1,118 adult AUF patients were enrolled at two sites in Abuja, Nigeria: The Defence Headquarters Medical Center (DHQMC), and the 063 Nigerian Air Force Hospital (NAFH). The DHQMC enrolled 557 adults, with a median age of 28 years, and 45% females, while the NAFH enrolled 561 cases, with a median age of 30 years, and 54% females. Muscle pains, joint weakness and headache were common in >90% of enrollees in both sites, whereas chills/rigors were more prevalent at the DHQMC (96%) than at the NAFH (61%). Malaria prevalence was 35% and 39% by microscopy with parasitemia density ranged from 40 to 492,000 parasite/µl and from 222 to 432,000 parasite/µl in DHQMC and NAFH, respectively. RDT detected 37% and 41% of cases at the DHQMC and NAFH, respectively. Microscopy positive/PfHRP2 RDT negative cases were less than 3.5% at both sites. Malaria qPCR performed on 965 samples showed higher positive detection rates than microscopy and RDT with 52% at the DHQMC and 57% at the NAFH. Malaria detection rates in enrolled cases varied significantly according to the season, reaching a maximum of 100% during the wet season, and a minimum of 0% in the dry season. Malaria data obtained with the three detection techniques showed a 78% concordance and indicated that 58% of cases tested positive for malaria with at least one technique. The qPCR panel showed that *Salmonella* was detected in 3% and 0.4% of samples at the DHQMC and the NAFH, respectively, whereas Epstein–Barr virus was only detected at the DHQMC. Our data confirm the high burden of malaria in Nigeria. The detection of AUF cases during malaria low season, along with the high negative qPCR detection rates for AUF pathogens, suggest a need for more advanced molecular tools that provide broader information about febrile disease epidemiology and etiology.

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PLASMODIUM FALCIPARUM HISTIDINE RICH PROTEIN 2/3 DELETIONS AND REPEAT MOTIFS IN INDIA: CHALLENGES IN RAPID DIAGNOSTIC TESTS - BASED MALARIA DIAGNOSIS

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Rapid diagnostic tests (RDTs) for malaria use the histidine-rich protein 2 (PfHRP2) for the detection of *Plasmodium falciparum,* with cross-reactivity extending to PfHRP3, a structural homolog. In this study, we have examined the gene deletions and sequence variation in the *Pfhrp2* and *Pfhrp3* gene in *P. falciparum* isolates from Chhattisgarh state, India, and correlated these variations with RDT reactivity. A total of 264 *P. falciparum* positive samples were PCR amplified for *Pfhrp2* and *Pfhrp3* genes and subsequently sequenced. Amino acid sequences were analyzed for repeat variations and their association with RDT reactivity. Among the samples, *Pfhrp2* and *Pfhrp3* showed 3.8% and 14% of gene deletion respectively. Nucleotide sequences for the *Pfhrp2* gene were successfully obtained from 101 and 95 sequences were acquired from *Pfhrp3*. *Pfhrp2* exhibited 15 distinct repeat motifs, and *Pfhrp3* showed 10. Notably, no correlation was found between variations in the size of *Pfhrp2* repeat types 2 and 7 and the performance of a commercial RDT at low parasite densities. The study suggests that gene deletions and sequence diversity in *Pfhrp2* and *Pfhrp3* genes in the Chhattisgarh state are unlikely to adversely affect the effectiveness of currently used PfHRP2 baaed RDTs. However, a larger-scale study encompassing other endemic states in India is recommended over time for a comprehensive understanding.

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UNCOVERING TREATMENT GAPS: A CLOSER LOOK AT MALARIA CASE MANAGEMENT IN A DISTRICT REFERRAL HOSPITAL IN GHANA, 2023

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Malaria remains a significant global public health concern, notably in the WHO African region, where it continues to rank among the leading causes of mortality and morbidity. Effective case management plays a pivotal role in malaria control efforts, yet concerns persist regarding poor adherence to established guidelines on management. We assessed adherence to malaria case management guidelines to inform interventions aimed at strengthening case management practices. A cross-sectional study was conducted, involving patient records of 350 suspected malaria cases systematically sampled from the Outpatients' Department of Tema General Hospital in Ghana. Data extracted were signs and symptoms, malaria testing, and treatment. The proportion of cases prescribed antimalarials and compliance with the Test, Treat, and Track policy (T3) were determined. Chi-squared tests and logistic regression were conducted for potential associations. Among the 350 cases reviewed, 91% (318/350) underwent testing by either microscopy or malaria Rapid Diagnostic Test. More than half (53%, 186/350) received antimalarial prescriptions, with 47% (87/186) receiving prescriptions prior to receipt of test results. About 26% (50/192) of suspected cases testing negative received antimalarials. Prescription of antimalarials was significantly associated with age (p=0.007), prescriber category (p=0.006), and requests for laboratory investigations (p<0.001). Treatment adherence to guidelines was observed in 60% (211/350) of cases, with significant variations among prescribers (p=0.001). Only 17% (60/350) of patients were scheduled for follow-up; 37% (22/60) attended the follow-up sessions. Although testing rate for suspected malaria cases was notably high, adherence to malaria case management guidelines suggested room for improvement, with lack of comprehensive tracking of cases. Implementing measures to increase adherence and track cases is needed to optimize malaria management outcomes.

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COST-EFFECTIVENESS COMPARISON OF MALARIA DIAGNOSIS SCENARIOS WITH SYSMEX XN-31 IN A NON-ENDEMIC AREA.

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Malaria diagnosis in non-endemic areas relies frequently on screening with RDT or molecular method followed by microscopic confirmation. The majority of laboratories in non-endemic areas receive a low number of suspected malaria cases with a low positivity rate. This epidemiological context underpins the need for innovative diagnosis methods. In the context of limited resources for medical care, the cost-effectiveness of diagnosis workflow is a major argument for decision makers and final buyers. The objective was to measure in monetary and non-monetary values the cost-effectiveness of the most current standards of care compared to scenarios with Sysmex XN-31 haematology analyser. A decision tree allowing visualization of the different diagnosis pathways was built. The structure of the study population was based on the real cohort of patients attending health care at Lyon university hospital for suspected malaria in 2023. The costs of intervention and controls were calculated by the addition of the direct + indirect costs (working time including training, quality proficiency and operational execution).An incremental cost-effectiveness ratio (ICER) was used to compare the difference between the costs and health outcomes of intervention and controls. The intervention (XN-31+microscopy) was the most effective scenario. Microscopy was weakly dominated by the intervention, and both LAMP+microscopy and RDT+microscopy were strongly dominated. This cost-effectiveness analysis was needed to clarify the real price of malaria diagnosis according to the different scenarios available. Considering both the workload of each method and their respective diagnosis accuracy, it appears that the association of microscopy to XN-31 is the best scenario from a monetary and non-monetary perspective.

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IDENTIFYING SUBGROUPS WITH DECREASED PERFORMANCE CHARACTERISTICS OF MALARIA RAPID DIAGNOSTIC TESTS

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The point-of-care malaria rapid diagnostic test (MRDT) is a crucial and cost-effective diagnostic tool, allowing prompt treatment to decrease the high burden of malaria morbidity and transmission. In a 2011 systematic review of real-world MRDT performance in uncomplicated malaria compared to microscopy or polymerase chain reaction (PCR), the average sensitivity and specificity of the most common tests was 95% or greater. However, recent data on MRDT performance show a more nuanced and complicated picture, suggesting that the sensitivity and specificity of the tests can vary significantly with age and some other characteristics. Under the aegis of the Malawi International Center of Excellence in Malaria Research (ICEMR), we evaluated the performance characteristics of MRDT in population subgroups when compared to quantitative PCR based on 1324 symptomatic health center visits conducted between 2019 and 2021, representing 510 participants (average of 2.6 visits/participant). 46% of

malaria PCR tests and 36% of MRDTs were positive; 85% of +PCR tests also had a +MRDT. As expected, the likelihood of a +MRDT was higher during the rainy (60%) compared to the dry (54%) season (p=0.04). Those with +MRDTs were more likely to report fever and headache (74% vs 52% for fever, 59% vs 38% for headache, p<0.05 for both). Those with +MRDTs were more likely to report vomiting (26% vs 8%, p<0.05), but less likely to report diarrhea (4% vs 10%, p<0.05) or cough (16% vs 39%, p<0.05). There were 174 false negative (24%) and 50 false positive (9%) MRDT results. Overall, the sensitivity of MRDTs was 67% and the specificity was 91%. MRDT sensitivity was the lowest among subjects aged < 2 years (46%), and the highest among those 5-15 years (83%). Parasite densities in false -MRDTs were generally <100 per microliter and varied significantly with age in both false -MRDTs and true +MRDTs. The widest range of parasite densities in false negative results were in those 5-15 years. Parasite density of true +MRDT results decreased with age. In our study, MRDTs performed less well than expected in certain populations, which may inform deployment and development of these important tools.

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FALSE NEGATIVE MALARIA RAPID DIAGNOSTIC TESTS ON A LACTATE DEHYDROGENASE-BASED KIT AMID INCREASING *PLASMODIUM OVALE* PREVALENCE IN KENYA

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Malaria rapid diagnostic tests (mRDTs) are widely used tests in resource limited settings to guide prompt malaria case management. The *P. falciparum* specific histidine-rich protein-based (*Pf*HRP2) mRDTs are commonly used and occasionally in combination with the *Plasmodium spp* lactate dehydrogenase (*p*LDH) specific band to detect infection containing non-*falciparum* malaria. Besides ongoing efforts to evaluate HRP2/3 deletions causing false negative *P. falciparum* diagnoses, it is increasingly important to establish the accuracy of pan-*p*LDH band given the increasing frequency of non-*falciparum* infections for effective case management. Here, we characterize polymorphisms causing false negative diagnosis of non-*falciparum* infections using combo mRDTs. In 2023-2024, 105 blood samples from febrile individuals at a health facility were tested for presence of malaria using combo mRDTs followed by microscopy and PCR to confirm malaria presence and determine species composition. Genotyping of polymorphisms within the *p*LDH gene of associated species is ongoing. Out of 105 samples tested using HRP2 and pan-pLDH bands of the mRDT, 84 were confirmed positive for malaria, whereas 6 samples (5.71%) failed to react to these mRDT bands but were positive through microscopy. Molecular analyses revealed that 94/105 samples were positive for malaria by PCR including those that had failed to react to both test bands. Assessment of species composition showed that *P. falciparum* (*Pf*) was the most prevalent, found in 80 samples (85.10%), followed by *P. ovale wallikeri* (Pow) 5, (5.32%), *P. malariae* (*Pm*) 2, (2.13%) and *Pf-P. ovale curtisi* mixed infections 2, (2.13%). Notably, the six infections that were unreactive by both the HRP2 and pan-*p*LDH bands comprised 4 *P. ovale wallikeri* and 2 *P. malariae* infections. A review of clinical data confirmed that these patients presented with classical symptoms of malaria in absence of *P. falciparum*. These findings underscore the urgency for enhanced surveillance and diagnostic accuracy, suggesting a reevaluation of the shift towards pan-pLDH based diagnostics in areas where non-falciparum species are prevalent.

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UNUSUAL PRESENTATION OF MALARIA IN A PEDIATRIC PATIENT DELAYING DIAGNOSIS

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A six months old female child from Terai region of Nepal presented with fever, vomiting, and bloody stool for three months. She was referred to Tribhuvan University Teaching Hospital, Kathmandu. Despite various investigations and treatments, including high-dose antibiotics for Pyrexia of unknown origin (PUO), the patient remained unwell and her health condition was deteriorating and got admitted to the PICU. Laboratory findings revealed pancytopenia with polychromasia. It was already 14 days of her PICU when a Peripheral blood examination revealed the presence of malarial parasites, suggesting specifically *Plasmodium vivax*. Subsequent Rapid kit test also support the diagnosis. Prompt treatment with Tab. Chloroquine and Tab. Primaquine resulted in complete recovery.

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A PHASE 1B STUDY TO CHARACTERIZE THE SAFETY AND PHARMACOKINETIC/PHARMACODYNAMIC RELATIONSHIP OF MMV367 (GSK701) IN ADULT PARTICIPANTS EXPERIMENTALLY INFECTED WITH BLOOD- STAGE *PLASMODIUM FALCIPARUM*

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The rapid spread of antimalarial drug resistance presents a major threat to malaria control and necessitates the development of new antimalarial compounds with novel mode of action. MMV367 is a first-in-class, fast acting, orally bioavailable antimalarial co-developed by MMV (sponsor) and GSK with potent activity against *Plasmodium falciparum*, including resistant strains. Safety, tolerability, and pharmacokinetics were recently evaluated in a first-in-human study (NCT05507970) with results supporting progression of MMV367 as a potential new treatment for uncomplicated malaria. We therefore undertook a Phase 1b volunteer infection study to characterise the pharmacokinetic/pharmacodynamic (PK/PD) relationship of MMV367 in healthy adults experimentally infected with blood-stage *P. falciparum* (NCT05979207). Twelve participants were enrolled across 2 cohorts of 6 participants. Participants were inoculated with *P. falciparum* infected erythrocytes and treated on day 8 with different single oral doses of MMV367, including subtherapeutic doses to observe recrudescence. In cohort 1, participants were dosed with 20 mg (n=3), 90 mg (n=2) or 1500 mg (n=1). Parasite clearance was rapid in all participants, with a median (95% CI) observed clearance half-life of 3.04 (2.78 - 3.37), 3.97 (3.58 - 4.46) and 3.11 (2.72 - 3.64) hours for the 20 mg, 90 mg, and 1500 mg doses, respectively. Parasite recrudescence occurred in only 1 participant (treated with 20 mg), requiring rescue treatment on day 22. In cohort 2, participants were dosed with 3 mg (n=3), 5 mg (n=2), or 10 mg (n=1). All 6 participants received rescue treatment with artemether-lumefantrine by day 4 post administration of MMV367 and recrudescences allowed identification of the PK/PD relationship. The 12 participants experienced a total of 211 adverse events (median 19, range 6 - 38). The majority were mild to moderate and

consistent with clinical symptoms of malaria. There were no serious adverse events. In summary, this study supports the further clinical development of MMV367 in patients as a single dose treatment of uncomplicated malaria.

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DOSE-OPTIMIZATION OF THE FIXED-DOSE TRIPLE COMBINATION ANTIMALARIAL THERAPY ARTEMETHER-LUMEFANTRINE-AMODIAQUINE

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Artemisinin-based combination therapy (ACT) is the first-line therapy for uncomplicated *falciparum* malaria. Triple-ACTs (TACTs) have emerged as a treatment option to combat declining efficacy of ACTs and to prevent the development of drug resistance. In this study, we aimed to develop an optimal fixed-dose regimen of artemether-lumefantrine-amodiaquine through population pharmacokinetic modelling and simulation. Three published pharmacokinetic models were used to simulate concentration-time profiles of competing dose regimens. Two publicly available data bases were used to generate virtual patients with biologically plausible weight-age combinations; NHANES from the US CDC (n = 53,833) and the SMAC network (n = 26,051). The pharmacometric model for each drug was applied to simulate a total of 1,000 patients for each bodyweight and dosing regimen. All pharmacometric simulations were performed in NONMEM. Simulated concentration-time profiles were compared between standard and optimal dosing. To minimize the extent of modifications needed to combine two existing treatments, the current dosing ratio of artemether-lumefantrine (20/120 mg) was retained, with the addition of 40 mg amodiaquine. This drug-to-drug-ratio was kept throughout the dosing bands in order to simplify manufacturing, implementation, and further development of a fixed-dose co-formulated product. The standard 4 dosing bands were transformed to 5 dosing bands to achieve more equivalent exposure in all weight groups and to reduce fluctuations in peak concentrations. The proposed optimal dosing was constructed to achieve equivalent drug exposure to artemether-lumefantrine-amodiaquine in small children compared to adults, while safeguarding that no patients received higher peak concentrations of amodiaquine compared to current dose recommendations. In conclusion, an optimal fixed-dose TACT regimen was developed to maximise the chance of cure by providing a somewhat increased mg/kg dose of artemether-lumefantrine in small children and large adults, while minimising the risk of adverse events associated with high doses of amodiaquine.

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PRE-REFERRAL RECTAL ARTESUNATE IN CHILDREN WITH SEVERE MALARIA: ANY BENEFIT?

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Malaria still poses a major health risk in Sub-Saharan Africa and untreated *Plasmodium falciparum* infections can progress to severe malaria and death, especially in young children. The first line treatment of severe malaria is parenteral artesunate, but this treatment requires adequate healthcare facilities to be able to administered in an effective and safe manner. In rural malaria-endemic areas, the access to appropriate care could involve prolonged transportation. Therefore, pre-referral rectal artesunate could be a life-saving option to keep the patient stable before adequate facilities can be reached. In the present study, observed data from intravenously and rectally administered artesunate in children with malaria were analyzed to determine the pharmacokinetic properties and the bioavailability of rectal artesunate. Concentration-time measurements of artesunate and dihydroartemisinin were collected from a clinical trial conducted in the Democratic Republic of Congo. The study was designed as cross-over trial in which the child randomly received rectal or intravenous artesunate at enrollment and the alternative regimen 12 hours later. All patients received intravenous quinine at the same time for safety reasons. Pharmacokinetic data was analysed using NONMEM. Artesunate and dihydroartemisinin was successfully described by a two-compartment disposition models with one transit compartment describing the absorption of the rectal formulation. The estimated absolute bioavailability of the rectal formulation was low with a high variability between patients. The final model was linked to an existing pharmacodynamic model, describing parasite density, and used to simulate the clinical impact of the rectal formulation. According to these simulations, even with low bioavailability, the rectal formulation resulted in enough concentrations of artesunate and its metabolite, to eliminate malaria parasites while transporting the patient to an appropriate health care facility. In conclusion, these findings add to existing knowledge and strongly encourage the use of rectal artesunate as a pre-referral treatment.

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THE EFFECT OF SINGLE LOW-DOSE PRIMAQUINE TREATMENT FOR UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA ON HEMOGLOBIN LEVELS IN ETHIOPIA: A LONGITUDINAL COHORT STUDY

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To interrupt residual malaria transmission and achieve successful elimination of *Plasmodium falciparum* in low-transmission settings, the World Health Organization recommends the administration of a single dose of 0.25 mg/kg (or 15 mg/kg for adults) primaquine (PQ) combined with artemisinin-based combination therapy (ACT) without glucose-6-phosphate dehydrogenase (G6PD) testing. However, due to the fear of hemolysis in patients with G6PD deficiency (G6PDd), PQ use is not widely practiced. Hence, this study aimed to assess the safety of a single low dose of PQ administered to patients with G6PD deficiency. A longitudinal cohort study was conducted with patients treated for uncomplicated *P. falciparum* malaria with either single-dose PQ (0.25 mg/kg) (SLD-PQ) + ACT or ACT alone. Microscopy-confirmed uncomplicated *P. falciparum* malaria patients visiting health facilities in Arjo Didessa, Southwest Ethiopia, were enrolled in the study from September 2019 to November 2022. Patients with uncomplicated *P. falciparum* malaria were followed up for 28 days through clinical and laboratory diagnosis for G6PD levels and hemoglobin (Hb) concentrations. Hb data were taken on days (D) 0, 7, 14, 21, and 28 following treatments with SLD-PQ + ACT or ACT alone. A total of 249 patients with uncomplicated *P. falciparum* malaria were enrolled in this study. Of these, 83 (33.3%) patients received ACT alone, and 166 (66.7%) received ACT combined with SLD-PQ treatment. The median age of the patients was 20 years. G6PD deficiency was found in 17 (6.8%) patients, 14 males and 3 females. There were 6 (7.2%) and 11 (6.6%) phenotypic G6PD-deficient patients in the ACT alone and ACT + SLD-PQ arms, respectively. No difference in mean Hb levels ($P = 0.157$) was observed in patients treated with ACT + SLD-PQ (mean Hb = 0.45 g/dL; 95% CI = 0.39 – 0.52) post-treatment compared to patients treated with ACT alone (mean Hb = 0.30 g/ dL; 95% CI = 0.14 – 0.47). Our findings showed that single low-dose primaquine (SLD-PQ) treatment for uncomplicated *P. falciparum* malaria is safe and does not increase the risk of hemolysis in G6PD deficient patients.

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REPEAT IVERMECTIN MASS DRUG ADMINISTRATIONS FOR MALARIA CONTROL II: PRIMARY OUTCOME

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Ivermectin (IVM) can kill malaria vectors that blood feed on IVM-treated people and thus may be an effective malaria vector control tool. We conducted a parallel design, double-blind, placebo-controlled cluster-randomized control trial in Burkina Faso over two consecutive years to test the safety of repeated, high-dose IVM mass drug administrations (MDA) and their efficacy for reducing incidence among children when distributed during seasonal malaria chemoprevention (SMC). Fourteen villages (clusters) were randomized 1:1. Exclusion criteria for IVM MDA included those <90cm, pregnant, or taking SMC. Participants received 3 consecutive 300 µg/kg IVM or placebo doses monthly during the rainy season. The primary outcome was incidence in children ≤10 years as assessed by weekly active case detection. Adverse events (AEs) were monitored in all participants. In the IVM and control arms, 4091 and 3525 participants including 1403 and 1262 cohort children were followed in 2019 and 2020, respectively. All clusters received new dual-ITN Interceptor® G2 in October 2019. The weekly malaria incidence rate per 100 person-weeks in the IVM and control arm was 1.78 and 1.84, respectively (IRR = 0.96; P = 0.87). The risk of AEs among MDA-eligible participants in the IVM arm was lower than among those in the control arm (risk ratio = 0.63; P = 0.0049). Membrane feeding data with treated human sera demonstrated the strong mosquitocidal activity of the drug. Blood fed *Anopheles gambiae* s.l. mosquitoes captured in IVM clusters the week after MDA in 2019 had decreased survival relative those captured from control clusters (P < 0.0001), but there was no difference in these survival rates among mosquitoes captured three weeks after MDA. EIR did not differ between arms (IVM = 0.010, control = 0.011). Repeated high dose IVM MDA was safe when integrated with SMC, but did not reduce incidence among children relative to placebo MDA, despite evidence that mosquito survivorship in the first year was reduced in the IVM arm at least a week following MDA. Confounding factors included unexpectedly low incidence over the trial and dual-chemistry LLIN distribution in the middle of the study period.

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ASSESSMENT OF THE ANTIPLASMODIAL EFFECTS < TOXICITY STUDY OF ENDOPHYTES FUNGI EXTRACT ISOLATED FROM *ALSTONIA BOONEI* DE WILD

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Despite all strategies implemented to eradicate malaria, it remains one of the main causes of death worldwide. This is particularly related to the expansion of multidrug-resistant strains of *Plasmodium* species of which *Plasmodium falciparum* is the most prevalent. This study aimed to assess the antiplasmodial < toxicity profiles of extracts from endophytic fungi of *Alstonia boonei*. Endophytic fungi from different parts of *A. boonei* were isolated using in Potato Dextrose Agar (PDA), Sabouraud Dextrose Agar (SDA) < Czapek Dox Agar (CDA) media. The isolates were identified < grouped morphologically and molecularly. Each fungus was grown in a liquid medium < the ethyl acetate extracts prepared were evaluated for antiplasmodial activity < for both larval using *Artemia salina* larvae < acute toxicity using rat as models. Following the isolation, 73 endophytic fungi in total, with 28 in PDA, 26 in SDA and 19 in CZA. Thirty-four (44) morphologically distinct < 35 molecularly different endophytic fungi with molecular weights ranging from 500 to 750 base pairs were obtained. Each of the 35 endophytic fungi were shown to belong to either of the following genera: *Fusarium spp, Trichoderma spp, Acremonium spp, Alternia spp, Lasiodiplodia spp, Chaetomium spp, Xylaria spp < Emericellopsis spp* with 04 non-sporulating fungi. Extracts from the 35 fungi showed IC_{50}s (inhibitory concentration 50%) ranging from 3.86 to 32.69 µg/mL against *P. falciparum* 3D7 < 5.34 to 76.28 µg/mL against *P. falciparum* Dd2 laboratory strains. The acute < larval toxicity tests showed that endophytic fungi extracts were not toxic on larvae < on rats. They therefore deserve to be exploited further as sources of potential antimalarial agents.

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IDENTIFICATION OF INHIBITORS OF MOSQUITO STAGES OF *PLASMODIUM FALCIPARUM* DEVELOPMENT USING AN *IN VITRO* CULTURE SYSTEM

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We recently generated a new strategy for malaria control based on killing *Plasmodium falciparum* parasites in the mosquito vector using inhibitors delivered via treated surfaces such as bed nets. The discovery of novel inhibitors that can be incorporated onto mosquito nets, however, has so far been hindered by the inability to perform high-throughput screens for compounds that kill the sporogonic stages of parasite development. While efficient *in vitro* systems of sporogonic stages have been generated for rodent malaria parasites, studies are still lagging for human parasites, despite some progress. Here, we show the development of an *in vitro* culture system for *P. falciparum* mosquito stages that allows the reliable production of ookinetes and oocysts with improved yields and that can be used for high-throughput screens. We used the previously described transgenic reporter line NF54-HGL, which expresses a fusion of the green fluorescent and firefly luciferase proteins, to culture parasites *in vitro*. Ookinete and oocyst formation were achieved in the presence of insect cells and matrigel in optimized media conditions. After cell number optimization, we assessed this system in a 96-well plate format to test the inhibitory activity of several compounds with known mechanism of action against ookinete and oocyst development. Parasite viability was evaluated through live cell imaging for ookinetes, while a simplified bioluminescence-based assay was employed for day 7 oocysts and then validated also through live cell imaging. Novel drugs were identified with potent multistage activity or stage specificity activity at 1 uM, including the *Pf*PI4K inhibitor KDU692 (ookinete -specific activity), the *Pf*DHODH inhibitor DMS265 (oocyst -specific activity), and the putative *Pf*CARL inhibitor GNF179 (multi-stage activity). Current studies are focused on extending the drug screening to libraries with novel chemotypes and on the development of a high-throughput live cell imaging system.

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ACCELERATING ANTIMALARIAL DRUG DISCOVERY WITH A HIGH-THROUGHPUT SCREENING FOR FAST-KILLING COMPOUNDS

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The significance of fast-killing properties has become increasingly crucial for the advancement of next-generation lead compounds in antimalarial drug discovery, as the expedited action of these compounds has the potential to alleviate resistance concerns and enhance patient compliance with antimalarial medications, thereby addressing prominent issues associated with artemisinin-based combination therapies (ACTs). The present study introduces a high-throughput screening (HTS) approach using 1536-well plates, employing *Plasmodium falciparum* lactate dehydrogenase (PfLDH) combined with nitroreductase (NTR) and turn-on fluorescent probes to evaluate the inhibition of the growth of the asexual blood stage of malaria parasites. We applied this method to assess the parasite reduction ratio (PRR) and successfully screened a large number of compounds in a 384-plate format over a short period, simplifying the time-consuming conventional method. Our high-throughput PRR enables the early identification of fast-killing hits during the screening stages, while also facilitating the continuous monitoring of such properties in newly synthesized compounds through structure-activity relationship (SAR) studies. This approach accelerates the development of innovative fast-killing antimalarial drugs within the framework of phenotypic drug discovery campaigns.

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HIGH THROUGHPUT SCREENING IDENTIFIES COMPOUNDS WITH NANOMOLAR ANTIPLASMODIAL ACTIVITY AGAINST THE ASEXUAL STAGE PARASITES

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The emergence of artemisinin-resistant malaria parasite highlights the need for new drugs with novel mechanisms of action against Plasmodium infection. To identify such new compounds, we conducted a high-throughput screening campaign (HTS) using a robust fluorescent technique at a single-dose concentration of compounds included in the Nagoya Chemical Library. Primary HTS identified 1,365 hits (among 36,160 compounds) at a cut-off inhibition of 68.65%, established by the empirical rule of standard deviations (3×SD). A subset of 896 compounds was prioritized for dose-response assays following elimination owing to cytotoxicity against mammalian cells and the requirement to achieve a 1% hit rate for structure disclosure. This subset was subsequently tested for inhibitors of the mitochondrial electron transport chain (MtETC), which is the most validated target, using the 3D7-yDHODH transgenic parasite strain alongside the wild-type 3D7. We have successfully identified 23 compounds showing complete parasite inhibition at nanomolar ranges, even at the lowest tested dose (12 nM) against 3D7, and seven compounds targeting MtETC showing > 100-fold shift in EC50 (3D7 vs. 3D7-yDHODH strains). A total of 435 compounds exhibiting ≤ 6.5 µM EC50 have been prioritized for further assays against a panel of Dd2 parasites harboring mutations in well-known drug target genes as an attempt to distinguish hit compounds with unknown or similar mechanisms of action. The MtETC-targeting compounds will be subjected to kinetic studies against the recombinant PfDHODH enzyme for further validation, and compounds that elicit unknown mechanisms of action will be used to raise resistant mutants, followed by whole-genome sequencing for target elucidation.

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NOVEL DRUG DISCOVERY FOR *PLASMODIUM FALCIPARUM* MALARIA

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Malaria attributable mortality is increasing and the spread of parasites resistant to the artemisinin family of compounds threatens to exacerbate this trend, thus underscoring the urgent need to identify novel anti-malarial drugs. We propose that *P. falciparum* PfGARP is a high value druggable target based on: 1) its surface expression on iRBCs, 2) its absence of amino acid homology with host proteins, 3) its absence of significant sequence variation, 4) the requirement for PfGARP for *in vivo* survival, and 5) the ability of antibody binding to PfGARP to rapidly kill parasites without engaging immune effector functions. To develop a drug based on PfGARP binding, we screened the 30 million compound CTS-FIU library to identify compounds that inhibit binding of anti-PfGARP to rPfGARP protein. We reason that compounds which bind to the same region of PfGARP targeted by parasite-lethal anti-PfGARP antibodies will be enriched for effective, PfGARP targeting anti-malarials. We identified 2 sub-libraries containing compounds which bind to PfGARP. Using our positional scanning method, we deconvoluted one sub-library (>45k compounds based on a bis-cyclic guanidine-*S*-butyl scaffold) to 7 compounds which kill 3D7 strain *P. falciparum* parasites with IC_{50} ~ 25-50nM. We focused on one of these highly active compounds, #19, and demonstrated it had similar killing activity against several drug resistant parasite strains (Dd2, CamWT_C580Y). Compound #19 had an IC_{50} >50uM for cytotoxicity as measured in several human cell types including PBMCs, lung epithelial (A549), macrophage (THP-1) as well as bacteria (*E. coli*) giving it a selectivity index >1,000. Compound #19 is freely soluble in aqueous vehicles and, when delivered SQ, has a half-life of 17 hrs in mice. When dosed SQ at 5mg/kg, compound #19 rapidly cleared parasites in the *P. falciparum*/NSG model. We are evaluating the *in vitro* efficacy of compound #19 in freshly isolated parasites from our field sites and evaluating mutagenic/genotoxic potential (Ames, micronucleus), cardiac toxicity (hERG), and vehicle formulations to advance compound #19 as a parenteral treatment for severe falciparum malaria.

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DIHYDROARTEMISININ-PIPERAQUINE AS AN ALTERNATIVE TO SULFADOXINE-PYRIMETHAMINE FOR INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY: A META-ANALYSIS OF MATERNAL, BIRTH, AND INFANT OUTCOMES

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High-grade *Plasmodium falciparum* resistance to sulfadoxine-pyrimethamine (SP) in East and Southern Africa prompted a series of trials comparing intermittent preventive treatment in pregnancy (IPTp) with SP to dihydroartemisinin-piperaquine (DP), a highly efficacious artemisinin-based combination therapy. We conducted an individual participant data random-effects meta-analysis of 9 trials involving 7,533 HIV-uninfected women with singleton pregnancies that led WHO to continue recommending IPTp-SP. We previously reported that IPTp-SP was associated with increased fetal growth and newborn birthweight despite a lower risk of malaria outcomes with IPTp-DP. Here, we provide new findings regarding the impact of these regimens on maternal, birth, and infant outcomes. Compared to IPTp-SP, IPTp-DP was associated with a 69% [95% CI: 45%–82%] lower incidence of clinical malaria during pregnancy, a 56% [26%–74%] lower risk of placental parasitemia detected by histopathology, microscopy, RDT, or PCR, and a 17% [0%–31%] lower incidence of moderate maternal anemia (Hb<9 g/dL). Effects were similar in primi- and multi-gravidae (p-interaction≥0.53). Compared to IPTp-DP, IPTp-SP was associated with higher mean weekly maternal weight gain (30 g [14-46]). At birth, the risk of small-for-gestational age was 14% [3%–24%] lower in the IPTp-SP arm. Among multigravidae, underweight and stunting at birth were 39% [14%-56%] and 24% [8%–37%] lower with IPTp-SP. These effects were not observed in primigravidae: 31% [-10%–92%] and 16% [-8%–46%] higher in the IPTp-SP arm, respectively. By age ~2 months, the risk of stunting remained lower in the IPTp-SP arm in multigravidae 18% [3%–30%], but not in primigravidae (-16% [-7%–46%]) (p-interaction<0.001). The risk of being underweight by ~2 months was 27% [6%–44%] lower in the IPTp-SP arm, with no differences between gravidity subgroups (p-interaction=0.79). IPTp-DP was associated with reductions in malaria, regardless of gravidity. However, IPTp-SP was associated with improved birth and infant outcomes, particularly in multigravidae. Trials evaluating a combined regimen of DP+SP for IPTp are warranted.

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SAFETY AND FEASIBILITY OF INTEGRATING MASS DRUG ADMINISTRATION FOR HELMINTH CONTROL WITH SEASONAL MALARIA CHEMOPREVENTION IN SENEGALESE CHILDREN: A RANDOMIZED CONTROLLED, OBSERVER-BLIND TRIAL

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The overlap in the epidemiology of malaria and helminths has been identified as a potential area to exploit for the development of an integrated control strategy to achieve the WHO targets of eliminating malaria and helminths by 2030. We conducted a randomized controlled, observer-blind trial, to assess the feasibility and safety of combining mass drug administration (MDA) for schistosomiasis and soil-transmitted helminths (STH) with seasonal malaria chemoprevention (SMC) among children living in Senegal, West Africa. Children aged 1-14 years were randomized 1:1:1, to receive Vitamin A and Zinc supplements on Day 0 (control group); or praziquantel on Day 0 (treatment group 1); or albendazole and praziquantel on Day 0 (treatment group 2), followed by SMC drugs (sulphadoxine-pyrimethamine/amodiaquine) on Days 1-3 in the control and treatment groups. Safety assessment was performed by collecting adverse events from all children for six subsequent days following drug administration. Pre- and post-intervention, blood, urine, and stool samples were collected from the study participants for determination of haemoglobin concentration, microscopy, and PCR assays. From 9-22 June 2022, 627 children were enrolled and randomized as described above. Mild-to-moderate, transient vomiting was observed in 12.6% (26/206) in treatment group 2, 10.6% (22/207) in treatment group 1, and 4.2% (9/214) of children in the control group (p=0.005). No statistical difference was observed in the prevalence of malaria-helminth co-infection before and after intervention (p=0.26). Malaria parasitaemia was much higher in the control group than in the intervention arms (p=0.03). Children who received praziquantel and SMC drugs had a lower risk of developing severe anaemia than those who received SMC drugs alone. Integration of MDA for helminths with SMC drugs was safe and feasible among Senegalese children. These findings boost the public health recommendations for a paradigm shift from parallel, top-down disease control programs to integrated, locally relevant, evidence-based, and sustainable child health policies and their delivery.

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DEVELOPMENT AND PRE-TEST OF A RISK BENEFIT ASSESSMENT TOOL TO SUPPORT PROGRAMMATIC DECISION-MAKING REGARDING *PLASMODIUM VIVAX* RADICAL CURE TREATMENT OPTIONS IN LATIN AMERICA AND THE CARIBBEAN

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In Latin America and the Caribbean, where *Plasmodium vivax* is the dominant malaria species, there are efficacy, adherence, and safety challenges associated with the radical cure options currently recommended (or implemented) in the region. New and/or alternative regimens include double dose PQ (7 mg/kg total dose over 14 days, ddPQ14), PQ administered over 8 weeks (6 mg/kg total administered weekly, PQ8wks) and tafenoquine (300mg single-dose, TQ, not yet recommended by the World Health Organization, but is being incorporated in Brazil). Different delivery strategies can also improve safety and effectiveness, including supervision of treatment, as well glucose-6-phosphate dehydrogenase (G6PD) rapid point-of-care testing to prevent G6PD deficiency-related hemolysis that can occur with any radical cure regimens. In consideration of these options, we developed a risk benefit assessment (RBA) tool to support decision-making regarding the selection of a safe and effective treatment scheme to use at national or subnational levels. The RBA tool requires inputs of the malaria epidemiological data (i.e., the number vivax cases, # relapses and/or recurrences episodes, # hemolytic events, etc.) from the national health information system. A decision tree approach is used to compare estimated number of recurrences for different radical cure treatment schemes. An interactive ShinyApp tool, in English or Spanish, https://ucsf-mei.shinyapps.io/RiskBenefitTool_en/ or https://ucsf-mei.shinyapps.io/RiskBenefitTool_es/, respectively, enables the user to provide input values regarding the local epidemiology of malaria, G6PD deficiency, and hemolytic risk. To inform how radical cure approaches can be tailored for local contexts, we share modeled results from low and high hemolytic risk settings in Colombia. A main limitation of the tool includes scarce data on hemolysis and recurrence risks associated with different treatment regimes. Nonetheless, the tool provides a framework upon which these variables and/or new data may be incorporated in the future.

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MALARIA HEALTHCARE SYSTEM OF PAKISTAN AMIDST CLIMATE CRISES: A SWOT ANALYSIS

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Pakistan continues to bear a heavy burden of malaria. By 2021, case incidence was reduced by 40% from 2015. The 2022 floods resulted in a fivefold increase in malaria cases, with 2.1 million new infections and damage to over 1000 health facilities. Sindh had 53.5% of flood-related cases, with 117,282 from Thatta district. About 28.9% of Pakistanis reside in malaria-prone areas, with P.vivax accounting for 80% of all malaria cases. This SWOT analysis of Pakistan's healthcare system focuses on critical issues that must be addressed to combat malaria.Our analysis identifies challenges in the healthcare system, such as data fragmentation, poor resource allocation, noncompliance with treatment guidelines, and drug shortages, mainly primaquine. Investing in the current infrastructure of primary care clinics, microscopy facilities, and health information systems is necessary. True disease burden measurement is critical for executing control strategies but is limited by insufficient training and lab facilities in endemic areas. By integrating health information systems with real-time monitoring, mHealth can enhance disease surveillance, optimize resource allocation, and alleviate drug shortages. Furthermore, electronic prescriptions can help assure treatment adherence. However, rising temperatures, political unrest, and unrestricted access to antimalarials pose a considerable threat. The approval of the malaria vaccine, together with global commitment to malaria elimination provides a chance to develop an advanced malaria care plan that uses tested and field-usable methods for ending malaria in Pakistan. To address malaria and climate-related health challenges, local and global partners must invest in monitoring and diagnostic infrastructure, training on treatment standards, and an electronic disease surveillance dashboard. This improves public health and resource allocation. Our analysis recommends stakeholders assist Thatta to become a model for malaria elimination strategies. In conclusion, climate issues in Pakistan necessitate urgent upgrading of all malaria control strategies to eliminate malaria by 2035.

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A SCOPING REVIEW OF PATIENT ADHERENCE TO ANTIMALARIAL DRUGS

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Patient adherence has been a constant global challenge for effective antimalarial treatment and prophylaxis. This scoping review was carried out to map out patient adherence to antimalarial drugs and explore recent evidence (2013-2023) from countries where malaria is still a public health problem. A comprehensive search was performed using PubMed, EMBASE, and CINAHL databases. Reference lists from the included studies were also hand-searched. Covidence software was used to conduct the different steps of this review. Three independent reviewers screened the title and abstracts, reviewed the full-texts, and extracted the data. In total, 132 studies were included in the final review, which comprised studies measuring patient adherence to falciparum antimalarials (n=42), vivax radical cure (n=15), both falciparum antimalarials and vivax radical cure (n=7), intermittent preventive treatment of malaria for pregnant women (n=23), mass drug administration (n=14), antimalarial travel chemoprophylaxis (n=21), and other forms of antimalarial chemoprophylaxis (n=10). Most studies were from the African region (82; 62.1%), followed by Asia-Pacific (24; 18.2%), North America (11; 8.3%) and Latin America (8; 6.1%). The adherence reported ranged from 4-100%, with a majority of studies reporting 50-90% adherence (67; 55.4%). Around half of the studies were observational (n=67), and patient self-reporting was the most-used technique to measure adherence, either through an interview (n=21), as a questionnaire (n=38), or combined with manual pill count (n=26) and other techniques (n=24). Only 15 studies (11.3%) reported any intervention to improve patient adherence, with SMS reminders (n=5), home visits or partial supervision (n=5), and drug packaging (n=2) being the major interventions, with relatively mixed success. These findings suggest that although there have been improvements in new products addressing patient adherence in the last decade, this remains a significant barrier. Effective interventions will require deeper consideration of underlying factors and practical challenges to bring about positive behavior change.

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NORMALIZED COMPONENTS OF HEALTH SYSTEMS STRENGTHENING IN DELIVERING MALARIA TREATMENT SERVICES: A 3-YEAR IMPLEMENTATION STUDY

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In Indonesia, the Papua provinces carry the highest malaria burden. Health systems strengthening activities were rolled out in an implementation study at five public health clinics in southern Papua to improve malaria case management:(1) providing patients with a unique identifier to identify recurrences, (2) monitoring artemisinin combination therapy (ACT) and primaquine doses accuracy, (3) observing the first doses of both antimalarial drugs, (4) patient education to motivate adherence,

and (5) home visits by community health workers (CHWs) to encourage treatment adherence. As part of the study, periodic continuous quality improvement (CQI) meetings were held with quantifiable targets set by the health workers and clinic managers themselves. Qualitative methods were used to study the processes of the implementation. The Normalization Process Theory (NPT) was used to assess the level of integration of the intervention into the system. Between October 2019 and August 2023, 93 participant observations, 11 focus group discussions (FGDs), and 68 interviews were conducted. The intervention includes setting up a desk called '*malaria corner*' at the clinics to deliver the activities. In the 3 years of implementation, health workers quickly integrated dose checking but observation of the first dose was hindered by scarcity of drinking water and snacks and a prolonged shortage of antimalarials in 2022. Adherence education was given to patients and their caregivers with varying degrees of detail. Existing CHWs delivery of adherence monitoring at home was improved by additionally providing them with incentives. While not all activities are normalized, several components have been modified and embedded into routine practice, although this was limited by personal and structural barriers and other programmatic activities. Our study highlights the complexities of strengthening health system, which is a crucial step in decreasing malaria transmission through better case management.

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TRACKING AND SCALING UP OF SERVICE PROVISION TO FOREST GOERS AND MOBILE AND MIGRANT POPULATIONS FOR CONTROLLING OF LOCAL MALARIA TRANSMISSION IN FORESTED AREAS OF MYANMAR

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The forest goers and the mobile and migrant populations (MMPs) in Myanmar are a risk group for malaria. The U.S. President's Malaria Initiative (PMI) in Myanmar funded University Research Co., LLC and its consortium of partners in collaboration with the National Malaria Control Program to improve access to these essential services among marginalized and at-risk groups, including forest goers and MMPs. We assessed the odds of positive malaria rapid diagnostic test (RDT) among forest goers and MMPs compared to static resident populations, considering the geographic area, programmatic coverage, age, sex, and provider type. This analysis used de-identified, programmatic malaria case data (from both passive and active detection) from January 2020 to December 2023 from 31 townships of Kayin and Rakhine States and the Tanintharyi Region for descriptive analyses, chi-square tests of association, and logistic regression to understand whether forest goers and MMPs were more vulnerable than the static resident populations to being infected with malaria. Overall, there were 864,159 tests and 40,029 positives, revealing a test positivity rate of 4.6%. The proportion of forest goers and MMPs among those tested in 2023 was 21.4%, which increased by 30% than those tested in 2020. Compared to static residents, forest goers, and MMPs were at a 9.7 times greater odds ratio (95% CI: 9.5-9.9) of positive RDT after controlling for other covariates, including sex, age group, provider type, and geographic areas. Stratified analyses showed that forest goers and MMPs had 10.0 times higher odds ratio (95% CI: 9.8-10.2) of positive RDT than those of static residents after adjusting sex and 11.0 times higher odds ratio (95% CI: 10.8-11.3) after adjusting age group. Among the migrants, males had a 2.0 times higher odds ratio than females (95% CI: 1.9-2.1). Findings support the importance of designing specific strategies to reach forest goers and MMPs with malaria services. Additionally, forest goers and MMP-specific services should be scaled up, and the reasons why male forest goers and MMPs were at higher risk than female forest goers and MMPs should be explored.

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USING A MULTI-PRONGED APPROACH TO TARGETING *PLASMODIUM VIVAX* TO SHARPLY REDUCE INCIDENCE

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By the end of 2023, Cambodia had all but eliminated *Plasmodium falciparum (Pf);* from late October 2023 through March 2024, only 3 cases were recorded in the country, and the bulk of malaria cases are now due to *P. vivax (Pv)*. CNM and USAID/PMI through the CMEP2 Project applied lessons learned from *Pf* elimination efforts to develop a multi-pronged strategy to eliminate *Pv* in 14 operational districts in 6 Provinces. The strategy layered multiple activities to produce maximum effect: (i) To combat relapses, *Pv* radical treatment was implemented for *Pv* patients with normal Glucose 6 Phosphate Dehydrogenase (G6PD) test results. A 14-day primaquine (PQ) regimen initiated in early 2021 was shifted to a 7-day PQ regimen in mid-2023 to improve completion rates. In May 2023, CNM and CMEP2 began piloting an 8-week PQ regimen in 8 health facilities (HFs) in 2 ODs of Pursat Province for *Pv* patients with deficient and intermediate G6PD test results. (ii) Integrated Drug Efficacy Surveillance (iDES)has been implemented in 10 HFs in 3 ODs of Pursat and Battambang Provinces since the beginning of 2023. Every individual diagnosed with malaria is enrolled for comprehensive follow-up for either 42 days (*Pf, P. malariae [Pm], & P. knowlesi [Pk]*) or for 90 days (*Pv & P. ovale [Po]*). In 2023,100% of patients enrolled in iDES following *Pf/Pm/Pk* infection and 79% of those enrolled following *Pv* infection completed the full course of treatment. No one tested positive for malaria during the follow-up period. (iii) Preventive interventions targeting forest goers were established due to the elevated infection risk in this group secondary to exposure to higher transmission areas in forested areas. Through 24/7 stationary teams at identified potential entry/exit points, all forest goers were tested for malaria, and either treated if positive or given artesunate pyronaridine for 3 consecutive days as intermittent preventive treatment (IPT) if negative. As Cambodia works to achieve elimination of all malaria species by 2025, introducing and sustaining multi-pronged intervention efforts targeting specific populations will be important, particularly for the elimination of Pv.

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PRIVATE COMMUNITY PROVIDERS' EXPERIENCES ON *PLASMODIUM VIVAX* RADICAL CURE TOOLS: EVIDENCE FROM MYANMAR

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The Partnership for Vivax Elimination (PAVE) supports Myanmar's national malaria control program to achieve malaria elimination goals, focusing on effective Plasmodium vivax case management. PAVE developed a new set of tools including Standard Operating Procedures, Counseling Form, and Directly Observed Treatment (DOT) form to enhance P. vivax treatment. Training on these tools was provided to 420 private community malaria providers across Mandalay, Kachin, Mon and Shan regions in 2022. A qualitative assessment, involving 30 in-depth interviews, assessed providers' experiences with the new tools. Data were analyzed using thematic analysis. Findings indicated that most providers could effectively utilize the forms, although some initially faced challenges, often resolved with supervisor assistance. Providers perceived that the forms ensured proper Primaquine dosing and follow-up visits, aligning with National Treatment Guidelines. Challenges to having four follow-up visits included

transportation difficulties and distance, resulting in some providers resorting to phone calls instead of physical visits. Adherence to urine collection in the initial treatment phase was generally high, but declined over time. Patients and providers lacked clarity regarding sulfur-containing medications. However, providers recognized numerous benefits of using the Counseling Form, including improved medication adherence and understanding of treatment duration and side effects. Feedback on the DOT form was positive, with providers highlighting its role in preventing missed doses and assisting patients' understanding of medication regimens. Suggestions for improvement included developing a manual to ensure consistency in providers' form completion. The study highlights private providers' favorability of new tools for managing P. vivax with Primaquine, indicating potential benefits. It underscored the importance of continued support and refinement, such as developing comprehensive manuals for consistent form utilization. This research signifies progress towards effective malaria elimination strategies in Myanmar.

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ADVANCING MALARIA ELIMINATION IN BRAZIL: PRIORITIES AND STRATEGIES FOR RESEARCH AND ACTION

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Malaria constitutes a notable public health challenge in Brazil, particularly in the Amazon region, which accounts for 99% of reported autochthonous cases. In 2022, Brazil initiated the National Malaria Elimination Plan. Subsequently, in June 2023, the Brazilian MoH convened a meeting involving members of the scientific academy and state representatives to deliberate on and establish research priorities concerning malaria. This initiative underscores our unwavering dedication to eradicating this disease. The creation of the Research Priorities Matrix aimed at identifying primary knowledge gaps and allocating resources toward research endeavors supportive of malaria elimination efforts. Prioritization of technological advancements in case surveillance, encompassing data analysis and predictive modeling, holds paramount importance in expediting the detection and timely treatment of Plasmodium infections across diverse transmission settings. By focusing on these pivotal domains, we can ensure targeted and efficacious endeavors toward achieving our objective of malaria elimination. Consequently, there will be enhanced precision in detecting parasite reservoirs, including asymptomatic and subpatent infections, particularly in regions striving for malaria elimination. Furthermore, advancements in diagnostic techniques and novel therapeutic approaches will aid in mitigating relapses attributed to *Plasmodium vivax*, the species accountable for roughly 85% of malaria cases in the country. The development of novel tools for entomological surveillance necessitates efficacious management of Anopheles vectors, including the evaluation of resistance to presently utilized insecticides. The endeavor to eliminate malaria in Brazil represents a viable and sustained strategy contingent upon substantial political contributions and reinforced commitments among federal entities. Therefore, the delineation of research priorities assumes critical significance in guiding concerted actions toward malaria elimination in Brazil, ensuring effective allocation of financing and resources to support these endeavors.

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HEALTH EDUCATION FOR MALARIA ELIMINATION IN BRAZIL - MALARIA LEADERSHIP COURSE

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In Brazil, despite the significant reduction in cases over the last decade, malaria is an example of partially successful elimination, mainly due to the spatio-temporal fluctuation cases malaria associated with the weakening of malaria health services in states and municipalities. In this context, it was proposed a course to train leaders to fight against malaria - *Leadership Course to Malaria Control and Elimination*. The primary objective of this course is to strengthen local health services by multidisciplinary training health professionals who work directly to malaria elimination in the Brazilian Legal Amazon. The training courses will be held in 9 states of the Brazilian Amazon organized by the National Malaria Control Program in association with representatives of the malaria research institutions. The methodology consists of problematizing heterogeneous malaria transmission scenarios in terms of management, policy, surveillance, diagnosis and treatment and health education to malaria elimination. To date, two malaria leadership courses have been held. These courses were attended by Municipal Supporters for Malaria Prevention, Control and Elimination from 34 Amazonian municipalities with a high malaria burden in Brazil, and 63 health professionals representing the states of the Brazilian Amazon that are close to malaria elimination - Maranhão, Mato Grosso and Tocantins. The average age of the participants was 39 years old (range: 29 to 69 years), with 53.4% of the participants being female. Around 81.8% of the participants had a university degree, with 64 (72.8%) having completed at least one postgraduate course. There was a homogeneous participation of health professionals working in malaria management, diagnosis and treatment and entomological surveillance and vector control. As a final evaluation of the participants, all of them reported that they would use the knowledge acquired during the courses in their work routine in the fight against malaria. It is expected that this course provides technical and scientific knowledge to develop sustainable and feasible local actions to support malaria elimination in Brazil.

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COVERAGE AND IMPACT OF A PROGRAMMATIC MASS DRUG ADMINISTRATION CAMPAIGN FOR MALARIA IN SOUTHERN MOZAMBIQUE USING ROUTINE SURVEILLANCE DATA

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Between December 2022-February 2023, a programmatic Mass Drug Administration (pMDA) was implemented in Mozambique by the National Malaria Control Program in the administrative post of Chidenguele (Manjacaze district, Gaza province), where the estimated population according to administrative data is 59,271. All eligible individuals aged ≥6 months were targeted to receive two rounds of the antimalarial dihydroartemisinin-piperaquine. This study evaluates the coverage of the pMDA and its impact on malaria incidence. Coverage was estimated using programmatic data collected during the pMDA. Impact was evaluated

through a controlled interrupted time series analysis using selected health facility catchment areas from the neighbouring district of Zavala (Inhambane province) as the comparison area. We assessed whether there was a change in malaria incidence after the introduction of the intervention in the pMDA versus the comparison group and whether there was a change in the malaria trend over time after the intervention compared to the pre-intervention period in the pMDA versus the comparison group. Negative binomial regression was performed, using monthly malaria case counts from the routine surveillance system as the dependent variable and adjusting for confounders. Population coverage (individuals reached [absent+present]/total population) was 63.4% in round 1 (R1), and increased to 92.0% in round 2 (R2) after optimising the delivery strategy based on lessons learnt in R1. Programmatic coverage (individuals treated/target population) increased from 41.2% in R1 to 69.7% in R2. Absences and exclusions in R2 accounted for 8.7% and 6.9% of the target population, respectively, whereas 6.7% refused to participate and 8.0% were not reached. Preliminary results from the impact evaluation will be available to be presented at the Meeting. Reaching 80% programmatic coverage, as recommended by WHO, is difficult even with high rates of population coverage, mainly due to absences and exclusion criteria. Routine data is an important source of information that can be used to evaluate the impact of interventions implemented programmatically.

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ENHANCING THE DESIGN OF RANDOMIZED TRIALS IN MALARIA ELIMINATION SETTINGS: A SIMULATION STUDY OF THE RING TRIAL DESIGN

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In malaria elimination settings, chemoprevention and vector control interventions are often reactive and focal: they target people who live in "rings" around index cases. Usually, cluster-randomized trials (CRTs) are used to evaluate ring interventions, but they may have low statistical power due to strong spatiotemporal clustering and low incidence in elimination settings. An alternative design that may have higher statistical power is the ring trial design, which was used to evaluate the Ebola vaccine but has not yet been used for malaria interventions. This design randomizes rings as index cases are detected. We compared statistical power of cluster-randomized and ring trials in a simulation study. We fit cluster-level malaria hazard functions using data from a trial conducted in a setting with low malaria incidence (50-100 cases per 1000 person-years) and strong spatiotemporal clustering in Namibia (NCT02610400). We simulated a ring intervention delivered within 500 meters of index cases in the intervention arm. In CRTs we randomized 56 administrative areas as clusters at baseline. In ring trials, we randomized rings as index cases occurred. For each design, we estimated intention-to-treat effects with robust standard errors and statistical power in 1,000 simulated trials. We examined different levels of intervention effectiveness, spillover effects, baseline incidence, spatial clustering, and treatment coverage. For all baseline incidence levels, ring trials had statistical power greater than or equal to CRTs. In transmission settings with incidence of 50 per 1,000 person-years, CRTs were powered at 80% to detect a minimum reduction in incidence of 60%, while ring trials were powered to detect a minimum reduction of 44%. For a lower effect size where incidence was reduced by 30%, power in both trial designs was less than 80% but power was 25.5% higher in the ring trial (54.5%) vs CRT (29.0%). CRTs had lower false positive rates than ring trials with larger differences at high baseline incidence. Our findings suggest that ring trials are a promising alternative to CRTs for evaluating ring interventions in malaria elimination settings.

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STRATEGIES TO ACHIEVED *PLASMODIUM FALCIPARUM* ELIMINATION IN CAMBODIA: PRACTICAL APPROACHES AND FINDINGS

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In 2018 there were 18,458 *Plasmodium falciparum* cases in Cambodia. With World Health Organization support, Cambodia began implementing targeted strategies to interrupt remaining transmission and reach *P. falciparum* elimination. Strategies were implemented in a phased approach: Intensification Plan 1 (IP1, Oct 2018 to Oct 2019), Intensification Plan 2 (IP2, Nov 2019 to Dec 2020), and Last Mile (LM, Dec 2020 to Dec 2023). The Village Malaria Worker (VMW) program was reactivated in 2018 after four years of disruption. As a result, testing increased by 15% between 2017 and 2018 (213,585 to 245,563). VMW testing constituted 55% of all tests in 2018, and the number of cases decreased by 31%, from 27,077 to 18,458. IP1 was launched in 2018 and included the 30 health center catchment areas (HFCAs) with the greatest malaria burden. During IP1, 4,725 P. falciparum cases were detected. In 2019, IP2 expanded to 36 HFCAs. During IP2, 1,092 P. falciparum cases were detected. A Controlled Interrupted Time Series (CITS) analysis demonstrated an accelerated decline in cases in IP1 and IP2 areas compared to non-IP areas. In 2021, LM was implemented to ensure each locally acquired P. falciparum case triggered a comprehensive investigation and tailored response. By 2023, 185 villages implemented full or partial LM. An analysis of the impact of LM showed the largest reduction in total cases in LM areas compared to partial and non-LM areas. In 2023, there were 34 cases nationwide and only 3 cases reported in the 4th quarter, a 99% case reduction in 5 years. From 2018-2023, there was a significant increase in malaria testing alongside a dramatic reduction in *P. falciparum* cases. The strategies of each elimination stage helped the country reduce the number of *P. falciparum* malaria cases to a negligible number, paving the way to malaria elimination.

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IMPROVING ADHERENCE AND RADICAL CURE OVERAGE FOR *PLASMODIUM VIVAX* THROUGH THE IMPLEMENTATION OF G6PD TESTING AT POINTS OF CARE IN CAMBODIA

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Cambodia aims to eliminate malaria by 2025. Following a 99% drop in *Plasmodium falciparum* (Pf) cases since 2018, *P. vivax* (Pv) infections now represent 95% of the 1,384 cases in 2023. Unlike Pf, Pv has a hypnozoite stage that requires radical cure with primaquine (PQ) to prevent relapse and achieve elimination. Due to the possible life-threatening side effects of PQ in G6PD-deficient patients, the WHO recommends G6PD testing to guide the administration of PQ. In 2020, the National Center for Parasitology Entomology and Malaria Control (CNM) enrolled males with mono or mixed Pv weighing ≥20 kgs in a radical cure pilot program in 88 health facilities (HF) across 4 provinces over 13 months. The pilot aimed to assess the feasibility of implementing qualitative point-of-care G6PD testing and a 14-day PQ scheme. Among 2,861 enrolled patients, 1,281 (45%) were G6PD tested, 959 (33.5%) had normal G6PD activity and received PQ, though just 78% completed treatment. HF staff also reported difficulty completing referrals for G6PD testing due to the high costs and time associated with travel to the HF. In 2021, CNM expanded the radical cure program to 324

HFs in 21 provinces and switched to quantitative G6PD tests so non-pregnant/breastfeeding females were now eligible. To address the gaps from the pilot, CNM introduced referral incentives for CHWs to accompany patients to HFs in 2022 and transitioned from a 14- to 7-day PQ scheme in 2023. As a result, 60% (678/1,129) of all eligible patients initiated radical cure in 2023. The proportion of patients successfully referred to HF increased from 42% in 2021 to 88% in 2023 while adherence increased from 87% to 96%. However, some coverage gaps remain, including 187 patients who were not G6PD tested and 264 (28%) G6PD-deficient patients who were ineligible for the 7-day PQ scheme. In response, CNM piloted 8-week PQ radical cure (0.75 mg/kg target dose) for deficient or intermediate patients and plans to implement this nationwide in 2024. Cambodia's experience demonstrates the feasibility of implementing successful radical cure strategies and serves as an example for other countries striving for malaria elimination.

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THE ACCEPTABILITY AND FEASIBILITY OF ROUTINE CLINICAL FOLLOW-UP FOR SHORT COURSE RADICAL CURE TREATMENT FOR *PLASMODIUM VIVAX* MALARIA: A COMPARATIVE ANALYSIS OF CAMBODIA AND ETHIOPIA

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Plasmodium vivax malaria requires a combination of drugs targeting both the blood and liver stages (hypnozoites) of the parasite (radical cure). The only available antimalarial drugs to clear hypnozoites are primaquine and tafenoquine, which can cause hemolysis in glucose-6-phosphate dehydrogenase-deficient patients. Although higher, shorter doses of primaquine have been proven more effective, they also increase the risk of hemolysis. Therefore, to support safety and improve adherence to a complete course of treatment, a clinical review three days after commencing primaquine has been proposed. It is unclear what type of clinical or laboratory-based assessments are acceptable and feasible for health providers and patients in different contexts and how such follow-up visits can be integrated into routine malaria care. Between March and September 2023 we conducted focus group discussions (FGDs) with *P. vivax* malaria patients and healthcare providers. The FGDs incorporated an interactive visual exercise for participants to explore and co-design a suitable day 3 review for their setting. Ten FGDs were completed in three health facility catchment areas in Pursat, Cambodia and six FGDs in four health facility catchment areas in Arba Minch, Ethiopia (total of 57 participants). Preliminary results suggest that distance, infrastructure, continuity of care, workload, and quality of care impact upon perceptions of where and how the follow up should be conducted. Collaboration across health care levels and the involvement of community health workers in monitoring as well as community engagement and sensitization regardless of chosen location were regarded as critically important. Selected procedures for the review were shaped by participants' perceptions of shorter, higher primaquine doses and how respondents understood the day 3 review visit, capacity, and costs to patients and health system. The findings and methodological approach outlined will inform the design and implementation of suitable follow-up strategies to increase safe delivery of novel radical cure options in different epidemiological and health system contexts.

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IMPLEMENTATION OUTCOMES OF 1-3-7 FOCUS INVESTIGATION FOR MALARIA IN A LOW TRANSMISSION SETTING IN SOUTHERN PROVINCE, ZAMBIA: A MIXED METHODS STUDY

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Since 2016, eleven countries have been certified as malaria free, but none of these are in continental Africa, where elimination challenges are unique. The 1-3-7 surveillance approach requires case reporting, case investigation/classification, and focal classification/responsive follow-up to be completed one, three, and seven days, respectively, after index case diagnosis. This approach is not dissimilar from reactive case detection as done in Zambia today, but it adds real-time short-messaging-service (SMS) reporting for each malaria case at each step (rather than weekly reporting) and with it, layers of monitoring, accountability, and data transparency. China, Thailand, Myanmar, and other countries deploy 1-3-7, citing high fidelity to deadlines and broad acceptability, yet 1-3-7 has yet to be widely deployed in Africa. This mixed-methods study evaluated implementation and service outcomes of 1-3-7 in a rural area of Choma District Zambia. Select outcomes were fidelity, feasibility, acceptability, efficiency, and equity. These were assessed through quantitative analysis of program metadata and qualitative analysis of semi-structured interviews with program personnel. Barriers and enablers to success and potential scale-up were also assessed. Fidelity was moderate with 61% of cases being reported. Network coverage was a common challenge to feasibility that likely affected reporting rates and fidelity. A large portion (64%) of cases diagnosed at the health facility were not eligible for follow-up per 1-3-7 criteria. Distance from the health center was a key barrier to feasibility and equitable reach of services. Reporting times were faster in areas where transmission was thought to be higher and slower in areas with poor network coverage. The program was widely accepted, and these results provided nuanced guidance to make modifications for 1-3-7 ahead of future scale-up.

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TRAVELERS WITH SUBMICROSCOPIC *PLASMODIUM SPP*. INFECTIONS CONTRIBUTE TO MAINTAIN RESIDUAL MALARIA IN TWO RURAL COMMUNITIES FROM THE PERUVIAN AMAZON REGION

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The movement of parasites through human mobilization is an important challenge to malaria elimination programs worldwide. This study aims

to identify malaria parasites in followed-up travelers going in and out of two rural communities in the Peruvian Amazon region to understand their contribution to maintaining residual malaria. Weekly active and passive case detections, as well as screening populations, were performed from February to August 2021 and 2022 in Libertad and Urcomiraño communities in Mazan district. Whole blood samples were collected for microscopy and qPCR diagnostics. A questionnaire specifically designed for travelers was applied to gather information about travel duration and reasons, visited communities, and other relevant sociodemographic information. From 678 people included in the study, 21.2% (144/678) traveled from Libertad and Urcomiraño to other communities in the last month. 119 malaria cases were detected during the study period, 89% (106/119) were submicroscopic infections, and 21.0% (25/119) were detected in travelers. Human mobilization was heterogeneous, and strong connectivity with other communities and creeks was found in the social network analysis; Mazan (out-degree=80) was the most frequent destination. Family affairs (40%) were the principal reason for traveling. Multilevel logistic regression analysis using balancing methods showed that male individuals over the age of 18 with travel history in the last month were the risk factors associated with malaria (p-value<0.001). These results show that human mobilization has an important role in the maintenance of residual malaria, and they will become the reservoirs of transmission and a challenge for the current elimination plan in the Peruvian Amazon.

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INCREASING CERTAINTY AROUND IMPACT OF SEASONAL MALARIA CHEMOPREVENTION: A MODELING FRAMEWORK USING ROUTINE DATA SOURCES IN BURKINA FASO

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Evidence from randomized controlled trials has demonstrated that Seasonal Malaria Chemoprevention (SMC) can prevent around 75% of malaria cases. However, there has been an increase in cases reported at health facilities in Burkina Faso since SMC implementation. This could indicate changes in treatment seeking or reporting, or that SMC is not achieving the desired effect. We developed a framework utilizing a mathematical model to assess whether impact is consistent over time, across different metrics, and among various population subgroups. We calibrated the Imperial College transmission model to slide prevalence in 65 districts in Burkina Faso (household surveys 2010-2018) using maximum likelihood. Included in the model were rainfall, net use, and treatment. We allowed for increases in treatment seeking by using the total consultation rate for all illness in the dry season when there are negligible malaria cases. We found that children in districts with SMC administration had significantly lower odds of prevalent malaria infection during the SMC protective period (OR 0.38, 95% CI 0.29-0.52, p<0.001) and remained lower for up to two months post-SMC. Modeled prevalence estimates by district aligned with prevalence data, indicating the anticipated impact of SMC at 70% coverage (Spearman correlation coefficient: r=0.66, p>0.001; r=0.76, p>0.001; r=0.60, p>0.001; in 2010, 2014, 2017, respectively). Health facility case data increased in total over time but the proportion of cases in children under-five years old who receive SMC decreased when compared to those aged 5-14, who do not receive SMC. The decrease in the proportion of cases under-five coincided with the introduction of SMC at different years in different districts (2014-2019). These findings correlate with modeled predictions (r = 0.60, p>0.001). We found evidence of seasonal variation in the proportion of cases under-five pre-SMC, that might obscure impact of SMC. We were able to replicate these patterns by including non-malarial fevers that would be counted as cases at the health facility due to incidental asymptomatic parasitaemia. Estimated cases averted will be presented.

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MOLECULAR INVESTIGATION OF RECURRENT *PLASMODIUM MALARIAE* INFECTION IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Plasmodium malariae is a neglected malaria parasite associated with clinically significant symptoms. Recent surveys confirm wide distribution of *P. malariae* across African countries where it often co-circulates with *P. falciparum.* Persistent *P. malariae* infection has been reported decades after initial confirmed infection. In this study, we are developing a multilocus sequencing approach to differentiate *P. malariae* re-infection from persistent infection in a longitudinal study conducted from 2015 to 2017 in Kinshasa, Democratic Republic of the Congo (DRC). Among 9,089 samples from 1,565 participants, 58 participants had recurrent *P. malariae* infections, comprising 131 *P. malariae* infections. Six *P. malariae* infections identified among six individuals from the same health area were selected. We Sanger sequenced partial *P. malariae csp* and *ama1* genes in four samples, then amplified and sequenced six *P. malariae* microsatellite loci in three samples using Oxford Nanopore MinION platform. Sequencing data was analyzed using an in-house pipeline for base-calling, filtering, demultiplexing, trimming, alignment, consensus sequence extraction, and determination of microsatellite repeat number. *Csp* and *ama1* sequencing showed 54 and 3 single-nucleotide differences, respectively, between the four samples tested; *csp* repeat analysis is ongoing. Microsatellite analysis confirmed distinct repeat numbers in three of six loci between all three samples tested. Optimization of a pooled *csp* and microsatellite Nanopore sequencing approach and analysis pipeline is underway. We will evaluate the assay performance by comparing results to Illumina whole-genome sequencing data generated from 13 infections derived from 5 participants. After methods optimization, we will apply it to all *P. malariae* samples. Our preliminary findings suggest that *csp* and microsatellites can be used to differentiate re-infection from relapse within one health area of Kinshasa, DRC. Combining sequencing results with available clinical and demographic data, we aim to improve our understanding of recurrent *P. malariae* infections in the DRC.

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MATHEMATICAL MODELING TO OPTIMIZE THE COHORT MONITORING TO ESTIMATE INCIDENCE RATE AND TIME TO FIRST INFECTION IN MALARIA-ENDEMIC SETTINGS

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It is important to evaluate the effectiveness of interventions against malaria. Key epidemiological endpoints are incidence rate and time to first malaria infection, typically estimated through longitudinal cohort study. However, the methods used to evaluate the endpoints are not standardized, such as the frequency of monitoring and the type of tests. We used the Imperial malaria transmission model to simulate different scenarios in malaria endemic settings (Entomological Inoculation Rate [EIR] = 10). Assuming a 30% reduction in an individual's EIR by intervention in a closed population of 10,000 with 10% intervention coverage, we estimated protective effectiveness (PE) defined as relative risk reduction by comparing cumulative incidence rates and time to first infection between intervention and control groups over 18 months post-intervention. We explored four scenarios with different visit intervals (7-, 14-, 28-, and 60-day intervals) for active

case detection alongside passive case detection, where participants seek healthcare upon developing symptoms. Through 100 simulations for each scenario, we observed that the cumulative incidence of infection decreased with longer visit intervals for both rapid diagnostic tests (RDT) and polymerase chain reaction (PCR). However, the estimated PEs did not vary across different visit interval scenarios. The median estimated PEs were 0.14, 0.13, 0.16, and 0.16 by RDT and 0.12, 0.12, 0.14, and 0.14 by PCR among 7-, 14-, 28-, and 60-day intervals, respectively, in terms of cumulative incidence. For the outcome of time to first infection, the median estimated PEs were 0.11, 0.14, 0.14, and 0.14 for RDT and 0.11, 0.15, 0.15, and 0.15 for PCR, respectively, for the intervals. Our results suggest that intensive monitoring, such as weekly or biweekly visits, may not always be necessary for evaluating malaria interventions. The results likely depend on the sample size and transmission intensity of the target population. Investigators should optimize cohort monitoring approaches during the study design phase, taking logistical aspects into account in field settings.

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ASSESSING ENTOMOLOGICAL MEASURES OF INDIVIDUAL *PLASMODIUM FALCIPARUM* INFECTION RISK

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While the aggregated entomological inoculation rate (EIR) is often associated with parasite prevalence at the population level, it is unclear whether mosquito data collected at finer spatial and temporal scales reflect heterogeneity in infection risk. With data from a longitudinal cohort that includes passive and active surveillance of participants and household-level mosquito captures and sporozoite rates (SR), we tested associations between multiple spatiotemporal models of EIR and individual risk of P. falciparum infection. We used data collected from 454 children aged 0.5-5 years in 244 households between 2011-2017 in three Ugandan districts: low-EIR Jinja, intermediate-EIR Kanungu and high-EIR Tororo. Vector densities and SRs were assessed monthly in each household using CDC light traps. Modeling each site separately, we predicted the distribution of EIRs at each household using combinations of spatial, temporal and spatiotemporal smooths of each entomological metric. We then assessed the association between predicted household-level EIR and individual malaria incidence using Poisson generalized additive mixed effects models. Data from Jinja were fit better (AIC) by a model that used fine-scale estimates of vector density and averaged SR temporally over the study period, while data from Kanungu and Tororo were fit better by a model that used fine-scale estimates of SR and averaged vector density temporally. The EIR-incidence relationship varied between sites, with positive associations in the Kanungu (IRR 1.85, 95% CI 1.45-2.35) and Jinja models (IRR 1.68, 95% CI 1.28-2.20) and no association in the Tororo model (IRR 1.25, 95% CI 0.95-1.65). These results show the relationship between EIR and malaria incidence may depend on local transmission dynamics and be strongest at intermediate-EIR sites. They also underscore the challenges of using individual captures to estimate individual malaria exposure.

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SPACE-TIME SENSITIVE MODELING OF SUBCLINICAL MALARIA PREVALENCE AT THE VILLAGE LEVEL IN LOW ENDEMIC AREAS OF MYANMAR USING RANDOM FOREST MODEL

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Malaria elimination progress in Myanmar has slowed down in recent years. Predicting malaria risks helps identifying targeted strategies in resource limited setting. This study estimated the temporal variation in subclinical malaria prevalence at village level in low endemic areas and quantified the impact of different socio-demographic, climatic and environmental drivers. A cross-sectional study was conducted using lot-quality assurance sampling in 67 villages across two townships in low endemic area of Myanmar. Data was collected in the wet and dry season of 2018-2019. Finger prick blood was collected from 11,128 asymptomatic individuals to detect subclinical malaria using ultra-sensitive polymerase chain reaction. We analyzed the effect of occupational risk, human utilization of landscape, climatic and environmental factors over-time to predict the subclinical malaria prevalence using machine learning approach (random forest model). The prevalence of subclinical malaria at individual level was 0.9% (*Plasmodium falciparum)*, 3.9% (*P. vivax)* and 4.9% (any malaria). At village level, <2% of people were subclinical malaria positive (ranged 0.7%-52%). Random forest model using potential and least correlated factors explained 41.5% (*P. falciparum),* 58.4% (*P. vivax)* and 58.3% (any malaria) of variance. Despite relatively low overall performance, the error rate of the models is very low. Fraction of croplands within a 2km buffer around villages was found to be the most important predictor for subclinical malaria, followed by frequency of interaction with water bodies, logging activities, fraction of managed and natural forest within the 2km buffer, greenness of vegetation and farming as the self-reported occupation. Findings suggest that in low endemic areas, the influence of village level socio-demographic, climatic and environmental factors is not sufficient to reliably predict the rate of subclinical malaria. Though the models' predictive power is limited, the very low error rate indicates high validity predictions. Incorporating temporal potential predictors in higher malaria endemicity will likely improve model performance.

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PREVALENCE OF SUBCLINICAL MALARIA AND ITS POTENTIAL RISK FACTORS IN LOW TRANSMISSION SETTING IN MYANMAR: A COMMUNITY-BASED SURVEY

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Despite ongoing efforts, malaria remains a global significant public health issue. Myanmar continues to experience a persistent prevalence of malaria infections in subnational elimination areas. Subclinical malaria contributes the persistent infection through asymptomatic carriers. This study identified the prevalence and potential risk factors for subclinical malaria in low transmission areas. A cross-sectional study was conducted using lot quality assurance sampling in 64 villages in two townships of Mandalay Region, Myanmar. Samples and data were collected from 11,128 asymptomatic individuals between Feb-Dec 2018. The questionnaire identified socio-demographic characteristics, travel history, mosquito exposure, population mobility and malaria history. Malaria infection was detected by rapid diagnostic test (RDT) and ultrasensitive polymerase chain reaction (usPCR) as a gold standard. Multiple logistic regression was performed to examine the potential risk factors for the prevalence of subclinical malaria infections. A total of 11,114 were involved in the final analysis (7,676 from Singu and 3,438 from Thabeikkyin). The mean age of participants was 31.3 years (SD 18.81) and the majority were dependent (25.2%). The prevalence of subclinical malaria by usPCR was 4.9% any malaria, 0.9% *P.falciparum*

and 3.9% *P.vivax.* Prevalence was very low for RDT (0.13% any malaria, 0.08% *P.falciparum* and 0.05% *P.vivax).* Multiple logistics regression shows that younger age group (< 29 years) (aOR=1.30, 95%CI=1.08-1.58), male (aOR=1.62, 95%CI=1.34-1.96), outdoor workers (aOR=1.40, 95%CI=1.14-1.72), having activities related to higher mosquito exposure (aOR=3.70, 95%CI=2.61-5.23), and having taken anti-malaria drug in the past 2 months (aOR=2.34, 95%CI=1.50-3.64) were significantly associated with subclinical malaria. The evidence showed the undeniable significance of subclinical malaria in low transmission areas. Policymakers should continue surveillance of subclinical malaria and tailor interventions to effectively control malaria transmission in high-risk populations to achieve malaria elimination.

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BLOOD TRANSFUSIONS FOR CHRONIC MALARIA ANEMIA IN PRISONERS OF WAR ON THE THAI-BURMA RAILWAY 1943-1945

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Blood transfusion is an important intervention for severe anemia caused by chronic relapsing vivax malaria. Sixty thousand Allied Prisoners of War (POW) worked on the Imperial Japanese Army's railroad from Thailand to Burma during 1942-5. From mid-1943 a blood transfusion service was run by the prisoners themselves to rescue severely ill fellow prisoners who were otherwise unlikely to survive the war. Approximately 1/3 of all POW did not survive the war largely due to a combination of starvation, ill-treatment and infectious diseases including cholera and malaria. Extant transfusion records (1251 recipients, 1189 donors) in ledger books held by the UK National Archives at Kew were accessed and analyzed. Survival to the end of the war in September 1945 was determined from Commonwealth War Graves Commission records. The records examined indicate that freshly donated whole blood was manually defibrinated and transfused following cross matches based on POW medic sera. Overall survival to the end of the war was 74% of recipients and 88% of donors. Post-war survival rates for the main diseases associated with anemia in transfusion recipients were 53% for malnutrition, 59% for dysentery, 68% for skin ulcers, and 90% for malaria. Most donors died in transport ships sunk on their way to Japan. By 1945 the vast majority of blood transfusions were given for severe anemia caused by chronic (nearly monthly) relapsing vivax malaria. Although the POW situation was admittedly extreme, eliminating residual liver parasites to prevent chronic vivax relapses and the resulting severe anemia does directly contribute to adult survival from *Plasmodium vivax*.

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PERFORMANCE METRICS DURING A MALARIA OUTBREAK RESPONSE; LESSONS FROM EVALUATION IN AN ARID, EPIDEMIC-PRONE COUNTY IN KENYA

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In January 2024, Marsabit County experienced a malaria outbreak with 750 confirmed cases, 12% (90) of whom had severe malaria. This was following heavy rains that displaced 1000 households and increased mosquito population. Epidemic preparedness and response (EPR) strategies were in place, but how the strategies performed was not known. We sought to measure the response timeliness and identify bottlenecks and enablers of system performance.We used the WHO guidelines to conduct an Early Action Review (EAR). We reviewed county weekly malaria surveillance data, EPR dashboard trends since December, and outbreak reports at the Marsabit Public Health Emergency Operations Centre. We calculated the time to detect, notify, and respond to the outbreaks against a benchmark of the 7-1-7 global target of detection within seven days from emergence, notification within one day of detection, and completion of early response actions within seven days of notification. Key informant interviews (KII) were held with the surveillance and response team members. Data analysis was done thematically. The outbreak was detected in 16 days, notified in 7 days, and early response activities were completed in 41 days. Staff capacity included case management, entomologic surveillance, genomic surveillance, and laboratory quality assurance. Stakeholders supported vector control and laboratory diagnosis. Primary health facilities did not monitor EPR dashboards, lacked rapid response teams, pan-specie malaria rapid diagnostic tests, and under-reported cases. Malaria surveillance is additionally challenged by nomadic pastoralism, cross-border disease spread, and changing vector and parasite distribution. KII elicited bottlenecks and enablers for the observed performance and proposed recommendations to strengthen future responses. Through an EAR, we identified areas for outbreak response improvement including facility-level EPR data monitoring, feedback, and support for clinical and diagnostic supplies decision-making. There is a need to strengthen malaria surveillance, diagnosis, and treatment in epidemic-prone border counties.

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ASSOCIATION OF A LONG-TERM CARRIAGE OF SUBPATENT *PLASMODIUM FALCIPARUM* PARASITES WITH CLINICAL MALARIA ATTACKS IN A LOW TRANSMISSION AREA IN SENEGAL

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In low malaria transmission areas, asymptomatic *Plasmodium*-infected individuals contribute to the low-level of residual malaria. In Dielmo (Senegal), long-term monitoring of malaria exposed populations upon the implementation of preventive and control measures has been key to document the reduction of malaria incidence to the point that elimination is being envisaged. Attention is now directed towards the asymptomatic *Plasmodium* carriers that are believed to sustain clinical malaria cases. This study comprehensively elucidates the contribution of asymptomatic *P. falciparum* carriage in clinical malaria in such low-transmission areas. The research followed from June 2014 to December 2022 two cohorts of qPCR-positive (Group 1) and negative (Group 2) individuals (44 in each group) matched by age and sex, and their movements and malaria episodes were tracked. Blood samples were taken biannually for parasite detection using Cytochrome b-based qPCR. The spatial and temporal analysis utilized QGIS and R. Associations between the asymptomatic carriage and the occurrence of clinical malaria were examined using logistic regression model. Temporal follow-up of individual' infections revealed *P. falciparum* carriage was more frequent in Group 1 individuals. The qPCR positivity rate was significantly higher in Group 1 (19.69% vs 10.77%, p-value < 0.001), and an increased infection risk nearby asymptomatic carriers were found within households (odds ratio: 1.44, p = 0.53) and in neighbouring households (odds ratio: 2.64, p = 0.04). The high rates of neighbourhood infections correlated with increased individual infection risk and households with low asymptomatic carriers had fewer malaria cases (average 0.40 per household) compared to those with higher rates (1.33 to 1.5 per household). The study findings provide detailed evidence linking long-term subpatent *Plasmodium* carriage to residual malaria transmission and valuable insights to guide targeted interventions against asymptomatic carriers for elimination purposes.

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EFFECTS OF INTERMITTENT PREVENTIVE TREATMENT FOR MALARIA IN PREGNANCY ON INFANT GROWTH THROUGH AGE 1 YEAR

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Intermittent preventive treatment for malaria in pregnancy (IPTp) can improve birth outcomes, but little is known about whether it confers benefits to postnatal growth. We investigated the effect of IPTp on infant growth in Uganda and its pathways of effects using causal mediation analyses. We analyzed data from 663 infants born to mothers enrolled in a randomized trial of monthly IPTp with dihydroartemisinin-piperaquine (DP) vs sulfadoxine-pyrimethamine (SP) (NCT 02793622). Weight and length were measured from 0-12 months of age. Using generalized linear models, we estimated crude effects for DP vs. SP on length-for-age (LAZ) and weight-for-length Z-scores (WLZ) stratified by gravidity. We estimated average causal mediated effects (mean difference in Z) for placental malaria, gestational weight change, maternal anemia, preterm birth, birth length, and birthweight. We also assessed maternal inflammation as a potential mediator using the Olink Target 96 inflammation panel and maternal plasma samples collected at delivery in a random subsample (N=264). We adjusted mediation models for infant sex, gravidity, gestational age at enrollment, maternal age, maternal parasitemia at enrollment, education, and wealth. We found that SP increased LAZ by 0.18-0.28 Z from birth through age 4 months compared to DP, while DP increased WLZ by 0.11-0.28 Z from 2-8 months compared to SP among infants of multigravida. We did not observe an effect among primigravida. Mediators of SP included increased birth weight and length and maternal stem cell factor at delivery. Mediators of DP included placental malaria and birth length, maternal IL-18 and CD6 at delivery. In summary, SP improved growth by increasing birth size, DP improved growth by reducing placental malaria, and both influenced growth by reducing certain markers of maternal inflammation. In malaria endemic settings, IPTp may prevent infant growth failure among multigravida in the period of exclusive breastfeeding (0-6 months), when few other interventions are available. IPTp with combined SP+DP may improve child growth through multiple pathways among multigravida.

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MALARIA BURDEN IN INFANTS LIVING IN A HIGH MALARIA TRANSMISSION SETTING IN UGANDA

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An affordable malaria vaccine, R21, will begin to be deployed in Uganda and other African countries with high malaria transmission in 2024, with standard dosing beginning at 6 months of age. However, in infants under 9 months of age, the vaccine provides minimal protection and the only widely used tool for malaria prevention during this period is insecticide treated bed nets. To better understand the burden of malaria during this period, we enrolled a birth cohort of infants born to HIV-uninfected pregnant mothers enrolled in a clinical trial of chemopreventive regimens in pregnancy in Busia, Uganda, a high, perennial transmission setting. Infants are followed for all medical care in a dedicated study clinic, and routine assessments are conducted every 4 weeks. Parasitemia is measured by microscopy and quantitative PCR during routine visits, and symptomatic malaria measured by passive surveillance. At all visits, infants with fever and a positive thick blood smear are diagnosed and treated for malaria. The primary outcome is malaria incidence during the first 12 months of life. Between November 2022 and January 2024, a total of 832 infants aged 4-8 weeks were enrolled into the birth cohort and 267 had reached one year of age. During 457.3 person years (PY) of follow-up, a total of 588 episodes of malaria were recorded (1.29 episodes per PY). Of incident cases, 11 (0.2%) met the definition of complicated malaria (0.02 episodes PPY). Malaria incidence increased from 0.82 episodes PPY prior to 6 months of age to 1.97 episodes ppy from 6-12 months of age. Parasite prevalence measured by qPCR increased from 5% at 1-2 months of age to more than 40% by 6 months of age. Among infants who completed one year of follow-up, the cumulative risk of any parasitemia was 95%. The malaria burden prior to vaccination among infants living in this perennial transmission setting is quite high, increasing with age. Young infants in these settings would benefit from additional control interventions, such as monoclonal antibodies, perennial malaria chemoprevention, and or malaria vaccination initiated earlier in life.

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MATHEMATICAL ASSESSMENT OF THE ROLE OF INTERVENTION PROGRAMS FOR MALARIA CONTROL

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Malaria remains a global health problem despite the attempts to control and eradicate it. There is an urgent need to understand the current transmission dynamics of malaria and to determine the interventions necessary for control. We seek to develop a fit-for-purpose mathematical model to assess the interventions needed to control malaria in an endemic setting. To achieve this, we formulate a malaria transmission model to analyze the spread of malaria in the presence of control interventions. A sensitivity analysis of the model is performed to determine the relative impact of the model parameters on disease transmission. We explore how variations in the recruitment and management of malaria control interventions affect transmission. Results obtained from the study imply that the discontinuation of these interventions has a significant effect on malaria prevalence. Thus, the maintenance of interventions is imperative for malaria elimination. In a scenario study aimed at assessing the impact of long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS), and localized individual measures, our findings indicate that increased LLIN utilization and extended IRS coverage (with longer-lasting insecticides) cause a more pronounced reduction in the prevalence of symptomatic malaria compared to reduced LLIN utilization and shorter IRS coverage. Additionally, our study demonstrates the impact of localized preventive measures in mitigating the spread of malaria when compared to the absence of interventions. Our results indicate that achieving malaria elimination is associated with a high level of utilization and consistent funding of interventions. By identifying key transmission pathways and emphasizing the importance of intervention maintenance, our findings can guide decision-makers and stakeholders in their efforts to control malaria and improve public health.

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ATTRACTIVE TARGETED SUGAR BAITS FOR MALARIA CONTROL IN WESTERN KENYA (ATSB-KENYA): ENROLLMENT CHARACTERISTICS OF COHORT CHILDREN AND HOUSEHOLDS

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In western Kenya, we are conducting a cluster-randomized controlled trial to assess the impact of a new vector control tool, Attractive Targeted

Sugar Baits (ATSBs), on malaria burden in a cohort of children aged 1 to <15 years. Characteristics of the cohort, their households, and factors associated with baseline malaria prevalence are described here. Children were randomly selected by cluster (n=70) from a census database. Three consecutive cohorts were enrolled in March-April 2022, September-October 2022, and March 2023. ATSBs were deployed in March 2022. At enrolment, participants were tested for malaria by rapid diagnostic test (RDT). After enrolment a household survey was conducted. Household structures were classified as 'improved' (finished walls and roofs, closed eaves) or 'traditional' (all other construction). Data were analysed using a generalised linear mixed model to assess factors associated with baseline malaria prevalence. Of the 3,705 children screened, 220 declined and 523 were excluded. Overall, 2,962 children were enrolled with a median age of 8.5 years (IQR: 4.8, 11.8); 48% were female. Bednet use was reported more frequently in children aged 1-4 years (96%) than in those aged 5-15 years (84%, p<0.001). In the household survey, only 199/2,595 (8%) households were categorised as 'improved', as most houses had open eaves. While 99% of households owned at least one net, only 51% were adequately covered (at least one net per two household residents). Among 999 children enrolled in the first cohort (baseline), 498 (50%) tested positive by RDT. In an adjusted multivariable analysis, factors associated with RDT positivity included sub-county (Alego-Usonga vs Rarieda, adjusted odds ratio [aOR] 4.8; 95% CI: 2.7-8.5; p<0.001), house construction (traditional vs improved, aOR 2.8; 95% CI: 1.6-5.0; p<0.001), and age (5-<15 years vs 1-4 years, aOR 1.6; 95% CI: 1.1-2.4; p=0.009). The burden of malaria in children remains high in western Kenya. Strategies to ensure high bednet coverage and use, and additional tools such as ATSBs, are needed to intensify malaria control in western Kenya.

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INDOOR RESIDUAL SPRAYING IN SOURCE DISTRICTS IN SOUTHERN MOZAMBIQUE INFLUENCES CROSS-BORDER MALARIA TRANSMISSION IN KWAZULU-NATAL, SOUTH AFRICA

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Cross-border malaria control initiatives are important for malaria elimination efforts especially when low transmission countries share borders with high transmission countries. The main source of imported malaria into KwaZulu-Natal are Gaza and Inhambane in Mozambique. This province is targeting elimination, but low levels of transmission is being driven by imported malaria. To advance the provincial elimination agenda, the National Treasury decided to support indoor residual spraying (IRS) in southern Mozambique. Studies have shown that Gaza and Inhambane provinces in southern Mozambique are the main contributors to the imported cases detected in South Africa. The study area was conducted by analysing malaria cases in Guija district in Gaza province as well as in the districts of Inharrime, Panda and Zavala in Inhambane province, in Mozambique. All districts recorded above 95% IRS coverage. Malaria cases prior to the application of IRS was compared to cases post-spray. The imported malaria cases into KwaZulu-Natal were compared prior and post implementation of IRS in the four identified districts. Malaria data from 2019 to 2023 was used to complete this study. The number of imported malaria cases in KwaZulu-Natal increased from 534 to 602 in 2019 to 2023. Imported cases accounted for 86% of total cases in 2019 whilst in 2023 imported cases comprised 80% of total cases. Since all other factors were consistent over the time periods, it is plausible that IRS in the source districts influenced the number of imported cases entering KwaZulu-Natal. Guija and Zavala, showed no significant differences between baseline and endline prevalence data. Panda and Inharrime recorded statistically significant differences in the prevalence rates for the same period (p-value <0.001). This demonstrated that IRS in at least two districts were influenced by the IRS campaign. Cases in Panda remained static but prevalence in Zavala increased compared to baseline. Transmission in targeted districts in southern Mozambique were influenced by the IRS campaign and led to a decrease in the proportion of imported cases reported in KwaZulu-Natal between 2019-2023.

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HIGH PREVALENCE OF MALARIA AMONG REACTIVE CASES IN COMMUNITIES NEAR THE HOME OF THE INDEX CASES: IMPLICATIONS FOR MALARIA CONTROL

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Detecting and treating all malaria cases is crucial for effectively controlling malaria. This study aimed to assess the burden of malaria in the community from where patients sought treatment. From July to October 2022, we conducted a study in the Sile village of South Ethiopia to identify consecutive malaria patients (index cases) at a health post. We then conducted a cross-sectional community survey to investigate reactive malaria cases. Within 6 days of the index case's identification, all individuals residing in the same household as the index case and 30-35 nearby households were screened using a Rapid Diagnostic Test, with PCR utilised for confirmation. Parasite and gametocyte load were measured microscopically. Ethical approval was obtained from the Arba Minch University Institutional Review Board (IRB/1292/2022). 181 index malaria cases were identified, and of 2009 individuals screened in the community, 104 reactive tested positive (prevalence rate 5.2% (95% CI = 4.2-6.2). There were more men in index cases (58.6%) than in reactive cases (Fisher's exact test, 43.3%; P=0.014). The prevalence of *Plasmodium falciparum* was higher among the index cases (67.4%) than the reactive cases (39.4%; *P*<0.01). The corresponding rates of *P. vivax* cases were 30.4% among index and 45.6% among reactive (P=0.02). All index cases were symptomatic, and 21.2% of reactive cases had symptoms of malaria (P<0.01). The median *P. falciparum* parasite density (N=207/255; 72%) among index cases was 20320 parasites/µl and higher than 5010 among reactive cases (non-parametric test, *P*<0.01). For *P. vivax*, the median parasite density among index cases was 7900, and higher than 1428 among reactive cases (*P*<0.01). We analysed 212/255 slides for gametocytes; 56% did not detect any gametocytes. Of the remaining, the density was low and similar for the *P. falciparum* and *P. vivax* index and reactive cases. Asymptomatic people in the community were more likely to be females (OR=1.8; P=0.04) and were younger (9.7 vs. 18.2 years; P<0.01). Effective malaria control requires more sensitive diagnostic tools to identify cases in the community.

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FEBRILE PATIENTS IN ZAMBIA: WHERE DO THEY SEEK TREATMENT?

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Zambia has made substantial progress in improving access to malaria diagnosis and treatment throughout the country, with a focus on deploying community health workers (CHWs) in remote rural areas. However, bypassing the nearest CHWs in favor of more distant, higher-level facilities (HFs) is not uncommon. This study aims to assess the utilization of CHWs among individuals with fevers and identify the determinants of CHW use. We analyzed data of a prospective cohort aged 12 months to 14 years from 2022 to 2023, which was part of an attractive targeted sugar bait station trial beginning November 2021 in Western Province, Zambia. Treatment-seeking information was recorded at each participant visit. CHW and HF information, including geolocation, were obtained from DHIS 2 and Zambia Ministry of Health. Travel time for walking to the nearest providers was calculated using the Malaria Atlas Project's travel friction surface. Among 25,638 follow-up visits made to 4,494 enrolled children, 9,992 reported fever, with 4,664 of these reporting seeking treatment at HFs or CHWs. For 76.20% of visits that report treatment seeking, the travel time to the

nearest CHW was shorter than the time to nearest HF. The overall median travel times were 15.44, 47.73, and 43.06 minutes to the nearest CHW, nearest HF, and actual CHW/HF visited, respectively. Excluding visits with reported providers that could not be identified, only 14.35% went to a CHW (N=4,088). The primary regression model showed individuals with >1 complication were less likely to visit a CHW (OR:0.38 [0.23, 0.63]). Notably, for every additional 10 minutes that the nearest HF was farther away than the nearest CHW, the likelihood of choosing a CHW increased by 23% (OR: 1.23; 95% CI: 1.12, 1.36). Spatial variation was evident, with individuals in Luampa (OR: 3.95; 95% CI: 1.62, 9.64) and Nkeyema (OR: 11.87; 95% CI: 4.83, 32.17) being more likely to use a CHW compared to those in Kaoma district. Our study found that CHW utilization among febrile patients remains low ; however, stock-outs at CHW/HF facilities, which were not assessed in our study, may influence treatment-seeking behavior.

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AN UPDATE OF THE EPIDEMIOLOGICAL PARAMETERS OF MALARIA IN SCHOOL AGE CHILDREN IN KOLLE, A RURAL SETTING, MALI

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Kolle, Mali is a malaria research site since 1998. Several clinical trials have been conducted at this site. Currently, there is very few of data on the parasitological and entomological parameters of malaria in this area. This suggests a critical need of updating these parameters. We aimed to update the epidemiological and entomological parameters of malaria transmission in Kolle, and to better inform health policy makers and health care providers to fighting against malaria efficiently. The main objective of this study was to assess the parasitological parameters of malaria transmission during the low-transmission season at the Kollé basic school. A cross-sectional survey was carried out in Kollé, a village in the rural commune of Bancoumana. The main objective was to evaluate the parasitological parameters of malaria transmission at the Kollé primary school. To achieve these objectives, 205 children from different age groups from first to sixth grade and from kindergarten were included to take part in the cross-sectional survey. The study area consisted of all pupils in the first cycle and pre-school at the Kollé basic school. The choice of the primary school was justified by its accessibility at the time of the survey and the fact that most control interventions are focused on children under 5 and pregnant women. It was therefore deemed necessary to know the parasitological parameters of school-age children for future decision-making. The survey took place in January 2023, during the period of low malaria transmission. The survey provided a better estimate of the prevalence of malaria infection in schools and pre-schools. The prevalence of malaria infection obtained during this cross-sectional survey was 19.0%. Children aged 10 and 12 years were the most affected (24.3%,) followed by children under 5 years (22.2%). The proportion of gametocyte carriage varied with age and was higher in with children under 5 years of age (11.1 %). *Plasmodium falciparum* malaria is still the dominant parasite in endemic areas of Kolle, and older children are becoming more vulnerable to malaria infection.

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PSYCHOSOCIAL FACTORS ASSOCIATED WITH CARE SEEKING FOR MALARIA AMONG CAREGIVERS OF FEBRILE CHILDREN UNDER FIVE IN LIBERIA, 2021

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Increasing care-seeking for children with fever is important for malaria control. Measuring psychosocial factors associated with care-seeking is crucial as they may influence behavior. In 2021, the National Malaria Control Program and Breakthrough ACTION conducted a cross-sectional Malaria Behavior Survey in North-Central, South-Central, and Greater Monrovia regions of Liberia (high, moderate, and low malaria prevalence). Through cluster random sampling, 5,822 respondents were selected, including 609 caregivers of children under five who had a fever in the two weeks prior to the survey, and interviewed using a structured questionnaire. Descriptive and multivariate logistic regression analyses were used to measure the association between psychosocial factors and care-seeking. Results revealed that 55% of caregivers sought prompt and appropriate care, defined as care-seeking within one day of fever onset from a health facility or community health worker. Respondents who knew what appropriate care is were three times more likely to report prompt and appropriate care (adjusted odds ratio [aOR]: 3.1, 95% confidence interval [CI]: 1.2-7.9), and those who knew the importance of prompt care-seeking were eight times (aOR: 8, 95% CI: 3.0-21.3) more likely to report the behavior. Both knowledge indicators were gt90% in all areas and subgroups. Perceiving that seeking care is effective (aOR: 1.7, 95% CI: 1.1-2.6) was also associated with care-seeking; this belief was prevalent among 70% of respondents and lowest among those with less than primary education (64%). While not significantly associated with care-seeking, only 34% of respondents believed that most community members seek prompt and appropriate care for febrile children, and 9% believed that community members approve of prompt and appropriate care-seeking. These social norms may influence care-seeking. Social and behavior change programs can sustain high levels of knowledge about prompt and appropriate care-seeking, improve perceived effectiveness of prompt and appropriate care-seeking, and may also benefit from promoting supportive social norms for care-seeking

6402

ANALYSIS OF MALARIA PREVALENCE AND HEALTH SERVICES IN A GOLD MINING SITE IN WESTERN ETHIOPIA: A MIXED METHODS RESEARCH STUDY

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Malaria is a major public health issue in Ethiopia. Migration can influence the malaria transmission dynamics, with individuals relocating from malaria-free highland regions to malarious lowlands, potentially facing elevated risks of contracting malaria. Migrants may find it difficult to protect themselves against malaria and have limited access to diagnosis or treatment. Settlers in goldmining sites are one type of migrant, and are often neglected in malaria research, yet may have particularly high malaria risk. We conducted a malaria prevalence survey in a new goldmining settlement in the highly malarious Gambella Region, Ethiopia. We conducted interviews to collect socio-demographic data and assess participants' malaria knowledge, attitudes, and practices, aiming to identify correlations between these factors, malaria infections, and bednet access. Interviews were also conducted to comprehend community living conditions and healthcare accessibility. The overall prevalence of *P. falciparum* malaria in the study area was 39.7% (CI: 34.7%-44.4%). Young children were most likely to have malaria, with individuals aged 15-24 having 67% lower odds (aOR: 0.33; CI: 0.13-0.86) of infection compared to those aged 0-4 years old. Meanwhile, those aged 25+ had 75% decreased odds of infection (aOR: 0.25; CI: 0.10-0.65). Having access to bednets showed a protective effect against odds of malaria (aOR: 0.47; CI: 0.22-0.97) but access to bednets was low (12%, n=59). Participants described multiple barriers to access despite a desire for bednets. Individuals who relocated from low elevation areas with high malaria test positivity rates were more likely to test positive for malaria, as were those residing in densely populated households with multiple malaria cases. Conversely, individuals from higher elevations with low malaria test positivity rates, and those living in households with 5-10 occupants and <2 malaria infections, were more likely to have bednets. Future interventions within this goldmining community focusing on bednet distribution and increasing access to diagnosis and treatment would likely help alleviate the malaria burden.

6403

HOUSEHOLD STORM DAMAGE LIMITS ACCESS TO AND USE OF INSECTICIDE TREATED BEDNETS IN MOZAMBIQUE

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Insecticide treated bednets (ITNs) are the key malaria prevention tool. Mozambique has the fourth highest prevalence of *P. falciparum* malaria worldwide. Manica Province is located in the center of the country and has historically high malaria prevalence with seasonal peaks in incidence following the rainy season. The aim of our study was to determine if household damage in the aftermath of Cyclone Idai was associated with decreased ITN access and use. A cross-sectional community-based survey was administered from December 2019 to February 2020 in Sussundenga village. Additional data regarding demographics, occupation, and employment were collected. Participants were analyzed based on the binary outcome variable of self-reported ITN use on the previous night. Comparisons were made between use and non-use by the following demographic variables: RDT results, age, sex, number of household residents, knowledge of the cause of malaria, head of household employment status (full-time, or part-time/ seasonal), and amount of household damage endured during Cyclone Idai (none, minor, significant, or destroyed). Generalized estimating equations (GEE) logistic regression models were used to identify factors associated with ITN use. GEE logistic regression models were used to account for within household non-independence of household level variables (household cyclone damage, number of household residents, and head of household employment status). In the multivariable analysis household cyclone damage was treated as the primary exposure of interest with other variables (RDT results, age, sex, number of residents per household, knowledge of the cause of malaria, and head of household employment status) included as potential confounders. In this analysis household cyclone damage was shown to be associated with ITN use on the previous night. Minor household damage was associated with a 0.34 times lower odds of ITN use (95% CI: 0.15-0.78), significant damage was associated with a 0.26 times lower odd of ITN use (95% CI: 0.29-1.39), and destruction was associated with a 0.23 times lower odds of ITN use (95% CI: 0.11-0.50).

6404

PLASMODIUM VIVAX OUTBREAK AMONG INDIGENOUS COMMUNITIES IN PLAYA PATAXTTE, IZABAL, GUATEMALA: THE IMPORTANCE OF LOCALIZATION AND RESPONSE

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Guatemala has achieved remarkable progress in reducing malaria; all infections are due to *Plasmodium vivax*. Mid-year internal population movements in the country due to agricultural activities are linked to continued malaria transmission; this poses a threat to achieving the elimination goal. In November 2023, the national surveillance data showed that the El Estor (EE) district in Izabal, Guatemala, reported a high number of malaria cases. We used retrospective data from the surveillance system to describe the response of Mayan communities controlling a malaria outbreak in Playa Pataxte, EE district. A malaria mass screening and treatment of positive cases was coordinated between indigenous health workers and their communities. Malaria cases were confirmed using malaria rapid diagnosis in case of symptomatic cases and blood smears were collected in each person in the community for microscopic diagnosis. Data was collected during household visits using a simplified questionnaire. Malaria prevalence (P) was reported overall and among symptomatic/ asymptomatic people. Between December 4-18, 1157, people were screened for malaria with 35 cases of malaria (all *Pv*) diagnosed and treated in Playa Pataxte, EE. Of these, 25 cases were diagnosed using rapid tests among symptomatic patients. The median age of the cases was 24 years (y) (1 to 64 y). 60% of cases were male and most of them (67%) were in the 14-49 y group (economically active age). Overall, malaria P was 3.02% (P=2.42% in symptomatic vs. P=0.51% in asymptomatic). The outbreak was successfully controlled; all cases received full treatment as per national guidelines. Local communities received logistic and financial support from the national level and all fieldwork was conducted by Mayan people. Playa Pataxte is a remote area located in a forested area inhabited by Mayan people, mostly poor and historically engaged in farming activities. Malaria prevention interventions should be planned before harvesting time to prevent further outbreaks in EE. Community engagement demonstrated the importance of effective localization and response.

6405

PREDICTING MALARIA-SPECIFIC HEALTHCARE ACCESS AND UTILIZATION IN THE DEMOCRATIC REPUBLIC OF THE CONGO: A SYNTHESIS OF GEOSPATIAL, TREATMENT-SEEKING, AND PROVIDER-BASED DETERMINANTS

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The Democratic Republic of the Congo (DRC) observes the second highest number of malaria cases and deaths globally. Malaria morbidity and mortality are impacted by access to healthcare, which is influenced by a range of interrelated patient- and provider-based determinants. Increased travel times to healthcare service point locations (HCSPs) have shown to be associated with poorer treatment seeking behavior for malaria. Physical access to HCSPs, however, does not guarantee receipt of necessary, or quality, healthcare services. Health facility service readiness (HFSR), or the ability of an HCSP to diagnose and treat an illness, also impacts an individual's ability to access healthcare. A data-driven understanding of dynamics such as health service availability, treatment-seeking behavior, demographic data, and HFSR is imperative for designing interventions that remove barriers and improve access to malaria care. This research investigates the influence these factors have on healthcare service utilization in the DRC. A gravity model combining HCSP geolocation data, population estimates, friction surface-derived travel times, and reported HCSP service populations is used to re-define HCSP catchment areas in the DRC. A malaria-specific HFSR index is constructed using results from principal component analyses on data from the DRC Service Provision Assessment (SPA). An alternative HFSR index is also created using the same data source, however, adopting a non-weighted, additive approach. These indices are combined with gravity model outputs

and 2013-14 Demographic and Health Survey (DHS) data in a survey-weighted multivariable logistic regression model to investigate prediction capabilities of seeking treatment of fever in the formal sector for children under 5. Receiver operating characteristic (ROC) curves determine which combination of predictors, including HFSR indices, produce the most successful regression model. Results from this research can be used to refine estimates of key malaria indicators and inform targeting of malaria interventions in the DRC to improve access to and seeking treatment for suspected malaria.

6406

LONGITUDINAL ANALYSIS OF THE INFANT GUT MICROBIOTA REVEALS EARLY LIFE PREDICTORS OF MALARIA SUSCEPTIBILITY

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The gut microbiome is both influenced by and can influence susceptibility to malaria infection. The nature of these interactions in infancy, when the gut microbiome rapidly develops and profoundly impacts infant development, is understudied. We addressed this problem in a cohort of 47 infants in Goma, Democratic Republic of Congo. Stool sampled at 6 weeks and 3, 6 and 12 months of age, as well as at "sick" visits and following malaria treatment, was subjected to full length 16S rRNA gene sequencing. Overall, 17 infants had at least one malaria episode. No significant differences in alpha and beta diversity of gut bacteria were found between infants with an active malaria infection and those who never presented with malaria. However, decreases in alpha and beta diversity were observed in post-treatment samples relative to samples at time of diagnosis. Stratification of infants into "malaria" (infection at any time during follow-up) and "no malaria" groups revealed significant differences in abundance for 11 to 20 bacterial species at the four main time points. Infants with high abundance of *Bifidobacterium* were less likely to develop malaria whereas those with high abundance of *Klebsiella* were more susceptible. Of note, *Lactobacillus gasseri* and *Akkermansia muciniphila* tended to be more abundant among malaria-free infants relative to those who developed malaria, reaching significance prior to or at 6 months of age. At one year of age, those infants that carried *Bacteroides xylanisolvens* and *Bifidobacterium catenulatum* were more likely to have remained malaria free. Strikingly, machine learning and a random forest with the Boruta feature selection algorithm applied to 6 week gut microbiota predicted with 73% accuracy which infants would develop malaria in their first year of life, with key discriminating bacteria being Bifidobacteriaceae and Streptococcaceae. These data are consistent with other work that has identified key associations between the human and murine gut microbiota and malaria susceptibility, and provide impetus to functionally characterize gut microbiome signatures that can predict risk for malaria infection in infancy.

6407

PEAK PARASITEMIA AND CLINICAL FEATURES OF EXPERIMENTAL BLOOD STAGE MALARIA INFECTION

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Clinical trials entailing controlled human malaria infections (CHIMI) have become increasingly important to define the activity of investigational antimalarial drugs and vaccines. Where the activity of drugs or vaccines against the blood stages of Plasmodium falciparum is the parameter of interest, there is a need to balance collection of the largest amount of data to define parasite growth while protecting the safety of participants who are at risk of harm if parasite infection progresses beyond an acceptable level. To assist in defining a safe level of target parasitemia that can be reached in such studies before rescue treatment is administered, we undertook a retrospective analysis of peak parasitemia and adverse events among study participants undergoing CHMI via the induced blood stage infection model (IBSM) at a single centre, QIMR Berghofer, Brisbane, Australia. Data from 271 participants enrolled in 21 studies between 2010 and 2023 were available. Parasitemia was quantified using a validated qPCR method, and adverse event data were extracted from study reports. 5 participants were excluded from analysis (1 withdrawal; 4 early rescue treatment). Inoculum size varied from 1,800 parasitised red blood cells (pRBC), (n=129, 2,300 pRBC (n=9) to 2,800 (n=128); treatment day varied from day 7 post-inoculation (n=77), day 8 (n=182) to day 9 (n=7). Among the 266 participants analysed, the median peak parasitemia was 7,598 parasites/mL (Range: 30 - 393,678). 29 subjects had a peak parasitemia >50,000/mL. Adverse events of mild to moderate severity were common across all groups, and consisted of those commonly observed in early malaria (headache [n=197], fever [n=122], myalgia [n=116], leukopenia [n=30] and thrombocytopenia [n=11]). No participants developed clinical or laboratory features of severe malaria, and all adverse events resolved spontaneously. This analysis provides a useful framework for regulatory and scientific evaluation, and safety oversight of this important clinical trial system for drug and vaccine development for malaria.

6408

COMPARISON OF THE PERFORMANCE OF AUTO-REGRESSIVE MOVING AVERAGE (ARIMA) TIME SERIES MODELS AND FB-PROPHET IN THE PREDICTION OF MALARIA INCIDENCE IN UGANDA AT THE NATIONAL AND SUBNATIONAL LEVEL

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Malaria is caused by a protozoan parasite, genus *Plasmodium*, and is considered endemic throughout East Africa. According to the WHO Malaria report from 2020, there are an estimated 250 million cases each year, with over 94% of global cases in the WHO Africa region. With 5% of global cases, Uganda carries the third largest burden of malarial disease within sub-Saharan Africa. Despite years of focus on combatting malaria by the Ugandan Government and international implementing partners the incidence rate has risen dramatically. In 2023, Uganda instituted an incident command structure at the national level to systematically address the acute rise in case burden. Due to the stochastic nature of the recent rise in cases, appropriate need-based resource allocation has become a major challenge. To better identify areas at risk, we aimed to create an accurate prediction model of malaria incidence in Uganda. Using malaria case logs from DHIS2 dating back to 2020, we created auto-regressive moving average (ARIMA) models of malaria incidence in Uganda on a national and subnational level. We applied the same data to FB-Prophet, a pre-existing algorithm created by Facebook designed to model and predict univariate time series data by combining trends within the data and seasonal variations quickly and accurately. Once the forecasts for January through June of 2024 were complete, we then compared the performance of FB-Prophet with the newly generated ARIMA model. At the national level, the classic ARIMA model outperformed FB-Prophet in 2 out of 3 statistical accuracy tests (Mean absolute error 0.074 vs 0.081, Mean absolute percentage error 22.6 vs 30.2, Root mean square error 0.10 vs 0.085). At the subnational level, ARIMA again outperformed FB-Prophet in 12 (92%) of 13 regions modeled. Overall, both the classic ARIMA time series model and FB-Prophet performed well in forecasting malaria incidence at both the national and subnational level. This prediction capability can be used to assist policy makers to improve need-based resource allocation at the national and regional level throughout Uganda.

6409

MODELLING *PLASMODIUM VIVAX* AND *P. FALCIPARUM* CO-INFECTIONS WITH HETEROGENEITY IN MOSQUITO BITING EXPOSURE

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Plasmodium vivax and *P. falciparum*, two of the parasites causing human malaria, co-circulate in regions of Southeast Asia, Eastern Africa, and South and Central America. As anti-malaria efforts in the past decades primarily have targeted *P. falciparum*, the more resilient *P. vivax* has taken over as the predominant parasite. In the affected regions of the world, research is now focusing on identifying effective anti-*vivax* strategies. Modelling can help us identify and explore how both parasites interact on an epidemiological level and how this can impact the effect of these anti-malaria interventions. We present a novel compartmental model that investigates co-infections between these parasites while considering heterogeneity in mosquito biting exposure as a key factor shaping their entangled epidemiology. Heterogeneity in mosquito biting exposure, which has been shown to occur mostly in low-incidence settings, virtually reduces the effective population size, artificially keeping the prevalence over the whole population low, while forcing more coinfections than what we would expect. Through a systematic review we created a robust dataset on the prevalence of *P. vivax*, *P. falciparum*, and coinfections across different settings, which served as the foundation for model development. This data was also used to fit the model through Approximate Bayesian Computation. Finally, we used the model to conduct scenario simulations exploring two potential mechanisms of interaction between *P. falciparum* and *P. vivax* of particular public health relevance. First, we showed the added benefit of treating *P. falciparum* cases with radical cure targeting *P. vivax* liver stages in high-heterogeneity settings. Then, we explored the virtually unanswered question of the mechanisms governing *P. vivax* relapses, by simulating the previously proposed hypothesis that *P. falciparum*-induced fevers can trigger them.

6410

AN INVESTIGATION OF A *PLASMODIUM FALCIPARUM* ODYSSEAN MALARIA CASE IN AN INFORMAL SETTLEMENT, GAUTENG, SOUTH AFRICA, JANUARY 2024

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South Africa is nearing malaria elimination, with active transmission confined to low-altitude border regions recognized as endemic. However, occurrences of odyssean malaria persist, particularly in Gauteng Province, a non-malaria endemic area. Odyssean malaria results from malaria parasite-infected mosquitoes inadvertently transported to non-malarious regions through various transportation modes (sea, air, rail, road). On January 22, 2024, a suspected case of odyssean malaria emerged in an informal settlement in Gauteng, reported to the National Institute for Communicable Diseases. This study delineates the case investigation, epidemiology, identifies risk factors, and proposes preventive and control measures. An odyssean malaria case was defined as malaria confirmed by microscopy and/or rapid diagnostic test without travel history, with mechanical transmission excluded. Descriptive analysis of the case investigation was conducted, including clinical and laboratory record review, site visits, patient interviews, and entomological surveys for adult mosquitoes and larvae in potential breeding sites. Odyssean malaria was confirmed in an 11-year-old male presenting with fever, headache, confusion, dizziness, and malaise, with no history of blood transfusions or travel to malaria-endemic areas. *Plasmodium falciparum* trophozoites were detected on microscopy (<0.1% count), accompanied by bicytopenia and anemia. The case's household was in close proximity to busy taxi ranks frequented by commuters from malaria-endemic areas. No *Anopheles* mosquitoes or larvae were found in the household, but *Culex* mosquito larvae were observed in a man-made water well. The case likely contracted malaria from infective mosquitoes inadvertently transported from malaria-endemic regions via taxis, due to the proximity of the taxi rank to the household. Recommendations include covering the well and eliminating stagnant water to reduce mosquito breeding. Healthcare providers in Gauteng should maintain vigilance for malaria, considering it in the differential diagnosis even in patients lacking travel history to malaria-endemic areas.

6411

MALARIA OUTBREAK INVESTIGATION IN MARSABIT COUNTY, KENYA - MARCH 2024

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Malaria epidemiology in Kenya is heterogenous due to geographic and climactic differences. Marsabit, a semi-arid seasonal malaria zone with wide variation in temperatures (15°C—26°C) and rainfall (200—1000mm per annum), is inhabited by pastoralists. In Dec 2023—Jan 2024, it experienced increased rainfall. Malaria cases increased by 345% (934 from 210 in the same period the previous year). An outbreak investigation was conducted to guide prevention and control efforts. We reviewed surveillance data from Dec 2023—Feb 2024, abstracted data from 12 facilities that surpassed action thresholds (5-year weekly mean + 1.5 Standard Deviation), conducted data quality assessments and descriptive analysis of confirmed cases. We conducted environmental risk assessments, key informant interviews and focus group discussions with community members to assess knowledge, perception and practice on malaria epidemiology, case management, prevention and control. We summarized data using median, frequencies, and proportions. Of 757 malaria cases abstracted, 424 (56.8%) were male, 227 (30.7%) age 10-20 years (median 17, Inter Quartile Range=10, 28 years) and 421 (55.6%) diagnosed by *P. falciparum*-specific rapid diagnostic tests. Reporting accuracy was 90% and test positivity saw a >2-fold increase from 28.8% (Dec) to 65.7% (Jan). Species breakdown by microscopy was as follows: 94.9% *P. falciparum*, 2.7% *P. vivax* and 2.3% *P. ovale*. There were 90 (11.9%) severe malaria cases and 5 deaths (Case Fatality Rate 0.7%). Proximity to a national park, stagnant water, and sleeping outside during herding were observed and identified by community as potential environmental risk factors. An outbreak was confirmed with predominance of *P. falciparum* but also presence of other species. Risk factors for males 10—20 years included sleeping outdoors during herding. Leveraging community knowledge on malaria transmission and community engagement in malaria control efforts tailored for nomadic pastoralists may be helpful in this context. Strengthening microscopy and continued monitoring of malaria species should be considered to improve malaria surveillance.

6412

MODELING RECURRENT MALARIA EPISODES OF MALARIA USING MARKOV MULTIPLE-STATE MODELS: A CASE STUDY FOR DANGASSA, MALI.

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In malaria-endemic areas, the incidence of clinical malaria reported from health centers may be overestimated because of recurrent events for individuals living in these areas. It is not well-established how the recurrence

of malaria cases affects malaria reporting and resource allocation. This analysis assesses the characteristics of malaria recurrence in Dangassa, Mali. Longitudinal cohort data from April 2018 to December 2023 were obtained from the Mali International Centers of Excellence for Malaria Research (ICEMR) and classified by age, season, prevalence of resistance molecular marker, and multiplicity of infection (MOI). Markovian multiple-state models were used to determine malaria incidence at the individual level while accounting for undetected parasitemia or confirmed malaria illness states. Analyses were performed to determine the patient's transition probabilities per state. A total of 10,688 visits with patients presenting malaria symptoms during the passive cases were included. Patients who reached a confirmed state more than three times a year ranged from 9.1% in 2018 to 24.0% in 2023. Significant variation was observed within patient age groups, with 11.0%, 48.0%, 25.0%, and 9.6% for patients aged under 5 years, 5 to 9 years, and 10 to 14 years, and 15 years old and over, respectively. The transition probabilities were 7.6% for the undetectable group, 10.69% for those transitioning to the confirmed state, 72.0% for those remaining in the confirmed state, and 9.6% for those returning to the undetected state. Younger age groups shoed a higher probability of moving from undetected to the confirmed state than older groups. Seasonal variation also significantly affected state transitions. Molecular marker prevalence and yearly MOI were strongly associated with remaining in a confirmed state. The results of this study showed changes in the probability of malaria recurrence in a patient depend on several factors. Adapting control methods to transmission intensity with appropriate community use and compliance with malaria treatment are required to efficiently control the malaria burden in endemic areas.

6413

EFFECT OF RAINFALL AND TEMPERATURE ANOMALIES ON MALARIA INCIDENCE IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Climate change is one of the main factors that could affect future trend of malaria cases in endemic countries. This research aimed to investigate the effect of weather indicators on malaria cases in DRC. Monthly data on population and reported malaria cases were gathered from the DRC's national health management information system (HMIS) for all health zones 2018 and 2023. Monthly temperature and precipitation were estimated using remote sensing data from MODIS and from the Global Precipitation Climatology Centre. Time series analyses were performed to capture trends of malaria and weather indicators. The relationship between malaria incidence and weather indicators was investigated using generalized additive random effect models. From January 2018 to December 2023, 116,835,122 malaria cases were reported in DRC's HMIS. Malaria cases increased from 156.1 cases per 1,000 people to 182.6 cases per 1,000 CU5 (16.9%) from 2018 to 2023. The fraction of severe malaria cases among reported cases declined by 12.3% from 2018 to 2023. Average temperatures increased (mean overall increase: +0.5C°, 95% CI= +0.4C°; +0.7C°) and were correlated with a decrease of monthly precipitation (mean decrease: +12mm; 95% CI: +9 mm; +15 mm). Malaria incidence was significantly associated with weather conditions occurring in the previous 5 months. The association between malaria incidence and rainfall was larger than with temperature. Understanding the relationship-between malaria and climate could help health systems to adapt their surveillance and intervention approaches and strategies to climate change.

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GENETIC DIVERSITY OF *PLASMODIUM VIVAX* DUFFY BINDING PROTEIN IN ETHIOPIA AND COMPARISON WITH OTHER GEOGRAPHICAL ISOLATES

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Plasmodium vivax Duffy binding protein (PvDBP) is a merozoite surface protein located in the micronemes of *P. vivax*. The invasion of human reticulocytes by *P. vivax* merozoites depends on the parasite DBP binding domain engaging Duffy Antigen Receptor for Chemokine (DARC) on these red blood cells (RBCs). PvDBPII shows high genetic diversity which is a major challenge to its use in the development of a vaccine against *vivax* malaria. A total of 58 blood samples confirmed positive for *P. vivax* by Polymerase Chain Reaction (PCR) were included in the study to determine PvDBPII genetic diversity. PvDBPII were amplified using primers designed from reference sequence of *P. vivax* Sal I. Alignment and phylogenetic tree constructions using MEGA version 10.1.1. Nucleotide diversity and haplotype diversity were analysed using DnaSP, and haplotype network was generated with PopART. The mean age of the participants was 25 years, 5 (8.6%) participants were Duffy negatives. From the 58 PvDBPII sequences, seven haplotypes based on nucleotide differences at 8 positions were identified. Nucleotide diversity and haplotype diversity were 0.00267 ± 0.00023 and 0.731 ±0.036, respectively. Globally, a total of 39 haplotypes were identified from 223 PvDBPII sequences representing different geographical isolates obtained from NCBI archive. The nucleotide and haplotype diversity were 0.00373 and 0.845 ±0.015, respectively. The haplotype prevalence ranged from 0.45% to 27.3%. Two haplotypes were shared among isolates from all geographical areas of the globe. PvDBPII of the Ethiopian *P. vivax* isolates showed low nucleotide but high haplotype diversity. Among the Ethiopian *P. vivax* isolates, almost half of the sequences were identical to the Sal-I reference sequence. However, there were unique haplotypes observed in the Ethiopian isolates, which does not share with isolates from other geographical areas. Categorizing population haplotype frequency can help to determine common haplotypes for designing an effective blood-stage vaccine which will have a significant role for the control and elimination of *P. vivax*.

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POPULATION GENOMICS OF *PLASMODIUM MALARIAE* FROM FOUR AFRICAN COUNTRIES

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Plasmodium malariae (*Pm*) is already prevalent in some African regions and may become more prevalent as *P. falciparum* (*Pf*) declines. *Pm* has been more frequently identified in West and Central Africa, while it is generally rare in East Africa. While *Pf* and both *P. ovale* species (*Po*) have shown evidence of population structure in Africa, a previous study of *Pm* using microsatellites found no clear geographic structure and high intrapopulation diversity. To better understand this neglected but widespread malaria pathogen, we completed the largest genomic study of *Pm* to-date by performing hybrid capture and sequencing of 77 *Pm* isolates collected from Cameroon (n = 7), the Democratic Republic of the Congo (n = 16), Nigeria (n = 4), and Tanzania (n = 50) between 2015 and 2021. In addition, we selected 76 publicly available *Pf* genomes to spatially match the origins

of our *Pm* isolates. We found no significant geographic separation by principal component analysis among these 77 *Pm* isolates. The majority of isolates (92.2%, n = 71/77) were monoclonal. When comparing 1-1 gene orthologs to geographically matched *Pf* samples, we identified significantly less nucleotide diversity and lower SNP density in *Pm* compared to *Pf*. Genome-wide scans of selection identified several regions under either balancing or directional selection. In contrast to studies in *Pf*, *Po* and *P. vivax*, Tajima's D scans for balancing selection identified no orthologous antigens to falciparum vaccine candidates as top hits, while nS_L scans for directional selection detected no putative antimalarial resistance genes as top hits. Using a candidate gene approach to identify signatures of selection at these loci, six putative drug resistance markers (CRT, DHFR, DHPS, MDR1, MRP1, and MRP2) show significant evidence of selective sweeps as determined by the DH test, a combination of Tajima's D and Fay and Wu's H that is more robust to demographic influences than either test alone. Our findings of low genetic diversity and no geographical population structure suggest that *Pm* is atypical compared to other human malaria species and may be subject to distinct evolutionary pressures.

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GENE EXPRESSION NETWORKS IN STAGE-CONTROLLED *PLASMODIUM VIVAX* INFECTIONS FROM NORTHERN THAILAND: A WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS

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Genomic methods have identified virulence factors and antigenic targets in *falciparum* malaria; however, the virulence determinants of relapsing malaria, *Plasmodium vivax*, remain less well-known due in part to notorious challenges in culturing the parasite *in-vitro*. *P. vivax's* distinct ecology and propensity for recrudescent infection threatens future eradication efforts. We present the analysis of a weighted gene co-expression network for *P. vivax* from ten *ex-vivo* parasite stage-synchronized infections against various host clinical variables. *P. vivax* isolates, which were confirmed by microscopy to be in the predominantly early-trophozoite stage of bloodstream infection, were collected from ten patients in northeastern Thailand prior to treatment and cultured *ex-vivo* over a 48-hour period with sampling every 3 hours. Complete gene expression profiles were obtained using RNA-Seq. A co-expression network was constructed using the weighted gene co-expression network analysis (WGCNA) on the R statistical platform. Pairwise gene expression correlations across the cohort were used to develop a matrix of gene correlation coefficients. Using hierarchical clustering, the *P. vivax* genome was grouped into 22 gene modules which showed stability to resampling and at various soft-thresholding powers. Statistically significant correlations were identified between specific gene co-expression modules and clinical variables collected from patients, including baseline laboratory parameters, history of malarial infection, and sleep patterns. A functional enrichment analysis of these modules using PlasmoDB explored gene functions correlating with these clinical variables. Our identification of co-expressed gene modules, preserved across resampling and aligned to logical gene functions, in an unique parasite stage-controlled dataset, provides a platform for hypothesis-generation and further genome exploration of parasite virulence in *P. vivax* infections.

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USE OF GENETIC METRICS TO CHARACTERIZE MALARIA TRANSMISSION PATTERNS AND DISTINGUISH COTRANSMISSION FROM SUPERINFECTION IN BURKINA FASO

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Traditional malaria surveillance uses clinical information, rapid diagnostic tests (RDTs) or microscopy. These tools provide important information about clinical cases, but cannot provide comprehensive and detailed data on transmission dynamics or changes in the parasite population with intervention use. Molecular surveillance can provide more granular details about the modality of malaria transmission and promises to help guide intervention stratification and impact. Burkina Faso, with a high malaria burden, has recently introduced the RTS,S vaccine. Molecular strategies provide excellent tools for monitoring parasite population dynamics and threats to elimination including drug resistance. We conducted a pilot study at two National Malaria Control Program sentinel sites, Banfora and Kaya, with distinct malaria transmission contexts, and evaluated parasite population structure with a 24 single nucleotide polymorphism (SNP) genotyping tool for Plasmodium falciparum. The study objective was to describe basic transmission characteristics, to distinguish monogenomic from polygenomic infections, to quantify the relative cotransmission and superinfection levels using R_H, and to identify any clonal infections. We enrolled 937 febrile RDT+ individuals, 468 and 469 from Kaya and Banfora respectively. The results found a higher polygenomic fraction (0.61 [CI: 0.50, 0.72] in Kaya, compared to Banfora (polygenomic fraction of 0.46 [0.37, 0.56]). R_H analysis showed that the majority of the polygenomic samples (COI ≥ 2) from both Banfora (0.74, [0.62, 0.85]) and Kaya (0.76, [0.65, 0.88]) were the result of superinfection, and there was no evidence of clonal parasites, consistent with a high level of transmission. These baseline data provide critical information for evaluating intervention impact including malaria vaccination. Ongoing work will help generate a comprehensive picture of the genomic epidemiology landscape of parasites in Burkina Faso, and monitor changes to the parasite population structure as various interventions, including the RTS,S vaccine are being implemented.

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GENOME-WIDE ASSOCIATION STUDY OF GLOBAL *PLASMODIUM VIVAX* POPULATIONS PROVIDES INSIGHTS INTO THE EVOLUTION OF DRUG RESISTANCE

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Plasmodium vivax malaria is a serious global health concern, putting 3 billion people at risk each year. Resistance to chloroquine, the current front-line antimalarial drug for *P. vivax* treatment, has increased globally. Consequently, several countries, including Indonesia, which is the epicentre of chloroquine resistance (CQR), have now adopted dihydroartemisinin-piperaquine as a frontline treatment instead. Although several genes have been posited as putative determinants of CQR, including the multidrug resistance gene, *pvmdr1*, the evidence of this candidate in driving CQR is conflicting. Using a genome-wide approach, we perform a genomic analysis of 1,534 *P. vivax* isolates across 29 endemic countries, detailing population

structure, patterns of relatedness, selection, and resistance profiling, providing insight into putative drivers of CQR. Differential selection metrics applied between isolates from low-grade and high-grade CQR regions revealed sweeps in a locus proximal to *pvmdr1* and in transcriptional regulation genes, suggesting transcriptional control underpins CQR. Our investigation of the temporal dynamics of selective sweeps in 106 isolates from the high-grade CQR region Indonesian Papua between 2008-2017 revealed *pvmrp1* as an emerging candidate for piperaquine resistance. Overall, our work provides novel markers for resistance surveillance in candidate loci, supported by evidence of regions under recent directional selection in this continually evolving parasite.

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IMPACT OF SICKLE CELL GENOTYPES ON PEDIATRIC MALARIA OUTCOMES IN A HOLOENDEMIC *PLASMODIUM FALCIPARUM* TRANSMISSION REGION: INSIGHTS FROM A LONGITUDINAL STUDY

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Malaria remains a major health challenge in the World Health Organization African region. Pediatric patients (<5 years of age) accounted for 80% of malaria-related deaths in the region due to naïve immunity. Malaria exerts a strong selective pressure, resulting in a high prevalence of sickle cell trait (HbAS) and sickle-cell disease (HbSS). We examined the impact of the hemoglobinopathy on clinical outcomes in a pediatric cohort (aged 2-38 mos., n=1,619) followed for 36 mos. (>16,000 visits) in a holoendemic *Plasmodium falciparum* transmission region (Siaya, Kenya). Sickle-cell status, determined by hemoglobin (Hb) electrophoresis, identified 1,358 HbAA (homozygous dominant), 243 HbAS, and 18 HbSS children. We employed three regression models (logistic, Poisson, and Cox regression) to determine the relationship between the sickle cell genotypes and malaria outcomes [malaria episodes, severe malarial anemia (SMA, Hb<5.0 g/dL), and all-cause mortality], controlling for the following malarial risk factors: age at first visit, HIV status, sex, G6PD deficiency, alpha thalassemia, and time of last visit. HbAS confered protection against malarial episodes (IRR=0.809, *P*=2.22E-8; HR=0.815, *P*=6.7E-8) and SMA episodes (OR=0.511, *P*=0.175E-3; IRR=0.446, *P*=7.439E-5, HR=2.54,*P*=4.31E-3). Although HbSS was protective against malarial episodes (IRR=0.453, *P*=1.575E-6, HR=0.496, *P*=2.21E-5), carriage of the trait increased the risk of developing SMA (OR=6.841, *P*=5.125E-6, IRR=2.267, *P*=1.10E-2, HR=2.54, *P*=4.31E-3), and was associated with a seven-fold increase in all-cause mortality (HR=7.05, *P*=1.94E-4). The prospective longitudinal study shows that HbAS confers protection against both acquiring malaria and developing SMA. In contrast, while HbSS carriage is protective against malarial episodes, once infected, they have a 2.5 times greater risk of developing SMA and 7 times greater risk of mortality. In conclusion, findings here underscore the protective and detrimental roles of sickle cell genotypes in pediatric malaria, highlighting the complex interplay between genetic factors and malaria outcomes in endemic regions.

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EVALUATING HOW THE MEANING OF IDENTICAL BY DESCENT VARIES WITH MUTATION AND RECOMBINATION RATES

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Identical by descent (IBD) describes the genetic similarity between individuals resulting from shared ancestry. In the field of malaria genetic epidemiology, a high degree of IBD between individuals indicates proximity within a transmission chain. When integrated with epidemiological data, such as age or geographic location, IBD can help identify risk factors for transmission. However, the exact criteria for IBD remain unclear, especially regarding how recent the shared ancestry should be to classify two individuals or two gene segments as IBD. In this study, we applied coalescent simulations to explore interpretations of IBD across varying mutation and recombination rates. Genetic data were generated, and the proportion of IBD was estimated using a hidden Markov model-based method. This was followed by determining the time cutoff that best explained the estimated proportion of IBD. Our results show that the implicit cutoff period for designating IBD depends on recombination and mutation rates. An increase in the mutation rate or a decrease in the recombination rate loosens the criteria for IBD, thus increasing the probability of classifying samples as IBD. This observed trend can be partially explained by the number of generations that have experienced recombination, a parameter co-estimated with IBD proportion in the hidden Markov model framework. This variability exposes an inconsistency in IBD definitions across various mutation and recombination rates, indicating a need for a cautious interpretation of IBD, particularly when making comparisons across different transmission settings where effective recombination rates differ. Moreover, the number of SNPs used in IBD estimation can significantly alter the results. We recommend conducting sensitivity analyses to refine the understanding of IBD. Our study clarifies the meaning of IBD and provides critical insights into the interpretation of IBD. The findings have implications beyond malaria genetic epidemiology, extending to broader research that employs IBD concepts.

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DYSREGULATION OF VASO-OCCLUSIVE AND VASOCONSTRICTIVE MOLECULAR PATHWAYS IN PEDIATRIC PATIENTS WITH SICKLE CELL ANEMIA AND SEVERE MALARIA ANEMIA

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Malaria and sickle cell anemia (SCA, HbSS) represent significant health burdens, particularly in holoendemic *Plasmodium falciparum* regions such as Siaya County, western Kenya. Understanding the molecular landscape in children with SCA is crucial for improved therapeutics. As such, we explored the entire expressed blood transcriptome in children with severe

malarial anemia [hemoglobin (Hb)<6.0 g/dL], stratified into SCA and non-SCA (i.e., HbAA and HbAS). There were 2,820 differentially expressed genes (DEGs, FDR<0.05) with 2,110 upregulated and 710 downregulated in SCA. Canonical pathway enrichment analyses using MetaCore ™ revealed that SMA patients with SCA had enhanced dysregulation in established molecular networks for SCA: Role of Cell Adhesion in Vaso-occlusion (CAVO; FDR=4.778E-8), Role of Red Blood Cell Adhesion to Endothelium in Vaso-occlusion (RBCEVO; FDR=1.624E-4), and Role of Endothelin-1 in Inflammation and Vasoconstriction (E1IVC; FDR=4.835E-2). The pathways involved in vaso-occulsion (CAVO and RBCEVO) revealed that SCA was defined by increased transcripts for BCAM (+3.17), GLPA (+2.93), TfR1 (+1.94), VCAM1 (+1.35), and IL-1 alpha (+1.16), suggesting enhanced dysregulation of cellular adhesion, metabolism, iron homeostasis, endothelial activation, and inflammation. In addition, the pathway involved in vasoconstriction (E1IVC) demonstrated downregulation of EDNRA (-4.00), EDNRB (-2.32), IL-8 (-1.98), VEGFR1 (-1.65), and MAPK14 (-1.32) indicating a compensatory mechanism for improved blood flow in the context of endothelial dysfunction, tissue hypoxia, and vascular complications. These findings provide novel insight into the molecular interactions in children with SCA who develop severe malaria and the importance of considering both conditions concurrently for improved therapeutic interventions. We are currently investigating specific molecular mechanisms driving these dysregulations to develop targeted interventions tailored to this vulnerable population.

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DECLINING POLYMORPHISM OF THE C-TERMINUS MEROZOITE SURFACE PROTEIN 1 AMIDST INCREASED *PLASMODIUM KNOWLESI* TRANSMISSION IN THAILAND

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Recent reports from Thailand indicate a substantial increase in *Plasmodium knowlesi* cases over the past decade, with more than an eightfold increase in incidence by 2023 compared to 2018. In this study, we aim to investigate temporal changes in genetic polymorphisms associated with the increased transmission intensity of knowlesi malaria observed in Thailand over the past two decades. Briefly, genomic DNA from 25 recent *P. knowlesi* samples collected in Thailand from 2018 to 2023 underwent sequencing for the 42-kDa region of *pkmsp1*. Comparative analysis was conducted with 24 former *P. knowlesi* samples obtained from 2000 to 2009. Overall, 7 unique haplotypes were identified in recent samples, compared to 15 in former samples. Nucleotide diversity and haplotype diversity were lower in the recent period ($\pi = 0.016$, Hd = 0.817) than in the former ($\pi = 0.018$, Hd = 0.942). A significantly higher synonymous substitution rate was observed in both periods ($d_S - d_N = 2.77$ and 2.43, $p < 0.05$). Analysis of the 42-kDa region of *pkmsp1* revealed a decrease in the genetic diversity of *P. knowlesi* in Thailand, which is associated with higher transmission intensity. Purifying selection was evident, indicating that parasites carrying deleterious mutations were less likely to survive, leading to reduced genetic diversity over time. The remaining parasites demonstrated fitness and adaptability, reflecting the increased transmission intensity in recent years compared to former years. Population differentiation based on fixation index (F_{st}) revealed high genetic differentiation between parasite populations in central and southern Thailand or Malaysia. Conversely, the relatively lower F_{st} value between southern Thailand and Malaysia indicates a closer genetic relationship, possibly reflecting historical gene flow and shared ancestry between these neighboring regions. In conclusion, our findings highlight a decline in genetic diversity and evidence of purifying selection among the current higher incidence of *P. knowlesi* populations in Thailand, indicating an adaptive response to increased transmission intensity.

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PREDICTING THE FUNCTIONAL IMPACT OF STRUCTURAL VARIATION AT A *PLASMODIUM FALCIPARUM* SICKLE-ASSOCIATED LOCUS

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Malaria parasites impart a strong selective force on the human genome, but whether human resistance mechanisms in turn shape parasite variation is less well understood. However, it was recently discovered that protein-altering mutations in three regions of the malaria parasite genome - termed *Plasmodium falciparum sickle-associated (Pfsa)* 1-3 - are strongly associated with the human sickle haemoglobin (HbS) polymorphism, which is normally thought to confer significant resistance to malaria infection. A natural hypothesis is that these '*Pfsa*+' mutations enable parasites to infect, grow, and cause disease in HbS-carrying individuals (an 'HbS-protection escape' phenotype). Uncovering the biological function of these regions is therefore a research priority. Here, we focus on the *Pfsa3* region where structural variation has previously been identified, but the extent to which this variation contributes to the HbS-protection escape phenotype remains unclear. We develop statistical methods to call structural variation in short-read whole-genome sequence data from > 5,000 infections from the MalariaGEN Pf6 resource, and from severe infections from The Gambia and Kenya. Our analysis identifies a set of structural variants that segregate at this locus, including both deletions and a set of ancestrally-related complex duplication variants that are closely linked to the *Pfsa3*+ mutation. These variants are shared across African parasite populations, implying a single mutational origin of *Pfsa3*+, yet they vary widely in frequency. We confirm this structure by using long-read sequencing to assemble the haplotype of the Uganda Palo Alto (FUP-H) isolate, a lab-adapted isolate carrying all three *Pfsa*+ mutations, showing that it carries the longest duplication variant. Moreover, these duplications are predicted to carry novel gene segments which we confirm by analysing available RNA-seq data for FUP-H against this assembly. Whether these additional transcripts contribute to the HbS-protection escape phenotype is not yet known.

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DEVELOPMENT OF *PLASMODIUM FALCIPARUM* WHOLE GENOME SEQUENCING WORKFLOW USING OXFORD NANOPORE SEQUENCING TECHNOLOGY TO SUPPORT MALARIA MOLECULAR SURVEILLANCE IN TANZANIA

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Whole-genome sequencing (WGS) of *Plasmodium falciparum* is increasingly becoming important for malaria molecular surveillance (MMS) and studies of other pathogens. Currently, MMS data generation relies predominantly on using short-read amplicon and whole genome sequencing (WGS) technology despite their shortfalls; and this has limited studies of the complex genome of *P. falciparum.* This challenge is even greater in most of malaria-endemic countries with limited resources for MMS. This study aimed at developing and optimizing a long-read-based WGS assay with Oxford Nanopore Technology (ONT) to explore structural variations in *P. falciparum* genome. To reduce human DNA contamination, we focused on depleting human DNA and/or enrichment of *P. falciparum* DNA. Mock samples were created by mixing laboratory strains in different ratios with uninfected human whole blood. Three DNA enrichment approaches were explored: enzyme digestion (McrBc and MspJI), NEBNext Microbiome DNA Enrichment Kit (NMDEK) and selective whole genome amplification (sWGA).

Multiplex qPCR of single-copy *P. falciparum* and human genes were used to evaluate workflow performance. qPCR results showed a significant reduction of human DNA with NMDEK alone, as evidenced by an increase in cycle threshold (ct) value from 22 to 30. Additional use of sWGA reduced human DNA with ct value going from 30 to 35; and increased parasite DNA (ct values from 26 to 16). Sequencing quality, coverage, and depth were thoroughly examined; and showed that a combination of NMDEK and sWGA gave a high mean read quality of 21 (>99% accuracy), with over 90% coverage across the chromosomes, and 88% of reads mapping to *P. falciparum*. Additional validation with field samples is underway and the results will be available soon. This workflow effectively balanced sequencing quality, coverage, and depth, and showed high potential for deployment and use in MMS in malaria-endemic countries.

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SURVEILLING *PLASMODIUM FALCIPARUM* AT FIRST ANTENATAL CARE VISITS THROUGH GENOMICS IN MOZAMBIQUE

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Pregnant women at first antenatal care (ANC) visit constitute a promising sentinel group for gathering information about malaria transmission. With the aim of testing if ANC-derived transmission and genomic metrics are representative of the wider population, we recruited pregnant women during their initial ANC visit throughout eight provinces, characterized by both low and medium-to-high intensity of malaria transmission, from January to December 2022. Simultaneously, infection result by RDT form children aged two to ten at health facilities and DHIS2 were recorded. Finger-prick blood samples onto filter papers were collected. qPCR positive samples form a random selection of up to 100 RDT-positive and 100 RDT-negative samples per province from pregnant women (PW) and all RDT-positive samples from children was submitted to sequencing. A total of 3940 PW were recruited. *Pf* positivity rate at ANC by RDT was lowest in the southern region (5.8%[119/2045]) and highest in the northern (41.6%[571/1374]), p<0.001). The preliminary genomic results show that among PW, no validated or candidate mutations of artemisinin and chloroquine resistance and no validated marker to amodiaquine were observed. A high prevalence of the *pfdhps-pfdhfr* quintuple mutant was observed (91.8%). However, no *pfdhps* A581G mutations were observed in pregnant women, which has been associated with reduced effectiveness of sulfadoxine-pyrimethamine (SP) for chemoprevention during pregnancy. In ANC attendees, the proportion of polyclonal infections was 55.5%. On average, PW had a multiplicity of infection of 3.04. Effective multiplicity of infection, was lower at 1.6, while 1-Wright's inbreeding coefficient was 0.21. Among ANC users, population mean expected heterozygosity across the 165 microhaplotype loci ranged from <0.01 to 0.92, with a mean of 0.57 (95%CI:0.54-0.59). Additionally, genetic metrics will be compared between PW and children. This study provides genomic information for the validation of an ANC-based malaria surveillance approach, in order to improve the programmatic performance of malaria control and elimination activities in Mozambique.

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ANALYTICAL VALIDATION OF A CAPILLARY ELECTROPHORESIS METHOD TO GENOTYPE *PLASMODIUM FALCIPARUM* GENES *MSP1*, *MSP2*, AND THE NEUTRAL MICROSATELLITE MARKER *POLY-*α

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To assess antimalarial drug efficacy, therapeutic efficacy studies (TES) use genotyping methods to distinguish new *Plasmodium falciparum* (Pf) malaria infections from recrudescence. The World Health Organization (WHO) recommends utilizing capillary electrophoresis (CE) to genotype merozoite surface proteins 1 (*msp1*) and 2 (*msp2*) genes and a neutral microsatellite marker. This study describes the analytical performance and limitations of a CE assay to genotype *msp1*, *msp2*, and *Poly-*α. Analytical performance was measured using seven Pf control strains over a three-log concentration range. DNA was extracted from dried blood spots (DBS) and Pf was confirmed by a photoinduced electron transfer PCR (PET-PCR) assay. PCR amplification and CE conditions were optimized for three polymorphic loci: *msp1* gene families K1, MAD20, and RO33, *msp2* gene families FC27 and 3D7/IC, and *Poly-*α. The limit of detection (LoD), defined by the lowest number of parasites detected by all six assays, was 112 parasites per reaction. Inclusivity was demonstrated by testing Pf strains at a concentration near the LoD. Exclusivity was demonstrated by testing 15 non-falciparum Plasmodium samples and by BLAST analysis of PET-PCR primers against sequences to publicly available genetic sequence data. No false negative or positive reactions were detected, and no primer cross-reactivity was detected resulting in 100% analytical sensitivity and specificity. Reproducibility of the CE assay was determined by two operators testing six panels of eight samples. Of 48 available results, 48 were in agreement for 100% reproducibility. The analytical performance of the assay indicates that this PCR/CE assay is a sensitive, specific and reproducible method for genotyping *msp1*, *msp2* and *Poly-*α from DBS. This assay may be used to evaluate the performance of *msp1*, *msp2* and *Poly-*α genotypes to distinguish between new and recrudescent malaria infections in field TES samples.

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SURVEILLANCE OF *PFHRP2* GENE DELETIONS AND ASSESSMENT OF FALSE NEGATIVE RAPID DIAGNOSTIC TESTS OUTCOMES FOR MALARIA DIAGNOSTICS IN SENEGAL

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The reliability of rapid diagnostic tests (RDTs) based on the detection of the *Plasmodium falciparum* Histidine-Rich Protein 2 (PfHRP2) may be compromised by emerging *P. falciparum* strains with deletions in the *pfhrp2/3* genes. WHO recommends that countries assess the prevalence of these gene deletions to inform diagnostic strategies. Between 2021 & 2022, 3,144 febrile patients from Kolda, Kédougou, Kaolack, and Diourbel were screened during the malaria season using (1) an SD BIOLINE HRP2-based

RDT, (2) microscopy, & (3) PET-PCR for *P. falciparum* confirmation. Samples were further analyzed through a multiplex fluorescent magnetic bead-based antigen assay comparing *Pf*HRP2 & *Pf*LDH, & PCR to evaluate possible *Pfhrp2* deletion. From the total 3,144 samples analyzed, there were 1,800 that tested positive for malaria by RDTs. *P. falciparum* was detected by PET-PCR in 38 of the remaining 1,344 samples that tested negative by RDT (2.83% false negative). Of these 38 PET-PCR positive cases, microscopic analysis identified 6 cases with parasitemia levels above 200 parasites per microliter (detection threshold of the RDTs). The remaining 31 cases had parasite densities that fell below this threshold. Additionally, within the RDT-negative samples, we identified one case each of *P. ovale* and of *P. malariae* monoinfection. Notably, among the PET-PCR confirmed *P. falciparum* cases, *Pfhrp2* gene deletions were detected in these 6 cases using the One Step PCR protocol (CDC). These findings are being validated using long-range Oxford Nanopore Technology sequencing to both confirm the gene deletion, to evaluate if there is also deletion of the *Pfhrp3* locus, and to map the break points of the gene deletions. Given this preliminary data using the combined total of PET-PCR and RDT positive cases (n=1,838), the propotion of *Pfhrp2* gene deletions was 0.32% (6/1,838), which remains below the WHO's critical 5% threshold that suggests a reconsideration of the diagnostic strategy. While these results are undergoing validation, our preliminary findings underscore the critical need for continuous surveillance of HRP2-based RDTs in Senegal.

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GENOMIC EPIDEMIOLOGY OF MALARIA IN ZANZIBAR: DEFINING THE ROLE OF IMPORTATION AND LOCAL TRANSMISSION

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Zanzibar achieved and maintained low malaria prevalence of less than 1% for 15 years, but malaria elimination has proven difficult. Recent studies support that importation from mainland Tanzania is a major contributor, but local transmission, particularly with the recent increase in cases, remains important. To expand our understanding of the factors that drive imported malaria and local outbreaks, we have launched the Zanzibar and Imported Malaria (ZIM) study. We collected samples from individuals with positive malaria rapid diagnostic tests at 100 clinics in Zanzibar and 29 clinics in mainland Tanzania. Individuals also provided clinical, behavioral, and household data. To date, we have enrolled approximately 3,723 patients in Zanzibar and 7,270 patients in mainland Tanzania. Leveraging a highly multiplexed genotyping assay [molecular invasion probes (MIPs)], we are genotyping single nucleotide polymorphisms throughout the genome and targeted known and candidate drug resistance polymorphisms. Leveraging inheritance through identity by descent (IBD) analysis, we are comparing the genetic relatedness of isolates. To date, we have extracted 3792 and 1008 samples from mainland Tanzania and Zanzibar. A portion of these were sequenced (1212 from mainland Tanzania and 490 from Zanzibar) and after filtering to high quality samples, 552 (mainland Tanzania) and 182 (Zanzibar) samples were analyzed. These isolates show highly related parasite pairs/clusters within and between regions, including parasite isolates that are highly related between mainland Tanzania and Zanzibar. Antimalarial resistance polymorphisms are similar between mainland Tanzania and Zanzibar, despite using different antimalarials, suggesting importation having a large impact on the parasite population. The ZIM study is the largest study to combine genomics and epidemiology to study how parasite migration and importation occurs across the country to lead to better strategies to interrupt malaria transmission.

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EVALUATION OF THE *MSP1*, *MSP2*, AND *POLY-*α METHOD FOR DISTINGUISHING NEW INFECTIONS FROM RECRUDESCENCE

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Antimalarial drug efficacy studies often require genotyping of recurrent *Plasmodium falciparum* infections at the time of treatment and recurrent parasitemia to distinguish new infections (NI) from recrudescence (REC). In 2021, the World Health Organization (WHO) recommended the use of merozoite surface proteins 1 and 2 (*msp1* and *msp2*), and a neutral microsatellite (NMS) to classify NI and REC during therapeutic efficacy studies (TESs). This study compares the ability of two capillary electrophoresis (CE) genotyping methods, *msp1, msp2,* and *Poly-*α vs seven NMS (7NMS), to distinguish NI from REC. Amplification and fragment analysis was optimized for six polymorphic targets of the selected loci: *msp1* gene families K1, MAD20, and RO33, *msp2* gene families FC27 and 3D7/IC, and neutral microsatellite *Poly-*α. Fifty pairs of samples with recurrent infections, collected as dried blood spots (DBS) from four African TESs, were selected to investigate assay performance. Classification with *msp1, msp2,* and *Poly-*α match-counting was compared with 7NMS match-counting. In the match-counting approaches for both assays, REC was defined by the presence of a matching allele at all loci, NI was defined by the absence of matching alleles at any one locus, and inconclusive (INC) was defined by missing data at one or more markers and matched alleles at all amplified markers resulting in removal from further interpretation. Of the 50 pairs, 45 were classified as NI by 7NMS due to mismatch at one or more loci while 40 (88.9%; 95% CI: 76.1-95.6%) were classified as NI by *msp1*, *msp2*, and *Poly-*α match-counting. Four pairs were classified as REC by both methods (100%; 95% CI: 45.4-100%). Of the six remaining pairs, two were NI by 7NMS but REC by *msp1*, *msp2*, and *Poly-*α*,* three were NI by 7NMS but INC by *msp1*, *msp2*, and *Poly-*α due to *msp2* non-amplification*,* and one was INC by 7NMS due to *C2M34* non-amplification but REC by *msp1, msp2,* and *Poly-*α*.* The *msp1*, *msp2*, and *Poly-*α assay and match-counting method demonstrates high agreement (88%; 95% CI: 75.8-94.8%) with 7NMS match-counting and may be a valid approach to assess antimalarial drug efficacy in high malaria transmission areas.

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SEROLOGICAL BIOMARKERS FOR DETECTION OF ASYMPTOMATIC *PLASMODIUM VIVAX*-INFECTED INDIVIDUALS IN THE PERUVIAN AMAZON

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Loreto is a malaria-endemic region of the Amazon that maintains residual transmission of malaria via submicroscopic asymptomatic carriers. People with blood-stage *Plasmodium vivax* (*Pv*) parasitemia who do not feel sick (asymptomatic subjects) are thought to be clinically immune to malaria. We hypothesized that asymptomatic (Asym) *Pv*-infected subjects from the Peruvian Amazon induce different IgG antibody titers in an antigen (Ag)-dependent fashion compared to symptomatic (Sym) individuals. This study performed a bead-based multiplex assay in a Luminex platform to analyze IgG antibody levels against a 30-antigen panel of *Pv*. The study population consisted of a total of 108 individuals. Serum samples from healthy Australian negative controls with no previous history of malaria (n=20); endemic negative controls from Iquitos city (n=30) (no history of malaria in the past 3 years and no *Plasmodium* infection confirmed by microscopy and qPCR); and Asym (n=28) and Sym (n=30) Amazonian subjects with confirmed *Pv* infection were evaluated. RAU (relative antibody units) were compared between study groups for each antigen by permutation ANOVA. Asym relative to Sym subjects showed higher IgG antibody levels against *Pv* antigens: hypothetical protein (PVX_091710), PvMSP7, SIAP2, and CSP247. Interestingly, aside from PvMSP7, the other antigens corresponded to the sporozoite stage**.** These limited set of antigens are thus related to naturally acquired clinical immunity in Asym *Pv*-infected individuals from low transmission settings of the Peruvian Amazon.

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INVESTIGATING THE ROLE OF NON-VAR2CSA SPECIFIC ANTIBODIES IN PROTECTION FROM PLACENTAL MALARIA

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Placental malaria (PM) is caused by *Plasmodium falciparum*-infected erythrocytes (IEs) sequestration in placenta via chondroitin sulphate A, and antibodies to VAR2CSA have been associated with protection from PM and adverse pregnancy outcomes. There are no VAR2CSA specific vaccines available, whereas vaccines based on other parasite antigens have progressed to clinical trials. Their role in protection against PM is unclear. We investigated if antibodies to antigens other than VAR2CSA contributed to protection from PM. Plasma collected mid-pregnancy from Malawian infected pregnant women, with (n=75) or without evidence of PM (n=88) at delivery, was used to measure antigen-specific IgG, IgG1-4, IgA1, IgA2, IgM, interactions with Fc receptors and C1q to thirteen *P. falciparum* recombinant antigens. Phagocytosis of merozoites and placental binding IE by THP-1 cells and neutrophils, IgG binding to merozoites and to placental binding IE, and levels of adhesion-blocking Ig to placental binding IE, were also measured. Using univariate analysis, we observed twenty-seven antibody features were higher in women with PM ($P \leq 0.05$), with 19 being antibody features to merozoites (IgG to MSP3, PfRh5; IgG1 to AMA1, EBA175, MSP1-p19, MSP2, PfRh2a1; IgG3 to MSP3; FcγRIIA to AMA1; FcγRIIIA to AMA1; FcγRIIB to AMA1, MSP1-p19, MSP3, FcγRIIIB to AMA1, MSP3; IgA2 to AMA1, MSP1-p19; C1q to AMA1, PfRh2a1. Five antibody features were higher in women with no placental malaria ($P \leq 0.05$), including IgA1 antibodies to MSP2, MSP9, PfRh2a1, PfRh5 and C1q binding antibodies to PfRh5, as were antibodies to placental binding IE and adhesion-blocking Ig. Phagocytosis of opsonised IEs by THP-1 cells or of merozoites by neutrophils did not differ between groups. Data will be further analysed using logistic regression and principal components analysis, but little evidence that antibodies towards non-VAR2CSA proteins protect against PM was observed so far. The IgG binding and adhesion-blocking data suggest antibodies to VAR2CSA are protective. Antibodies to non-VAR2CSA proteins may be markers of exposure to PM rather than markers of protection.

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EVALUATE THE ROLE OF CYTOKINES AND CHEMOKINES IN THE DEVELOPMENT OF COMPLICATIONS IN MALARIA CAUSED BY *PLASMODIUM VIVAX*

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Plasmodium vivax can cause complicated manifestations, the mechanisms that lead to this situation are not entirely clear. The presence of parasite and parasite-derived components triggers the inflammatory response, which is characterized by the production of pro- and anti-inflammatory molecules. These molecules may be responsible for the damage observed in different affected organs in complicated malaria. Evaluate the role of cytokines and chemokines in the development of complications in malaria caused by *P. vivax*. Thirteen cytokines and chemokines were quantified in 106 people with malaria (severe and not severe) and 50 controls, with bead-based multiplex assay. The study variables were analyzed by non-parametric tests were carried with Prima and R statistical software. Fitting models with interaction to study the complication probability, using Lasso Regression with readjustment of Gamlss models of binomial family. IL-10, IL-6 and IFNg had higher concentration in the severe malaria group (<0.0001) and lower concentration of TGF- β (<0.0001), compared with non-severe malaria group and control group. IL-10, IL-6, IFNg showed a negative correlation with platelet count in severe malaria, IL-6 and IFNg specifically with severe thrombocytopenia; and a positive correlation between IFNg and transaminases, and IL-2 and creatinine. Lasso regression model suggests that IL-4, IL-10, CCL2 and TGF-β might be developed as prognostic for severity in *P. vivax* malaria. The inflammatory response during *P. vivax* infection can mediate the development of hematological, renal, and hepatic complications. TGF- β to protect against the development of complicated forms of *P. vivax* malaria.

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IGG ANTIBODY-MEDIATED COMPLEMENT FIXATION AND ACTIVITY AND ITS ASSOCIATIONS WITH PROTECTION AGAINST SEVERE MALARIA

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Plasmodium falciparum infected erythrocytes (IEs) sequestration leading severe malaria (SM) in children is primarily mediated by *P. falciparum* erythrocyte membrane protein 1 (PfEMP-1). The magnitude of Immunoglobulin G (IgG) to IEs has been associated with reduced risk of SM in children. IgG Antibodies mechanisms that might contribute to SM immunity include IgG that blocks IEs binding to cognate receptors or mediates IE opsonization for phagocytosis. Another IgG antibody mechanism is complement-dependent functional activities, however, can complement fix the problem of SM in children? To certain complement

mechanism in SM, a cohort of *P. falciparum* exposed children (n=84) from Benin was studied. We measured the ability of IgG antibodies to fix and activate complement using PfEMP-1 recombinant domains. We determined IgG antibody-mediated complement fixation and activity and its associations with protection against SM. Some children acquired IgG antibodies that effectively promoted complement fixation and activity on PfEMP-1 recombinant domains and complement fixation, C1q correlated with C3 activity. There was however limited evidence for membrane attack complex activity that is C5-9 activity on the PfEMP-1 recombinant domains. Importantly, a higher magnitude of complement C1q fixing antibodies was associated with reduced risk of SM for some domains. These findings provide new insights into mechanisms mediating immunity to SM in children and therefore, targeting the complement system on IEs could be a potential adjunctive therapy to address SM in children by modulating immune responses and enhancing protective immunity.

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MOSQUITO-*PLASMODIUM* IGG ANTIBODIES AND CLINICAL PRESENTATION OF MALARIA IN COLOMBIA

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Malaria remains the main vector-borne parasitic disease worldwide. Understanding mosquito vector biology during the malaria infection process is critical for the identification of novel markers of exposure which could be used to develop protective countermeasures against malaria infection. Recently, human immune responses against mosquito salivary protein (SP) have been used to measure mosquito bite intensity and disease risk. We previously identified *Anopheles darlingi* AdP4230 SP as immunogenic against sera from malaria infected populations in Colombia. Here, we evaluated IgG antibody levels measured against two novel mosquito peptides designed from An. darlingi AdP4230 SP to determine association with malaria clinical presentation. ELISA assays were performed to compare level of antibodies IgG by measure of optical density (OD) in serum samples from uninfected (n=50), malaria submicroscopic (n=70), and malaria microscopic (n=89) populations from Colombia during 2016-2018. In addition, an exposure malaria marker merozoite surface protein 1 (MSP1), was used to compare immunogenicity with novel mosquito peptides AdP4230. Our results showed that patterns of IgG antibody responses against the Ad4230 peptide 1 (AdP4230p1) and peptide 2 (AdP4230p2) are associated with clinical presentation of malaria. Higher median level of antibodies (OD:0.42) against AdP4230p1 were associated with symptomatic malaria and AdP4230p2 with both symptomatic (OD:0.25) / asymptomatic (OD:0.28) individuals, $p<0.05$. In addition, we observed a low positive correlation (Spearman Rho: 0.16-0.31, $p<0.05$) between levels of IgG antibodies against AdP4230p1 and AdP4230p2 versus age (median age: 21, IQR: 11-35), which was similar to those against MSP1. Our results showed that IgG responses against mosquito salivary peptides AdP4230p1 and AdP4230p2 could be use as biomarkers for malaria clinical presentation. These novel SG markers could be integrated with other malaria parasitic markers associated with exposure as part of improved malaria control strategies in civilian and military populations living in endemic areas.

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ASSOCIATION OF NOVEL IGG3 ALLELE WITH MALARIA IN CHILDREN FROM SEPIK REGION OF PAPUA NEW GUINEA

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Malaria causes death and severe illness in children under five years of age in malaria endemic regions. Recent work has established the importance of malaria-specific IgG3 in malaria immunity. IgG3 via its Fc region binds to Fcγ-receptors (FcγRs) on immune cells to instigate immunological defense against malaria. Changes in the amino acid sequences due to single nucleotide polymorphisms (SNPs) in IgG3-Fc regions give rise to IgG3 allotypes which can modulate IgG3 functions. A novel IgG3 allele, G3m29, was recently reported in pregnant women from Sepik, Papua New Guinea, and was shown to have enhanced affinity to FcγRIIa. We hypothesized that the prevalence of G3m29 in this population was associated with protection from *Plasmodium* species infections in children. In a longitudinal study cohort of children aged 1-3 years (N=203), with multiple *Plasmodium* species infections from the Sepik region in Papua New Guinea (PNG), we amplified the Fc region of IgG3 genes by polymerase chain reaction (PCR) using heavy chain constant domains 2 and 3 specific primers. We then used Sanger sequencing to identify SNPs and compared to the reference alleles of immunogenetics (IMGT) database. We identified that 78% of children in the cohort were either heterozygous (n=82, 40%) or homozygous (n=77, 38%) for G3m29. There were significantly fewer *Plasmodium* species infections in children with the novel G3m29 allele compared to non-G3m29 allele carriers (β= -1.736, 95% CI [-3.39, -0.079], $p<0.05$) measured using linear regression. This effect was most pronounced for numbers of *P. vivax* asymptomatic infections (β=-1.06, 95% CI [-2.01, -0.12], $p<0.05$). Moreover, novel G3m29 allele carriers also had significantly lower levels of total IgG and IgG1 to several *Plasmodium vivax* vaccine candidate antigens but no difference in IgG3 levels. Of note, IgG1 alleles were not associated with protection from malaria. In conclusion, the G3m29 allele is highly prevalent in the Sepik region of PNG and might be involved in protection against *P. vivax* infections. G3m29 also seems to alter IgG subclass distribution.

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MATURATION AND DIVERSIFICATION OF THE B AND T CELL RECEPTOR REPERTOIRES OVER 9 YEARS OF REPEATED MALARIA INFECTIONS

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The adaptive immune system identifies antigens through a vast array of antibodies (B cell receptors, BCRs) and T cell receptors (TCRs), known as the immune repertoire. Understanding the immune repertoires is key to comprehending the adaptive immune response in disease and infection. In malaria, natural immunity develops slowly: children living in regions with intense *Plasmodium falciparum* (*Pf*) transmission develop immunity to severe malaria within the first 5 years of life, but immunity to uncomplicated febrile malaria is not acquired until early adulthood. In a cohort in a malaria endemic region of Mali, we are performing longitudinal analyses using PBMCs from children with malaria infections over the course of nine years, including samples from two annual cross-sectional blood-draws and samples taken shortly after febrile malaria episodes. Using this unique set of samples, we are analysing the evolving immune repertoires to assess the impact of repetitive acute malaria episodes. To this end, *Pf*-specific and bulk B cells, as well as follicular helper and bulk T cells are sorted for BCR/TCR sequencing, while acquired phenotypic flow cytometry data are used for an analysis of cell subset distribution. BCRseq will be performed using a newly established highly sensitive BCRseq pipeline: cDNA synthesis with isotype-specific primers that target the Ig constant regions is followed by multiplex PCR with a primer pool targeting the 5′ leader regions of V genes. Finally, indexes are introduced by PCR to prepare the library for Illumina sequencing. Sequencing of the TCR β chain is performed using the QIAseq Targeted RNA Panel Human TCR kit. We will be able to detect specific clones that expand after malaria episodes and track their maturation over years, generating key insights into the longevity of malaria-specific B and T cell clones. Overall, we are generating unprecedented longitudinal data of interest to the general immunological community, that reveal the impact of repeated infections on the co-evolution of the BCR and TCR repertoires, yielding important information on the development and maintenance of naturally acquired immunity to malaria.

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THE CD4⁺T CELL MEMORY IN *PLASMODIUM FALCIPARUM* MALARIA

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The development of natural immunity against *Plasmodium falciparum* (*Pf*) malaria takes many years and is primarily mediated by antibodies and a Th1 $CD4^+$ T cell response against the blood-stage. Data from endemic areas indicate that natural immunity is short-lived and requires regular exposure. In contrast, experimental *Pf* infections or vaccinations of volunteers in Europe induce stable T and B cell responses. This raises the question of whether natural *Pf* infections interfere with the acquisition of long-term immunity. Our study aims to identify mechanisms influencing the induction of long-lived $CD4^+$ T cell memory in malaria. We hypothesize that the massive induction of co-inhibitory molecules during acute malaria inhibits the development of a long-lived T cell memory response to malaria. We are longitudinally studying the *Pf*-specific immune response in patients with acute malaria in Hamburg for 12 months. We will compare the T cell response of malaria patients with high and low expression patterns of co-inhibitory molecules. In addition, we will compare those malaria patients to individuals from controlled human malaria infection trials. Currently, we perform a detailed analysis of the immune cell responses during acute infection. We designed and validated a comprehensive 36-color flow cytometry panel for deep phenotyping of immune cells during acute infection with a special focus on T cells and immune checkpoints. Our preliminary results show a strong upregulation of the checkpoint inhibitors CTLA-4 and PD-1, and a trend towards upregulation of LAG-3 on $CD4^+$ T cells in malaria patients compared to healthy controls. Furthermore, $CD4^+$ T cells show an upregulation of the co-stimulatory molecule ICOS. Secondly, we will investigate *Pf*-specific T cell responses over 12 months to identify immunologic predictors of a long-lasting memory response. Subsequent analysis will try to decipher potential correlations between acute phenotypes and the persistence of *Pf*-specific $CD4^+$ T cell responses.

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INFLUENCE OF CYTOKINE RATIO (IL-10: TNF- α) ON ANAEMIA STATUS OF MALARIOUS CHILDREN IN SOUTH EASTERN NIGERIA

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Interleukin 10 (IL-10) production appears to be important in the induction and maintenance of immunity to *Plasmodium falciparum* in naturally exposed populations. Down regulation of TNF-α production and consequent resistance to severe malaria, has been linked to the ability to produce the immuno-regulatory cytokine (IL-10), while a relative deficiency in immuno-regulatory cytokine (IL-10) and lower ratios of IL-10 to TNF-α has been recorded in patients with severe malaria. Children aged 1-72 months who presents with fever or history of fever in the last 24 hours at the selected Outpatient's Department of the Health facilities were enrolled after obtaining Ethical approval from the Research, Ethical Committee of Federal University Teaching hospital Owerri Imo state. Blood samples were collected from respondents who consented for the diagnosis of malaria and anemia using outlined standard operating procedures (SOPs). Plasma/serum of all randomly selected children (both TEST and CONTROL) were freeze dried in aliquots of 100µl in cryovial tubes at –20°C until they were used for cytokine assays in accordance with the manufacturer's manual. The geometric mean parasite density of children positive by microscopy was 1764 parasites/µl of blood with a range of (12-220,000 000parsites/µl of blood). Anemia ranged from mild to moderate, there was no severe malaria anemia observed. A significant relationship was observed between anemia and fever ($p < 0.001$), febrile children had higher percentage of mild and moderate anemia than afebrile children (18.3% vs 15.0%) and (25.7% vs 15.0%). The geometric mean of IL10/TNF-α ratios of 2.8pg/ml, 2.1pg/ml and 1.7pg/ml were recorded for normal hemoglobin, mild and moderate anemia. The IL -10 and TNF concentrations increased respectively with advance in anemia while the IL-10/TNF ratio decreased as Anemia advances. Increased IL-10/TNF-α ratio is associated with increased hemoglobin concentrations in acute, uncomplicated *P. falciparum* malaria ($p<0.001$). Thus, lower levels of IL-10 over TNF- α may contribute to development of malaria complications such as anemia in addition to other factors.

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FICOLIN-1 IN PAEDIATRIC *PLASMODIUM FALCIPARUM* MALARIA AND ITS POSSIBLE ROLE IN PARASITE CLEARANCE AND ANAEMIA

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Plasmodium falciparum malaria causes significant disease, especially in children under five. A successful immune response to *P. falciparum* is a major determinant of clinical outcome. The ficolins are a family of lectins that act as Pattern Recognition Receptors that can activate the lectin complement pathway and may promote inflammation and facilitate opsonization and lysis of pathogens. Here, we have investigated the potential roles of ficolin-1 and ficolin-2 in the context of *P. falciparum* infection. We measured ficolin-1 and ficolin-2 concentrations in plasma from Malawian children (presenting with uncomplicated or cerebral malaria)

with and without P. falciparum malaria infection (healthy Controls) by ELISA. Using flow cytometry, we then assessed if ficolin-1 bound to infected red blood cells (iRBC) and whether it binds sialic acid on the iRBC, we also investigated whether ficolin-1 could promote lysis of iRBC in the presence of complete sera *in vitro*. Ficolin -1 and 2 plasma levels were measurable in children from all clinical groups. Compared to healthy controls Ficolin-1 concentrations were higher in children with uncomplicated (coef. (95% CI) 0.63, (0.22, 1.04)) and cerebral malaria (coef. (95% CI) 0.5 (0.01, 0.9)). Ficolin-1 levels were positively associated with peripheral blood monocyte (coef. (95% CI) 0.26 (0.02, 0.51)) and neutrophil counts (coef. (95% CI) 0.06, (0.00, 0.12)). Ficolin-2 was not associated with malaria infection or disease severity. Haemoglobin levels were negatively associated with ficolin-1 (coef. (95% CI) -0.38 (-0.68, -0.09)) and ficolin-2 plasma levels (coef. (95% CI) -0.36 (-0.68, -0.04)). Ficolin-1 bound more to iRBC compared to uninfected RBC and binding was reduced in a ficolin-1 mutant that does not bind to sialic acid. The addition of ficolin-1 to iRBC and uninfected RBC in the presence of serum was associated with increased RBC lysis. These results highlight a largely overlooked role for ficolin-1 in the immune response to *P. falciparum* infection and point to a potential role for lectins contributing to parasite clearance and anaemia by binding and promoting lysis of iRBC.

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ASSESSMENT FOR NEUTROPHIL EXTRACELLULAR TRAPS MARKERS IN *PLASMODIUM FALCIPARUM* MALARIA-INFECTED PREGNANT WOMEN IN A HIGH MALARIA BURDEN REGION

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Malaria infects millions worldwide and is particularly a problem in the vulnerable including pregnant women. Neutrophil extracellular traps (NETs) formation is an anti-microbial activity of neutrophils and NET structures are formed from nuclear and cytoplasmic components that can capture and kill pathogens. However, recent findings have shown that these NETs have a role in inflammation and may have serious consequences contributing to disease morbidity and mortality. What is the situation in malaria disease? This study was carried out to assess for markers of neutrophil activation and NETs in pregnancy and malaria infection. Ninety pregnant women aged between 18 and 40 years were recruited for this study. Blood and placenta samples were collected. The study population were grouped into two categories: 45 pregnant subjects infected with Plasmodium falciparum malaria and 45 apparently healthy pregnant subjects. Neutrophil elastase, myeloperoxidase, Citrulline H3, total white blood cell counts, white blood cell differential counts and haematocrit were assessed in blood. Sections of paraffin wax embedded tissues were stained with immunofluorescent dyes and examined for expression of NETs markers. Findings from this study show significantly different levels of neutrophil elastase and myeloperoxidase in malaria infected pregnant women (P>0.05). Total white blood cells, lymphocyte and neutrophil counts are significantly different as well when comparing the groups. There were differences in the expression of NET marker in the placenta from the malaria infected compared to the control group. Findings show interesting immunomodulatory effects, with possible implications for malaria disease pathogenesis and control in pregnancy.

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MEMORY CD8$^+$ T-CELLS SPECIFIC FOR CIRCUMSPOROZOITE PROTEIN EPITOPE SEQUENCE YLNKIQNSL RECOGNIZE AND KILL *PLASMODIUM FALCIPARUM* MALARIA INFECTED HEPATOCYTES

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Infected *Anopheles* mosquitoes transmit *Plasmodium falciparum* (*Pf*) sporozoites (SPZ) by inoculation in the skin. Only a few SPZ will migrate to the liver, where they infect roughly 1 out of 10^9 human hepatocytes and hide intracellularly. In the hepatocyte, the parasite will multiply to form ~30,000 merozoites within 7 days. In animal models, CD8$^+$ T-cells have been shown to play an important role in killing infected hepatocytes. However, the role of human CD8$^+$ T-cells protection against *Pf* liver stages remains incompletely understood. Elucidating this may crucially inform novel vaccine strategies. During hepatocyte invasion and the first days of replication, the *Pf* parasite expresses large quantities of circumsporozoite protein (CSP), a SPZ surface protein. Here we aimed to unravel if memory HLA-A*02 CD8$^+$ T-cells specific for the CSP epitope YLNKIQNSL can be activated *in vitro* to specifically recognize and kill malaria infected hepatocytes. We show that memory CSP YLNKIQNSL CD8$^+$ T-cells can be activated by co-culture with CSP-stimulated HLA-A*02 antigen presenting cells. Upon activation, CD8$^+$ T-cells show a 7-fold increase in activation markers CD137$^+$ and IFNγ^+. Furthermore, we demonstrate upregulation of granzyme B (p=0.03, mean 66%) and perforin (p=0.03, mean 19%). Subsequently, we find that these CD8$^+$ T-cells kill 98% of CSP epitope sequence YLNKI**Q**NSL stimulated hepatocytes (mean nucleus 230;SD 145) but do not kill when stimulated with aspecific epitope sequence YLNKI**K**NSL (mean nucleus 14200;SD 1200). Finally, we demonstrate that the CSP-specific CD8$^+$ T-cells kill 45% of exoerythrocytic forms (SPZ infected hepatocytes) when added 24 hours post infection. Killing increased to 55% when CSP CD8$^+$ T-cells were added 48 hours post infection. We thus provide unequivocal evidence that human CD8$^+$ T-cells specific for the CSP epitope YLNKIQNSL can specifically recognise and kill malaria infected hepatocytes. This finding underlines the importance of discovering novel T-cell epitopes expressed by *Pf* parasites in the liver stage to be included in the next generation of vaccines and provides a methodology to test killing capacity *in vitro.*

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BONE VOYAGE: HOW *PLASMODIUM* INFECTION DISRUPTS THE PLASMA CELL MICROENVIRONMENT IN THE BONE MARROW

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Malaria is a disease caused by protozoan parasites in the genus *Plasmodium* . *Plasmodium* infection is cleared in an antibody dependent manner, and plasma cells (PCs) are a type of immune cell that secrete high levels of antibody in response to antigen. After generation, these PCs home to the bone marrow to differentiate into long-lived PCs (LLPCs) if they receive the proper survival signals from other bone marrow resident cells. Individuals that live in malaria endemic regions can be reinfected with *Plasmodium*, indicating that the immune memory response against *Plasmodium* is impaired. It is hypothesized that LLPCs are crucial in protecting against *Plasmodium* reinfection due to their ability to continuously secrete *Plasmodium* specific antibodies. However, we have discovered that there is poor accumulation of LLPCs in the bone marrow of *P. yoelii*

infected mice. We hypothesize that *P. yoelii* impacts the bone marrow microenvironment, affecting the ability of PCs to differentiate into LLPCs. To test this hypothesis, we compared the 'unhealthy' bone marrow microenvironment that develops during *P. yoelii* infection to a 'healthy' bone marrow microenvironment developed during immunization. We analyzed bone marrow resident cell populations using flow cytometry, and characterized the number of antigen-specific PCs present in the bone marrow using ELISpot. In addition, we used fluorescent microscopy to characterize the distribution of these bone marrow resident cells in the LLPC microenvironment during *P. yoelii* infection compared to immunization. We observed a decrease in the number of bone marrow resident cells involved in providing PCs with signals to differentiate into LLPCs during *P. yoelii* infection. There are also fewer of these cells present in the bone marrow of *P. yoelii* infected mice compared to immunized mice. *P. yoelii* infection is negatively impacting the composition of the bone marrow, which may contribute to the poor accumulation of LLPCs following *P. yoelii* infection.

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NOVEL ASSAY TO ASSESS THE SEROLOGICAL EQUIVALENCE OF VACCINE-INDUCED RESPONSES TO CRITICAL MONOCLONAL ANTIBODIES

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Circumsporozoite protein (CSP), the primary surface antigen of the *Plasmodium falciparum* sporozoite and has been the target of many pre-erythrocytic malaria vaccine candidates. Due to the lack of confirmed immune correlates of protection induced by CSP-specific responses, assessing vaccine efficacy through surrogate immunological parameters is currently not possible. Controlled human malaria infection (CHMI) remains the only way to assess protective vaccine efficacy through clinical trials but comes with great cost and time. Since induced antibodies appear to mediate protection, we have developed a novel equivalence assay to improve our ability to down-select vaccine candidates. This multiplex assay, known as the CSP-based assay for serological quantification and equivalency (CBASQE), generates the CSP-epitope specific profile in preclinical and clinical samples (serum/plasma) and assesses the equivalence of these antibodies to functionally relevant monoclonal antibodies across key regions of CSP in a species-independent assay. Results inform the ability of vaccine formulations to induce epitope-specificities considered to be critical for protection. Here, we demonstrate the potential of the assay to accurately identify protected vs. non-protected recipients of CSP-based vaccine thus revealing the crucial role of specific CSP-regions/epitopes in mediating protection. Moreover, we report the evolution of these epitope-specific humoral responses throughout a three-dose vaccination regimen, answering the question whether booster vaccinations only quantitatively impact the immune response (e.g., expansion of specific clones) or also impact the quality of the response (e.g., changes in the epitope-specific profile). Lastly, we discuss how this method can be modified for other antigens and disease models if functionally relevant monoclonal antibodies or the respective protective antigen(s) are available in that model.

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BURKHOLDERIA GLADIOLI PRODUCTION OF ARSINOTHRICIN TO LIMIT TRANSMISSIBILITY OF *PLASMODIUM FALCIPARUM* WHEN INTRODUCED INTO THE *ANOPHELES GAMBIAE* MIDGUT

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Burkholderia gladioli (GSRB05) is a bacterial rice rhizosphere microbe which produces arsenic-containing arsinothricin (AST) -- resulting in Bacterial Panicle Blight (BPB), a negative feedback loop of the rice life cycle. Here, evidence exists for GSRB05 production of AST, a Glutamine Synthetase I (GSI) inhibitor. Subsequently, NH4+ accumulates, causing a largely toxic local environment for the rice's soil, leading to rice growth limitations and BPB syndrome. This is a negative feedback loop that may mirror a naturally occurring process of inhibition of malarial transmission. Evidence exists for GSRB05's presence in the midgut the *Anopheles gambiae* (A.g.) mosquito, and that through production of AST creates a hypertoxic microenvironment with buildup of NH4+ thus preventing malarial transmission. Fundamentally, we have a naturally occurring microbe, with its concomitant broad spectrum arsenic containing antibiotic in GSRB05, and AST, respectively. The production of AST causes selective inhibition of prokaryotic GSI and lack of significant deleterious effect on eukaryotic (including human) GSII -- meaning that GSRB05 (and AST) exposure to humans is safe. In terms of an effective intervention, the critical step is introduction of GSRB05 into the midgut of the A.g in a manner that is effective, efficient, inexpensive, and practical on a broad scale. This has been attempted successfully in other analogous situations. AST is non-toxic to human cell lines. But arsenic is. Arsenic naturally exists in the soil in many environments where A.g. can proliferate. Two bottle necks for A.g. mosquito proliferation are: (a.) blood feeding and (b.) moist soil larvae growth. Introducing GSRB05 in the soil where Arsenic already exists could mitigate malarial transmissibility with no added potential risk to humans during (a.) because GSRB05 and AST are safe in humans; while simultaneously allowing maximal introduction of AST in the A.g. midgut in (b), creating a hypertoxic microenvironment for malaria there. Fundamentally this may lead to less need for anti-malarial pesticide, drug, or vaccine use while still minimizing malarial transmission.

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THE LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE (LSHTM) HUMAN MALARIA TRANSMISSION FACILITY: AN OPEN FACILITY FOR EXPERIMENTAL TRANSMISSION STUDIES OF *PLASMODIUM* PARASITES

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The Human Malaria Transmission Facility was established in December 2020 at the London School of Hygiene & Tropical Medicine (LSHTM), supported by a Biomedical Resources grant from the Wellcome Trust, to provide research groups worldwide with access to *Anopheles* spp. mosquitoes infected with human malaria parasites. The facility now boasts a history of successful transmission experiments through vigorous optimisation of methods. Our specialist team works with collaborators to design and execute studies relating to the transmission of *Plasmodium* parasites. Experiments have been carried out to investigate various stages of the malaria transmission cycle using *Plasmodium* spp. gametocytes grown *in vitro* in the laboratory or collected directly from clinical samples received in the UKHSA Malaria Reference Laboratory and fed to insectary-reared *Anopheles* mosquitoes via artificial membrane-feeding. A variety of experimental end points can be analysed, depending on the specific research question. This includes but is not limited to imaging of ookinetes, measuring prevalence and intensity of oocysts in the midgut lining, sporozoite positivity and intensity within the salivary glands of infectious mosquitoes, and oocyst genotyping. The facility supports studies of the impact of transgenic *P. falciparum* lines on transmission capabilities, studies of the relationships between mosquito microbiome and malaria transmission, xenomonitoring of parasite prevalence in non-vector blood-feeding insects, and investigations of the influence of parasite drug resistance on fitness for mosquito infection, as well as investigations of the effects of insecticides and endectocides on sporogony. Furthermore, we have been able to infect mosquitoes with clinical isolates with varying anti-malarial resistance phenotypes, providing insight into the effects of drug resistance and providing proof-of-principle that various *P. falciparum* strains,

of different origins, can be transmitted to mosquitoes in the facility. We will present examples of results obtained from studies with UK and international collaborators.

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ASSESSING THE IMPACT OF DRUG RESISTANCE ON MALARIA TRANSMISSION

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The development of resistance to antimalarial drugs presents one of the greatest threats to malaria control and results in increased malaria morbidity and mortality. The emergence and propagation of drug-resistant *Plasmodium* spp. are intrinsically tied to the diverse forms assumed by the parasite and the variety of environments it traverses, from the mosquito midgut and salivary glands to human hepatocytes and erythrocytes. Changes in parasite fitness and transmissibility to mosquito vectors can affect the spread of resistance. Several studies have shown that the development of atovaquone-resistant parasites in mosquitoes is impaired or halted suggesting their transmission could be limited in the field. This data reflects that a fitness cost could be potentially associated with the bc1 genotype, which causes a sizeable reduction in the onward probability of infection relative to wild type parasites in the absence of atovaquone. In a series of independent experiments, we have carried out he selection of atovaquone and pyrimethamine resistant parasite mutants in the *Plasmodium berghei* mouse model using an inadequate therapeutic regimen dose to expand our knowledge on drug-resistant transmission. Mutational changes underlying the resistance were identified to be S110N in dihydrofolate reductase for pyrimethamine and M133I, Y268N and V284F in cytochrome b for atovaquone resistant parasites. We have evaluated the effect of these mutations on parasite transmission stage development, and we have conducted *in vivo* efficacy studies. In addition, we have included the evaluation of clinical isolates and we have monitored its growth and development in anopheles mosquitoes and its transmissibility to mice engrafted with human hepatocytes and erythrocytes.

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EXPERIMENTAL INFESTATION OF *ANOPHELES GAMBIAE* WITH *PLASMODIUM OVALE* ISOLATES FROM PATIENTS WITH UNCOMPLICATED MALARIA

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Herein, we investigated *Plasmodium ovale* development dynamic within the mosquito vector *Anopheles gambiae* using fresh field isolate parasites from the locality of N'tjiba, Mali. We conducted an experimental study from April to December 2023 at the Malaria Research Training and Center laboratory in Bamako on samples from Faladjè, capital of the commune of N'tjiba. The study included all volunteers aged 12 months or older, presenting to the health center and having *P. ovale* infection by light microscopy as well have provided their informed consent/assent. Following determination of the parasite density and species, venous blood sample was taken and sent to Bamako in an incubator set at 37°C and dried blood spots (DBS) were made for molecular identification. The blood collected was used to feed adults *An. gambiae s.s,* Kisumu strain aged 3-5 days through an artificial membrane. The dissection was carried from the 3rd to the 14th day post feeding in search of oocysts. Positive midguts were fixed with 4% paraformaldehyde for morphological identification. For each carrier, at least 20 mosquitoes were dissected per dissection day. Oocysts were observed on the midguts from 3rd to 14th day post feeding. The prevalence of infected mosquitoes among positive samples varied between field isolates and days of dissection. It varied from 4.08% to 81.8% for days 3, 4, 6, 7, 8, 9, 10, 11, 12, 13 and 14 post feeding. The oocyst load was low for all on of the days of dissection, with an average varying from 1 to 7 oocysts per midgut (min = 1, max = 30). Until day 14 post feeding, the majority of oocysts were still intact. *P. ovale* oocysts were spherical with a well-defined rounded edge and the presence of parasitic pigments. *P. ovale* is efficiently transmitted by *An. gambiae s.s*, Kisumu strain in N'tjiba. The oocysts are clearly visible from day 7 until day 14 post feeding where the majority is still intact.

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PRELIMINARY CHARACTERIZATION OF *PLASMODIUM FALCIPARUM* SPLICING FACTOR 3A SUBUNIT 2 (SF3A2) GENE IN GAMETOCYTE DEVELOPMENT

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The burden of malaria remains a major global public health problem especially among pregnant women and young children in sub-Saharan Africa. Development of transmission-blocking interventions and global eradication efforts rely on understanding the mechanisms underlying the development of the parasite's sexual forms, known as gametocytes, which is the only transmissible stage of the parasite to the mosquito vectors. Currently, limited knowledge exists regarding the genetic factors and mechanisms governing gametocyte development. Here, we investigate the role of pre mRNA metabolism required for gametocyte development of P. falciparum, studying the role of SF3A2 of the U2 SnRNP complex. SF3A2 of the spliceosome complex was previously identified as essential for gametocyte development in a large-scale genetic screen of piggyBac mutants. Although the SF3A2 piggyBac mutant had no observable defect in asexual intraerythrocytic development, this piggyBac mutant exhibited reduced abundance and incomplete development of gametocytes compared to the isogenic NF54 wild-type parent post induction for gametocyte culture. Further characterization of the P. falciparum SF3A2 mutant by scRNAseq identified aberrant transcription and splicing of canonical gametocyte genes. As part of the intranuclear U2 SnRNP spliceosome complex, the essential function of SF3A2 appears to be integral in regulating early gene expression during gametocyte development. These findings lay the groundwork for further investigations on the importance of nuclear RNA processes in the context of sexual stage development vital for mosquito infections and transmission of malaria parasites.

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MALARIA RISK STRATIFICATION: A CRITICAL TOOL FOR MALARIA CONTROL AND ELIMINATION IN HIGH BURDEN COUNTRY, CASE OF MALI

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Malaria risk stratification is an approach for identifying different transmission zones and prioritizing the implementation of control measures. As part of the development of the new 2024-2028 strategic plan, the stratification was done to take into account World Health Organization (WHO) guidelines and to target interventions appropriately. Data collection covered all 75 health districts (HDs) in 2022. Data collected included malaria cases (confirmed and suspected), supplemented by national survey data and a literature review on malaria and entomology in Mali. Adjusted incidence was calculated by taking into account health data reporting, malaria

diagnostic positivity and health facility attendance rates at health district level. Mixed interventions were defined on the basis of adjusted incidence, prevalence, seasonality, vector resistance to pyrethrinoids and parasite distribution by region. Four strata have been defined according to the 2017 WHO Malaria Elimination Framework. The majority of HDs (54) are ranged in high and moderate transmission, i.e. 84% of the population (~18 million). *Plasmodium vivax* was identified in two regions with a prevalence ranging from 4% - 22%. In this regard, specific Pf/Pv RDTs will be used for diagnosis in these regions. Vaccination has been recommended for all HDs with high and moderate transmission. Seasonal Malaria Chemoprevention (SMC) is maintained in 57 HDs. Both Dual-insecticide ITNs and PBO ITNs will be used in high prevalence area on the basis of insecticide resistance distribution. For cIPTg, HDs with high and moderate transmission coverage rates have been targeted to implement this intervention. Finally, to delay drug resistance with Artemether Lumefatrine (AL), Dihydro-artemisinin-Piperaquine (DHA-PPQ) will be introduced as a first line treatment along with AL in 5 high burden regions. Malaria stratification is a critical for strategic planning and appropriate deployment of malaria control interventions. It requires a multi-disciplinary team as well as recent and reliable data, with periodic updates.

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ASSESSMENT OF MOSQUITO FEEDING ASSAYS TO MEASURE ENDPOINTS IN CHILDREN FOR FUTURE TRANSMISSION BLOCKING TRIALS

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A vaccine to interrupt malaria transmission will be a valuable tool for elimination and control of malaria. Recently, progress has been made in malaria vaccines for young children with the R21 and RTS,S vaccines now approved in several sub-Saharan African countries. However, additional control measures are needed to supplement existing vaccines and extend protection to all vulnerable individuals. Transmission blocking vaccines (TBV) that reduce the number of infected mosquitoes have shown promising results and Phase 1 studies to test the two vaccines in combination are planned in Mali this year. TBV are unique in their action by killing parasites in the mosquito vector rather than human host. To accurately measure their efficacy, TBV require specialized assays such as the direct skin feeding (DSF) assay and direct membrane feeding assay (DMFA). Here we investigate the performance of both feeding assays and determine the adverse events related to direct skin feeding in Bancoumana, Mali. From November 2023 to February 2024, we recruited 200 volunteers aged 5-17 years who completed monthly visits including a blood smear and RDT. All RDT positive participants completed a DSF along with 10 participants who were RDT negative on each calendar day that feeds were performed. Additionally, the first 20 RDT positive individuals completed a DMFA, as well as 2 participants who were RDT negative. In total 252 DSF were conducted - 92 from RDT positive individuals. Of the RDT positive individuals, 8 feeds (8.7%) yielded a positive infection with a total of 67 positive mosquitoes recorded (1.9%). 124 DMFA were performed of which 4 out of the 92 RDT positive individuals (4.3%) yielded a positive infection with a total of 12 positives mosquitoes (0.34%). No positive feeds (either DSF or DMFA) were recorded in RDT negative individuals. We will discuss mosquito feeding parameters such as: mosquito feeding rate, survival rate, infection rate and feed positivity rates. We will also discuss the safety of the DSF procedure which yielded one Grade 1 adverse event overall. Data from this study support DSF as a surrogate assay for measuring the efficacy of TBV in future field trials.

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COMMUNITY ACCEPTABILITY OF ATTRACTIVE TARGETED SUGAR BAITS IN A CLUSTER RANDOMIZED CONTROLLED TRIAL IN WESTERN KENYA

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Attractive Targeted Sugar Baits (ATSBs) are a novel malaria vector control intervention that aim to attract and kill mosquitoes. We conducted a qualitative evaluation of community perceptions of ATSBs alongside an ongoing cluster-randomised trial in western Kenya evaluating ATSB impact on malaria incidence. ATSB were deployed in March 2022, with 2 ATSB stations hung outside on walls and replaced every 6 months over 2 years. Between May and October 2023, 12 in-depth interviews (IDIs) and 30 focus group discussions (FGDs) were conducted with 303 community members aged 13 to 83 purposively selected from intervention clusters. Interviews were conducted in Dholuo, Kiswahili, or English, recorded, and transcribed verbatim to English. The interview guides, conceptual framework, and evaluation objectives were used to create predetermined codes for the domains of potential barriers and facilitators to ATSB acceptability and high coverage. Data were coded and organized using NVivo 12, and data within each code were assessed. Patterns among themes and across types of respondents were identified and interpreted. Initially, most participants were unsatisfied that ATSBs did not eradicate mosquitoes. By the second year of deployment, most participants associated ATSBs with positive experiences, such as reduced mosquitoes and malaria; and compensation and free treatment in some sub-studies, which increased acceptability. Some participants were still unsatisfied with ATSBs due to perceived ineffectiveness but opted to have them for the benefit of doubt and their trust in the research implementors. Other barriers to ATSB acceptability included perceived bias in the selection of participants for sub-studies and activities, religious ideologies and ATSB leakage. Periodic community engagement to understand and address community concerns greatly improved the acceptability of ATSBs. Notably, high ATSB coverage of over 98% was maintained throughout the study period with minimal consent withdrawal. The information on factors influencing community acceptance of ATSBs can guide future sensitization and education of communities about ATSBs.

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A SYSTEMATIC REVIEW OF THE COST OF DELIVERING SEASONAL MALARIA CHEMOPREVENTION

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Seasonal malaria chemoprevention (SMC) is a cost-effective intervention for preventing malaria in children. SMC includes monthly doses of antimalarials during high transmission periods and has been implemented in 17 countries. To inform future planning and resource allocation, there is a need to understand the cost of SMC delivery, especially as new malaria preventive technologies are being adopted. This systematic review aims to determine the financial and economic costs of SMC delivery from provider and patient perspectives. Six databases were reviewed in accordance with the PRISMA guidelines. We included studies published between 2012 and 2023 which focused on the cost of SMC delivery and included a defined costing methodology. Two authors reviewed each study to ensure criteria were met and extracted relevant cost data. Results were adjusted for

inflation and study quality was assessed using the CHEERS checklist. We identified 4,034 studies, of which six met the inclusion criteria, including results from nine countries. The number of children targeted for SMC varied from 104,225 to 2,020,597. The total financial cost per child covered by SMC ranged from $1.71 to $12.46 and the total economic cost from $2.11 to $29.06. The Incremental cost-effectiveness ratio (ICER) per clinical case averted ranged from $5.41 to $138.03, ICER per DALY averted from $24.51 to $182.88, and ICER per death averted from $688.86 to $18,418.81. While some components (e.g. training, drugs and supplies) were universally costed, others (e.g. transport, per diem) were only incorporated into some calculations, leading to discrepancies in aggregate cost estimates for SMC delivery. Costing methodologies, reporting, and the intervention scale varied by study, limiting comparability. As most studies only captured SMC costs from a provider perspective, important household costs may have been overlooked. Given emerging malaria preventive technologies (e.g. monoclonal antibodies and malaria vaccines), understanding SMC cost implications is critical to ensure evidence-based resource allocations and improved efficiency.

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EQUITY IN ACCESS TO IPTP3+ AMONG WOMEN WHO ATTENDED ANC4 IN 12 SUB-SAHARAN COUNTRIES, BEFORE AND AFTER WHO RECOMMENDATION CHANGES

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Intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is a proven intervention for preventing malaria in pregnancy. The World Health Organization (WHO) initially recommended that pregnant women receive at least two doses of IPTp in 2004 and revised this recommendation in 2012 to three or more doses (IPTp3+). Although this recommendation has been in place for over 10 years, no country has met their target of 80% coverage of IPTp3+. The primary platform for delivering IPTp is through antenatal care (ANC), however despite women attending four or more ANC visits (ANC4+), they often do not receive the minimum three doses of IPTp. To understand how IPTp coverage changed for different demographics of pregnant women since the 2012 recommendation, a secondary analysis of women who attended ANC4+ was conducted using data from 12 countries with population-based surveys completed before and after countries adopted the 2012 WHO recommendation. If multiple surveys were available, the most recent were used. IPTp3+ coverage for women who attended at least four ANC visits was compared against demographic indicators including wealth, education, urbanicity, and age. While 8 of the 12 countries showed better access to IPTp3+ among the lowest wealth quintile (pro-poor) before the revised recommendation and more equitable access after, no demographic indicator was significantly associated with an increased likelihood of receiving IPTp3+ across the twelve countries included in this analysis. In the pooled analysis, IPTp3+ access was pro-poor in earlier surveys [concentration index (CI): -0.03] and moved to being more equitable between high and low wealth quintiles in later surveys (CI: 0.01). There are many known barriers to ANC attendance, but the barriers to receiving SP while attending ANC are less well documented. This analysis found that demographic indicators often associated with health inequity are not associated with reduced access to IPTp3+ among women who attended four or more ANC visits. Further analysis is needed to understand key factors associated with low IPTp coverage among pregnant women attending ANC.

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COMMUNITY-BASED STRATEGIES TO INCREASE UPTAKE OF INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY WITH SULFADOXINE-PYRIMETHAMINE IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW, META-ANALYSIS, META-ETHNOGRAPHY, AND ECONOMIC ASSESSMENT

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Community-based approaches may increase uptake of intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP). We assessed the effects of community-based approaches on IPTp-SP and antenatal care (ANC) coverage, and barriers and facilitators to implementation in sub-Saharan Africa. We undertook a meta-analysis and meta-ethnography. We searched online databases for trials, mixed-method, qualitative and cost-effectiveness studies evaluating community health worker (CHW) promotion of ANC and/or IPTp-SP delivery (cIPTp) with no language restriction up to March 20, 2024. Information on interventions, IPTp doses, ANC visits, and barriers/facilitators were extracted. Meta-analysis (random effects) was conducted comparing effects on two-or-more (IPTp2+), three-or-more IPTp doses (IPTp3+), one-or-more (ANC1+) and four-or-more ANC visits (ANC4+). We followed Noblit and Hare's method of meta-ethnography to synthesize qualitative findings, using reciprocal translation and line-of-argument synthesis. A theory for increased cIPTp uptake was developed. A summary of cost and cost-effectiveness studies was done. Of 4755 records screened, 23 reporting on 15 studies were included. CHW involvement was associated with an increase in IPTp2+ (pooled RR [pRR] 1·48, 95% CI 1·24-1·75, 12 sub-studies, I^2 94·7%) and IPTp3+ (pRR 1·73, 95% CI 1·19-2·50, 10 sub-studies, I^2 97·5%), with no decrease in ANC4+ (pRR 1·17, 95% CI 1·00-1·36, 13 sub-studies, I^2 90·3%). Barriers to cIPTp included women's fear of side effects, lack of knowledge, lack of trust in CHWs, and sociocultural factors. Community sensitization, engagement of husbands, pre-established CHW networks and trained and supported CHWs facilitated cIPTp. Incremental cost-effectiveness ratios ranged from $1·1 to $543 per DALY averted. Community-based approaches increased IPTp coverage and may have a positive impact on ANC visits in addition to being cost-effective, though there was high heterogeneity among studies. Community sensitization and engagement in addition to established, trained, and supported CHWs can facilitate cIPTp delivery and uptake.

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ASSESSMENT OF EPIDEMIOLOGIC IMPACT ON MALARIA FOLLOWING DRONE-BASED LARVICIDING WITH *BACILLUS THURIGIENSIS ISRAELENSIS IN* TWO DISTRICTS OF MADAGASCAR, 2022

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In Madagascar, rice is cultivated throughout the country near human housing. Rice paddies are key habitats for the larvae of the *Anopheles* mosquito, which transmits malaria. Malaria burden in Madagascar is heterogeneous, with persistently high or increasing incidence in some areas despite repeated national distributions of insecticide-treated bednets and years of support for malaria case management. In 2022, we conducted a feasibility study of drone-delivered *Bacillus thurigiensis israelensis* (Bti), a bacterial larvicide, as a possible adjunct intervention in two districts with a high density of rice paddies. Bti was applied every two weeks to paddies within one km of human housing in a subset of villages within 3 of 15

communes in Ankazobe District and 3 of 9 communes in Morombe District from February to June 2022, which is typically within the malaria high-burden season. Using commune-level data from DHIS2, we used malaria case counts from 2021 and 2022 to compare communes that received larviciding (Bti) and those that did not (comparison) in a random intercept model, adjusted for district, to explore the difference-in-difference (DID). Median case counts per commune in 2022 were lower in both arms in both districts (Ankazobe: Bti = 2451 [interquartile range (IQR) 2,155, 3,716] in 2021 and 331 [IQR 247, 1160] in 2022; comparison= 1,614 [IQR 816, 2,737] in 2021 and 358 [IQR 123, 903] in 2022. Morombe: Bti= 1,970 [IQR 1,908, 3,383] in 2021 and 1,289 [IQR 1,249, 2,548] in 2022; comparison= 2,254 [IQR 1,804, 2,847] in 2021 and 1,384 [IQR 902, 2,018] in 2022). The DID was not significant (p=0.3). Although the intervention was not designed to fully cover all villages in each commune, and the number of communes available for analysis was small, biweekly larviciding with Bti throughout the high-transmission season was not associated with reductions in malaria burden that could be measured at the commune level using routine data. Future assessments of the epidemiologic impacts of larviciding would benefit from access to more geographically granular health data, more complete intervention coverage, or larger sample sizes.

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THE EFFECT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY (IPTP) ON THE MATERNAL INTESTINAL MICROBIOME AND ITS RELATIONSHIP WITH FETAL GROWTH

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The IMPROVE trial was a double-blinded randomized controlled trial in Kenya, Tanzania, and Malawi that compared monthly intermittent preventive treatment of malaria in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) vs monthly IPTp with dihydroartemisinin-piperaquine (DP), alone or combined with a single course of azithromycin (DP+AZT). IPTp with SP was superior to DP and DP+AZT at improving maternal weight gain and fetal growth despite demonstrating inferior antimalarial activity relative to DP. The mechanism by which SP protects against low birthweight may involve changing the maternal intestinal microbiome to support increased release of nutrients and energy. For example, expanding the Prevotellaceae family of intestinal bacteria has been shown to increase mono- and di-saccharide release from dietary glycans such as mannan and galactan leading to improved weight gain in children with undernutrition. We are characterizing the intestinal microbiomes of 152 trial participants at enrolment (16 - 28 weeks gestation) and, again, near delivery (32 - 35 weeks). DNA was extracted from stool samples and the V3-V4 region of 16S rRNA genes from an initial 19 sample pairs were amplified and sequenced using Illumina MiSeq. Analysis of the first 19 pairs revealed diverse and dynamic microbiomes. The Prevotella component of the microbiome expanded between enrolment and delivery in women who received SP (11.1% +/- 9.4% at enrolment compared with 31.0% +/- 29.3% near delivery) with 6 out of 7 sample pairs showing an increase. In contrast, the size of the Prevotella compartment in the DP and DP+AZT groups remained the same (17.3% +/-21.5% at enrolment compared with 19.8% +/- 22.8% near delivery) with only 5 out of 12 sample pairs showing an increase (P=0.04). These data support Prevotella expansion as a possible non-malarial mechanism through which SP increases birthweight and is in line with data from other studies demonstrating improved weight gain in children. We will present full length 16S rRNA gene sequencing and metagenomics for the remaining 133 sample pairs to confirm this finding and identify other components associated with fetal growth.

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ANTIPLASMODIAL AND INSECTICIDAL ACTIVITIES OF THIRD GENERATION IVERMECTIN HYBRIDS

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Current antimalarial therapeutic and vector control strategies are threatened by the development of drug resistance. Hence, new tools to control this infectious disease, particularly drugs that can act throughout the complex life cycle of *Plasmodium* parasites, malaria's etiologic agents, are needed. Ivermectin (IVM), an endectocide used in mass drug administration to treat neglected tropical diseases, has shown promising potential for malaria control, either indirectly, by killing the mosquito vector, or directly, by impairing the parasite's development. Although IVM was shown to impact the liver stage bottleneck of infection in the mammalian host, its effect on the subsequent, symptomatic blood stage of infection remains controversial. Aiming to develop compounds that could efficaciously tackle both the liver and blood stages of *Plasmodium* infection, we have previously designed two generations of IVM hybrid conjugates in which the IVM macrolide is covalently linked to antimalarial pharmacophores, yielding compounds with increased antiplasmodial potency, relative to IVM. However, one of the most potent antiplasmodial compounds lacked the insecticidal activity displayed by the parental IVM molecule. Seeking to recover this crucial feature of IVM, while improving its antiplasmodial activity, and stemming from our previous structure-activity relationships, we have designed a third-generation of hybrid IVM molecules. Here, we present the evaluation of the liver stage, blood stage, and insecticidal activities of these newly developed compounds. We further assess, for the first time, the blood stage activity of the most potent hybrids *in vivo*, in a rodent model of *Plasmodium* infection. Collectively, our results provide key structure-activity relationships to guide the rational design of new molecules, supporting the subsequent pursuit of the clinical development of IVM hybrids as potential antiplasmodial drugs.

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ASSESSING THE 2023 SCHOOL-BASED INSECTICIDE-TREATED NET DISTRIBUTION IN KONO DISTRICT, SIERRA LEONE

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Insecticide-treated nets (ITNs) are a key malaria prevention and control tool. In Sierra Leone, the National Malaria Control Program (NMCP) targets universal ITN access through triennial mass distribution campaigns and continuous distribution through routine channels (such as antenatal care visits, etc). The 2021 Malaria Indicator Survey reported higher national malaria prevalence in children ages five through nine than in children under five. To cover this at-risk population, in 2023 PMI Evolve supported

the NMCP and the Ministry of Basic and Senior Secondary Education to conduct a school-based distribution (SBD) of piperonyl butoxide-synergist ITNs in 531 schools across Kono District, reaching about 89,000 students in classes 1, 3 and 5. A cluster random sample household survey, stratified by presence of a child in a targeted class, was conducted at 950 households to assess ITN use and access one month after the SBD. Key informant interviews (KIIs) were also conducted with 26 donor, government (national and sub-national) and other stakeholders. SBD was successful and led to significant increases in ITN access and use. Population access in intervention households (those with at least one child in class 1, 3 or 5) was significantly higher than in non-intervention households (69% vs. 46%, p<0.001). Household ownership of at least one ITN was also significantly higher in intervention households (93% vs. 65%, p<0.001), as was ownership of one ITN per two people (40% vs. 21%, p<0.001) and population-level ITN use (71% vs. 49%, p<0.001). KIIs highlighted funding dispersion delays and a need for more social behavior change communication. They also showed that rather than staggering recipient classes, the SBD could target consecutive classes (e.g. classes 1-3). Staggering is the global standard. However, while pilot SBD ITN uptake was high, unincluded community members expressed dissatisfaction. The consecutive approach may be more acceptable while reducing operational costs. To strengthen the scale up of SBD nationally, the NMCP and its partners should decide which roll out strategy to pursue and resolve other identified challenges.

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KNOWLEDGE, ATTITUDES, PRACTICES AND SATISFACTION OF DIGITAL PAYMENT BY OPERATORS OF THE INDOOR SPRAYING CAMPAIGN AGAINST MALARIA IN THE HEALTH DISTRICT OF KOUMPENTOUM (SENEGAL)

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Digitizing the payment of healthcare workers could improve their well-being, that of patients and the performance of the healthcare system. The aim of this study is to identify factors associated with satisfaction with digital payment by applicators of the intra-domestic insecticide spraying campaign against malaria in the Koumpentoum health district. This is a descriptive and analytical cross-sectional study. Data collection took place from January 16 to 28, 2023. Sampling was exhaustive. Data were collected via a questionnaire from applicators of the 2022 indoor insecticide spraying campaign. We performed a descriptive, bi-variate analysis. Logistic regression was used to identify factors associated with satisfaction. Data were analyzed using R software version 4.2.2. A total of 159 applicators were interviewed. The proportion of men was 67.92%, 61.01% were married and 58.49% had a monthly income of less than 50,000 CFA francs. The average age was 26.96 +/- 5 years, and 94.07% had studied in French. Health workers represent only 15.09% of the working population. Almost all (97.48%) were familiar with the definition of digital payment and its use. Acceptability of digital payment in healthcare was 92.43%. Satisfaction was 94.41%, the main reasons being speed (92.59%), security (85.93%), convenience (84.44%), ease of use (83.7%), traceability (80%) and anonymity (77.04%). In multiple logistic regression, only perceptions of safety and speed were predictive of applicator satisfaction. Digitizing the payment of healthcare workers is a major challenge for the healthcare system. It should be taken into account in mass public health campaigns to improve performance.

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LEVERAGING COMMUNITY HEALTH WORKERS TO SUSTAIN UNIVERSAL BED NET COVERAGE IN RURAL UGANDA: A PILOT FEASIBILITY STUDY

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Long-lasting insecticidal nets (LLIN) are a cornerstone of malaria control programs but sustaining target coverage levels, defined as 1 LLIN per 2 household members, between mass distribution campaigns is challenging. We evaluated the feasibility of a novel distribution strategy leveraging community health workers (CHW) operating in an integrated community case management (iCCM) program. We conducted cross-sectional household surveys in two villages in Kasese District to assess (i) baseline and (ii) post-intervention LLIN coverage and parasite prevalence (PfPR). The intervention consisted of an open-label, pilot feasibility trial in which CHWs in both villages were trained to measure household LLIN coverage when a child is RDT positive. CHWs in the intervention village also distributed LLINs to households below target levels. At baseline 92 (28%) of households had at least 1 LLIN with 20 (6%) meeting universal coverage. Parasitemia $PfPR_{2-10}$ was 36% in the control and 9% in the intervention villages, respectively. Between July and September 2023, CHWs evaluated 311 children <5 years of age with 61% of those tested have a positive RDT in each village. In the intervention village, all 100 LLINs were distributed with the median number of 3 LLINs required to meet universal coverage by each household. Post-intervention, 12 (8%) of households in the intervention village reached universal coverage and only 2 (2%) in the control village. The percentage of children <5 years old who slept under a LLIN increased from 16% to 32% compared to a decrease from 29% to 11% in each village, respectively. In interviews, CHWs conveyed favorable opinions of the distribution method. Our results demonstrate low proportions of universal LLIN coverage near the end of the 3-year distribution cycle. LLIN distribution through iCCM appears feasible and may supplement mass distribution campaigns, with marked trends improvements in children sleeping under LLINs in the intervention village.

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IMPLEMENTATION PERFORMANCE OF INSECTICIDE TREATED NET (ITN) DISTRIBUTION THROUGH THE HEALTH FACILITIES IN TANZANIA: FIVE YEARS OF EXPERIENCE (2018-2022)

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Routine distribution of insecticide-treated nets (ITNs) to pregnant women at antenatal care (ANC) and to infants through the Expanded Programme for Immunization (EPI) has been a primary mechanism of maintaining population access to ITNs. As the implementation performance of these channels has not been assessed, we conducted a historical analysis of bed net issuing rates through ANC and EPI channels over five years (2018-2022). The team used monthly data from District Health Information

System 2 (DHIS2) on ITN distribution across 6,790 health facilities in 26 regions of mainland Tanzania. Descriptive analyses were conducted to separately assess the performance of ITN issuing rates through ANC and EPI across time, region, health facility, ownership (public/private), setting (urban/rural), and malaria transmission strata. Performance was categorized as "good" if all women or infants attending ANC or EPI received nets in a given month. Across all years and facilities, ANC outperformed EPI with "good" issuing rates of 83% and 70%, respectively ($p<0.001$). Issuing rates started low, about 44% and 34% in 2018, and increased to 93% and 80% in 2022, for ANC and EPI, respectively. Public facilities performed better for both ANC (89%) and EPI (76%) compared to private facilities (53% and 42%, respectively) ($p<0.001$). Dispensaries and health centers performed better than hospitals and clinics for both ANC and EPI issuance ($p<0.001$). Ruvuma region had the best performance, and, in most regions, performance improved markedly in the first year but then increased at a very slow rate. Rural areas had higher performance (72%) during ANC visits compared to urban areas (51%) ($p<0.001$). Across epidemiological strata, ITN issuing rates during EPI activities were notably higher in high (79%) and moderate (76%) transmission epidemic strata compared to low (54%) and very low (65%) ($p<0.001$) strata. By 2022, Tanzania substantially improved ITN issuance via ANC and EPI compared to 2018 levels. Exploration of the reasons for differences among analyzed variables in issuing rates are recommended to understand additional characteristics of high performing facilities.

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COMBINING SEASONAL MALARIA CHEMOPREVENTION WITH A MULTI-STAGE PRODUCT FOR MALARIA PREVENTION: A MATHEMATICAL MODELLING STUDY

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In recent years, research and development programs for vaccines, monoclonal antibodies, and small molecule drugs have led to significant advancements in preventing Plasmodium falciparum malaria. Innovations include products that target multiple stages of the parasite life cycle that, if approved, might be deployed as part of a comprehensive prevention strategy. To effectively prioritize vaccine and drug candidates for clinical development, evidence is needed to understand the benefits of combining both single- and multi-stage tools with malaria chemoprevention. We used an individual-based malaria transmission model to estimate the impact of combining seasonal deployment of a novel therapeutic with seasonal malaria chemoprevention (SMC) in children under five. Our model combined emulator-based methods with explicit models of intervention dynamics for vaccines, monoclonal antibodies, and long-acting injectable drugs with both pre-erythrocytic and blood stage activity. We estimated reductions in the cumulative incidence of uncomplicated and severe malaria throughout childhood relative to SMC alone. Results indicated that, when a pre-erythrocytic product was combined with SMC, lasting protection was needed to limit the impact of delayed malaria after children were no longer eligible for interventions. Depending on prevalence setting and SMC deployment, a protection half-life of more than 230 days was required for a pre-erythrocytic product with 50% initial efficacy to achieve a more than 5% reduction in cumulative incidence of severe malaria by ten years old. Higher duration and efficacy were required when SMC's deployment was optimized. Adding blood stage activity increased impact on cumulative severe malaria throughout childhood. Our modelling quantifies the benefits of combining multi-stage therapeutics for malaria prevention with SMC by estimating their possible impact on malaria burden throughout childhood. This evidence articulates the need for a novel tool to fill an existing gap in malaria prevention tools, thus informing the selection of multi-stage therapeutics for malaria prevention.

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IDENTIFICATION AND MAPPING AREAS WITH AN INCREASED RISK O MALARIA TRANSMISSION AMONG HARD-TO-REACH HIGH-RISK GROUPS IN RWANDA

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Malaria continues to be a significant public health concern in Rwanda, posing a risk of infection to the entire population. Understanding the spatial distribution of high-risk populations is crucial for targeted interventions. Malaria high-risk groups as hard-to-reach people are estimated at 3.4% (413,367) of the Rwandan population from mapping assessment of 2022. This research focuses on mapping malaria hotspots among hard-to-reach high-risk groups in Rwanda, aiming to identify and map areas with an increased risk of malaria transmission. A mixed-methods approach study integrates Matchbox assessment of 262 participants, comprising 22 individual interviews and 240 for focus group discussions (FGDs) and rapid assessment data (455participants for FGD). Integration of geospatial data, demographic information, and malaria incidence records into Geographic Information System (GIS) analysis illustrated the precision of hotspots mapping of high-risk groups.The findings reveal that 17.6% (80/455) reported fever cases in the past two weeks, with 22% (100/455) experiencing malaria in the last nine months (2 episodes). Of those, 68% (309/455) sought care at health centers, 12% (37/309) bought malaria drugs without a diagnostic test, and 7% (7/100) received community-level treatment. Female Sex Workers (FSWs) had the highest malaria incidence (30.5%; 30/95), followed by seasonal workers (28.8%; 19/66), bicyclists (20%; 15/75), People with Disabilities (PWD) (18.8%; 9/48), and cross-border traders (18.4%; 7/38). Reported barriers included a lack of repellent (80%; 356/455), insufficient knowledge (70%; 317/455), outdoor activity delays (69%; 312/455), lack of updated information (60%; 273/455), and limited access to care (9%; 42/455). This study successfully mapped and identified malaria hotspots among hard-to-reach high-risk groups in Rwanda, providing a valuable tool for precision public health interventions. This strategic approach enhances resource allocation for Rwanda's malaria elimination efforts allowing optimization of the impact of malaria control objectives.

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INSECTICIDE TREATED NET (ITN) TARGETED MASS CAMPAIGN (TMC) FOR MALARIA PREVENTION IN THE KAGERA REGION, TANZANIA: IMPLEMENTATION PROCESSES, OUTCOMES AND CHALLENGES

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Kagera region, Tanzania, has been receiving continuous distribution of insecticide-treated nets (ITNs) through antenatal clinics and school net programs over the past 10 years. However, in 2023, a Targeted Mass Campaign (TMC) in Kagera was conducted in response to high malaria prevalence (18%), low population access to ITNs (62% vs. 80% national target), and confirmed partial artemisinin resistance. We aimed to document the process, outcomes, and challenges of TMC implementation in Kagera. We quantified the estimated number of required ITNs using the standard formula, population (from national census data 2022) divided by 1.8. Planning and advocacy meetings were held at the regional and council levels. Training was conducted to orient volunteers, village leaders, and ward leaders on using the TMC Management Information System (TMC-MIS), household registration, ITN issuance , data management,

and accountability. Targeted supportive supervision and mentorship were informed by TMC-MIS data based on low registration and issuance rates at different levels. A total of 190 ward executive officers, 790 village leaders, and 2,476 volunteers were trained from 192 wards in all six councils of the Kagera region. We quantified a need of 1,713,815 ITNs, of which 1,693,318 (98.8%) were issued through 2,104 issuing points, covering an estimated 3,094,278 people. TMC-MIS challenges included poor internet connectivity in hard-to-reach villages that slowed registrant data uploads and TMC-MIS server failure due to data overload, preventing data upload. We conducted a total of 287 and 217 targeted supervision visits at the village level during household registration and ITNs issuance respectively contributing to the timely mitigation of observed challenges. Real-time digital ITN data entry, monitoring, and intervention by trained volunteers, leaders, and supervision teams aided in identification and prompt mitigation of challenges during TMC ITN distribution.

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PREGNANCY DESIRES AND MALARIA PREVENTION IN SUB-SAHARAN AFRICA

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Trends in antenatal (ANC) attendance and malaria in pregnancy prevention are suboptimal in sub-Saharan Africa. It is unclear to what extent pregnancy desires influence these outcomes. This study explores the relationships among women aged 15 - 49 years old in 19 sub-Saharan African countries. Secondary data analysis of recent (2018-2023) Demographic and Health Surveys was conducted among women who had a live birth in the past year preceding the survey and stated whether the index child was wanted then, later or not at all (N= 45,200). Other outcomes included early ANC defined as the first visit within the first trimester, ANC retention (at least four (ANC4) or eight (ANC8) contacts), mosquito net use and intermittent presumptive treatment in pregnancy (IPTp). Control variables included age, residence, religion, education, household wealth, parity, country and year of survey. Overall, 25% of women did not want the index pregnancy when it happened had early ANC with intercountry variation ranging from 13% in Madagascar to 48% in Gabon. Not wanting a pregnancy was associated with reduced odds of early ANC (aOR: 0.67, 95% CI: 0.63, 0.71), ANC4 (aOR: 0.68; 95% CI: 0.64, 0.73), ANC8 (aOR: 0.83; 95% CI: 0.73, 0.94), mosquito net use (aOR: 0.88; 95% CI: 0.82, 0.94) and IPTp (aOR: 0.88; 95% CI: 0.83, 0.95). Women who did not want the pregnancy were more likely to be single, 15 - 24 years or older than 34 years old, urban, non-Christian, with a secondary education, from poorer households and have two or more children less than five years old. Women's pregnancy desires influence their uptake of care services and subsequent malaria prevention behaviors. Study findings corroborate the need for a multi-sectoral approach to optimizing malaria in pregnancy outcomes. Integration of reproductive health services, malaria service delivery and behavior change interventions can help to improve pregnancy intentions and outcomes in order to ensure healthier pregnancies, women and children.

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ASSESSING MISSED OPPORTUNITIES IN ROUTINE LONG-LASTING INSECTICIDE-TREATED NETS DISTRIBUTION AMONG PREGNANT WOMEN ATTENDING PUBLIC HEALTH FACILITIES IN TARGETED COUNTIES IN KENYA

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To prevent malaria in pregnancy (MIP), the World Health Organization recommends universal coverage of at-risk pregnant women with long-lasting insecticide-treated nets (LLINs), which are routinely accessed through antenatal care (ANC) clinics. The Kenya Malaria Strategy aims to protect 100% of at-risk individuals in the lake endemic zone (LEZ), coastal endemic zone (CEZ), and highland epidemic-prone zone (HEZ) through LLINs. Biannual malaria commodities review meetings facilitate inter-county discussions on malaria commodity management best practices and identify gaps. LLINs issued to pregnant women are recorded in the ANC register, summarized in the integrated summary report (MOH 711), and replicated in the malaria commodities report (MOH 743) monthly. This information is uploaded to the Kenya Health Information System (KHIS). At the time of the review meeting, the number of new ANC attendance and LLINs dispensed recorded in MOH 711 for September 2023 was downloaded from KHIS. The total number of LLINs dispensed and recorded in the two summary tools was compared. The overall reporting rate for MOH 711 and 743 was 98% of the total no. of reports expected, with 2% over-reporting for LLINs dispensed in MOH 743. The median months of stock for LLINs was 5 months, with none of the counties reporting stock out. Notably, about 9,200 (10%) of the pregnant women attending the first ANC clinic did not receive ITNs despite the availability of the commodity within the county. The HEZ achieved the least coverage at 85%, while the LEZ achieved 98%. Data discordance indicated over-reporting on the commodities reporting tool, and data quality audits should be carried out to improve reporting. The Ministry of Health should intensify the development of health workers' capacity in reporting and social behavior change in communities as some counties reported pregnancy stigma and negative cultural perceptions of pregnancy among teenage and older (over 35 years) mothers, resulting in poor ANC and LLIN uptake.

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DETERMINANTS OF NON-USE OF LONG-LASTING INSECTICIDE-TREATED NETS (LLIN) AMONG MOTHERS OF CHILDREN UNDER 5 YEARS OLD: A SECONDARY ANALYSIS OF DATA FROM THE USAID NOTRE SANTÉ KNOWLEDGE ATTITUDES AND PRACTICES SURVEY

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Malaria remains a major public health challenge in Guinea, negatively impacting the economy and particularly affecting children under 5 years old (CU5) and pregnant women. In October 2023, the USAID Notre Santé Activity, implemented by RTI International, undertook an in-depth study of the knowledge, attitudes, and practices (KAP) related to malaria prevention and treatment of women with CU5 in the Conakry, Kindia, Boké, and Labé regions. Based on the hypothesis that socio-demographic factors, level of malaria knowledge, and disease attitudes play a role in the use of LLINs in these households, a secondary analysis was undertaken to study those factors. Statistical approaches included descriptive statistics, Chi Square and t tests, and logistic regression to pinpoint factors associated with LLIN non-use. The study included 1460 women of whom 31.4% did not sleep under a LLIN the previous night. Household dialogue about malaria, positive attitude towards LLIN repair, self-efficacy and favorable social norms were associated with increased LLIN use (p less than 0.05). The impact of ethnicity (p less than 0.001) and marital status (OR-1.85, p=0.03) on non-use of LLINs highlights the need to integrate cultural and relational issues in malaria control programs. The positive association between household size and non-use of LLINs (OR=1.07, p less than 0.001) raises questions about net use in the contexts of limited or shared resources. Contrary to expectations, women with higher levels of education were less likely to use LLINs (OR=1.19, p less than 0.001). Comparison with studies in other African regions reveal that while some dynamics, such as the impact of household size, appear to be universal, other factors vary, such as the influence of education or access to electricity, highlighting the importance

of local context in developing malaria prevention strategies. This research is part of a broader approach aimed at identifying more effective prevention and treatment strategies, accounting for local context and needs.

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CHALLENGES IN ESTIMATING COVERAGE INDICATORS FOR PERENNIAL MALARIA CHEMOPREVENTION (PMC) WHEN COMBINING STANDARD ROLLOUT PLUS CATCH-UP APPROACHES: LESSONS LEARNED FROM PILOT IMPLEMENTATION IN DEMOCRATIC REPUBLIC OF CONGO (DRC)

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The DRC recently introduced PMC targeting children under 2. Implementation began in December 2023 in 4 health zones in Kongo Central province. DRC opted for a model based on the administration of Sulfadoxine-Pyrimethamine (SP) at six contacts aligned with the expanded immunization program (EPI) and Vitamin A (Vit A) calendar, i.e. at 10 and 14 weeks of age, 6, 9, 12 and 15 months. This corresponds to the timing of DTP2, DTP3, Vit. A at 6 months, Measles1, Vit A at 12 months and Measles2. A monitoring and evaluation plan was developed and defined various indicators to be tracked, including coverage indicators. The monthly coverage of each PMC dose is estimated the same way as the corresponding EPI antigens or Vit A using the same expected monthly population. To maximize coverage during the rollout phase, all children between 10 weeks and 15 months of age were targeted. Children received their first dose of PMC anytime between the age of 10 weeks and 15 months. With this approach, the monthly coverage of each PMC dose cannot be reliably compared with the corresponding EPI antigen or Vit A. In February, there were 4,591 doses of PMC 1 for 2,223 doses of DTP 2 delivered. This discrepancy will likely continue until the cohort is composed solely of children who received their first PMC dose at 10 weeks. The length of time will depend on the country specific schedule, and in DRC this will take 12 months. An overall PMC coverage indicator is used to track the performance of PMC against corresponding EPI antigens and Vit A during the initial rollout phase and guide decision making for improvement. This indicator compares the total number of PMC doses administered during the period (i.e 7,297 in January and 7,963 in February), regardless of age, to the total number of children expected for the 6 EPI and Vit A contacts, as well as the total number of children who received any EPI antigen or Vit A (7,152 in January and 7,302 in February) during the 6 contacts in the same period. This indicator showed better correspondence and suggested an increase in use of health services with an increase in the EPI/Vit A performance, probably boosted by the enthusiasm generated by the introduction of PMC.

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QUALITY AND PERFORMANCE OF COMMUNITY-OWNED RESOURCE PERSONS FOR MALARIA COMMUNITY CASE MANAGEMENT (MCCM) IN HARD-TO-REACH COMMUNITIES IN TANZANIA, 2023

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In 2022, because policy prohibited malaria testing by community health workers, Mainland Tanzania introduced community case management of malaria (mCCM) by retired health professionals called Community-Owned Resource Persons (CORPs) to enhance the equity and reach of malaria service delivery in remote, high burden communities. To assess CORPs mCCM service delivery, we analyzed data collected by Council Health Management Teams (CHMT) during the two initial rounds of supportive supervision (SS). Training, equipment, and monthly stipends were provided to 33 CORPs providing mCCM services in 36 villages in Nsimbo and Tanganyika districts in Katavi region. Local government provided artemether-lumefantrine (AL), malaria rapid diagnostic tests (mRDTs), reporting tools, and SS. CHMTs used a standard checklist to assess service delivery, including patient volume, commodity management, community leader engagement, and overall competency. CHMTs assessed 33 (100.0%) CORPs in round 1 and 28 (84.8%) in round 2. From March to September 2023, CORPs conducted 15,437 mRDTs. Of these, 4,795 (31.1%) tested positive for malaria. Of these, all were diagnosed with uncomplicated malaria, and all were treated with AL. During stockouts of AL (24.3% round 1, 14.0% round 2) and mRDTs (28.3% round 1, 7.4% round 2), CORPs did not provide mCCM. Across both rounds, 70% of CORPs engaged community leaders for community mCCM sensitization. CORPs meeting overall competency standards was 54% in round 1 and 92% in round 2. Most improved competency areas included: stockout reduction, tool use (e.g., proper OPD summary filing [39% to 96%]), and mRDT quality control (e.g., recording start/reading time [83% to 96%]). CORP-administered mCCM improved over two SS rounds but was limited by stockouts. To improve service delivery, commodity availability should be paired with continued SS and other evidence-based supports. These findings are likely to be generalizable to future cadres of CHWs implementing the test and treat approach to mCCM.

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THE ECONOMIC BENEFITS OF INDOOR RESIDUAL SPRAYING IN RWAMAGANA DISTRICT, EASTERN PROVINCE, RWANDA

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Malaria continues to be a major public health concern in Africa and particularly in Rwanda. Malaria reduces labor productivity as it affects people's ability to work, children misses school. Indoor residual spraying is one of the key interventions used to control malaria in Rwanda; however, few studies have evaluated its economic outcomes. This study aims to investigate the economic returns from investment in malaria control using IRS with Rwamagana district with 484,953 inhabitant. Malaria morbidity data were retrospectively collected through Rwanda Health Management Information System. Projected malaria cases in the absence of IRS intervention was done using the linear regression in Epi Info and adjusted for seasonal effects. The economic benefits were estimated using the minimum average cost of USD 8.67 for treating a simple episode of malaria case which includes direct cost and indirect costs. The IRS has been implemented for the first time in Rwamagana from June 2019. It is conducted on annual round and with more than 98% coverage. Two types of insecticides have been used on rotation every two years, Pirimiphos methyl 300 CS and Fludora Fusion 56.25 WP. Malaria cases were reduced by 95 percent from 235,320 cases in 2018 before IRS to 11,067 cases in 2023 while the incidence dropped from 959 to 23 cases per 1000 persons respectively. From June 2019 to December 2023, the projected malaria cases in absence of IRS are estimated to 4,431,401 and 239,08 reported malaria cases. The estimated averted malaria cases are 4,192,320 cases. The total cost for conducting IRS was USD 9,385,661 including both Insecticides and operation costs. The total estimated cost to treat malaria

cases in absence of IRS is 36,347,412 USD. The benefit due to averted outpatient malaria cases is estimated to 26,961,751 USD with benefit-cost ratios of 2.9 and the average IRS cost per Capita is 19.4 USD. IRS in Rwamagana district have high economic returns, its cost is much lower than benefits related to the averted malaria cases. Funding Malaria Control using IRS have good return on investment and in preventing malaria and saving lives.

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ASSESSING PATTERNS IN BEDNET USE USING ACCELEROMETER-BASED MONITORING IN COTE D'IVOIRE

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Malaria has not declined despite the wide-scale distribution of long-lasting insecticide treated bednets. One explanation could be that the timing of use may not correspond with the timing of vector exposure. Surveys about bednet use are prone to recall and social desirability bias and only give a snapshot of bednet use the previous night. Remote monitors of bednet use can provide objective measurements of whether a bednet is in use or not over time. This observational study deployed accelerometer-based bednet monitors in 3 regions of Cote d'Ivoire representing different malaria transmission settings: urban Yamoussoukro, peri-urban Tiassalé and rural Korhogo. The objective was to characterize patterns in bednet use and assess differences between regions. Bednet use monitors were attached to the side of one bednet in each household. Accelerometer data was classified using a previously trained random-forest machine learning algorithm (Koudou et al. 2022). Mixed-effects regression models were employed to account for multiple measures per household. Logistic regression models were used for binary outcomes and generalized linear models for continuous outcomes. Fifty households were followed for a mean of 115 nights each (5,749 total nights). Overall, bednets were unfurled at 8:26 pm (95% CI: 8:20 pm - 8:39 pm) and folded up at 6:13am (95% CI: 6:03 am - 6:23am). Mean bednet use was 10.3 hours per night (95% CI: 9.8 - 10.9). Both Yamoussoukro (-1.3 hours; 95% CI: 0.5 to 2.5; p=0.042) and Korhogo households (-1.5; 95% CI: -0.0 to 3.0; p=0.054) used their bednets less compared to Tiassalé. Overall, households did not use their bednets on 4.8% of nights (95% CI: 2.2% - 7.4%), but there were no significant differences between regions. Within regions, there was substantial heterogeneity along both of these metrics and evidence of outlier households. These findings suggest that remote bednet monitoring could be utilized by National Malaria Control Programs to identify the behaviors, households and regions with sub-optimal prevention practices, thus allowing behavior change campaigns to be tailored to ensure maximum impact in improving malaria prevention.

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ANALYZING THE IMPACT OF MALARIA PREVENTIVE INTERVENTION ON MALARIA TEST POSITIVITY RATES: A FOUR YEAR STUDY IN ADAMAWA STATE NIGERIA

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This study analyzes malaria testing and positivity rates in Adamawa State, Nigeria, from January 2020 to December 2023. The data include information on Rapid Diagnostic Tests (RDT) and Microscopy methods. The study considers the demographic characteristics of the state, including its diverse population and urban or rural settings. In 2023, Management Sciences for Health conducted a large-scale campaign for Insecticide Treated Nets (ITNs) and supported the Seasonal Malaria Chemoprevention campaign. The study aims to analyze the effectiveness of these campaigns in reducing malaria incidence. This data-driven exploration will inform future malaria elimination strategies and form a foundation for evidence-based decision-making in malaria prevention and elimination programs. The data used is from Nigeria DHIS2 to calculate Test Positivity Rates (TPR) for both RDT and Microscopy, analyzing monthly fever cases, malaria-positive cases, and those tested by RDT and Microscopy. The results reveal average dropping trends in malaria testing positivity rates over four years of SMC and ITN implementation in Adamawa State from 80% to 77%, 76%, and 75% in 2020, 2021, 2022, and 2023, respectively. While the overall average yearly number of persons presenting with fever continues to increase progressively from 59,567 in 2020 to 68,475 in 2023, the TPR demonstrated positive variations, providing insights into the efficacy and effectiveness of prevention and vector control strategies in the state, because we recorded malaria incidence rate declined from 7% (January) to 3% (December) in 2023. The analysis highlights the need for continuous monitoring and assessment of malaria testing processes and reporting in Adamawa State to optimize elimination vector control interventions. The study recommends regular evaluations of testing methodologies, and targeted interventions in high malaria positivity regions. In conclusion, monthly and yearly variances in malaria case patterns are determined, highlighting the impact of SMC and ITN interventions on the rate of malaria incidence in the states.

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RECONSIDERING INDOOR RESIDUAL SPRAYING COVERAGE TARGETS: LEVERAGING HIGH-RESOLUTION OBSERVATIONAL DATA FROM BIOKO ISLAND TO ESTIMATE THE DOSE-RESPONSE CURVE

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Indoor residual spraying (IRS) has long been one of the cornerstones of malaria vector control, and high to extremely high coverage levels (at least 80-85%) have historically been recommended as necessary to ensure a community effect. This claim has little empirical evidence due to the difficulty of conducting high-quality studies. Here we present results from a retrospective analysis of five years (2016-2020) of programmatic IRS and annual malaria indicator survey (MIS) data from Bioko Island, estimating how IRS effect size varied with coverage. The first 15 years of IRS implementation on Bioko targeted the entire island, but the years analyzed targeted high-risk areas based on *P. falciparum* prevalence (PfPR) in the previous year. The implementation of a spatial decision support system on Bioko links household-level IRS and MIS data to map sectors (100m x 100m grid cells), which we use as the primary unit of analysis. Despite the observational nature of the data and non-random selection of areas to target, this period provides a sensible setting for the application of causal inference techniques, given the increased variation in achieved coverage and the relatively simple and well-understood mechanism for assigning treatment. In a causal inference framework, we define multiple coverage variables using different spatial scales (the map sector and 100m, 200m, and 300m buffers around sectors), and use MIS covariates to debias the relationship between coverage and PfPR. The analysis suggests a possible threshold for community protection at much lower coverage levels than previously thought, though extremely high coverages may provide additional benefit. This casts some doubt on the necessity of 80-85% coverage targets, and more importantly, points to the need for more research on the relevant coverage thresholds for IRS, the potential mechanisms causing the observed behavior, and other drivers of IRS effect size heterogeneity.

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SEASONAL MALARIA CHEMOPREVENTION COVERAGE SURVEY STRATEGIES TO SUSTAIN HIGH COVERAGE THROUGHOUT CAMPAIGN ARE NEEDED BENIN 2023

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Benin assessed 2023 seasonal malaria chemoprevention (SMC) coverage of four monthly SMC cycles consisting of three daily medicine doses [sulfadoxine-pyrimethamine + amodiaquine (SPAQ) on day one; AQ on days two and three] given to a target of 432,710 children aged 3-59 months. A weighted, cluster-randomized sample of SMC-receiving households (sample size, 3403 children) from 15 communes was surveyed four weeks post-campaign. In six communes, distributors gave day-one doses; education to caregivers included AQ dose administration for days two and three (DOT1). In nine communes, distributors gave all doses each cycle (DOT3) along with SMC education. A questionnaire regarding one randomly selected, age-eligible child per household was administered to caregivers; data including demographics, number of doses per cycle, reasons for refusal, and education provided by the distributor were recorded using Survey Solutions software on a smartphone and analyzed with SPSS. Caregivers of 3573 children (1932 [54%] male; mean age 29 months) completed surveys; 452 (13%) had no SMC for diverse reasons (e.g., refusal, absent). In DOT1 and DOT3 communes, 1565/1663 (94%) and 1556/1910 (81%) children received at least one SPAQ dose, respectively. For DOT1, three SMC doses were taken by 1531 (92%), 1503 (90%), 1469 (88%) and 1106 (67%) children, for cycles one to four, respectively; for DOT3, these doses were 1486 (78%), 1415 (74%), 1306 (68%) and 1114 (58%), respectively. In total, 2137 (60%) children took all 12 doses. Reasons given by 65 caregivers who refused SMC for their child included father's absence for permission (n=24, 40%), and medicine safety concerns (n=27, 42%). Of 3121 caregivers, 2684 (86%) reported that distributors taught them about SMC benefits and 1092 (35%) were educated to manage adverse events. Coverage with at least one SPAQ dose was high; however, SMC coverage declined with each successive cycle. Lower coverage in DOT3 sites may reflect challenges finding children and caregivers at each visit. Areas to improve include uptake of all SMC doses, particularly in later cycles, and effectively teaching key information to caregivers.

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ENHANCING OFFLINE DATA COLLECTION SYSTEMS THROUGH HYBRID DATA MANAGEMENT: INSIGHTS FROM THE BOHEMIA CLINICAL TRIAL

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The BOHEMIA clinical trial, conducted in Mozambique and Kenya, investigated the impact of mass ivermectin administration on malaria control. Utilizing a comprehensive database of over 600,000 entries collected via Open Data Kit (ODK) on tablets, the trial showcased the benefits and challenges of electronic data capture in remote settings. Despite its efficiency, maintaining data integrity posed significant challenges due to digital literacy gaps and connectivity issues, necessitating innovative solutions for data quality assurance.The trial's data management strategy highlighted several hurdles, including data errors such as typographical mistakes, geolocation inaccuracies, and duplication. To mitigate these issues, the data collection system was enhanced with validation checks and warnings, complemented by a dynamic analysis script for identifying and addressing anomalies. This multi-tiered approach, bolstered by independent data reviews, ensured the robustness of the cleaning process. Crucially, the trial underscored the importance of human oversight alongside technological solutions. Direct feedback mechanisms and continuous communication between data managers, field supervisors, and collectors were vital in refining the data cleaning methodology. This process not only improved data accuracy but also fostered a transparent and replicable system, essential for the trial's success.This mixed-methods approach—combining technological tools with human insight—proved effective in overcoming the challenges of data collection in resource-limited settings. The BOHEMIA trial's experiences offer valuable lessons for future global health research, emphasizing the need for adaptable and resilient data management strategies in the face of connectivity and literacy barriers.>

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EVALUATING A PROGRAMMATIC MALARIA MASS DRUG ADMINISTRATION IN MOZAMBIQUE: MIXED-METHODS ANALYSIS OF OPERATIONAL PERFORMANCE

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The World Health Organization (WHO) recommends Mass Drug Administration (MDA) to reduce malaria transmission in low-transmission settings, with a target coverage of at least 80%. Developing effective and sustainable programmatic delivery strategies is key to achieving high impact.From Dec 2022 to Feb 2023, two rounds of programmatic MDA (pMDA) were conducted in Chidenguele (Gaza province), Mozambique, targeting an estimated population of 59,271. Door-to-door distribution using a satellite imagery-based mapping tool was conducted. To evaluate its operational performance (including acceptability, adoption, fidelity, feasibility, and appropriateness), we conducted a mixed-methods evaluation with a community household survey (HHS, n=770), a health facility survey (HFS, n=28), and field observations (FO, n=149). Out of the HHS participants (HHSp) eligible to receive medication, 96.0% (568/592) accepted taking the medication. All HFS participants (HFSp) and 91.3% (703/770) of HHSp agreed that taking antimalarials even if not sick was acceptable as a prevention strategy. Similarly, all HFSp and 84.1% (648/770) of HHSp agreed that the intervention was appropriate to decrease malaria transmission in the community. Programmatic coverage (% of survey participants treated), a proxy of feasibility, was 73.9% (569/770) and operational coverage (% of individuals treated among participants present during the pMDA) was 90.2% (569/631). In 74.5% (111/149) of the FO, the distribution team correctly informed family members about the purpose of the visit, in 86.6% (129/149) asked for verbal consent to conduct the visit and treat them, and in 60.4% (90/149) explained the importance of completing the full treatment (fidelity). In rounds 1 and 2, 86.0% (24/28) and 96.0% (27/28) of HFSp were very willing to adopt the campaign procedures respectively.Despite the pMDA delivery strategy being implemented with good operational performance and being well accepted by the community and implementers, achieving 80% coverage is challenging and requires high engagement from partners, community, and policymakers.

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GENETIC LINKAGE OF DRUG RESISTANCE GENOTYPES TO CONTINENTS USING *PFS47* AND *PFCPMP* FOR TRAVEL-ASSOCIATED *PLASMODIUM FALCIPARUM* MALARIA CASES WITH AN UNREPORTED TRAVEL HISTORY (USA, 2018-2021)

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Travel-related malaria cases are regularly encountered in the United States where the Centers for Disease Control and Prevention (CDC) performs national surveillance through characterization of *Plasmodium falciparum* drug-resistance genotypes. An important aspect of antimalarial resistance surveillance is understanding its geographic distribution. However, CDC often receives malaria case data lacking a travel history. To complement drug-resistance surveillance at CDC, in addition to sequencing loci associated with resistance, amplicons of *Pfs47* and *Pfcpmp* are sequenced as markers of geographic origin. Here, we use these markers to classify *P. falciparum* to a continent and compare sequence-based classifications to travel histories provided for a subset of U.S. travel-associated malaria cases reported to CDC from 2018-2021 (n=380). We built 10 classification models by training a Naïve Bayes classifier using *Pfs47* and *Pfcpmp* sequences from >10,000 publicly available (MalariaGen) *P. falciparum* genomes of known origin to predict an isolate's continental origin. The classifier's performance was evaluated by comparing predictions obtained for 10 sets of 627 MalariaGen genomes (excluded from the 10 training datasets to test the trained models) from Africa (n=267), Asia-Oceania (n=338), and Latin America (n=22), plus 243 CDC cases with travel histories; 234 obtained sufficient sequencing coverage; 231 reported travel to Africa, one to India, one to Costa Rica, and one to the Dominican Republic. The classifier was 98% accurate, where incongruent classifications included a Costa Rican travel case classified to Africa, a Sierra Leone case classified to Asia, and on average, 16 Asian MalariaGen samples were misclassified to Africa. Of the CDC cases with unknown travel histories (n=137), one obtained insufficient sequencing coverage, 135 samples were classified to Africa, and one to Latin America. Given the importance of understanding the geographic distribution of drug-resistance, this work will improve domestic malaria surveillance efforts by linking geographic information to more cases.

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EFFECTS OF FACILITY BASED MALARIA SURVEILLANCE MONITORING AND EVALUATION MENTORSHIP MODEL ON DATA QUALITY IN KAKAMEGA COUNTY, KENYA

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In Kenya malaria data is reported through routine health information systems. There are data quality challenges in this system. Enhancing healthcare workers' knowledge and skills is one way of enhancing malaria surveillance monitoring and evaluation and improving the availability of quality data for decision making. This paper describes the impact of the facility based malaria surveillance mentorship model on data quality in Kakamega County, Kenya. This retrospective study analysed data collected during routine malaria data quality assessments before and after implementing the facility based malaria surveillance mentorship program. Data quality indicators. A total of 35 mentors were trained, 1,403 healthcare workers mentored in all 225 targeted health facilities. There were significant improvements in data completeness, timeliness, and accuracy following the mentorship program. Timely reporting increased from 96% to 99%, completeness of reports from 96% to 100%. Data accuracy improved for several key malaria indicators. Cross checks revealed discrepancies between baseline and round two assessments, with reduced accuracy in cross checks between laboratory and pharmacy registers. There were documented positive effects of facility based mentorship on malaria data quality through improvements in the data quality aspects. There is need for a routine capacity building of healthcare workers on best practices in data management and reporting, with emphasis on the newly recruited staff and ensuring continuity of data quality efforts.

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ANTI-MALARIAL DRUG RESISTANCE INTELLIGENT ADAPTIVE GEOSPATIAL SURVEILLANCE SYSTEM

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Disease monitoring resources are limited, so improvements are required to achieve comprehensive geographic mapping and real-time situational awareness. This optimization would help to improve resource allocation and reduce logistics and other costs. Countries with vast differences in population density and access to healthcare, as well as vast geography and terrain, use multiple distinct Antimalarial Drug (AD) treatments. All of these complications make mapping of AD resistance a challenging task. Despite the challenges, this study employs a novel approach to identify potential study sites for AD medication monitoring. The methodology also overcomes the limitations in existing data on the geographical distribution of AD resistance in *Plasmodium Falciparum* (Pf). We sought to identify locations with high median resistance marker prevalence and uncertainty. As a test case, we use updated WWARN molecular surveyor from India and neighbouring countries to examine the prevalence of resistance-conferring mutations in pfdhfr/pfdhps for sulfadoxine/pyrimethamine and pfk13 for artemisinin derivatives. This information was then used to develop geostatistical models to identify districts with the greatest potential for reducing predicted uncertainty while also verifying the expected high median resistance marker prevalence. A dynamic dashboard was also created using RShiny to make the site selection process more dynamic. The dashboard classifies districts as having high, medium, or low malaria endemicity. Sites in these areas can then be chosen based on practicality. This ensures that decision-making is supported by quantitative data derived from geographic models, making it easier to select appropriate locations for potential AD resistance surveillance. We demonstrated the efficacy of our technique in identifying areas for medication resistance surveillance in Pf malaria in India. With minor modifications, this technique could be used to improve the efficacy of surveillance initiatives in any other part of the world with a small dataset.

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GUIDING LOCALIZED SEASONAL MALARIA CHEMOPREVENTION STRATEGIES WITH ANTENATAL CARE-BASED MALARIA SURVEILLANCE IN TANZANIA

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As of 2022, 17 countries in sub-Saharan Africa have implemented seasonal malaria chemoprevention (SMC), providing over 49 million children with at least one dose that year. WHO recommends using clinical case reports or rainfall data to inform SMC implementation, but clinical case reports are influenced by treatment seeking behaviour and only detect symptomatic infections. Outside the Sahel, correlations between rainfall and malaria burden are not well characterised. Malaria surveillance at antenatal care (ANC), which has been conducted nationally in Tanzania since 2014, could provide an alternate means to estimate seasonal malaria burden. Here, we fit an established mathematical malaria model within a Bayesian framework to estimate unobserved indicators of malaria transmission and simulate the impact of SMC strategies in candidate locations identified by the Tanzania National Malaria Control Programme. Monthly reports of malaria testing and positivity among pregnant women at first ANC between 2016 and 2022 were obtained from the Tanzania Ministry of Health. We used a particle Markov Chain Monte Carlo algorithm to fit the *malariasimulation* model to ANC prevalence. Estimated trends in adult mosquito emergence rates were then used to simulate counterfactual scenarios with varying SMC timing and rounds across 23 councils. Percent reduction in annual cases was calculated for each scenario. Overall, our results suggest that SMC could be effective. However, we also identified substantial variation in seasonal trends in malaria prevalence at ANC across candidate councils despite similar rainfall patterns. For example, in a hypothetical four round SMC campaign beginning in January, annual cases in Itigi district council, Singida Region, were reduced on average by 72.3% (95% confidence interval [CI]: 65.4-81.1%) compared with only a 37.8% (95%CI: 37.5-38.0%) reduction in Malinyi district council in Morogoro Region. ANC-based malaria surveillance data are a powerful tool for not only identifying ideal locations for SMC intervention, but also to adapt SMC timing and frequency to the local context.

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FALSE ALARM ON A MALARIA "OUTBREAK" LINKED TO IRREGULARITIES IN MALARIA DIAGNOSTIC SUPPLY: A CALL TO STRENGTHEN SUPPLY CHAIN MANAGEMENT — SIERRA LEONE, MAY-AUGUST 2023

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Malaria transmission in Sierra Leone is intense and perennial, accounting for 40% of clinical consultations. Medical workers diagnose suspected malaria cases using rapid diagnostic tests (RDT) and microscopy, with results reported to the Health Management Information System (HMIS) as monthly aggregates. We investigated a striking increase in confirmed malaria cases reported to HMIS, impacting all ages and districts during May-August 2023 and peaking in June. We first analyzed national and health facility HMIS data to assess RDT stocks, testing rates, and confirmed case counts. To control for transmission variations, 2023 data was compared to the same month's average from 2019 to 2022. We then visited four facilities in two districts with concurrent elevations in malaria cases to identify root causes through analysis of case registers and staff interviews. Investigation revealed inconsistent RDT distribution to and use by facilities. National RDT distribution spiked in May 2023, when 551,888 RDT test kits were delivered compared to the May 2019-2022 mean of 53,121. This was the largest single-month distribution on electronic record. Subsequently in June 2023, 386,343 tests were performed compared to the June 2019-2022 mean of 282,656 (37% increase); tests performed by community health workers increased to 92,817 from a mean of 25,899 (260% increase); and confirmed cases increased to 273,835 from a mean of 187,527 (46% increase). The four visited facilities reflected national trends: June 2023 had 1,910 confirmed cases compared to a 2019-2022 mean of 483 (300% increase). Staff reported recurrent RDT stockouts, with all facilities reporting a greater than 1-month RDT stockout immediately preceding their spike in cases. In conclusion, the 2023 spike in reported malaria cases was likely related to increased testing following an unusually large distribution of RDTs. Fluctuations in RDT availability impede the ability to recognize true case variations. Sierra Leone and its partners can strengthen supply chain logistics and health commodity stock tracking to ensure a consistent supply of RDTs and improve interpretation of surveillance data.

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QUALITY OF MALARIA ROUTINE SURVEILLANCE DATA IN GHANA, 2023

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Ghana changed its focus from malaria control to elimination in 2023. Accurate and reliable surveillance data play a pivotal role in shaping public health interventions and strategies. Recognizing the critical importance of data quality in informing evidence-based decision-making, a comprehensive assessment of routine malaria data was conducted to assess the accuracy of reported malaria data in Ghana. We conducted a descriptive cross-sectional assessment using records reviews across 28 health facilities in 10 regions of Ghana selected using a multistage approach. Source documents reviewed included patient folders, monthly statements of inpatient, and monthly summaries. Data was also extracted from the DHIMS-2. Indicators extracted were confirmed malaria cases and admissions. The accuracy of malaria data was assessed using the Malaria Routine Data Quality Assessment Tool. Verification Factor (VF) was calculated as the number of cases counted from the source documents divided by the reported value in DHIMS-2. VF between 0.9 and 1.1 indicated an acceptable accuracy level, VF of >1.1 indicated over-reporting and VF <0.9 indicated under-reporting. Malaria admissions were over-reported in seven out of the 10 regions. Only data reported in Greater Accra Region (VF = 0.92) and Central Region (0.90) were within acceptable level. Only facilities using paper-based (VF = 0.95), Phone Book (VF = 1.06), and Medlink (VF = 0.91) recorded acceptable levels. Government-owned facilities (VF = 2.43) had the highest level of poor data quality followed by quasi-governmental (VF = 2.02). Malaria admissions were thrice over-reported in the period evaluated. Health facilities using Smile and LHIMS software had the highest over-reporting. Coaching on data validation was organized for health information officers in the facilities assessed. The Ghana Health Service needs to strengthen data validation and verification activities in all health facilities across the country.

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TOWARD ZERO MALARIA IN THE DOMINICAN REPUBLIC: INTEGRATING IMPORTED INFECTIONS INTO SURVEILLANCE STRATEGIES

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Confirming malaria elimination requires evidence of the sustained absence of locally acquired cases. If infections are imported, they do not reflect local transmission and provide a critical piece of information to accurately determine between local elimination and ongoing transmission risk. Additionally, a health system's ability to confirm and report imported infections indicates its strength and functionality. The aim was to enhance the precision of system sensitivity and the probability of an area being malaria-free in the Dominican Republic by integrating data on imported malaria cases into the Freedom From Infection (FFI) model. This novel statistical framework, designed to probabilistically demonstrate the absence of malaria using routinely collected health system data, was adapted to incorporate information on imported infections. The study analysed detailed health facility data, including routine malaria surveillance data and questionnaires on health system factors from 48 facilities between 2019 and 2023. Initial analysis of the standard FFI model indicated that, out of 2688 facility-months observed, 387 months had a high probability of being free from infection, with 7 out of 48 facilities maintaining this probability in the last 36 months. However, the revised model, which included imported cases, showed an increase to 714 months and 12 facilities, respectively. By adjusting for the detection of imported infections and their impact on local transmission and surveillance effectiveness, the model offers a refined approach to evaluating elimination status. This improvement in reflecting reality enables public health officials to formulate intervention strategies and allocate resources more effectively, ensuring decisions are grounded in accurate assessments of malaria status. This method's significance extends beyond the Dominican Republic, providing a crucial strategy for regions similarly aiming to differentiate between imported and indigenous cases of malaria, thereby guiding more strategic and impactful public health actions.

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ASSESSMENT OF THE MALARIA SURVEILLANCE SYSTEM IN ELIMINATION-TARGETED NORTH BANK REGIONS, THE GAMBIA

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A strong malaria surveillance system is essential for achieving malaria elimination. In 2023, case-based surveillance (CBS) began in North Bank Regions (NBR), The Gambia, providing a unique opportunity to assess the malaria surveillance system in an elimination setting. Using the WHO Malaria Surveillance Assessment Toolkit, a rapid assessment comprised of a desk review and quantitative interviews with regional (n=5) and health facility (HF; n=29) staff was conducted from January-February 2024. The routine and CBS systems in NBR are functional with several strengths and areas for improvement. NBR HF reporting and participation rates were high: 100% and 92%, respectively, in the routine system and 100% for both rates in the CBS system. Private sector reporting and care-seeking were low, 62% and 16%, respectively. The community level does not participate in CBS, and foci investigation and response are not yet operational. Data for decision-making are used at national and regional levels but are limited at NBR HFs—40% do not use data and case classification rates varied, 64%-77%. Routine quality assurance activities are not done regularly at all health levels. The DHIS2 Tracker for CBS is considered accessible, flexible, stable, and has visualization capacities, but its integration capability has not been implemented and there is no master facility list. The national surveillance guideline is available at NBR regional health directorates (100%) and HFs (97%), but there is no supervision guideline. Despite half of planned trainings being conducted, all NBR regional and most HF staff said they received training in 2023. In consultation with country and partner stakeholders, recommendations were developed to improve the representativeness of routine and CBS systems, ensure availability and access to resources, strengthen data integration and linkage across systems, strengthen data analysis and use, and improve processes for ensuring high quality data. These recommendations will form the basis for a roadmap to guide prioritization of activities among stakeholders that will accelerate and expand malaria elimination efforts in The Gambia.

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PREGNANT WOMEN AS A SENTINEL POPULATION FOR GENETIC SURVEILLANCE OF MALARIA IN THE DEMOCRATIC REPUBLIC OF CONGO

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Genomic surveillance is a valuable tool for detecting changes in the drug susceptibility of malaria parasites, allowing rapid modification of preventive and curative treatment strategies when needed. To address some of the challenges of implementing surveillance in the most fragile settings, we investigated whether pregnant women attending antenatal care (ANC) services could serve as a more pragmatic sentinel population than the conventional target of children. We conducted a prospective malariometric survey in Kinshasa, Democratic Republic of Congo (DRC), between 2021 and 2023. The study recruited pregnant women attending ANCs regardless of age or trimester of pregnancy, as well as children under 14 years old living in the same area. A total of 4,001 women and 2,794 children participated in the study. While most enrolled women were asymptomatic regardless of parasitaemia, 19% tested positive by rapid diagnostic test (RDT). In contrast, 49% of children tested positive by RDT, with 71% reporting malaria-like symptoms in previous days. Blood samples were taken from positive cases to characterise and compare the genomes of *Plasmodium falciparum* isolates using the SpotMalaria genotyping platform. Comparison of allele frequencies in a 100-SNP barcode revealed a strong correlation between the parasite populations in pregnant women and children ($r=0.99$, $p<0.001$), with overlapping confidence interval at 98 out of 100 SNPs. This indicates that parasite populations were minimally differentiated between the two cohorts. Furthermore, the comparison of antimalarial resistance marker frequencies showed minimal or non-significant differences in variants within *dhfr*, *dhps*, *crt*, *mdr1* and *kelch13* genes. These findings suggest that, in a malaria endemic fragile context, the genomic surveillance of antimalarial drug resistance in pregnant women attending ANC services, can provide comparable results to those of children, with logistical and ethical advantages in implementation.

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IMPROVING THE APPROACH TO MONITOR AND REPORT ON COVERAGE OF MALARIA INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY: TIME FOR A RETHINK

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Malaria in pregnancy (MIP) is a maternal and neonatal health issue that continues to result in an estimated 10,000 women and 100,000 infants dying each year. With bednets and prompt case management, intermittent preventive treatment during pregnancy (IPTp) administered during antenatal care (ANC) contacts is the main intervention to prevent and mitigate against MIP effects. For it to be effective at a population level, WHO recommends 80% coverage of at least 3 doses of IPTp (IPTp3). However, as of 2024, no country has reached the 80% target. Indeed, of all malariometric indicators,

MIP is the indicator where endemic countries probably lag most. While this is due to a myriad of factors (e.g., low ANC coverage, SP shortages) we believe that this is also due to limitations in the monitoring and reporting of MIP indicators, specifically IPTp. We posit that the ratio of ANC contact to IPTp coverage, specifically ANC1+ (at least one ANC clinic visit) /IPTp1+ and ANC4+/IPTp3+, should be an added mandatory programmatic indicator for National Malaria Control Programs to monitor MIP efforts. In theory, if pregnant women attending ANC services were to receive IPTp at every ANC visit, the number of IPTp doses administered should track closely with the number of ANC visits, ideally in a 1:1 ratio. Publicly available data from nationally representative surveys conducted in 17 countries in the past five years were analyzed. Findings indicate that while many countries are close to meeting recommended ANC4+ targets, IPTp3 coverage is lagging behind. Thus, while the ANC1+/IPTp1+ ratio is tracking well (i.e., is close to 1), IPTp coverage diverges from ANC coverage with increasing number of ANC visits. Also, the ratio between ANC and IPTp at national level also often differs from the ratio at subnational levels, highlighting geographic areas ripe for programmatic intervention. Identifying countries where the differential in ANC and IPTp coverage is wide, both nationally and sub-nationally, may help identify barriers and facilitators in reaching the recommended IPTp3 coverage targets, as well as in the design of approaches that maximize the impact of MIP control efforts.

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MALARIA EPIDEMICS IN LOW AND VERY LOW BURDEN AREAS OF TANZANIA AND ALERT THRESHOLD SENSITIVITY FOR DISTRICT-LEVEL EPIDEMIC DETECTION, 2022-2023

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Malaria epidemics are associated with increased morbidity, mortality, and health system strain. Epidemic alerts and thresholds can provide context to routine data reviews and guide pre-emptive programmatic action. In 2023, the National Malaria Control Program in Tanzania has established weekly 50th and 75th percentile administrative area-specific thresholds for epidemic alerts and epidemics, respectively, from District Health Surveillance System 2 (DHIS2)-based outpatient department (OPD) case counts for the previous five years. We used the World Health Organization definition of an epidemic as weekly malaria cases exceeding the epidemic thresholds for two consecutive weeks. Using established weekly thresholds, we described the number of district-level epidemics that occurred in 2022 and 2023 in 56 low and very low malaria transmission districts and investigated the sensitivity and positive predictive values of the alert threshold for detecting malaria epidemics during the four weeks before the epidemic. All 56 district councils reported 52 weekly data points, creating a total of 5,824 district-weeks under analysis for 2022 and 2023. During 2023, annual OPD cases were 175,083 with median weekly cases of 18 (range: 0=39) cases and a weekly 75th percentile epidemic threshold of 35 (range: 17-55) cases. Over the two-year period, malaria epidemics occurred in 1,014/5,824 district-weeks (17.4%). At least one epidemic occurred in 49 (87%) districts. Of 1,014 district-weeks with epidemics, 838 reached the alert threshold four weeks before the actual epidemic (82.6% sensitivity), while 176 epidemics occurred without reaching the alert threshold (17.4% false negative). There were 2,236 epidemic alerts: 838 (37.5%) true and 1,398 (62.5%) false. Current epidemic detection algorithms have low sensitivity and very low positive predictive value, indicating inefficiency. Upstream data quality issues and lack of field data to confirm outbreaks indicate more work must be done before threshold-based programmatic actions can be recommended.

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MALARIA SURVEILLANCE DATA ANALYSIS, GA EAST MUNICIPALITY, GHANA, 2023

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Malaria remains a significant cause of morbidity and mortality in Ghana. In the Ga East municipality, the case fatality rate increased from 0.006 in 2018 to 0.015 in 2022. The malaria surveillance data in Ga East municipality was analysed to determine the burden, distribution, and gauge the effectiveness of malaria prevention and control initiatives and compare current reporting to the expected levels over a five-year period. An analysis was conducted on malaria surveillance data reported between 2018 and 2022 in Ga East municipality from the DHIMS 2 database. Data was extracted between February 2023 and April 2023. Summary descriptive analysis was performed on the data to generate frequencies, proportions, rates, and thresholds. The findings were presented in tables, charts, and maps.Out of the 261,588 malaria cases suspected, 98.8% (258,475/261,588) were tested, of which 22.1% (57,155/258,475) were positive. Females accounted for 58% (33,144/57,138) of the morbidity. Females in age group 20-34 years recorded the highest proportion of malaria, 18% (10,322/57,138) of cases in the municipality. The overall case fatality rate was 0.003% (4/57,155). Ashongman recorded the highest prevalence of 305 per 1,000 population, and the least prevalence of 82 per 1,000 population was recorded at Taifa. An overall malaria mortality rate of 0.14 per 10,000 population was recorded. Malaria prevalence varied by age and sex in the municipality, with females in 20-34 age groups having the highest incidence of malaria cases. The municipality missed two outbreaks in Abokobi and Haatso sub districts. Dome sub district recorded the highest under-5 years positivity rate. Malaria incidence declined gradually throughout the evaluation period whiles case fatality rate increased. The municipality achieved the WHO targets throughout the evaluation period. The Public Health unit of the health directorate and the NMCP should focus on case management training for all sub-districts.

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QUANTIFYING THE SUITABILITY OF WATERSHED-BASED AREAL UNITS FOR MALARIA MODELING IN THE PERUVIAN AMAZON REGION

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The Amazon rainforest is one of the most important malaria hotspots worldwide. In Latin America, and particularly in Peru, the highest historical cases of malaria are concentrated in the Loreto department. The relationship between malaria and meteorological factors has often been modeled using administrative boundaries, which limits the natural geographic distribution of boundaries. We leveraged village-level data on *Plasmodium vivax* and *P. falciparum* cases (2009 - 2023) in the Peruvian Amazon rainforest to assess the performance of multiple spatial aggregation strategies (administrative and watershed-based) for malaria spatio-temporal models. After geolocating malaria cases, we used an Integrated Nested Laplace (INLA) approximation to build the spatio-temporal models for each malaria species, considering multiple components related to climate, vegetation, and bodies of water as predictors. Overall, 316,566 malaria cases were reported and geolocated, of which 79.2% were caused by *P. vivax* and 20.85% by *P. falciparum*. The model based on a hydrographic basin unit (level 6 of hydrobasin) showed the best prediction performance of *P. falciparum* and *P. vivax* cases, compared to traditional administrative

boundaries, evaluated using the Deviance Information Criterion (DIC) and Watanabe-Akaike Information Criterion (WAIC). However, it was observed that the best combination of variables for *P. falciparum* was associated with vegetation and bodies of water, while *P. vivax* showed a better association with climatic components, vegetation, and bodies of water, with Root Mean Squared Error (RMSE) values of 54.1 and 140.1 and Residual Standard Error (RSE) values of 0.56 and 0.40, respectively. These new hydrographic basin-based units could be useful tools for improving the specifications of future models and early warning systems.

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CONSISTENT POST MARKETING SURVEILLANCE ASSURES QUALITY OF ANTIMALARIAL MEDICINES IN KENYA

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Malaria accounts for 13-15% of outpatient consultations in Kenya, with 4,000 lives lost annually. Access to quality assured antimalarials is crucial for effective malaria prevention and treatment. Kenya's medicines regulatory agency, with the national malaria program, implements a structured risk-based quality surveillance system to monitor the quality of antimalarials. The quality of artemisinin-based, quinine and sulfadoxine -pyrimethamine (SP) antimalarials sampled across the supply chain from both public and private health care facilities across Kenya were analyzed for the period between 2010-2023. Screening and compendial testing showed continuous improvement in the antimalarial product quality; from 84% in 2010 to 100% in 2019 and has been sustained onwards. Registered antimalarials were 49% less likely to fail quality screening as compared to non-registered ones. For compendial testing, 488 out of 622 samples (95%) passed lab tests. Based on the compendial testing results, several regulatory actions like product recalls and legal prosecution were implemented. Routine risk-based post-marketing quality surveillance of medical products is critical in assuring quality and mitigating risks from substandard and falsified products. Consistent investment in monitoring the quality of antimalarials ensures safe, quality treatment, thereby contributing to reducing malaria-related morbidity and mortality. Regulatory enforcement of antimalarial quality standards has helped to significantly reduce the presence of poor quality antimalarials in Kenya.

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IMPROVEMENTS IN INTERMITTENT PREVENTIVE TREATMENT FOR MALARIA IN PREGNANCY (IPTP) STOCK AND COVERAGE INDICATORS FOLLOWING DECENTRALIZATION OF SULFADOXINE-PYRIMETHAMINE (SP) PROCUREMENTS, TANZANIA, 2020-2023

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Malaria in pregnancy (MiP) is associated with adverse health outcomes. Intermittent preventive treatment for malaria in pregnancy (IPTp) with Sulfadoxine-Pyrimethamine (SP) is a key MIP intervention. In 2020, Tanzania decentralized SP procurement, requiring facilities to procure SP. We examined SP availability and determinants of IPTp dose 3 (IPTp3+) coverage in Tanzania following this change from 2020 through 2023. IPTp3+ coverage determinants were assessed using standardized Malaria Services and Data Quality Improvement (MSDQI) supportive supervision (SS) checklists. IPTp3+ coverage was obtained from monthly reports of pregnant women receiving IPTp3+ out of all expected (number received 1st ANC). We modeled determinants of IPTp3+ using the Poisson regression with the dependent variable being the monthly number of women receiving IPTp3+ at health facilities offset by the number expected to receive IPTp (1st ANC). Of the assessed 7,559 facilities, 86% had the recommended RCH staffing; 85% had sufficient RCH equipment/supplies; 57% displayed current information, education, and communication (IEC) materials; and 54% had RCH reference materials available on average during the study period. Over the study period, SP stockouts were 13%; 16.5% in 2020 and 8.4% in 2023. Overall IPTp3+ coverage was 67%; 62% in 2020 and 72% in 2023. SP stockouts were associated with a 47% decrease in IPTp3+ coverage (incidence rate ratio=0.53, 95% confidence interval: 0.52-0.54%). Other significant IPTp3+ coverage determinants were: reference material availability, equipment and supply availability, displayed IEC/SBC materials, urban residency, high transmission stratum, and no heavy rains at the time of SS. SP availability at the facility is the strongest determinant of IPTp3+ uptake. Availability and coverage of IPTp improved over the three years following decentralization of SP procurement to health facilities, and it was higher on average than the average of 63% IPTp3+ coverage reported over 2018—2019, the two years before decentralization. This suggests IPTp3+ coverage gains can be made in the context of decentralized SP procurement

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TRENDS OF MALARIA BURDEN IN KENYA: MAPPING INCIDENCE TO TARGET INTERVENTIONS, 2019-2023

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Malaria remains a substantial public health concern in Kenya, despite a decline in prevalence from 11% in 2010 to 6% in 2020. Disruptions in health service delivery due to COVID-19 pandemic and climate change have impacted on malaria control efforts. We determined the geographical distribution and trends of malaria burden in Kenya. We analyzed retrospective malaria data extracted from the Kenya Health Information Systems, 2019-2023 by assessing the key malaria indicators. Malaria incidence rate was calculated as malaria cases per 1,000 population at risk. Confirmed malaria cases were done using both microscopy and RDTs. The annual blood examination rate (ABER) was calculated as the number of examinations of blood slides for malaria by microscopy per 100 population. Malaria case fatality rate (CFR) was assessed as a percentage based on malaria deaths per malaria admissions. Geospatial maps were developed in QGIS to visualize incidence patterns at sub-national levels. The confirmed malaria cases reduced from 4.7 in 2019 to 4.0 million in 2020, subsequently, the cases increased to 5.0 million in 2023. Malaria incidence increased from 97 in 2019 to 105 in 2023. The ABER reduced from 25 tests in 2019 to 22 tests in 2021 and later increased to 27 tests per 100 population in 2023. The malaria admissions decreased from 36,766 in 2019 to 11,555 in 2021 and deaths decreased from 1,043 in 2019 to 769 in 2021. In 2022 the malaria admissions increased to 29,941 as the deaths declined further to 219. The CFR increased from 2.8% in 2019 to 6.7% in 2021 and reduced to 0.7% in 2022. The incidence maps showed increased malaria transmission intensity overtime especially in the Lake endemic and Turkana counties. The malaria indicators assessed demonstrate a reverse trend for the achievements gained in malaria control. Despite decrease in malaria admissions and deaths, the CFR increased due to delayed care seeking by the community and the scale up of community case management improved access to malaria services. The incidence maps can be used to refocus targeted interventions.

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FINANCIAL AND ECONOMIC COSTS OF CARE FOR FEBRILE ILLNESS IN A MALARIA ENDEMIC REGION OF WESTERN KENYA - FINDINGS FROM A CROSS-SECTIONAL COMMUNITY SURVEY, 2022 - 2023

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In Kenya, malaria accounts for an estimated 13-15% of outpatient department consultations. Quantifying the costs associated with care seeking is important to understand the burden of health seeking and malaria care. We used data from a continuous cross-sectional household survey conducted between August 2022 - July 2023 in Rarieda sub-county, western Kenya to describe the costs of seeking care for febrile illness and to assess factors associated with financial (transport, registration/ consult, or laboratory) and economic (travel and wait time) costs. Of 6,708 consented participants, all ages, 5.8% (387/6,708) reported a fever in the two weeks prior. Of those, 59.4% (230/387) reported seeking care and 44.8% (103/230) of care seekers tested positive for malaria. Most (82.2%, 189/230) sought care at only one location. Care was sought at least once, 52.6% of the time in the formal public sector (facilities or community health volunteers), 32.6% of the time in the informal sector (pharmacies, retail outlets, or traditional medicine), and 17.0% of the time in the formal private sector. Financial costs were reported by 59.6% (137/230), with a median cost of $1.21 USD (IQR: $0.80 - $2.99) consisting of 48% transport, 41% consult, and 12% lab costs. Economic costs were reported by 41.3% (95/230), and median travel and waiting time was 2 hours (IQR: 1 - 3). In an adjusted Tweedie generalized linear regression model, household wealth, age, medical insurance, public or informal sector visit were not related to financial or economic costs; visiting a private facility was associated with $5.78 USD (95% CI: $0.69 - $10.88) higher financial costs ($p<0.05$). The majority (94.8%, 218/230) reported taking drugs for their illness. The median cost of treatment was $0.24 USD (IQR: 0 - 1.21) and did not differ significantly by malaria test positivity. Our findings provide an overview of the costs associated with care seeking for febrile illness in western Kenya. Financial and economic costs were low, but higher in the private sector. Two-part models (cost vs. no-cost and cost distribution) will be explored to account for high proportion of persons reporting zero-costs.

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EXTERNAL VALIDITY OF BED NET INDICATOR ESTIMATES FROM RANDOM DIGIT DIAL MOBILE PHONE SURVEYS CONDUCTED IN TANZANIA

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Malaria is a leading cause of morbidity and mortality among children under-5 and pregnant women in Tanzania. The national malaria programs (NMP) in Tanzania mainland and Zanzibar recommend the distribution and use of bed nets as the primary intervention for malaria prevention. Net coverage indicators help guide NMP strategies; however, the usual source of such indicators, national-scale household surveys, are expensive and occur infrequently. To rapidly estimate bed net coverage across Tanzania, two mobile phone surveys were conducted in 2017 and 2022. Regional-level bed net indicator estimates from these two random digit dial (RDD), interactive voice response surveys were compared against the 2017 Tanzania Malaria Indicator Survey (MIS) and the 2022 Tanzania Demographic and Health Survey (DHS) (both population-based household surveys), respectively, to assess their external validity. The core malaria indicators estimated via the RDD surveys were 1) households with at least one bed net of any type, 2) households with at least one bed net of any type per two de facto household population, and 3) de facto population access to a bed net of any type. When compared to the regional-level estimates similarly calculated from the 2017 and 2022 household surveys, the RDD estimates exhibited an average bias of -9.67 and -9.91 for indicator one, -3.39 and -5.29 for indicator two, and -10.63 and -11.97 for indicator three. Adjusted R-squared values were small for all three indicators, ranging between 7.9-40.5%, suggesting poor model fit for the simple linear regression of RDD against DHS/MIS values. The lack of DHS/MIS and RDD data point pairs at extreme values likely prevented regression lines from being more closely aligned with the 45° line of equality. Both mobile phone surveys underestimated indicator three by about 11-12 percentage points at the national level. If used for program planning, underestimation may prompt bed net distribution channels to increase output or trigger mass campaigns to occur sooner than necessary. However, in the context of malaria prevention, this prompt may assist in achieving program targets of reducing malaria burden.

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SITUATIONAL ANALYSIS OF THE TOWNSHIP-LEVEL MALARIA SURVEILLANCE SYSTEM IN RAKHINE STATE AND TANINTHARYI REGION OF MYANMAR

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Malaria remains a significant public health challenge in Myanmar. The various malaria control and elimination efforts in Myanmar necessitate a robust township-level surveillance system to identify gaps and target interventions effectively. This situational analysis was conducted as part of the U.S. President's Malaria Initiative Digital Community Health Initiative to understand key surveillance gaps; strengthen the township-level surveillance system to enable timely, effective, and decentralized interventions; and advance progress to eliminate malaria in Myanmar by 2030. The analysis focused on four key areas of the surveillance system: performance, context and infrastructure, technology and processes, and behavior. A mixed-methods approach, including a desk review, interviews, and observation, was used for this analysis. Structured questionnaires were adapted from the WHO Surveillance Assessment Toolkit and key informant interviews were conducted with implementing partners to collect data across all 27 townships in Rakhine State and Tanintharyi Region in 2024. Data management practices followed standard protocols to ensure confidentiality and data security. Findings were triangulated to provide a comprehensive understanding of the malaria surveillance system in townships. Initial findings showed that Mrauk-U and Palaw townships encountered increased population migration, increased drop-out of integrated community malaria volunteers, and limited distribution of commodities due to security issues. Opportunities to strengthen the township-level malaria surveillance system through enhanced capacity building, strengthened collaboration with partners, and the utilization of context-specific interventions were also identified. Results will be disseminated to key stakeholders to share main surveillance gaps uncovered. A similar approach would benefit other areas of Myanmar, and those insights can inform adaptive strategies aimed at optimizing the malaria surveillance system in Myanmar and advancing progress towards elimination goals.

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EVALUATING THE PERFORMANCE OF THE ELECTRONIC COMMUNICABLE DISEASE SURVEILLANCE (ECDS-MMS) IN VIETNAM: A TAILORED MALARIA SURVEILLANCE ASSESSMENT STUDY

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In 2020, Vietnam rolled out an electronic communicable disease surveillance, the eCDS-MMS, which covers 43 diseases, including malaria. This system is utilized by all communes, districts, provinces, health facilities and other public hospitals. In 2022, the system was updated to align with the national malaria surveillance guidelines, known as Decision 4922. The National Malaria Control Program (NMCP) decided to conduct an in-depth evaluation of the updated system to understand gaps and make needed adjustments. The NMCP utilized the WHO surveillance assessment toolkit and conducted a tailored review using mixed methods from July 15th to December 31st, 2023. A total of 71 indicators were assessed, of which 27 comprehensively evaluated the performance of eCDS-MMS. Samples for the service delivery survey were selected using a stratified random sample of communes based on the 2022 risk stratification, which categorized communes by levels of malaria risk. In total, 29 provinces, 52 districts, and 75 communes comprising of 156 health facilities were selected. Each indicator in the survey was classified as met, partially met, or not met based on specific criteria of that indicator. The results indicated that overall, the surveillance system was operating well with 92% of the indicators meeting the criteria defined in the toolkit. Despite the high overall score, some key areas for improvement were identified. Specifically, the proportion of cases seeking care within 48 hours of symptom onset (54%), the timeliness of focus investigation (not met), the consistency of the malaria inpatient details (partially met), and the concordance of core variables between paper-based registers and eCDS-MMS (78%) remain lower than expected. The assessment revealed a well-functioning malaria surveillance system in Vietnam through eCDS-MMS, capable of detecting and responding to malaria cases. However, to enhance the reliability and effectiveness of eCDS-MMS, the country should increase awareness campaigns for early detection, streamline reporting procedures to ensure timeliness, and accuracy of reporting to achieve malaria elimination in the country.

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HEALTH FACILITY LED DATA UTILIZATION TO SUPPORT IMPROVED COMMODITY AVAILABILITY AND SERVICE DELIVERY IN RESPONSE TO MALARIA EPIDEMICS IN BUKEDI REGION, UGANDA

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Since 2021, Uganda has faced malaria epidemics. Sub-national led surveillance and data use is critical for districts to better manage malaria outbreaks and improve service delivery. In March 2023, the Uganda National Malaria Control Division (NMCD), with support from Clinton Health Access Initiative (CHAI) conducted a landscape assessment in Budaka and Kibuku districts in Bukedi region, Eastern Uganda, identifying minimal malaria surveillance and data use in public facilities, impacting stock management and treatment for patients. Between May and November 2023, NMCD and CHAI supported public facilities in both districts to improve routine data review and use for improved surveillance, stock monitoring and decision making, in addition to case management mentorships. Districts were supported to develop malaria epidemic response plans which included rolling out health facility malaria surveillance and weekly review meetings. NMCD developed physical Malaria Surveillance Charts enabling facilities to plot weekly cases against epidemic thresholds, deaths and stock. Facilities were trained on tracking malaria burden and stock availability using these charts, and established data review committees (DRCs) for weekly review of malaria data. By October 2023, 100% of facilities established DRCs and 78% were holding weekly meetings, compared to 0% in March. Utilizing weekly malaria data, facilities promptly addressed issues by creating time-bound action plans. The overall action completion rate was 53%, with 41% of actions recorded as on-going and 6% incomplete. Facilities completed 75% of stock management actions due to the urgency required to alleviate stock challenges, correlated with ACT stock availability increasing from 92% to 97%, and 45% to 85% for artesunate. This correlated with improved treatment rate for uncomplicated malaria (75% to 97%) and severe cases (45% to 85%). Providing facilities with simple physical tools, training, and continuous QI focused mentorships for malaria surveillance and stock management generates ownership of data and increases decision making at health facilities for improved service delivery.

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PERSPECTIVES OF KEY STAKEHOLDERS ON THE USE OF INFRARED SPECTROSCOPY FOR MALARIA SURVEILLANCE

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As malaria-endemic countries move towards elimination, it becomes imperative to closely monitor the effectiveness of essential interventions and allocate resources strategically. The WHO Global Technical Strategy for Malaria Elimination, suggests that countries should integrate surveillance as a core intervention alongside efficient vector control and case management. Unfortunately, most countries still lack adequate capacity for vector surveillance and intervention monitoring and most African malaria vectors express varied ecological and biological traits, making their detailed surveillance challenging yet critical to optimize control. Emerging techniques in spectroscopy have been considered to address these limitations since they can be performed quickly without expensive reagents or replacement parts compared to alternatives such as polymerase chain reaction (PCR). Near-infrared (NIR) and Mid-infrared (MIR) spectroscopy coupled with machine learning techniques have an incredible potential for mosquito characterization, age-grading, detecting sporozoites, and determining insecticide resistance status in wild-caught mosquitoes This multi-country study aims to explore the perspectives of key African stakeholders regarding the utilization of infrared spectroscopy for malaria surveillance. Through in-depth interviews with policy makers, technicians, researchers, funders and other relevant stakeholders involved in malaria surveillance efforts. The study seeks to investigate their experiences, opinions, and perceived utility of infrared spectroscopy in the context of malaria control and prevention. Preliminary findings suggest that most researchers were previously unaware of the potential applications of infrared tools in malaria surveillance. However, upon receiving more detailed information about the technology, all expressed eagerness to integrate it into their regular surveillance activities. Stakeholders have also emphasized the need for robust evidence to persuade decision-makers, as well as need for comprehensive capacity building initiatives across African institutions.

6500

ACCURACY OF REPORTING OF MALARIA RAPID DIAGNOSTIC TESTS IN UGANDA

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To assess the accuracy of malaria rapid diagnostic test (RDT) results recorded in health facility registers, we conducted an observational study in two high-burden regions (Busoga and Lango), Uganda. Two districts in each region were purposively selected. Public health facilities (levels II and III) in each district were considered eligible based on three years of complete data and an average of at least 50 RDTs performed monthly. Facilities were grouped into four strata based on patient volume and test positivity rate (TPR). From each stratum, one facility was randomly sampled, resulting in a total of 16 facilities. At each selected facility, using a smartphone application, study staff captured the image of each RDT administered and the corresponding RDT result and patient data recorded in the register. Cohen's kappa was used to determine the level of agreement between the HCW RDT result and that of a trained, external panel that reviewed all of the RDT images and recorded their interpretation. Between June and November 2023, 45,838 RDTs were reported, of which 40,049 (87%) were recorded by the study and 33,429 (83%) complete records were included in the final analysis. The majority of patients tested by RDT (67%) were female, and 43% were 15 years or older. The TPR based on the outpatient register was 62%. Overall, there was a high level of agreement (kappa 0.82; 95% confidence interval 0.79, 0.84) between HCW and external reader results, with no significant variation observed over the study period. Considering the external result as the gold standard, 7% and 2% of HCWs' results were considered 'false positive' (FP) and 'false negative' (FN), respectively. The proportion of FP RDTs was higher among facilities in Lango (8%) compared with the Busoga region (5.5%), while both FP and FN were higher among persons aged 15 years or older (8.2% and 2.2%, respectively) compared to those aged less than five years (5.8% and 1.3%). These findings suggest that RDT results reported in the registers of Ugandan public facilities are largely accurate. However, reasons for higher rates of disagreement in the Lango region and among older patients need to be investigated.

6501

SETTING UP A SUSTAINABLE ACTIVE SURVEILLANCE SYSTEM IN SOUTHERN ANGOLA: PROGRESS TOWARDS MALARIA ELIMINATION IN THE SOUTHERN AFRICA REGION.

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Angola has a wide malaria transmission heterogeneity ranging from high transmission in the north and central parts of the country to low and very low transmission in southern bordering areas with Namibia. Since 2017 Angola has been supporting regional elimination efforts through the implementation of robust interventions to eliminate *foci* of transmission in border areas, and as a result, supporting elimination efforts in neighboring Namibia. In the southern provinces of Cunene and Cuando Cubango, new surveillance strategies were developed and piloted such as case line listing, case investigation, reactive case detection, *foci* classification and *foci* investigation. Malaria paper-based case line listing started in November 2022 in 5 health facilities and was later expanded to 53 health facilities. A DHIS2 based malaria case notification tracker system was developed and has been used since September 2023. A total of 7 malaria focal points, 7 statisticians and 53 health workers from selected health facilities were trained. The results showed the variability of transmission across the targeted region. In total, 1137 confirmed cases were notified and classified. A total of 1,074 cases (95%) were classified as Local 1 (sleeping within the same household) and 3 were classified as imported. After conducting entomological capacity building trainings among local focal points, *foci* investigations are currently being implemented to localize vector breeding sites and classify the foci as well as give information for response decision-making. Results highlight the importance of having a robust and integrated active surveillance system to target existing *foci* of transmission in southern Angola. As data becomes more detailed and available, further efforts should be made to implement reactive case surveillance approaches and *foci* management interventions to progress towards malaria elimination.

6502

INTRODUCTION OF THE RTS,S MALARIA VACCINE IN BURKINA FASO: RESULTS FROM THE FIRST SUPPORTIVE SUPERVISION

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Burkina Faso introduced the RTS,S vaccine into its expanded vaccination program on February 5, 2024. Following the recommendations of the World Health Organization, a supervision was conducted to assess the state of readiness. This supervision, which took place a few days before the introduction of the new vaccine, was carried out in all selected districts. This article describes the initial vaccination efforts in Burkina Faso.This is a secondary data analysis conducted from February 2 to 10, 2024, using the Kobo tools during the first supervision of the RTS,S introduction into the expanded vaccination program.The first supervision covered 95 health facilities (HF) across the 27 selected districts. All HFs received the necessary financial resources for preparatory activities of the vaccine introduction. Coordination teams were established, and 99% of HF managers were briefed. Supply replenishment was effective in 99% of HFs, with 84% starting on February 5, 2024. The vaccine was correctly administered by 92% of health workers, registration was well documented by 88% of vaccinators, and 92% reminded mothers of the next visit. Less than a quarter (14%) of HFs had received communication and social mobilization materials before the first vaccinations. There were almost no rumors about the vaccine in the community, and no mothers refused the vaccine. Overall, the main challenges encountered were the unavailability of updated data management tools, limited community mobilization, and insufficient cold chain capacity.The initial on-the-ground results are satisfactory despite the challenges faced during the introduction of the malaria vaccine in Burkina Faso. Future challenges will include monitoring vaccinated children and scaling up to the remaining 43 districts in the country.

6503

PFS230D1 24- AND 60-COPY SINGLE COMPONENT MALARIA TRANSMISSION BLOCKING NANOPARTICLE VACCINES ELICIT A POTENT AND DURABLE RESPONSE UPON VACCINATION

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Although the number of cases of and deaths associated with malaria had been declining prior to the COVID-19 pandemic, forward progress has since stalled, and there were an estimated 249 million cases and 608,000 deaths

worldwide due to malaria in 2022 according to the WHO's World Malaria Report 2023. Tragically, most of these deaths were children under the age of 5. With the rise in parasite resistance to anti-malarial drugs, a malaria vaccine is desperately needed. Malaria vaccines can be broken down into three major classes: Pre-erythrocytic vaccines, Blood Stage vaccines, and Transmission Blocking vaccines (TBVs). TBVs function by reducing disease transmission by breaking the continuous cycle of infection between the human host and the mosquito vector, specifically by reducing/inhibiting the infection within the mosquito after feeding on an infected human. The gametocyte surface protein Pfs230 is a leading TBV candidate. Pfs230 is a large multi-domain protein and most antibodies with transmission reducing activity (TRA) map to Domain 1 (D1). Here we show that both a 24-copy and 60-copy nanoparticle composed of Pfs230D1 genetically fused to either ferritin or the catalytic domain of dihydrolipoyl acetyltransferase protein (E2p), respectively, result in single-component self-assembling nanoparticles (Pfs230D1-ferritin and Pfs230D1-E2p) that have high stability, homogeneity, and production yields. Pfs230-ferritin and Pfs230D1-E2p nanoparticles also correctly present potent human transmission blocking conformational epitopes within Pfs230D1 as shown by the ability of human mAbs possessing high TRA to bind to the nanoparticles. Both nanoparticles elicited potent and durable antibody responses with high TRA after two vaccinations of New Zealand White rabbits when formulated in two distinct adjuvants suitable for translation to human use (Alhydrogel and AddaS03) that was maintained for 4.5 months post vaccination. These single-component nanoparticle vaccines may play a key role in malaria control and have the potential to improve production pipelines and cost of manufacturing of a potent and durable TBV.

6504

SINGLE IMMUNIZATION WITH GENETICALLY ATTENUATED *PLASMODIUM FALCIPARUM ΔMEI2* (GA2) SPOROZOITES INDUCES HIGH LEVEL PROTECTION AGAINST A CONTROLLED HUMAN MALARIA INFECTION

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Malaria vaccines consisting of metabolically active *Plasmodium falciparum (Pf)* sporozoites have the potential to offer a better and more durable protection than the currently deployed subunit vaccines. Recently, we demonstrated the unequivocal superior protective efficacy of late-arresting genetically attenuated parasites (GA2) as compared to its early-arresting counterpart (GA1) against a controlled human malaria infection (CHMI). We found high level protection accompanied by potent circulating cellular memory responses, presumably against late liver stage antigens. So far, malaria vaccines have always been tested in regimens of three or more immunizations, but the necessity of multiple immunizations in inducing strong cellular response and high protective efficacy remains unknown. Encouraged by the previous results, we explored whether such responses and protection could also be induced after a single immunization. An effective simple regimen will facilitate vaccine implementation and will significantly reduce costs. To address this critical knowledge gap, we investigated the protective efficacy and cellular memory formation upon a single GA2-immunization administered through the bites of 50 GA2-infected mosquitoes in a randomized double-blind placebo-controlled clinical trial in healthy malaria-naive adults. By testing the preliminary efficacy of this simplified regimen with a homologous CHMI six weeks later, we found 9/10 GA2-immunized participants to be sterile protected, as compared to 0/5 mock-immunized participants (infectivity controls). GA2-immunized participants had a significantly higher frequency of *Pf*-specific polyfunctional CD4+ T cells than the controls within both central and effector memory compartments. This unprecedented 90% protective efficacy upon only one GA2-immunization shows the potency of cellular immune memory formed against GA2-derived late liver-stage antigens, further underlining their importance. Moreover, our study provides strong support for the further clinical development of malaria vaccines based on late-arresting genetically attenuated parasites.

6505

CHARACTERIZING THE SEROLOGICAL IGG REPERTOIRE OF TANZANIAN CHILDREN VACCINATED WITH NOVEL MALARIA BLOOD-STAGE CANDIDATE RH5.1/MATRIX-M ADJUVANT

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For the first time, malaria blood-stage vaccine antigen Reticulocyte Binding Protein Homologue 5 (RH5), a protein found on the surface of *Plasmodium falciparum* merozoites, has been tested in a Phase 1b clinical trial (NCT04318002). RH5 has the potential to provide superior protection compared to previous blood-stage vaccine candidates due to its low levels of polymorphism and role as an essential component of a non-redundant erythrocyte invasion pathway. Further, previously characterized anti-RH5 antibodies exhibit protective properties, such as the ability to inhibit parasite growth *in vitro*. The vaccine, consisting of an engineered RH5 variant termed RH5.1 (Draper Laboratory, Oxford) with Matrix-M™ adjuvant (Novavax), is designed to induce high, long-lasting, and protective antibody titers. In the trial, n=11 healthy Tanzanian children between 5-17 months old, a population susceptible to *P. falciparum* infection, were administered two monthly doses of 10 µg RH5.1 with 50 µg Matrix-M followed by a delayed booster dose six months following the first dose. The highest anti-RH5.1 titers observed in humans to date (median 723 µg/mL; range: 450-1436 µg/mL) were seen 14 days post-boost (Silk et al. 2024, *medRxiv*). Polyclonal IgG isolated from plasma also showed the highest level of functional GIA observed in humans to date following vaccination; all 11 children exhibited >60% GIA at 2.5 mg/mL (median 88%; range: 73-97%), a benchmark previously witnessed to predict blood-stage protection in *Aotus* monkeys (Douglas et al. 2015, *Cell Host Microbe*). To further examine the robust antibody response seen within this cohort, we completed high-throughput B cell receptor sequencing (BCR-Seq) alongside high-resolution, bottom-up tandem mass spectrometry (Ig-Seq) (n=3 donors). By cross-comparing the BCR- and Ig-Seq data sets, we determined the full-length VH and VL sequences of the most abundant circulating plasma IgG lineages in each individual child. The identified plasma lineages were subsequently expressed as recombinant monoclonal antibodies and functionally characterized for epitope specificity and *in vitro* parasite growth inhibition activity.

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VALIDATION OF CIRCULAR RNA VACCINE PLATFORM FOR MALARIA TRANSMISSION BLOCKING VACCINE

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Plasmodium vivax is a major malaria parasite that causes acute illness in millions of people each year. A vaccine that interrupts parasite transmission (transmission-blocking vaccine, TBV) will contribute to the elimination of malaria but no such vaccine has been approved to date. We have recently demonstrated that the nucleoside-modified mRNA formulated with lipid nanoparticle (mRNA-LNP) vaccine targeting a leading transmission blocking antigen of *P. vivax*, Pvs25, has ability to elicit long-lasting transmission-blocking immunity. A new vaccine platform using circular RNAs (circRNAs) to express target protein antigens has demonstrated improved stability, protein expression capacity and several advantages that facilitate its use as cost-effective vaccines. In this study, we developed and evaluated a lipid nanoparticle (LNP)-encapsulated circular Pvs25 RNA vaccine (circPvs25). *In vitro* protein protection and immunogenicity in mice of a circPvs25 vaccine was tested and compared with that of a linear nucleoside-modified Pvs25mRNA-LNP vaccine (linear Pvs25). The direct membrane feeding assay was utilized to assess the capacity of vaccine induced antibodies to block the parasite development in the mosquitoes. We observed similar levels of protein expression of our unpurified circPvs25 and purified linear PVS25 in Western blot, flow cytometry and immunofluorescence assays. Pvs25-reactive antibodies were induced by a single immunization of either circPvs25 or linear Pvs25. A booster immunization with the same vaccine significantly increased the Pvs25-specific antibody titer, and a higher antibody response was observed in circPvs25-circPvs25 homologous vaccination. Both homologous circPvs25 and homologous linear Pvs25 immunization showed strong transmission reducing activity with ability to completely block parasite development in mosquitoes and robust memory B cell and T cell responses. With the ability to induce complete transmission-blocking activity, the circPvs25 RNA vaccine holds a strong promise for further development/testing in non-human primates.

6507

A WHOLE ORGANISM *PLASMODIUM VIVAX* BLOOD STAGE VACCINE PARTIALLY PROTECTS AOTUS MONKEYS AGAINST A HOMOLOGOUS EXPERIMENTAL INFECTION

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Previous studies achieved sterile immunity in Aotus monkeys following two repeated exposures to Plasmodium vivax blood stages. This pilot study aimed to protect Aotus monkeys using a crude P. vivax whole organism antigen (pvWAg) adjuvanted with Al(OH)3, delivered intramuscularly (i.m.), in a prime-boost immunization scheme against a homologous challenge. Using a 47% Percoll cushion, the band (mostly trophozoites and schizonts) was washed with PBS, subjected to three cycles of freezing and thawing, and adsorbed onto $Al(OH)_3$ to obtain a concentration of 50 µg per 0.1 mL. Five Aotus monkeys were immunized i.m. three times in alternating thigh muscles with 50, 100, and 100 µg of the crude immunogen at 0, 2, and 5 weeks respectively, while one control received the adjuvant alone. Three weeks after the last immunization, all animals including a malaria-naïve infection control, were challenged intravenously (i.v.) with 50,000 parasites of the homologous *P. vivax* AMRU-1 strain. Parasitemias were monitored daily using the Earle & Perez (1932) method, and blood samples were collected pre-immunization and post-challenge to determine the antibody immune response by ELISA. After the challenge, all animals tested positive for infection between days 8 and 9 post-inoculation (PI). Parasitemia peaked in the control animal at 115.9 x 10^3/µL on day 15 PI. In contrast, immunized animals -except for one animal requiring treatment for high parasitemia (120.0 x 10^3/µL on day 14 PI)- exhibited 7-fold lower parasitemias (Mean ± sd = 16.1 x 10^3/µL on day 15 PI; n = 4) compared to the inoculation control. The total parasitemia area under the curve (AUC) excluding the non-responder, was 88.4 in the immunized group (n = 4) compared to 231.8 in the controls (n = 2) ($P<0.0001$; F test). Similarly, survival curves, with the endpoint being rescue treatment, were significantly different in the immunized group compared to the controls ($P=0.0254$; Gehan-Breslow-Wilcoxon test). This pilot study demonstrates that a crude pvWAg adjuvanted with Al(OH)3 provides partial protection in Aotus monkeys against a homologous P. vivax challenge.

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ACCEPTABILITY AND FEASIBILITY OF ADMINISTERING RTS,S/AS01 MALARIA VACCINE TO SCHOOL-AGED CHILDREN IN SOUTHERN MALAWI.

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School-age children (SAC) in sub-Saharan Africa have a significant malaria burden and are recognized as reservoirs for malaria transmission. We explored whether the RTS,S/AS01 malaria vaccine, which the WHO approved in 2021 for use in children under age five, could be feasibly and acceptably administered through schools to SAC. These data were collected as part of a clinical trial to assess the efficacy of the vaccine in preventing malaria morbidity in SAC. Qualitative data grounded within the Theoretical Framework of Acceptability were gathered and mapped onto seven domains: affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy. Using purposive sampling with maximum variation, we selected 116 participants (ages 10-71 years) to capture diverse perspectives in 16 focus group discussions: SAC (N=44), caregivers (N=40), community health workers (N=12), and Learner Treatment Kit teachers/dispensers (N=20). Framework analysis highlighted and interpreted key patterns within and across groups of participants and themes within the context of implementation. Results indicate that implementing the malaria vaccine in schools is highly acceptable and feasible due to accessibility, other school-based health programmes, and confidence to invite school-going siblings to participate. Most caregivers stated that the vaccine was aligned with their values, as fewer children reported being sick and absent from school. However, community members perceived high opportunity costs due to the deviation from daily routines for caregivers and SAC to access all three doses. Additional barriers affected demand and uptake included competing priorities and limited understanding of the purpose of the vaccine, as some expected it to eliminate malaria. Mixed feelings toward this vaccine also involve persistent misconceptions, misinformation, and conspiracy theories affecting uptake of the 2nd and 3rd doses. Addressing misinformation is important for optimal uptake, requiring multi-sectoral support and coordinated efforts of both Health and Education Ministries.

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IN-SILICO ANALYSIS OF *PLASMODIUM FALCIPARUM* SURFACE PROTEINS AND MONOCLONAL ANTIBODIES TO DESIGN MALARIA VACCINE

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Efforts to develop effective vaccines against *Plasmodium falciparum*, the deadliest malaria-causing parasite, have intensified with the aid of computational methods. This research focuses on utilizing in-silico analysis to explore the interactions between *Plasmodium falciparum* surface proteins and monoclonal antibodies (mAbs) as potential targets for vaccine development. Through comprehensive literature review and bioinformatics tools, twenty-three (23) key surface proteins of the parasite were identified, and their structural characteristics elucidated, even in instances where experimental structural data was unavailable. Concurrently, mAbs are computationally analyzed to assess their potential in recognizing and neutralizing these surface proteins. The resulting insights into the dynamics and stability of antibody-antigen interactions provide crucial understanding of immune responses essential for vaccine design. Integration of computational findings aids in the identification of promising vaccine candidates, which can subsequently undergo experimental validation for assessment of immunogenicity, safety, and efficacy. This study underscores the significance of computational approaches in accelerating the discovery and development of vaccines against malaria caused by *Plasmodium falciparum*, offering a promising avenue for combating this global health menace.

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ASSESSMENT OF PARENTAL/CAREGIVER PERCEPTION AND ACCEPTANCE OF THE MALARIA VACCINE IN A CONFLICT-AFFECTED REGION IN CAMEROON

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Malaria poses a significant challenge to public health in Cameroon, with an annual estimate of 2.7 million infections and 11,000 deaths. The development of the first malaria vaccine (RTS, S) and its subsequent pre-qualification by the WHO has provided an additional tool in the fight against this deadly disease. Consequently, African countries, including Cameroon, have expressed interest in integrating the vaccine into their standard immunization programs. In preparation for this rollout, evaluating the public's comprehension and willingness to accept this vaccine was essential. The Study employed a cross-sectional descriptive design involving 444 caregivers attending Infant Welfare Clinics. Data was collected over one month, and questionnaires were administered to those who consented to the study. Qualitative analysis using SPSS was done to have the most significant variables. Our study revealed that a significant % of caregivers (83.6%) were aware of the malaria vaccine, and half (54.5%) were willing to accept vaccination. It's important to note that caregivers, as key players in the vaccination process, were twice as likely to vaccinate their children in urban areas than their rural counterparts. However, this difference was not statistically significant. The findings underscore the importance of comprehensive information, education, and communication about the malaria vaccine before its implementation. This is particularly crucial in rural areas where vaccine hesitancy is prevalent. By implementing effective communication strategies, we can empower caregivers to make informed decisions for malaria vaccination, to sustainably reduce the malaria burden.

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PHASE 1A CLINICAL TRIAL OF SAFETY AND IMMUNOGENICITY OF RH5.1 AND R78C WITH MATRIX-M™ ADJUVANT IN UK ADULTS - A NOVEL COMBINATION VACCINE CANDIDATE AGAINST THE *PLASMODIUM FALCIPARUM* BLOOD-STAGE RH5-CYRPA-RIPR (RCR) INVASION COMPLEX

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The *Plasmodium falciparum* RH5-CyRPA-RIPR (RCR) hetero-trimeric invasion complex, part of a larger pentameric complex, is a highly conserved and essential blood-stage malaria vaccine target. A soluble protein vaccine candidate, called "RH5.1", targeting the full-length reticulocyte binding protein homologue 5 (RH5) component of the complex is the most advanced clinically, but RH5-interacting protein (RIPR)- and cysteine-rich protective antigen (CyRPA)-based vaccines have not previously been tested in clinical trials. Here we assessed "R78C", a new soluble protein antigen comprising RIPR EGF domains 7-8 fused to CyRPA, alone and combined with RH5.1, formulated with Matrix-M™ adjuvant, in a first-in-human Phase 1a trial. Healthy, malaria-naïve UK adults (N=32) were recruited into four groups: i) 10 µg RH5.1 alone, or ii) 10 µg R78C alone in a delayed (0-1-6 month) vaccination regimen; iii) the combination of 10 µg R78C admixed with 10 µg RH5.1 in a delayed (0-1-6 month) regimen; or iv) the combination of 10 µg R78C and 10 µg RH5.1 with both proteins admixed for the first two doses (at 0-1 months) and with the third and final doses given separately at 6 and 7 months. All vaccinations were given with 50 µg Matrix-M™ adjuvant. Vaccinations to-date (April 2024) have been well tolerated with no safety concerns. The most commonly reported adverse events (AEs) were injection site pain and fatigue. Solicited AEs were generally mild-moderate in severity and all spontaneously resolved within 7 days. Functional immunogenicity is being assessed via the growth inhibition activity (GIA) assay, and IgG titres to the individual antigens and to the RCR-complex are being assessed by ELISA and these data will be presented. RH5.1 formulated with Matrix-M™ has shown clinically significant efficacy against clinical malaria in a Phase 2b field trial as a standalone blood-stage vaccine. Initial immunogenicity data from this trial suggest that the combination of R78C and RH5.1 may induce a superior antibody response (as compared to RH5.1 alone) and support onward clinical testing. A Phase 1b trial is planned to start in Tanzania in April 2024 with a Phase 2b trial in 2025.

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PRE-CLINICAL AND CLINICAL EFFICACY OF ATTENUATED AND KILLED WHOLE PARASITE MALARIA BLOOD STAGE VACCINES TO LIMIT DISEASE

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Subunit vaccines against the blood stages of malaria have shown limited efficacy. All candidates have aimed to induce antibodies to interfere with merozoite invasion. Polymorphism of B-cell epitopes is the major obstacle. We have championed a different approach, relying on the entire antigenic

composition of the parasite delivered in a way to maximize induction of cellular immunity. Our first candidate consisted of ring-stage parasitized red cells attenuated using seco-cyclopropyl pyrroloindole analogs. These induced strong clinical and parasitological immunity to different rodent parasites. A clinical trial involving malaria-naive adult volunteers vaccinated using chemically attenuated magnet-purified *Plasmodium falciparum*-parasitized red cells was undertaken. We have now shown that vaccination leads to strong cellular responses involving Th1 and Th2 cytokine-secreting T-cells. We screened antibody responses to randomly chosen antigenic fragments of 271 PfEMP1 and 78 other blood stage antigens and observed baseline responses to the vast majority of antigens. Two volunteers were completely protected from a blood stage challenge infection with no parasites detected by PCR. This proof-of-principle study laid the groundwork for a whole parasite vaccine in which the parasite antigens were frozen prior to admixing with a liposomal adjuvant, CAF01. Pre-clinical work using the *P. yoelii* model demonstrated long-lived protection against clinical disease and parasite burden (>9 months in mice) with induction of Th1 and regulatory cytokines. CD4+ T-cells were critical. Infection post-vaccination strongly boosted clinical and parasitological protection. Vaccine-induced protection was also augmented by prior infection. In advance of moving to a clinical trial, we modified this vaccine to block induction of antibodies to human red cells using methoxy polyethylene glycol (mPEG) treatment of *P. falciparum*-parasitized magnet-purified red cells. mPEG treatment did not reduce vaccine efficacy in a *P. yoelii* model. The vaccine has now completed formal toxicological evaluation with no adverse findings. The trial will commence in Q3 2024.

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IN SILICO EVALUATION OF PREDICTED *PLASMODIUM FALCIPARUM* EPITOPES IN LEADING VACCINE CANDIDATE ANTIGENS

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Plasmodium falciparum is the most lethal and common human malaria parasite. Epitope-based vaccines could overcome existing limitations of currently recommended malaria vaccines by targeting conserved and immunogenic regions within multiple discrete antigens presented in pre-erythrocytic, erythrocytic, and sexual stages. We hypothesize that *in silico* tools can incorporate parasite protein diversity and host HLA allele frequency data to identify and rank multiple predicted epitopes. Through literature review, 42 malaria proteins were identified as nonredundant, conserved, and essential for either hepatocyte or erythrocyte invasion or transmission, making them ideal targets for a multistage malaria vaccine. Using leading vaccine candidate protein sequence datasets constructed from *P. falciparum* samples collected in highly endemic areas, we predicted and evaluated epitopes with high affinity for regional HLA alleles. After performing quality control filtering and sequence clustering, we used NetMHCpan to predict CD4+ and CD8+ T-cell epitopes. To score and rank epitopes, we developed a heuristic-based weighting model integrating the following: 1) predicted binding affinities between epitopes and MHC receptors, 2) HLA allele frequency in endemic regions, and 3) sequence conservation. By characterizing predicted epitope distribution across the protein and comparing results to peptide regions with positive or negative immunogenicity and low or high HLA restriction by *in vitro* and *in vivo* assays, we validated weighting model performance in assigning epitope scores. As a proof of principle, we first examined epitopes within the most studied vaccine candidate, circumsporozoite protein (CSP). Our model scored CSP epitopes in multiple conserved and HLA-nonspecific regions as strong candidates with positive immunogenicity, validating the methodology. We plan to refine this model and continue in-depth analyses of predicted and ranked epitopes for the remaining protein candidates to ultimately contribute towards the design of a multistage, multiepitope vaccine for preclinical evaluation.

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INNOVATIONS IN MALARIA VACCINE DEVELOPMENT PROGRAM (IMV)

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The Innovations in Malaria Vaccine Development (IMV) contract is designed to solve key underlying challenges in the preclinical development and clinical evaluation of next-generation *Plasmodium falciparum* malaria vaccines. The IMV contract is funded by the U.S. Agency for International Development and implemented by PATH and sub-partners. A core strategy of all IMV projects is to identify and advance next-generation malaria vaccine candidates that will induce more potent and durable immune responses interfering with critical steps in the parasite life cycle—namely, the infection of hepatocytes and progression to asexual blood-stage infection. By focusing on the potency of immune responses, IMV projects aim to increase the durability of protection of future vaccines—an important limitation of the first-generation vaccines RTS,S/AS01 and R21/Matrix-M. The IMV program consists of three workstreams: the circumsporozoite protein (CS) workstream; the blood stage (BS) workstream, focused on RH5 and other antigens in the RH5 complex; and the combination (CS+BS) workstream, exploring the preclinical and clinical challenges and opportunities of combining CS and BS vaccines. With an international consortium, including Johns Hopkins University, Scripps Research, the Statens Serum Institut, the University of Oxford, and the University of Texas at Austin, along with USAID government partners the National Institute of Allergy and Infectious Diseases, the Naval Medical Research Command, and the Walter Reed Army Institute of Research, the IMV program is making progress in all three workstreams. Important milestones include establishing RTS,S as a benchmark in a preclinical model of malaria infection, now available for comparison testing of novel CS-based vaccine candidates, and evaluating a particle-based RH5-based BS vaccine candidate in a Phase 1 clinical trial. We will present an overview of key accomplishments, platforms of interest (such as mRNA-LNP and other nanoparticles), lessons learned, and future directions. We will also highlight IMV-funded work being presented at ASTMH 2024 and in scientific literature.

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HEALTH SYSTEMS CAPACITY STRENGTHENING FOR MENINGITIS SURVEILLANCE AND SAFETY SIGNALS MONITORING: LESSONS FROM THE RTSS/AS01 MALARIA VACCINE PILOT EVALUATION IN GHANA

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Meningitis constitutes a major public health burden and presents a diagnostic challenge for many resource-limited health systems. It accounts for over 5 million new cases and about 300,000 annual deaths mainly among children under 5 years. Survivors may suffer lifelong neurological and hearing impairment. Based on safety signals observed from the pivotal phase III trial of RTSS malaria vaccine, there was the need for enhanced meningitis surveillance and monitoring of these safety signals during the WHO led malaria vaccine implementation (MVIP) in routine health systems in Ghana. Baseline capacity assessment was carried out involving 20 referral Hospitals within 6 regions in Ghana prior to the MVIP. Eight (8)

hospitals serving both vaccine implementing and comparator districts were selected as sentinel hospitals for the safety cohort event monitoring using standardized questionnaire deployed on digital surveillance platform. Trial interventions were implemented based on identified gaps and their impact on meningitis surveillance and cerebral malaria were evaluated. Prior to the MVIP in 2019, baseline lumbar puncture (LP) rate among eligible children was 0.25% across assessed hospitals. The underlying reasons for the low LP rates included limited health worker capacity to perform LPs, few paediatricians and medical officers, inadequate laboratory equipment and reagents to process and analyse cerebrospinal fluid samples and lack of motivation to perform LPs. The interventions instituted included regular refresher trainings on LPs, health worker incentives, supportive supervision and monitoring, supply of reagents and logistics and incorporation of a meningitis alert algorithm into the digital platform for early notification to perform LPs. We observed a significant increase in LP rate from 0.25% at baseline to 78% as at December, 2022 for all eligible children. Sustained health systems strengthening is key for effective meningitis surveillance in routine health facilities. Lessons learnt during the vaccine implementation have implications for future safety events monitoring in health systems in Ghana.

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CHARACTERIZATION OF THE IMMUNE RESPONSES INDUCED BY THE *PLASMODIUM FALCIPARUM* BLOOD-STAGE VACCINE CANDIDATE, RH5.1/MATRIX M™, IN A PHASE IIB TRIAL IN BURKINABE 5-17MONTH OLDS

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There are promising advances in vaccines against *Plasmodium falciparum* (*Pf*) malaria, with both R21/Matrix-M™ and RTS,S/AS01 now licenced. However, these vaccines are only partially effective against clinical malaria and induce no blood-stage immunity to neutralise parasites that may emerge from the liver. Development of an effective blood-stage malaria vaccine therefore remains crucial for a future multi-stage vaccine approach. The reticulocyte-binding protein homologue 5 (RH5) is essential for erythrocyte invasion, has limited polymorphism, and antibodies induced by RH5 have demonstrated *in vivo* efficacy against blood-stage malaria challenge in non-human primates (NHPs). This protection has been strongly correlated with anti-RH5 serum IgG antibody concentration and *in vitro* functional growth inhibition activity (GIA), requiring a threshold of >60% GIA at 2.5mg/mL purified total IgG for protection. In a Phase Ib trial in Tanzania (NCT04318002), assessing full-length recombinant protein RH5 (RH5.1) with Matrix-M™ (MM) adjuvant in 5-17month old children, we reported the highest levels of GIA in human participants to date, now above the defined correlate of protection in NHPs. We therefore progressed to a Phase IIb, double-blinded, block randomised, controlled trial (NCT05790889) in Siglé, an area of seasonal transmission, in Burkina Faso, to assess safety, efficacy and immunogenicity of RH5.1/MM. A total of 360 5-17month olds were randomized to receive 3x 10 µg doses of RH5.1 with 50µg MM (2 groups of N=120 children, in a 0-1-2 month or a delayed 0-1-5 month regimen) or 3x doses of the rabies vaccine, Rabivax-S (2 groups of N=60 children, in a 0-1-2 or 0-1-5 month regimen). Type of vaccine delivery system, regimen and demographic characteristics of vaccinees have been shown to have substantial impact on anti-RH5 immune responses in studies to date. Here, we report the effects of monthly vs delayed third dose regimen on humoral response magnitude, quality and durability, as well as functional GIA assessment of antibody responses in the first opportunity for correlation with clinical malaria outcome for RH5-based vaccines.

6517

CREATING SUPERIOR PFSPZ VACCINES FOR MALARIA BY GENETICALLY CROSSING WEST AND EAST AFRICAN *PLASMODIUM FALCIPARUM* TO PRODUCE PFSPZ WITH GREATER ANTIGENIC DIVERSITY AND POTENCY

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Plasmodium falciparum sporozoite (PfSPZ) vaccines are the only malaria vaccines to have 100% vaccine efficacy (VE) against heterologous CHMI, sustained VE for 2 transmission seasons in Africa without boosting, and VE against highly divergent Pf in Papua, Indonesia. PfSPZ vaccines are based on a W. African isolate, NF54. Their VE is primarily mediated by cellular immunity against potentially 1000's of protective CD8+ T cell epitopes expressed in the Pf liver stage. Target epitopes vary among Pf isolates and genetic divergence from NF54 increases with geographic distance from W. Africa. Furthermore, NF54 SPZ do not invade/develop in hepatocytes as well as other Pf strains, thereby limiting immunogenic potency. To enhance VE against divergent Pf, an approach is to mix PfSPZ from parasites from different geographic regions. However, the 5-10x fewer PfSPZ/mosquito produced by other Pf strains relative to NF54 makes this approach cost prohibitive. We hypothesized that by genetically crossing strains of Pf from E. Africa with NF54, we could produce a hybrid parasite that made as many PfSPZ as NF54, had greater invasion/development in hepatocytes than NF54, and by having critical epitopes from both parental strains, would have better VE against E. African Pf than PfSPZ (NF54) without losing VE against W. African Pf. Thus, we generated pan African hybrids by crossing NF54 with 3 E. African Pf strains (MAL31 Malawi, NF165 Malawi and HL1209 S. Sudan). All 3 crosses gave rise to PfSPZ which transitioned through humanized FRG huHep mice and RBC stage parasites were cloned resulting in 60, 31 and 17 clones respectively. We then selected hybrids that 1) had a balanced representation of a) both parental genomes, b) genes implicated in protective immunity that were highly transcribed in PfSPZ and liver stages; 2) produced high numbers of PfSPZ; and 3) developed in hepatocytes better than NF54. This resulted in identification of 2 pan African recombinant hybrids, AV27 & AVD7, that met all criteria. We are creating late arresting replication competent parasites, PfSPZ-LARC2 (AV27 & AVD7), by deleting genes for *Mei2* and *LINUP*, and plan GMP production and clinical trials.

6518

IMPLEMENTATION COSTS OF A SCHOOL-BASED RTS,S/AS01 MALARIA VACCINATION PROGRAM IN MALAWI

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Costs are increasingly considered key outcomes in implementation research given their importance in informing health intervention programmatic decisions. We assessed implementation costs of a school-based RTS,S/AS01 vaccination program piggybacked on a trial assessing the effects of vaccinating school-aged children in 5 primary schools in Malawi. In the trial, learners aged 6 to 16 years received 3 doses of RTS,S/AS01 vaccines administered by health workers at monthly intervals. The present study

objectives were to estimate the total start-up and post start-up costs for the school-based RTS,S/AS01 vaccination program, cost per fully vaccinated learner and project total costs of implementing the program at national level. We adopted a provider perspective, combining Ministry of Health and Ministry of Education perspectives. Micro-costing approach was used to identify, quantify and value resources used for the main strategy activities including micro-planning, training of health workers, community mobilization and sensitization, procurement and delivery of RTSS vaccines. Trial related costs were precluded. The total costs for the school-based RTS,S/AS01 vaccination program were $23,141. Of this, $7,846 (34%) were incurred during the start-up phase. During this phase, community mobilization and sensitization, health worker trainings, briefings of health facility and district executive members were the main cost drivers accounting for 52, 27 and 8% of the cost, respectively. For the post-start-up phase, RTSS vaccines and supplies, health worker allowances and supervision were the main cost drivers accounting for 79, 16 and 5% of the costs, respectively. The average costs per learner with 1, 2 and 3 RTS,S/AS01 doses (fully vaccinated) were $11.72, $13.51 and $14.75, respectively. [Work is ongoing to extrapolate costs at national level]. School-based RTSS malaria vaccine delivery strategy appears a low cost intervention to implement and may be affordable at scale. Implementation strategy re-configuration focusing on cost driving activities has the potential to improve efficiencies and further lower implementation costs.

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RHESUS MODELS FOR PRE-ERYTHROCYTIC STAGE SPOROZOITE VACCINES AGAINST MALARIA

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There are no animal models or *in vitro* assays that indicate a human will be protected against malaria by a pre-erythrocytic stage sporozoite(SPZ) vaccine. Based on murine models, the prevailing hypothesis is that protective immunity is mediated by antigen specific, tissue resident CD8+ T cells in the liver. This hypothesis correlated well when CD8+ T cell responses in the livers of rhesus macaques immunized IV or subcutaneously with *Plasmodium falciparum* (Pf) SPZ were compared with clinical efficacy of PfSPZ Vaccine administered by these routes. We performed protective efficacy studies in rhesus macaques with vialed, cryopreserved *P. knowlesi* (Pk) SPZ administered IV, to develop a reliable model to interrogate protective immunity in the liver that cannot be addressed in humans. In the 1st study with irradiated PkSPZ we achieved 66% (4/6) sterile protection at 8 weeks after last vaccination (3 doses of 10^6 PkSPZ), and a significant difference compared to controls in pre-patent period in non-protected macaques. The 2nd and 3rd studies used infectious PkSPZ co-administered with chloroquine (PkSPZ-CVac [CQ]), that provides increased breadth and magnitude of protective antigens since the parasite replicates in the host, but is arrested in the blood. In these studies, we achieved sterile protection of 50% (3/6) at 13 weeks (3 doses of $2x10^5$ PkSPZ) and 60% (3/5) at 12 weeks (3 doses of $4x10^5$ PkSPZ) after last immunization and a significant delay in pre-patency in unprotected animals. In the 4th study, we immunized with a Pf vaccine, PfSPZ-LARC2 which overcomes the logistic limitations of administering chloroquine with PfSPZ-CVac and there was no cross-species protection against challenge with PkSPZ. These data demonstrate it is more difficult to achieve high-level protection with PkSPZ immunization in rhesus than with PfSPZ Vaccine or PfSPZ-CVac (CQ) in humans, with the latter demonstrating 100% vaccine efficacy at 10-12 weeks with 3 doses of $5x10^4$ to $2x10^5$ PfSPZ. The reasons for this and the results of systems immunology/serology assessments of the sera, PBMCs, and lymphocytes from the liver and spleen will be presented.

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PFSPZ VACCINE ELICITS PFCSP ANTIBODIES THAT CROSS-REACT WITH OTHER *PLASMODIUM FALCIPARUM* PROTEINS AND CORRELATE WITH PROTECTION FROM MALARIA

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Two WHO-approved malaria vaccines, RTS,S and R21, are subunit vaccines containing a fragment of the *Plasmodium falciparum* (Pf) circumsporozoite protein (CSP). Such vaccines mediate protection at the liver stage of infection that wanes over time. Enhancing the breadth of vaccine-induced immunity may improve efficacy and durability of next-generation vaccines. PfSPZ Vaccine is comprised of live, attenuated sporozoites, presents thousands of Pf proteins in addition to PfCSP, and has also been shown to be protective at the liver stage of infection. We conducted parallel seroprofiling studies of PfSPZ Vaccine-induced antibody responses in 3 clinical trials of PfSPZ Vaccine on (1) whole protein and (2) linear peptide microarrays. We tested baseline and post-vaccination sera from a subset of 42 malaria naïve participants: all received 3 or 4 doses of PfSPZ Vaccine followed by controlled human malaria infection (CHMI) three weeks later. Following vaccination and CHMI, 29 vaccinees demonstrated sterile protection. Protein and peptide microarrays identified 22 and 75 immunoreactive proteins respectively and a common subset of 5 proteins for which antibody responses were higher in protected vs. not-protected vaccinees: CLAMP (PF3D7_1030200), MSP5 (PF3D7_0206900), DOC2 (PF3D7_1211200), GSK3 (PF3D7_0312400), and an uncharacterized protein (PF3D7_0720500). Peptide sequences associated with differential antibody responses were found to have sequence homology with PfCSP. Two PfCSP-binding monoclonal antibodies, mAb4 and mAb10, also bound the same 5 proteins and putative epitopes, suggesting that some antibody responses to PfSPZ Vaccine elicited by PfCSP are cross-reactive with multiple other Pf proteins. Hierarchical clustering grouped cross-reactive responses into high and low groups with a higher proportion of protected vaccinees clustering into the high group. This work highlights the importance of considering the possibility of broadly cross-reactive antibodies in seroprofiling studies and demonstrates a correlation between broad seroreactivity and vaccine efficacy.

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RESULTS FROM A PHASE III STUDY TO ASSESS THE SAFETY, IMMUNE RESPONSE, AND LOT-TO-LOT CONSISTENCY OF EUTCV SINGLE-DOSE AND MULTI-DOSE FORMULATION COMPARED TO THE COMPARATOR VACCINE TYPBAR-TCV® IN HEALTHY AFRICAN ADULTS AND YOUNG CHILDREN 6 MONTHS TO 45 YEARS OF AGE

Birahim Pierre Ndiaye[1], Lucy Koech[2], Ndeye Sakha Bob[3], Niles Eaton[4], Winnie Keter[2], Siry Diye[1], Badara Cissé[1], Vajra Allan[4], Yeong Ok Baik[5], Chankyu Lee[5], Howard Her[5], Sookyung Kim[5], YoungJin Choi[5], Moussa Dia[6], Emily Locke[7], Gamou Fall[6], John J. Aponte[8], **Patricia Njuguna**[9]

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Typhoid fever remains an important public health problem, especially in low- and middle-income countries (LMICs). Safe water, sanitation, and hygiene (WASH) interventions alongside vaccines play a vital role in preventing the spread of typhoid. Two conjugate vaccines against *Salmonella enterica* serovar Typhi (*S*. typhi), which have been administered to millions of children and shown to be safely co-administered with other routine childhood vaccines, have been prequalified by the World Health Organization (WHO). Previous studies demonstrated the comparable safety and reasonable immunogenicity of a third vaccine, EuTCV (EuBiologics Co. Ltd.), relative to other typhoid conjugate vaccines when delivered as a single dose. This Phase III study (PACTR202112680671189), conducted at IRESSEF at Sandiara, Senegal, and KEMRI/WRP at Kericho, Kenya, enrolled 3,219 healthy African adults and young children 6 months to 45 years of age to assess the safety, immune responses, and lot-to-lot consistency of EuTCV single-dose and multi-dose presentations. Measles-rubella and yellow fever vaccines were co-administered to infants aged 9 to 12 months (Cohort 3, n=1,012), alongside the typhoid conjugate vaccine. The objectives of the study were to evaluate: i) non-inferiority of single-dose and multi-dose vial formulations of EuTCV compared with Typbar TCV® at 28 days post-vaccination in Cohort 3 and ii) the safety of single-dose and multi-dose vial formulations of EuTCV compared to that of Typbar TCV® in all participants. Throughout the study, all participants were followed for safety, with reporting on local and systemic adverse reactions 7 days post-vaccination, unsolicited adverse events 28 days post-vaccination, and serious adverse events during the entire study period until Day 181. In Cohort 3, immunogenicity assessments included typhoid (anti-Vi polysaccharide geometric mean titer and seroconversion rates 28 days and 6 months post-vaccination) and seroconversion rates following measles, rubella, and yellow fever vaccination. We report the results of this Phase III study which will be submitted as part of the PQ dossier.

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MOLECULAR CHARACTERIZATION OF MULTIDRUG RESISTANCE *E.COLI* RECOVERED FROM DIARRHEAGENIC CHILDREN UNDER FIVE YEARS FROM MUKURU INFORMAL SETTLEMENT, NAIROBI, KENYA, BASED ON WGS ANALYSIS

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High genomic plasticity within *E. coli* enables it to acquire and accumulate genetic material through horizontal gene transfer. In this study, we sought to investigate the virulence genes, phylogroups, antibiotic resistance genes, plasmid replicons, MLST, and cgMLST of multidrug-resistant E.coli recovered from diarrheagenic children under five years from Mukuru Informal Settlement, Nairobi Kenya. A total of 26 MDR strains had their DNA extracted, and Whole Genome Sequencing was done using the Illumina HiSeq 2500 platform. Twenty-six *E.coli* assemblies were analyzed using web-based bioinformatics tools at the Centre for Genomic Epidemiology and EnteroBase. The isolates were categorized into four main phylogroups, where 10/26 (38.5%) belonged to the B2 phylogroup, 4/26 (15.4%) belonged to D, 3/26 (11.5%) belonged to A, 1/26 (3.8%) belonged to B1, while 8/26 (30.8%) were not determined. FimH30 was predominantly found in the most frequent phylogroup B2 and Sequence Type(ST) 131. The most common Beta-lactam resistance genes were $bla_{\text{Tem 1B}}$ and $bla_{\text{CTXM 15}}$, followed by fluoroquinolone resistance genes (*qnrS1* 6/26(23.1%), *qnrB4* 2/26 (7.7%), and *aac(6')-Ib-cr,* 8/26(30.8%)). A total of 40 diverse virulence genes were detected among the isolates. 13 different STs were isolated from the *E. coli* genomes, which included ST 131, ST 3036, ST 38, ST 10, ST 12569, ST 15271, ST 2076, ST 311, ST 3572, ST 394, ST 453, ST 46 and ST 1722. Only two isolates (2/26, 7.7%) from the Municipal City Council (MCC) clinic were genetically related. Additionally, the most abundant plasmid replicon identified belonged to the IncF family followed by the Col family. Of 26 isolates, 15 had at least one nonsynonymous mutation in the housekeeping genes *gyrA (p.S83L), gyrA (p.D87N), parC (p.S80I), parC (p.E84V), parC(p.S57T),* and *parE(p.I529L),* associated with resistance to fluoroquinolones. The study highlighted the first *E.coli* ST46 to harbor the *NDM5* gene encoded in Col(BS512), IncFII(pRSB107), and IncFIB(AP001918) plasmid replicons in Kenya. We further demonstrated the diversity of MDR *E. coli* associated with diarrhea in an endemic setting in Kenya.

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ASSOCIATION OF GUT REDOX POTENTIAL WITH SEVERE ACUTE MALNUTRITION AND STUNTING IN HOSPITALIZED CHILDREN

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Redox potential is a composite measurement of factors influencing gut microbiota. Secretion of reactive oxygen species from gut epithelium in response to intestinal injury, chronic infections and inflammation increases gut redox potential. This imposes 'oxidative stress' leading to gut dysbiosis characterized by decline in beneficial microbes like *Bifidobacterium* accompanied by increase in aerotolerant pathogens like *Enterobacteriaceae*, resulting in diarrhea and malnutrition. Furthermore malnutrition, specifically severe acute malnutrition (SAM), is associated with inadequate intake of energy as well as qualitative lack of micronutrients leading to low antioxidant levels, again increasing gut redox potential and oxidative stress. This altered redox dynamics and invasion by aerotolerant bacterial pathogens highlight the need for antibiotics that further promote gut dysbiosis. This creates a vicious cycle of oxidative stress, gut dysbiosis and malnutrition. In this study, we aimed to explore the association of gut redox potential with malnutrition among 6-24 months old hospitalized children. This cross-sectional study was conducted on 200 children aged between 06-24 months getting admitted in icddr,b Dhaka Hospital and Dhaka Shishu Hospital. 50 of these children had weight-for-length Z scores (WLZ) <-3, and were considered as the SAM group. Anthropometric, socio-demographic and food frequency questionnaire data was recorded and 2g of stool was collected for assessing gut redox potential using redox meter. The mean gut redox potential for stunted and SAM children was 183.92±22.36 and 191.68±25.98; while the same for non-stunted and non-SAM children was 178.11±24.75 and 175.91±22.23, respectively. After inclusion of factors affecting malnutrition into the multivariate linear regression model, a statistically significant association was observed between gut redox potential and SAM ($p<0.05$; OR 1.02; 95% CI 1.01-1.05). The mean gut redox potential was higher in stunted children and significantly higher in children suffering from SAM. Increased gut redox potential was found to have a significant association with SAM.

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GENOTYPIC DIVERSITY AND ANTIMICROBIAL RESISTANCE DETERMINANTS *IN SALMONELLA* TYPHI ISOLATED FROM CHILDREN LIVING IN INFORMAL SETTLEMENTS IN NAIROBI, KENYA

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Whole genome sequencing (WGS) is a tool for disease diagnostics and identification of multi-drug resistant genotypes of enteric pathogens globally. In typhoid-endemic regions, WGS of *Salmonella* Typhi (*S*. Typhi) has identified haplotype 58 as one of the dominant MDR haplogroups. This case-control study reported on AMR and genotypic diversity of *S*. Typhi from children in Mukuru and Kibera informal settlements. From 2013 to 2018, children ≤ 16 years in 4 health facilities in Nairobi County were recruited if they had a fever; $\geq 38^0$C with or without diarrhea. Controls were recruited if they came for vaccinations and presented with non-typhoid-related symptoms. All participants provided stool samples that were

subjected to culture and antimicrobial susceptibility testing for phenotypic analysis of AMR. *S*. Typhi isolates that showed resistance to ampicillin, co-trimoxazole, and chloramphenicol were considered as MDR and subjected to WGS. DNA of 90 *S*. Typhi was extracted for WGS. Sequencing was done using Illumina Nextseq2000 platform. The raw reads were *de novo* assembled and pathogen-watch was used for analysis. Of the sequenced isolates, 60(67%) were confirmed to be *S*. Typhi. All of the *S*. Typhi belonged to the sequence Type 1 and genotype 4.3.1 (Haplotype 58). Out of the 60 *S*. Typhi strains 40(67%) were found to have plasmids, out of which 38(95%) had the IncHI1A/IncHI1B (R27) plasmids. The distribution of *S*. Typhi in cases and controls was; 31(51%) and 30(49%). The 60 *S*. Typhi isolates were observed to have AMR determinants of 6 antibiotics with ampicillin (*bla TEM-1D*) as the most common; 59 (98%) of the isolates. Point mutations conferring reduced susceptibility to quinolones were detected in 42 (70%) of *S*. Typhi isolates, 14(33%) *gyrA_S83Y*, and 28/42 (67%) *gyrB_S464F*.This study reports 4.3.1 (H58) as the most dominant *S*. Typhi genotype. It is evident that H58 is responsible for the spread of MDR phenotypes that carry on IncHI1 plasmids. Circulation of H58 *S*. Typhi genotypes in Mukuru and Kibera informal settlements especially among asymptomatic individuals reiterates the need for mass vaccination as a control and prevention measure of Typhoid fever.

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SEROCONVERSION AND KINETICS OF VIBRIOCIDAL ANTIBODIES DURING THE FIRST 90 DAYS OF RE-VACCINATION WITH ORAL CHOLERA VACCINE IN AN ENDEMIC POPULATION

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Despite the successful introduction of oral cholera vaccines, Zambia continues to experience multiple, sporadic, and protracted cholera outbreaks in various parts of the country. While vaccines have been useful in staying the cholera outbreaks, the ideal window for re-vaccinating individual's resident in cholera hotspot areas remains unclear. Using a prospective cohort study design, 225 individuals were enrolled, re-vaccinated with two doses of Shanchol™ regardless of previous vaccination and followed-up for 90 days. Bloods collected at baseline before re-vaccination, at day 14 prior to second dosing and subsequently on days 28, 60, and 90. Vibriocidal assay was performed on samples collected at all five time points. Our results showed that anti-LPS and vibriocidal antibody titers increased at day 14 after re-vaccination and decreased gradually at 28, 60 and 90 across all the groups. Seroconversion rates were generally comparable in all treatment arms. We therefore conclude that vibriocidal antibody titers generated in response to re-vaccination still wane quickly irrespective of previous vaccination status. However, despite the observed decline, the levels of vibriocidal antibodies remained elevated over baseline values across all groups, an important aspect for Zambia where there is no empirical evidence as to the ideal time for re-vaccination.

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ETIOLOGY OF DIARRHEAL DISEASE CAUSING SEVERE DEHYDRATION IN INFANTS AND YOUNG CHILDREN RESIDING IN LOW AND MIDDLE INCOME COUNTRIES

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Acute infectious diarrhea remains a leading cause of death among young children, especially in low- and middle-income countries (LMICs). Given the limitations of available diagnostic testing in LMICs, a clinical syndrome or case definition frequently informs pediatric diarrheal illness management. Diarrhea with severe dehydration is a clinical syndrome with distinct clinical management per the World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) and the Global Task Force on Cholera Control (GTFCC) guidelines. We sought to characterize the pathogens in this group specifically using data from the Global Enteric Multicenter Study (GEMS). GEMS was a three-year prospective, case-control study of children aged 0-59 months with moderate-to-severe diarrhea (MSD) at seven sites in sub-Saharan Africa and South Asia. We used quantitative real-time PCR-based (qPCR) majority attribution models to assign the etiology of diarrhea as well as both IMCI and GTFCC guidelines to define severe dehydration. Among the 5304 cases of MSD with qPCR results, the IMCI or GTFCC guidelines classified 2,284 (43%) of the cases as having severe dehydration. Approximately one third of the cases with severe dehydration did not have any attributable pathogens (33% for the IMCI definition, 35% GTFCC). Pathogens attributed to severely dehydrated cases of diarrhea varied by age group. Rotavirus (30.9%), *Cryptosporidium* (12.0%), and ST-ETEC (10.3%) were the top pathogens for ages 0-11 months compared to *Shigella* (25.8%), rotavirus (19.3%), and ST-ETEC (10.3%) for those ages 12-23 months and *Shigella* (25.9%), *V. cholerae* (10.4%), and rotavirus (9.2%) for those ages 2-5 years. Most of the top pathogens attributed to severe dehydration were similar to those attributed to MSD for each age group. However, several pathogens, notably adenovirus and *H. pylori* were less frequently attributed to severe dehydrating MSD than to MSD overall. Vaccine and treatment advances should be targeted at pathogens associated with severe dehydration, given the potential morbidity caused by severe dehydration.

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ANTIRADICAL SCAVENGING AND UREASE INHIBITION POTENTIALS OF *DICTYOPHLEBA SETOSA* (APOCYNACEAE) AND ISOLATION OF ITS CHEMICAL CONSTITUENTS TOWARDS MANAGEMENT OF GASTRIC AND PEPTIC ULCERS CAUSED BY *HELICOBACTER PYLORI* ACTIVITIES

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This study is design to determine the antiradical scavenging and Urease inhibition potentials of *Dictyophleba setosa*, a medicinal liana native to central Africa used traditional as a vermifuge in children, as an alternative to manage peptic and gastric ulcers. The antiradical potentials of the DCM/MeOH crude extracts of the leaves (DSL), stem bark (DSS) and roots (DSR) of *Dictyophleba setosa* were determined by five different complementary methods (DPPH, CUPRAC, $ABTS^{\bullet+}$, metal chelating and β-carotene-linoleic acid assays). DSS showed to be a more powerful antioxidant compared to the standards BHA and α-tocopherol in the $DPPH^{\bullet}$, $ABTS^{\bullet+}$ and CUPRAC assays. That is, DSS (IC_{50} = 7.13 ± 0.21; IC_{50} =5.22 ± 0.53; IC_{50} =5.80 ± 0.12 µg/mL) respectively is at least 5 times more active than α-tocopherol and at least 2 times more active than BHA (IC_{50} = 19.82 ± 0.33; IC_{50} = 12.80 ± 0.08; IC_{50} = 25.50 ± 0.43 µg/mL) respectively. The urease enzyme

inhibition potentials of extracts carried out by determination of the amount of ammonia produced using the Indophenol method displayed IC_{50} values ranging from 30.48 ± 0.62 to 11.23 ± 0.38 µg/mL compared to Thiourea (IC_{50} = 8.15 ± 0.33 µg/mL) as standard among which DSS was the most potent. Purification of DSS using standard chromatographic techniques led to the isolation of fifteen secondary metabolites whose structures were elucidated by analysis of their spectroscopic data, three of which are reported for the first time. The isolates will be further evaluated for their urease enzyme inhibitory activity. These findings clearly indicate that the stem bark extract of *Dictyophleba setosa* can be used in the traditional pharmacopeia to prevent/manage gastric and peptic ulcers by inhibition of urease enzyme produced by *Helicobacter pylori.*

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PREVENTION AND MANAGEMENT OF TRAVELERS' DIARRHEA IN AN INTERNATIONAL WORKER IN GLOBAL OIL AND GAS COMPANY

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According to CDC, Travelers' diarrhea (TD) occurs in 30%-70% of travelers during a 2-week travel period, depending on the destination and season of travel. ExxonMobil (EM) has a global workforce with both short and long-term international travelers to areas with varied risks throughout the year. TD interferes with travel itineraries and business prospects, causing loss in productivity from absences. There may be significant medical costs with complications requiring hospitalization. TD results from ingestion of contaminated food and/or water and is defined as 3 or more loose stools in 24-hour period. In 2023 EM had over 61,007 international business trips in over 134 countries with majority of the locations with high-risk for travelers' diarrhea. The company has a robust pre-travel health process, which educates international travelers on disease prevention and health promotion. The pre-travel process includes a country-specific risk assessment, immunizations, medications, and travel education., ExxonMobil's global Emergency Medical Response System (EMERS), a 24-hour medical assistance for business travelers, provides mitigative services ranging from telephone consultation to medical evacuation. Highlight pre-travel health preparation including identifying health risks and education of preventive practices for TD. Retrospective review of annual EMERS calls for medical assistance from 2023, with focus on gastrointestinal related services. In 2023, 30% of travelers visited sites with increased risk for food and water borne diseases. Out of 217 EMERS calls, gastrointestinal illness (20) was the second most common health concern recorded. Over 9% of medical calls made where related to gastrointestinal disease such as gastroenteritis. The pre-travel health consultation is effective in preventing significant cases of TD. EM had only 9% of EMERS calls for gastrointestinal diseases and there was adequate mitigative response from travelers. A comprehensive travel preparation contributes towards achieving minimal cases, and no occurrence of serious illness events from TD cases.

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THE VALIDATION OF A LOW COST STOOL SPECIMEN PRESERVATION METHOD, COMPARING TIME AND TEMPERATURE STORAGE CONDITIONS

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Testing the nucleic acid (NA) from dried stool spots (DSS) on filter paper provides a simple method to detect enteric pathogens., especially in low-resource settings where cold-chain transport is not always available. The NA is stable, the samples are easily collected, stored, transported, and processed. We used qPCR to document the stability of NA on DSS samples over various times and temperatures. We prepared DSS samples with stools from patients infected with *Shigella* spp. (double-stranded bacterial DNA), rotavirus (double-stranded RNA virus) and norovirus (single-stranded RNA virus) on Whatman903 filter paper and compared to the gold standard, Qiagen-extracted stool samples. We will compare Qiagen-extracted NA from 200ul of frozen stool and 20ul stool-spotted filter specimens spotted the same day (Time Zero, T0), and stored at room temperature, 4°C, -20°C or -80°C. To date, we have evaluated the samples after 3 - 6 months of storage. The results suggest that NA extracted from *Shigella* spp. DSS had similar CT regardless of temperature of storage compared to Qiagen-extracted NA. Interestingly, rotavirus DSS had a lower CT at all temperatures (Mean CT: 20.62 at T0, 20.10 at RT, 20.49 at 4°C, 20.17 at -20°C, 20.37 at -80°C, $p<0.001$) when compared to Qiagen-extracted NA (mean CT 26.86). In contrast, norovirus DSS showed a significantly higher CT compared to Qiagen-extracted samples (Mean CT: 29.53 at T0, 30.12 at RT, 29.77 at 4°C, 29.44 at -20°C, 29.44 at -80°C versus CT 26.28, $p<0.001$). These results suggest that for a minimum of 3-6 months, NA on DSS samples is stable at RT for *Shigella* spp. and rotavirus detection, but there may be some loss in detection of norovirus when using DSS. However, we observed the loss is stable across all filter paper specimens, including T0. This suggests that degradation may occur during the initial spotting, with subsequent stability across time and temperature, suggesting that norovirus can also be preserved over time. These initial results show that DSS samples stored at room temperature may provide a simple method to enhance stool collection in global surveillance networks for diarrheal diseases.

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ANTIMICROBIAL RESISTANCE AND INTESTINAL SHEDDING OF NONTYPHOIDAL *SALMONELLA* AMONG CHILDREN UNDER FIVE YEARS AND CARRIAGE IN ASYMPTOMATIC HOSTS IN KENYA

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Nontyphoidal *Salmonella* (NTS) infection is characterized by self-limiting enterocolitis, but can become invasive resulting in bacteremia. *Salmonella enterica* serovars Typhimurium and Enteritidis (*S*. Typhimurium and *S*. Enteritidis) are the most common causes of NTS with the highest incidences reported in sub-Saharan Africa and in children ≤ 5 years. Since intestinal shedding could serve as a potential source of new infections in vulnerable individuals, this study aimed to determine rates of post-convalescent shedding in children under five years of age and corresponding age-matched controls in the community. This was a prospective case-control study in children from the Mukuru Informal settlement in Nairobi, between June 2021 and April 2023. Children presenting with fever for > 24 hours with or without diarrhoea were recruited. Blood and stool were collected, subjected to culture for NTS isolation, and identified through serology and PCR. Disk diffusion method was used to determine the antimicrobial susceptibility to 14 commonly used antibiotics. Fourteen days post-treatment, index cases, their household contacts, and randomly selected controls were followed up for a minimum of one month. Follow-up was stopped after three consecutive negative cultures from the stool. Of the 3,057 participants, 1.5% (46) were NTS-positive with 58.7% (27/46) being male. The positivity rate per age group was: ≤ 12 months (1.7%), 13-24 months (1.7%), 25-36 months (1.1%), 37-48 months (0.7%), and 49-60 months (2.2%). Intestinal shedding was observed in 26.1% (12/46) of the index cases with 66.7% of those being male. The longest duration of intestinal shedding was three months post-treatment. Among the healthy individuals, 3.7% were found to be shedding NTS. Resistance to Azithromycin, the current drug of choice for the treatment of invasive NTS, was observed in 13.8% of *S*. Typhimurium and 8.9% of *S*. Enteritidis with reduced susceptibility in 72.4% of *S*. Typhimurium and 82.2% of *S*. Enteritidis. This study demonstrates the need for vaccine introduction in the prevention of invasive NTS infections especially among young children in endemic settings.

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THE ROLE OF FERMENTED PICKLE CONSUMPTION ON THE GUT MICROBIOME OF WOMEN OF REPRODUCTIVE AGE IN RURAL PAKISTAN

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Gut microbiota-targeted diets can modulate microbial community and immune system, potentially preventing multiple health conditions linked to gut dysbiosis. Fermented foods containing Lactic Acid Bacteria (LAB) benefit the host by enhancing the availability of bioactive compounds and improving the gut microbiome. This study aimed to evaluate the effect of traditional fermented pickle consumption on the gut microbiome of women of reproductive age (WRA). In eight weeks of an intervention trial, a total of 210 healthy WRA were recruited from rural Matiari, Pakistan, and were divided into one control and 6 intervention groups (30 each) provided with fermented onion, radish, carrot, lemon-chili, water-based, and oil-based mango pickles respectively. Pre-intervention (week 0), end-of-intervention (week 8), and post-intervention (week 12) stool samples were collected. Among Onion and Lemon-chili (LC) intervention groups, 16S microbiome analyses showed a significant increase in α diversity [Observed α diversity at 0, 8, and 12 weeks: Onion (p= 0.01), LC (p=0.0005)] and variation in ß diversity [Onion: 0 to 8 weeks (p= 9e-04) and 0 to 12 weeks (p= 0.02), LC: 0 to 8 weeks (p= 0.02) and 0 to 12 weeks (p= 0.01)]. Most of the bacteria detected post-intervention belonged to *Actinobacteria* and *Firmicutes*. The linear discriminant analysis (LDA) at cut-off =2 showed an increase in *Actinobacteriota* (Week 8) and *Olsenella*, *Singui*, and *Intestinobacter* (week 12) among Onion while *Eggerthellaceae*, *Oscillospiraceae, Burkholderiales, Sutterellaceae, Coprococcus, Isoflavoniconvertens, Ruminococcaceae* (week 8) and *Erysipelatoclostridiaceae, Subdoligranulum, Marvinbryantia, and Fusicatenibacter* (week 12) among LC participants. Hence, fermented onion and lemon-chili pickles can be an affordable and socially acceptable microbiota-targeted diet that can potentially improve gut microbiota in WRA belonging to malnourished settings. Further studies will inform about the usefulness of such interventions for alleviating gut disorders.

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MISSED OPPORTUNITIES OF SYNDROME-BASED DIARRHEA MANAGEMENT GUIDELINES TO DETECT NON-DYSENTERIC *SHIGELLA* INFECTIONS IN KENYAN CHILDREN: FINDINGS FROM THE ENTERICS FOR GLOBAL HEALTH -*SHIGELLA* SURVEILLANCE STUDY, 2022-2024

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Current World Health Organization (WHO) guidelines recommend empirical use of antibiotics for children with dysentery, a proxy for suspected *Shigella*-attributed diarrhea. However, recent diarrhea etiology studies have highlighted the major contribution of *Shigella* to watery diarrhea, which is not covered by WHO syndromic guidelines. Leveraging data from the Enterics for Global Health (EFGH) Kenyan site, we quantify the burden of *Shigella* among Medically Attended Diarrhea (MAD) cases, outline the proportion missed by WHO guidelines, and characterize antibiotic management. We enrolled children aged 6-35 months with MAD, collected rectal swabs at enrolment, and tested for *Shigella* using the standard culture method. The susceptibility of *Shigella* isolates to a panel of antimicrobial agents was determined by the Kirby-Bauer disk diffusion method and the results were relayed back to clinicians to guide further management. We used logistic regression to estimate the odds of *Shigella* positivity based on dysentery. Between August 2022 to March 2024**,** we enrolled 1,158 MAD cases, of whom 66 (5.7%) had culture-positive *Shigella*. Nearly a quarter (15 of 73, 20.6%) of dysentery cases were *Shigella* positive compared to 51 of 1,084 (4.7%), watery diarrhea (odds ratio=5.24, 95% confidence interval 2.78-9.87). Although all 15 dysenteric cases were treated according to WHO guidelines, 43 of 51 (84.3%) non-dysenteric were not treated as per WHO guidelines. Among these non-dysenteric cases, 33 of 43 (76.7%) were prescribed other antibiotics with the leading antibiotics being metronidazole (34.9%), cotrimoxazole (25.6%), and amoxicillin (23.3%) which are not recommended for treatment of shigellosis. However, treatment of *Shigella* cases was revised based on culture and susceptibility results where appropriate Our data highlighted a substantial proportion of culture-positive *Shigella* cases are missed by WHO dysentery-based guidelines. Majority of children with *Shigella* and no dysentery ended up receiving an ineffective antibiotic. An effective *Shigella* vaccine holds promise for reducing not only diarrhea but also antibiotic use.

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DEVELOPMENT OF A RAPID, PORTABLE PCR ASSAY FOR *SHIGELLA* SEROTYPING

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Shigella species are a major cause of diarrheal disease worldwide, with *S. flexneri* and *S. sonnei* the predominant species in developing countries. Standard serotyping methods alone are expensive, vary in performance and lack the resolution to specific serotypes, which is important for surveillance and vaccine development and evaluation. Here we report the development of a multiplex PCR assay for *Shigella* serotyping, focussing on the proposed vaccine targets of *S. flexneri* 2a, 3a, 6 and *S. sonnei*. A total of 38 DNA samples were included in the initial screening (*S. flexneri* [n=22], *S. sonnei* [n=6], *S. boydii* [n=5] and *S. dysenteriae* [n=5]), and results compared to standard antisera serotyping method. Of the 38 samples tested, 34 (89.5%) had consistent results between phenotypic serotyping and PCR. All serotype 2 (*n=5*) and serotype 3 (*n=3*) samples were further classified as 2a (*gtrII* positive, *gtrX* negative) and 3a (*gtrX+oac* positive) respectively. Additionally, all six serotype 1 samples were initially positive for only the *oac* gene indicating serotype 1b. Intriguingly, of the four samples originally classified as serotype 4, samples 09 and 08 were positive for only *ipaH* (serotype Y) and *ipaH+gtrII* (serotype 2a) respectively, and samples 25 and 26 were positive for *gtrX* only (serotype X). All four samples were negative for the serotype 4 *gtrIV* gene marker. ONT sequencing and genomic *in silico* classification with ShigaPass confirmed the PCR results for samples 08 and 26, and identified the *optII* gene (involved in O-antigen modification) in samples 09 and 25, resulting in a WGS-based serotyping of Yv and Xv respectively. Once optimised, further testing will be performed on additional clinical *Shigella* DNA samples, as well as conducting large scale *in silico* screening. Additionally, amplicon detection will be transferred to dipsticks carrying antitags to tagged primers. We will also optimise our assay to work directly on bacterial cultures and clinical samples, to detect these four type strains in any suspected shigellosis sample during surveillance for vaccination programs or outbreak evaluation.

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ANTIBACTERIAL ACTIVITY OF *CORRYOCACTUS BREVISTYLUS* (SANKY) METHANOL EXTRACT AGAINST *STAPHYLOCOCCUS AUREUS* AND *ENTEROCOCCUS FAECALIS*

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Staphylococcus aureus and *Enterococcus faecalis* are two important pathogens associated with health-care associated infections. In 2017, the WHO published a list of bacteria for which new antibiotics are urgently needed, which included both bacteria in the highest priority group among gram positive bacteria. *Corryocactus brevistylus* (K. Schum. ex Vaupel) Britton & Rose, commonly referred to as Sanky is a Peruvian Cactaceae grown in the Andean regions with antioxidant properties, however, its antibacterial effect has not been studied yet. To determine the antibacterial effect of *Corryocactus brevistylus* (Sanky) methanol extract, against *Staphylococcus aureus* (ATC®25175) and *Enterococcus faecalis* (ATCC®29212). The methanol extract of *Corryocactus brevistylus* was prepared from freeze-dried fruit pulp. Agar diffusion test was used by preparing wells with the experimental solutions cultivated in aerobic conditions for 24 h at 37 °C. Six independent tests were prepared for each type of bacteria, using penicillin-streptomycin and clorhexidine 12% as positive controls. The MIC was determined using the microdilution method as described by the CLSI. Antibacterial effect of the methanol extract was observed with inhibition halos of 23.33 ± 0.72 mm and 24.34 ± 0.55 mm against *Staphylococcus aureus* and *Enterococcus faecalis*, respectively. Meanwhile, penicillin-streptomycin (10 U) showed an inhibition halo of 28.32 ± 2.6 mm and 22.84 ± 1.2 mm, respectively. Clorhexidine 12% produced halos of 26.8 ± 0.4 mm and 24.3 ± 0.4 mm, respectively. The minimum inhibitory concentration of the fruit extract was 0.83 mg/mL for *Staphylococcus aureus* and 0.21 mg/mL for *Enterococcus faecalis*. The experimental findings showed a favorable *in vitro* antibacterial effect of the methanol extract of *Corryocactus brevistylus* against *Staphylococcus aureus* and *Enterococcus faecalis*.

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THE INTRICATE RELATIONSHIP OF G-QUADRUPLEXES AND PATHOGENICITY ISLANDS

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Guanine-rich and cytosine-rich DNA can form four stranded DNA secondary structures called guanine quadruplex (G4) and i-motif, respectively. These structures widely exist in genomes and play important roles in transcription, replication, translation and protection of telomeres. The dynamic interplay between G4 structures and pathogenicity islands (PAIs) represents a captivating area of research with implications for understanding the molecular mechanisms underlying pathogenicity. This study conducted a comprehensive analysis of a large-scale dataset from reported 89 pathogenic strains of bacteria to investigate the potential interactions between G4 structures and PAIs. G4 structures exhibited an uneven and non-random distribution within the PAIs and were consistently conserved within the same pathogenic strains. Additionally, this investigation identified positive correlations between the number and frequency of G4 structures and the GC content across different genomic features, including the genome, promoters, genes, tRNA, and rRNA regions, indicating a potential relationship between G4 structures and the GC-associated regions of the genome. The observed differences in GC content between PAIs and the core genome further highlight the unique nature of PAIs and underlying factors, such as DNA topology. High-confidence G4 structures within regulatory regions of *Escherichia coli* were identified, modulating the efficiency or specificity of DNA integration events within PAIs. Collectively, these findings pave the way for future research to unravel the intricate molecular mechanisms and functional implications of G4-PAI interactions, thereby advancing our understanding of bacterial pathogenicity and the role of G4 structures in pathogenic diseases.

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WHOLE GENOME SEQUENCING OF A *CRONOBACTER SAKAZAKII* ST8 STRAIN ISOLATED FROM SPICE POWDER

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Cronobacter sakazakii is a Gram-negative, human-pathogenic bacterium that can survive in extreme dry conditions. This emerging opportunistic pathogen is recognized for causing acute meningitis and necrotizing enterocolitis in neonates, ageing, and immunocompromised individuals. It is linked predominantly to contaminated powdered infant formula (PIF) and to cause PIF-related sporadic cases and outbreaks worldwide. However, it has also been isolated from a wide variety of foods. Molecular characterization have indicated a high level of species-level genetic variation, comprising unique clonal complexes and sequence types, often associated with foodborne sickness and outbreaks. At present, application of whole genome sequencing (WGS) has improved bacterial typing and is widely utilized for correct strain identification to understand disease transmission. In this study, a *Cronobacter sakazakii*-like Gram-negative bacterial isolate SRL-104, from spice powder produced in the Caribbean Island nation, was recovered and analyzed. Initial microbial identification was accomplished on VITEK 2, RT-PCR, and MALDI-TOF MS based analysis, following FDA's Bacteriological Analytical Manual and manufacturer's recommended protocols. WGS was completed on an Illumina MiSeq system, using a Nextera XT DNA library preparation kit and a 250-bp paired-end read MiSeq Reagent v2 kit (500-cycle), following manufacturer's instructions. MALDI-TOF MS identified the *Cronobacter sakazakii* SRL-104 isolate as *Cronobacter sakazakii* with a high confidence value (99.9%). WGS analysis revealed the genome sequence of *Cronobacter sakazakii* isolate SRL-104 was 4,494,638 bp in length and distributed in 54 contigs. The analysis further confirmed the genome of *Cronobacter sakazakii* isolate SRL-104 to be Sequence Type 8 (ST8). *Cronobacter sakazakii* ST8 is considered as a highly stable clone with a high susceptibility to cause neonatal meningitis. Thus, MALDI-TOF mass spectrometry and WGS based analysis can be utilized for rapid and precise identification of infectious *Cronobacter sakazakii* strains of public health importance.

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SCREENING OF THE PANDEMIC RESPONSE BOX LIBRARY IDENTIFIED PROMISING COMPOUND CANDIDATES AGAINST EXTENSIVELY DRUG-RESISTANT *ACINETOBACTER BAUMANNII*

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Infections caused by antimicrobial-resistant *Acinetobacter baumannii* pose a significant threat to human health, particularly in the context of hospital-acquired infections. As existing antibiotics lose efficacy against Acinetobacter isolates, there is an urgent need for the development of novel antimicrobial agents. In this study, we assessed 400 structurally diverse compounds from the Medicines for Malaria Pandemic Response Box for their activity against two clinical isolates of *A. baumannii: A. baumannii* 5075, known for its extensive drug resistance, and *A. baumannii* QS17-1084, obtained from an infected wound in a Thai patient and displaying resistance to nearly all antimicrobial classes, including tetracycline. Among the compounds tested, seven from the Pathogen box exhibited inhibitory effects on the in vitro growth of *A. baumannii* isolates, with IC50s ≤ 48 μM

for *A. baumannii* QS17-1084 and IC50s ≤ 17 μM for *A. baumannii* 5075. Notably, two of these compounds, MUT056399 and MMV1580854, shared chemical scaffolds resembling triclosan. Further investigations involving drug combinations identified five synergistic drug combinations, suggesting potential avenues for therapeutic development. Our findings highlight gepotidacin, epetraborole, and eravacycline as promising candidates for further evaluation in murine wound infection models against multidrug-resistant *A. baumannii*. These compounds hold potential for addressing the critical need for effective antibiotics in the face of rising antimicrobial resistance.

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BURDEN OF MYCOBACTERIUM TUBERCULOSIS DRUG RESISTANT AMONG PRESUMPTIVE PULMONARY AND EXTRAPULMONARY TUBERCULOSIS PATIENTS AT AMBO GENERAL HOSPITAL WEST ETHIOPIA

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Drug resistant Mycobacterium tuberculosis is one of the serious public enemy out there that deterring progress made in tuberculosis cases and control in several countries including Ethiopia. Rifampicin resistance is an indicator for drug-resistant Mycobacterium tuberculosis, because it disclose the existence of more than 90% Isoniazid resistance. Early detection of drug-resistant tuberculosis is crucial for patient management and infection control. This study was designed to assess Burden of Mycobacterium tuberculosis, its Rifampicin-resistance pattern and associated factors among presumptive Pulmonary and Extra Pulmonary Tuberculosis patients at Ambo General Hospital, West Ethiopia. Hospital based cross-sectional study design was carried out from September 2, 2021 to March 27, 2022. Detection of Mycobacterium tuberculosis and resistance to Rifampicin pattern was determined by using GeneXpert MTB/RIF assay. Data were entered and analyzed by SPSS version 23.0. Bivariate and multivariate analyses were used to examine the relationship between dependent and independent variables. P-value was significant(<0.05) . A total of 322 presumptive tuberculosis patients were included in the study; of these, 52 (16.2%) of them were identified as having Mycobacterium tuberculosis by the GeneXpert MTB/RIF assay, 3/52 (5.8%) were resistant to Rifampicin and 6/52 (11.5%) patients were TB/HIV co-infected. From the total of M. tuberculosis detected 46 (16.1%) were identified in pulmonary and 6 (8.5%) were in extra-pulmonary presumptive patients. Rifampicin-resistant M. tuberculosis was detected in 3 patients who had a history of taking Anti-tuberculosis drugs and no in new patients. Previous history of tuberculosis treatment and having close contact history with tuberculosis patients were found as an important associated factors that enhance the Burden of tuberculosis. This indicates the mandate to make better and oversee the treatment protocol and prevention method to control the burden of tuberculosis.

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ANTIMICROBIAL RESISTANCE AMONG PATHOGENS CAUSING SURGICAL SITE INFECTIONS: TRENDS AND IMPACT OF THE COVID-19 PANDEMIC

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Surgical site infection (SSI) with antimicrobial resistant (AMR) bacteria is a progressing healthcare burden. This study assessed AMR in SSI cases at two University Hospitals in Egypt. A total of 361 cases were enrolled from March 2018 to September 2023: 154 cases pre-COVID-19 and 207 post-COVID-19. Identification and antibiograms of isolated pathogens were done by VITEK2. Up to four pathogens were isolated from 70% of the cases. ESKAPE-E (*E. faecium*, *S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, Enterobacter spp*., *E. coli*) constituted 88% of isolated pathogens. *E. coli* (30%), *K. pneumonia* (23%), *A. baumannii* (12%), and *P. aeruginosa* (9%) were the most frequently encountered pathogens. High AMR was observed among ESKAPE-E pathogens, with 15% pan-drug resistance (PDR), 43% extensive drug resistance (XDR) and 27% multi-drug resistance (MDR). *K. pneumoniae* (44%) had the highest PDR, and *A. baumannii* (79%) had the highest XDR. *Enterobacteriaceae* isolates showed lowest resistance rates against amikacin (27%) and meropenem (39%), whereas >85% were resistant to 3rd and 4th generation cephalosporins. Resistance of *Enterobacteriaceae* to meropenem, fluoroquinolones and cefoxitin increased post COVID-19, and lead to substantial increase in XDR and PDR in both *K. pneumoniae* and *E. coli*. *A. baumannii* lowest resistance rates were against colistin (7%) and minocycline (33%), whereas resistance against the rest of antibiotics ranged from 71% to 98%. Overall increase in *A. baumannii* resistance was observed post-COVID-19. For *P. aeruginosa*, colistin had the lowest resistance rates (11%), while resistance to the rest of antibiotics ranged from 56% to 82%. Prophylactic antibiotics were administered to almost all cases. Of these, 3rd generation cephalosporins were used in 86% of the cases, which may explain the elevated resistance rates against these antibiotics. Moreover, less restricted use of antibiotics during the pandemic may have contributed to the rise in resistance following the COVID-19 pandemic. This study highlights the significant AMR issue in Egypt, emphasizing need for updating guidelines for prophylaxis and empiric therapy.

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PHYTOACTIVITIES OF THE LEAF OF *VERNONIA AMYGDALINA* (BITTER LEAF) ON BACTERIAL INFECTIONS

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Anti-bacterial activities of the leaf of *Vernonia amygdalina* (bitterleaf) were tested on *Escherichia coli* and *Staphylococcus aureus*. Five concentrations 0.5g/ml, 1.0g/ml, 1.5g/m, 2.0g/ml and 2.5g/ml were used and the control experiment was carried out to compare the diameter zones or clearing from the extracts and already standardized antibiotics. Agar well plugs method was used for the tests. The bitter leaf extract was made with cold water. Nutrient agar was prepared and inoculated with the different bacteria strains after which wells were made in the in the media and bitter leaf extracts were poured on them. The cold-water extracts of *V. amygdalina* showed inhibitions on the five organisms according to concentration. The organism susceptibility varied with more inhibition to *E. coli, Pseudomonas aeruginosa, Salmonella typhi, Klebsiella pneumonia* and least to *Staphylococcus aureus*.

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FIVE-YEAR SURVEILLANCE OF ANTIMICROBIAL RESISTANCE IN ESKAPE PATHOGENS OF NOSOCOMIAL ORIGIN IN LIMA, PERU

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The increasing trend of antimicrobial resistance (AMR) among bacterial pathogens in nosocomial settings (NS) presents a global threat. Continuous surveillance of pathogens from NS is crucial due to their potential impact on patient outcomes, particularly in regions with limited resources. We conducted a prospective surveillance study of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter spp*. (ESKAPE) in six hospitals in Lima, Peru, from 2017 to 2021. Bacterial pathogens were isolated and identified in these hospitals and then transported under refrigerated conditions to the U.S. Naval Medical Research Unit SOUTH

for further analysis, including pathogen re-identification and antimicrobial susceptibility testing. A total of 1,465 bacterial isolates were recovered with *K. pneumoniae* (35.4%) being the most prevalent pathogen, followed by *P. aeruginosa* (31.4%), *A. baumannii* (15.4%), *S. aureus* (12.4%), and *E. coli* (5.4%). Overall, these pathogens exhibited resistance to between one and 12 different antimicrobial families (AFs). We found high rates of multidrug resistance (MDR, non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories) in 474 (91.5%) *K. pneumoniae*, 458 (99.1%) *P. aeruginosa*, 224 (99.6%) *A. baumannii*, 130 (71.08%) *S. aureus*, and 76 (96.2%) *E. coli* isolates. Furthermore, we observed significant differences between the means of the number of AFs from 2017-2019 compared to 2021 for *P. aeruginosa* (7.9 vs. 6.8, p<0.001) and *A. baumannii* (7.6 vs. 4.8, p<0.001). No significant changes in AMR trends over time were found for any antimicrobial category tested. The differences in AF resistance underscore the critical need for ongoing surveillance of antimicrobial resistance.

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RICKETTSIOSES AMONG HOSPITALIZED ACUTE FEBRILE ILLNESS ADMISSIONS, WESTERN AND CENTRAL PROVINCES, SRI LANKA

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Diagnostics for acute undifferentiated febrile illness (AUFI) are limited in lesser developed countries, such as Sri Lanka. Patient management is mainly based upon clinical case definitions. We aimed to determine the seroprevalence and importance of typhus group (TGR) and spotted fever group (SFGR) rickettsiae as AUFI pathogens during a study to determine the epidemiology and diagnostics for AUFI in Western and Central Provinces, Sri Lanka. Total of 800 patients (≥14years) hospitalized with AUFI (<7days) were recruited from 3 district general hospitals. Pan-*Rickettsia* qPCR assay (Rick17b) was performed on all study participants blood and/or eschar DNA samples. Cases were confirmed as *Rickettsia* spp. based upon positive triplicate qPCR results. In-house IgG (*Rickettsia typhi* for TGR and *Rickettsia conorii* for SFGR) enzyme-linked immunosorbent assays (ELISA) were performed on a sub-cohort with paired acute and convalescent (≥2 weeks) sera. Screening assays were performed on paired samples at 1:100 dilution to determine seroconversion. In the overall AUFI study cohort, there were 25/800 (3%) rickettsial infections diagnosed by qPCR (Rick17b). In the sub-cohort of participants with paired serology (n=492), the etiology of AUFI was determined as TGR and SFGR in 10 (2%) and 17 (3%), respectively. Overall seroprevalence (combined acute and previous infections) of SFGR (27/162, 17%) was higher in Central Province compared with SFGR (21/330, 6%) in Western Province. Seroprevalence of TGR in Central Province (13/162, 8%) was comparable with TGR (23/330, 7%) in Western Province. Only 11/42 (26%) of the acute rickettsioses diagnosed by PCR and/or ELISA, were clinically diagnosed rickettsial infection by the medical team on admission. Our results showed that rickettsioses represent an important under recognized differential diagnoses for AUFI in Sri Lanka. A combination of PCR and ELISA diagnostics will optimize management of patients and improve surveillance of rickettsioses.

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IDENTIFICATION AND ANTIMICROBIAL SUSCEPTIBILITY OF MILK PATHOGENS ISOLATED FROM MASTITIS INFECTED COW'S MILK IN ADO EKITI, NIGERIA

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Mastitis is the most common and economically significant disease affecting dairy cattle. It is the most important cause of economic losses to the dairy industry throughout the world. This study aimed to evaluate the profile of resistance pathogens isolated from mastitis infected cow milk in Ado-Ekiti. Different bacteria were isolated using standard Microbiological techniques and further characterized using biochemical methods and identified using API Kit. A total of 80 Milk samples from cows diagnosed with subclinical mastitis were collected from four dairy farms in Ado-Ekiti (Aba Erifun, Aba baba Medinat, Afao road and Irasa). Antibiotic susceptibility testing was conducted using the Kirby-Bauer disk diffusion method. The study revealed that highest prevalent pathogen was *Streptococcus agalactiae* 25/80 (31.25%) and *Staphylococcus aureus* 18/80 (22.5%) followed by *E. coli* 15/80 (18.75%). Antibiotic sensitivity test revealed that *S. agalactiae* revealed the highest sensitivity to ofloxacin, ciprofloxacin, gentamicin and resistance to amoxicillin and doxycycline; *S. aureus* revealed the highest sensitivity to ciprofloxacin, doxycycline and azithromycin and resistance to amoxycillin and gentamicin. *E. coli* revealed the highest sensitivity to azithromycin and chloramphenicol and resistance to amoxicillin and ciprofloxacin. Results indicate a need to educate the dairy farmers about mastitis (particularly subclinical), proper hygiene methods in milking and the public health implications of consuming contaminated raw milk.

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PREVALENCE AND RISK FACTORS FOR COLONIZATION DURING THE FIRST THREE MONTHS OF LIFE WITH THREE CRITICAL ANTIBIOTIC-RESISTANT PATHOGENS IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW, META-ANALYSIS, AND META-REGRESSION STUDY

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In low- and middle-income countries (LMICs), neonatal bacterial infections are mainly caused by *Enterobacterales* and *Staphylococcus aureus*, both significant contributors to mortality attributable to antimicrobial resistance. However, obtaining blood cultures in neonates, particularly in these settings, presents challenges, leaving a significant gap in our understanding. Given that bacterial colonization often precedes infection, we conducted a systematic review and meta-analysis to provide a comprehensive overview of the prevalence and risk factors for colonization with third generation-cephalosporin-resistant (3GC-R-E), carbapenem-resistant (CRE) *Enterobacterales*, and methicillin-resistant *S. aureus* (MRSA) during the first three months of life. Four databases were searched from January 1, 2000, to June 1, 2023, for cohort and cross-sectional studies conducted within LMICs that reported prevalence rates or risk factors for colonization with 3GC-R-E, CRE, or MRSA in infants up to 3 months of age. A random-effects model was used to compute the pooled prevalences. Out of the 2869 articles identified, 53 studies were eligible (N=40 for 3GC-R-E and CRE and N=13 for MRSA). The pooled prevalence of 3GC-R-E colonization was 31.1% (95%CI 20-45, τ^2 = 1.8), varying from 8.5% in the community to 54.3% in hospitalized patients. The risk of colonization with 3GC-R-E was found to increase with hospital birth, prior neonatal antibiotic intake, and prolonged rupture of membranes. *Klebsiella pneumoniae* was the most frequently identified species in newborns colonized with 3GC-R-E, before *E. coli*. The prevalence of carbapenem-R *Enterobacterales* colonization was 3.3% (1-11, τ^2= 7.1), and increased significantly other time, from 1.6% before 2018 to 23.9% afterward. The prevalence of MRSA colonization was 3.0% (1-9, τ^2 = 3.1). The prevalence of antibiotic-resistant pathogens colonization among neonates is high in LMICs, comparable to that reported in adults despite a limited exposure period. This highlights the need for additional research to identify transmission routes and to design targeted and effective preventive measures.

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INVESTIGATING THE ANTIPHAGE DEFENSE SYSTEMS IN STAPHYLOCOCCAL PHAGE SATELLITE

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Phage satellites are one of the mobile genetic elements encoded into the bacterial chromosome and rely on their helper phages (viruses that infect bacteria) to promote their horizontal transfer in a recipient bacterial host. Among these phage satellites are the phage inducible chromosomal islands (PICIs) with the size of genome typically around 12 - 15 kb, significantly contributing to bacterial adaptation and pathogenesis. PICIs are found in Gram-positive or Gram-negative, with the prototypical and best-characterised family being the *Staphylococcus aureus* pathogenicity islands (SaPIs), which include SaPI1 and SaPIbov1. SaPIs exploit the life cycle of their 'helper' phages upon prophage induction or phage infection. Once excised, the SaPI-encoded genes are packaged into phage-encoded structural components, interfering with phage packaging and reducing phage reproduction. Most SaPIs are packaged using helper phage machinery through a headful (*pac*) packaging mechanism. SaPIs interfere with *pac* phage reproduction through a variety of strategies, including the redirection of phage capsid assembly to form small capsids, which can accommodate the smaller SaPI genome. This process depends on the expression of the SaPI-encoded *cpm*A and *cpm*B genes encoded in operon 1 of the SaPI genome. However, another SaPI subfamily, including SaPIpT1028, can remodel helper phage capsids into small capsids without encoding *cpm*AB homologs. It opens new avenues for research, as the basis for this phage interference remains to be deciphered. The interference mechanism by SaPIpT1028 is dependent on a new SaPI-encoded gene, *rcp* (redirecting capsid packaging), encoding a protein involved in remodelling the phage capsid into a small capsid to package the SaPI genome. This study has also identified a novel interference strategy involving an accessory gene, *sma* (single-protein MazF-like antiphage system), encoded at the 5' region of the island genome, that offers protection to its recipient host and the SaPI-inducing phages from other phage infection, shedding light on PICI evolution and the mutual relationship between PICIs and their helper phages.

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IMPROVING SYPHILIS MOLECULAR DIAGNOSTICS: GENOME MINING-BASED IDENTIFICATION OF IDENTICAL MULTI-REPEAT SEQUENCES (IMRS) IN *TREPONEMA PALLIDUM* GENOME

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According to the World Health Organization (WHO) more than 7 million new *Treponema pallidum* infections were reported among people aged 15 – 49 years in 2020 globally, the majority of them in developing countries. Syphilis, which is caused by *T. pallidum* is transmitted through contact with active lesions of a sexual partner or from an infected pregnant woman to her foetus. Gold standard *T. pallidum* laboratory diagnosis methods include dark-field microscopy, silver staining, direct fluorescence immunoassays and the rabbit infectivity test. However, these tests are associated with false positive or negative results. The gold standard 16S ribosomal (rRNA) gene polymerase chain reaction (PCR) is used for routine amplification of *T. pallidum* conserved genes. Here we report on an ultrasensitive syphilis diagnostic method, based on de *novo* genome mining of the *T. pallidum* DNA to identify identical multi repeat sequences (IMRS) as amplification primers. We used genome-mining approaches to find IMRS distributed throughout the *T. pallidum* genome to design a primer pair that target four repeat sequences. Genomic *T. pallidum* DNA was diluted from 8.14×10^{4} to 8.14×10^{-2} genome copies/μ;l and used as template in the IMRS-based amplification assay. For performance comparison, 16S rRNA PCR assay was employed. Probit analysis was used to calculate the lower limit of detection of the *T. pallidum*-IMRS PCR and the conventional 16S rRNA PCR assays. Probit analysis confirmed that the *T. pallidum*-IMRS primers offered higher test sensitivity of 0.03 fg/μ;L compared to the 16S rRNA PCR (0.714 pg/μ;L). Using the *T. pallidum*-IMRS primers, we were able to observe considerable isothermal amplification of genomic DNA at a starting concentration of 0.01 pg/µL. *De novo* genome mining of *T. pallidum* IMRS as amplification primers can serve as a platform for developing ultrasensitive diagnostics for Syphilis and potentially a wide range of infectious pathogens.

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COMPARISON OF COMMERCIAL KITS FOR DNA EXTRACTION AND PRE-TREATMENTS OF SPUTUM SAMPLES FROM PATIENTS WITH TUBERCULOSIS FOR SEQUENCING

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Mycobacterium tuberculosis (MTB), a pathogen of global concern, causes one of the infectious diseases with the highest rates of morbidity and mortality. The challenge of incomplete treatment adherence leads to antibiotics worldwide. This is due to failure to comply with all doses, generating resistance, underscoring the necessity for timely and effective individualized diagnosis and treatment. Whole-genome sequencing (WGS) is pivotal for elucidating the complete DNA sequence of an organism, offering insights into the full spectrum of multidrug resistance, thus positioning it as a critical diagnostic tool. Our study focused on optimizing MTB DNA extraction from sputum samples for sequencing, comparing the efficacy of different commercial DNA extraction kits (n=39) and pre-treatments: NAOH-NALC and saponin (n=32). The comparative analysis revealed that the Quick-DNA Fungal/Bacterial Miniprep and Quick-DNA Miniprep Plus Kits outperformed the ZymoBIOMICS DNA Miniprep Kit in terms of DNA yield (91.19 ng and 77.87 ng, respectively, versus 50.06 ng). Quality assessment based on the 260/280 and 260/230 ratios favored the Quick-DNA Miniprep Plus kit (1.77 and 0.46). Additionally, sputum sample treatment evaluations indicated that saponin treatment yielded higher DNA quantities and better quality metrics (876 ng, 1.83, 0.98) compared to the NaOH-NALC treatment (54 ng, 1.56, 0.29). Quantitative PCR analysis to assess the proportions of human and MTB DNA demonstrated a reduction in human DNA with NaOH-NALC treatment followed by saponin, while the MTB DNA levels were similar across both treatments. In conclusion, for sequencing clinical sputum samples from MTB patients, the combination of DNA extraction using the Quick DNA Miniprep Plus kit and sample pre-treatment with saponin emerged as the most effective strategy.

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SEROPREVALENCE OF LEPTOSPIROSIS IN HORSE KEEPERS IN A REGION OF THE COLOMBIAN CARIBBEAN

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Leptospirosis is an endemic zoonotic disease with high distribution and worldwide prevalence. An analytical observational study was carried out with a cross-sectional approach that determined the seroprevalence and risk factors associated with occupational leptospirosis in horse keepers in the department of Córdoba, 2022-2023. After signing the informed consent, 112 blood samples were taken. to horse caretakers in 33 properties in the department of Córdoba to determine the seroprevalence of leptospirosis through the Microagglutination technique. An epidemiological survey was implemented to carry out the socio-demographic

characterization of the population under study and an association was established between risk factors and the presentation of occupational leptospirosis in equine caregivers through descriptive and inferential statistical analyses. The seroprevalence was 59.8% (n=67). Of the 67 horse keepers with antibody titers against Leptospira spp, 82.1% were associated with a serogroup, the most frequent being Australis. 17.9% were mixed and the most frequent association was with the Australis serogroup. Dairy work (p:0.041, CI:1.02-6.472, OR: 2.57) and frequenting dam-type water sources (p:0.026, CI:1.08-6.843, OR: 2.75) were established as risk factors. Research on horse keepers in Córdoba highlights the correlation between occupational and environmental factors with the prevalence of leptospirosis. There are occupational and environmental risks that deserve to be taken into account for the design of prevention and control strategies for the event by health authorities.

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UNDERSTANDING THE IMPACT OF MONOCULAR SEVERE VISION IMPAIRMENT AND BLINDNESS CAUSED BY FUNGAL KERATITIS IN TANZANIA

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A majority of current eye care surveys focus on the better-seeing eye, overlooking individuals with monocular problems, and underestimating the extent of eye conditions and the services required to treat them. Therefore, most current definitions and targets for monitoring ophthalmic services are unlikely to recognize the true burden of monocular blindness. There is very little data regarding the quality of life in individuals who are unilaterally blind or have severe visual impairment due to fungal keratitis, both in sub-saharan Africa and worldwide. This project will examine the impact of monocular visual impairment and monocular blindness due to fungal keratitis on people in Tanzania. A mixed-methods study will be conducted at Kilimanjaro Christian Medical Centre Hospital (KCMC) in Tanzania over six weeks. This study will constitute a quality-of-life survey and cross-sectional, semi-structured in-depth interviews. This study is an extension of a previous parent trial. A randomized control trial took place at KCMC starting September 2021 and set out to recruit patients with fungal keratitis to determine if topical chlorhexidine 0.2% in combination with topical natamycin 5% is superior to topical natamycin 5% alone. Participants will be organized into two groups based on World Health Organization visual acuity criteria: those with severe visual impairment or Blindness in the affected eye after treatment: (≤6/60 in the worse eye, presenting ≥6/18 in the better eye), and those with mild to no visual impairment in the affected eye after treatment: (presenting ≥6/18 in both eyes). Only those in the blind or severe visual impairment group will be eligible for interviews. Quality-of-life survey responses for the two groups will be compared to previous surveys completed by participants at the beginning of the clinical trial and 90 days after. Survey responses will also be compared between those who now have monocular blindness/visual impairment and those who do not. Using thematic analysis, interview transcripts will be coded and analyzed to identify common themes between interviews.

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ANTIBIOTIC PRESCRIBING PATTERNS AT OUTPATIENT CLINICS IN WESTERN AND COASTAL KENYA

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Antimicrobial resistant pathogens are a leading cause of morbidity and mortality worldwide, particularly in low- and middle-income countries, and the overuse and misuse of antimicrobials are key contributors. We aimed to identify factors associated with antibiotic prescriptions among persons presenting to clinics in Kenya. We performed a retrospective, descriptive cohort study of adults and children presenting to outpatient clinics in Western and Coastal Kenya, including reported symptoms, physical exam findings, clinician assessments, laboratory results and prescriptions. Data analysis was performed using R studio software. We reviewed 1,526 visits among 1,059 people who sought care from December 2019-February 2022. Enrollment was continuous apart from April-June 2020, when the study was paused due to the COVID-19 pandemic. Median age was 16 years (IQR 6-35) and 22% were under 5 years. All persons endorsed fever, and 44% reported onset within 48 hours of presentation. At least one provisional diagnosis was provided for 89% of encounters, and upper respiratory infection was the most common diagnosis (48%). 30% of malaria RDTs were positive and 3% of dengue RT-qPCRs were positive. Antibiotics were prescribed in 73% of encounters overall and in 84% among children under 5. In 48% of visits antibiotics were prescribed without a provisional bacterial diagnosis. In the multivariable model, factors associated with increased odds of an antibiotic prescription were the clinic in Western Kenya (OR 5.1, 95% CI 3.0-8.8), age less than or equal to 18 years (OR 2.1, 95% CI 1.4-3.2), endorsement of cardiorespiratory symptoms (OR 5.2, 95% CI 3.2-8.3), a negative malaria RDT (OR 4.0, 95% CI 2.5-6.8), and a provisional diagnosis that could be bacterial in etiology (OR 5.9, 95% CI 3.5-10.3). High rates of antibiotic prescriptions are common even when associated diagnoses are not bacterial. Compared to our 2014-2017 cohort, we found higher rates of antibiotic prescriptions among children. Improved diagnostics to rule in alternative diagnoses as well as stewardship programs are needed.

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SEVERE INFECTION AMONG YOUNG INFANTS IN DHAKA, BANGLADESH: EFFECT OF CASE DEFINITION ON INCIDENCE ESTIMATES

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Multiple definitions are used to denote severe infection (SI) in young infants including sepsis and serious bacterial infection (SBI). Heterogeneity in these definitions limits comparability of randomized controlled trials (RCTs) of infant SI prevention interventions. To inform the design of young infant SI prevention RCTs in low-resource settings, we estimated the incidence of SI in Bangladeshi infants aged 0-60 days and examined the effect of variations in SI definitions on incidence estimates. From 2020-2022, generally healthy newborns were recruited at two hospitals in Dhaka, Bangladesh. SI cases were identified through active surveillance at up to 12 scheduled community health worker home visits from ages 0-60 days or through caregiver self-referral. The primary SI case definition combined physician documentation of clinical signs and/or diagnosis of sepsis/SBI and either a positive blood culture or parenteral antibiotic treatment for ≥5 days. Incidence rates were estimated for the primary SI definition, the World Health Organization (WHO)

definition of possible SBI based on seven clinical signs, culture-confirmed SI, and five other alternative SI definitions. Among 1939 infants, the SI incidence rate using the primary definition was 1.1 (95% CI 0.93-1.4) per 1000 infant-days at risk, whereas the incidence using the WHO definition of possible SBI was 0.84 (0.69-1.0) per 1000 infant-days at risk. Culture-confirmed SI incidence was 0.026 (0.0085-0.081) per 1000 infant-days at risk. One third of primary SI definition cases met criteria through a physician diagnosis of sepsis/SBI rather than documentation of clinical signs. Of primary SI definition cases, 85% were identified following caregiver self-referral. The incidence of SI in young infants varied considerably by case definition. Using a clinical sign-based SI definition may result in missing a substantial proportion of cases identified by physician diagnosis of sepsis/SBI. If health facilities are accessible and caregivers seek care for infant illness, frequent scheduled home assessments by study personnel to identify infants requiring referral may not be warranted.

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CLINICAL PRESENTATION AND MANAGEMENT OF ECHINOCOCCUS INFECTION: A CASE REPORT

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We report the case of a 51-year-old male from Ecuador who presented to the Mayo Clinic Florida (MCF) for evaluation of an incidentally found hepatic lesion during evaluation of midepigastric pain that started in June 2023 after two days of riding his bicycle. He used over the counter antacids and proton pump inhibitors for a few days without any improvement of his symptoms and when the pain became debilitating, he sought care at a hospital in Ecuador. MRI abdomen from the outside facility was significant for focal hepatic lesions . He denied any pets or animal exposure including visits to farmland, sheep or other cattle. He has lived within the Ecuadorian city of Quito for his entire life except for a 5 year period during which he lived in Egypt. He does not have any exposure to rural areas and works as a consultant for an oil company. He is a meat eater and denies consuming undercooked or uncooked meat products. Our patient underwent sonographically guided needle aspiration of the 6.4 x 4.9 cm hepatic cyst with installation of 20 cc of 23.5% hypertonic saline. No fluid was aspirated from the smaller 3.2 x 2.8 cm cyst but it was injected with 3 cc of absolute ethanol with scolicidal intent. He was started on a three month course of 400 mg PO BID of Albendazole. Our patient underwent surveillance imaging at 3 months which showed stable hepatic cysts. He will continue to have 3 month surveillance followed by yearly imaging.

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ACTIVE MELIOIDOSIS SURVEILLANCE AMONG HOSPITALIZED PATIENTS WITH DIABETES MELLITUS IN BANGLADESH, JUNE 2021-MARCH 2024

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Melioidosis is an infectious disease predominantly found in tropical regions, caused by soil-borne bacterium *Burkholderia pseudomallei*. Melioidosis remains a neglected disease in Bangladesh. From 1961-2021, Bangladesh has documented around 85 cases. The incidence of melioidosis is believed to be much higher. To determine a more accurate incidence of melioidosis in Bangladesh, we initiated surveillance in June 2021 to detect *B. pseudomallei* infection in hospitalized patients at BIRDEM General Hospital. BIRDEM General Hospital is the largest diabetes hospital in Bangladesh which has 715 in-patient beds and more than 3500 out-patient visits daily. Adult patients with diabetes mellitus having clinical suspicions for melioidosis as per case definition were enrolled. As of 20 March 2024, a total of 693 were enrolled; 53% (n= 365) were male and the mean age of all patients was 58 years (range: 18-105). Of the 693 patients, 28 (4%) were culture confirmed for *B. pseudomallei*, 7 (25%) of whom died. The mean age of cases was 54 years (range: 25-70); male was predominant (82%), most patients (96%) had diabetes; 23 (82%) had fever; 7 (25%) had sepsis syndrome; 13 (46%) had skin abscess; 10 (36%) had pneumonia; 4 (14%) had organ abscess; 17 (61%) had urinary tract infection (UTI) and 13 (46%) had chronic Kidney disease (CKD). Most of the cases (n=22, 79%) were detected during June-November; 18 (64%) cases lived in rural areas and all cases originated from 17 districts. Patients with melioidosis were more likely to have soil exposure within the prior 30 days compared to those that did not (OR 2.6, 95% CI: 1.21-5.47). *B. pseudomallei* showed highest sensitivity to meropenem (100%), amoxicillin-clavulanate (100%), ceftazidime (100%), piperacillin (100%) followed by tetracycline (73%), cotrimoxazole (57%), and ciprofloxacin (35%). This hospital-based active surveillance provides evidence that the burden of melioidosis is higher in Bangladesh than previously documented. Active surveillance should be expanded with diagnostic facilities to understand the true country-wide melioidosis burden.

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TROPICAL SPASTIC PARAPARESIS AND ADULT T CELL LEUKEMIA-LYMPHOMA CO-PRESENTATION IN AN HTLV-1 PATIENT

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Human T-lymphotropic virus type 1 (HTLV-1) affects between 5 to 10 million people globally. In most patients the infection remains clinically inapparent. It carries a 5% lifetime risk of adult T-cell leukemia/lymphoma (ATLL) and a 2% lifetime risk of tropical spastic paraparesis (TSP), which are the most commonly described conditions associated with HTLV-1. Here we report a case of HTLV-1 infection in a patient presenting with both TSP and ATLL. A 53 year old woman from Lima, Peru presented for a 2 year history of facial erythema and skin changes on her legs. She also noted weakness and involuntary movements of her lower extremities for the past year, which had led to falls on three occasions, in addition to urinary retention in the last month. On skin examination, the patient was noted to have erythematous patches on her face, and scaly plaques on bilateral lower extremities. A dermal punch biopsy of the facial erythema was performed, which showed "moderate inflammatory infiltrate on the dermis with lymphocytes and histiocytes, which stained positive for the following: CD4/CD8 3:1; CD3+, CD7+, Ki-67 5-10%, suggestive of mycosis fungoides." A HTLV-1 test was performed via electrochemiluminescence immunoassay, which returned positive, confirming the diagnosis of adult T-cell leukemia/lymphoma. On neurologic exam, she was noted to have decreased tone of both lower extremities, and 4/5 strength in both upper extremities, and 3/5 strength in both lower extremities. She was additionally noted to have hyperreflexia of both patellar and achilles reflexes, positive bilateral Hoffman, Babinski, and Chaddock signs, and spasticity of both lower extremities, leading to a diagnosis of tropical spastic paraparesis in the context of HTLV-1 positivity. There has been only one other case of this co-presentation in the literature, in 1996. Given the rarity of HTLV-1 and its clinical manifestations, the co-presentations of these conditions represents a unique clinical entity and indicates the importance of evaluating patients with one manifestation of HTLV-1 for other conditions associated with the infection.

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PARASITES IN HISTOPATHOLOGY: A TEACHING HOSPITAL EXPERIENCE

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Accurately diagnosing parasitic infectious diseases is essential to ensure those diseases are appropriately treated. The diagnosis of parasitic infectious diseases is achieved in many parts of the world especially in the resource-limited regions, by the observation of parasite life-cycle stages on microscopy of biological samples like urine, stool, sputum, aspirates, and tissue biopsies. This study was done to evaluate the role of histopathology, which is the analysis of tissue biopsies, in the diagnosis of parasitic infectious diseases. This is a retrospective descriptive study that reviewed the clinical and pathological features of cases of parasitic infections diagnosed on tissue biopsies, from January 2014 to December 2019 in the Anatomical pathology department of the laboratory of University Teaching Hospital of Kigali. In total 23 cases of parasitic infections were diagnosed on tissue biopsy. The age of the patients ranged from 1.5 years old to 84 years old. The symptoms and their severity varied according to affected organs. The cases consisted of 14 cases of cysticercosis, 4 cases of schistosomiasis, 3 cases of echinococcosis, 1 case of genital filariasis, and 1 case of arthropod bite larva migrans. The cases of cysticercosis consisted of 7 cases of neurocysticercosis, 1 case of disseminated cysticercosis, and 6 cases of skin and intramuscular cysticercosis. The cases of schistosomiasis consisted of 1 case of intramedullary spinal schistosomiasis, 2 cases of female genital schistosomiasis, and 1 case of intestinal schistosomiasis. The cases of echinococcosis consisted of splenic, liver, and pancreatic cystic echinococcosis. Most of the parasitic infections that are diagnosed on tissue biopsy consist of parasitic infections of the central nervous system, those of the skin and soft tissues, and those of the female genital tract. Histopathology is very useful in diagnosing parasitic infectious diseases, some of which can be life threatening notably those affecting the central nervous system.

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FREQUENCY OF FEVER AMONG CHILDREN AGED 0 TO 15 AT BAMAKO COMMUNE IV DISTRICT HOSPITAL IN 2023, MALI

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Despite progress in the fight against malaria in recent years in Mali and the sub-region, fever remains the most frequent reason for consultations in health facilities. The aim of this study was to identify the current causes of fever in children in Mali. A prospective cross-sectional study was conducted from February to November 2023 at the pediatric ward at the district hospital of the commune IV of Bamako. The study population concerned all patients received in routine consultation aged 0 to 15 years. A paper questionnaire was used for data collection. The entry was made in EPI data and the SPSS 25 software was used for data analysis.A total, we included 501 patients including 308 cases of fever, a frequency of 61.5%. Among the febrile cases, the male sex increased with 54.6%, the age group under 5 years represented 59.4% of the cases. The majority of patients lived in rural areas with 53.9%. Malaria was the leading cause of fever with (69.5%) followed by acute respiratory infections (26.6%) of Gastroenteritis (4.5%) of Salmonellosis (3.6%), oral candidiasis (2.9%) and malnutrition (0.6%). Most cases of fever were recorded in the months of (July August September) during the rainy season and in the months of (February and March) during the dry season. No significant variation between fever and age range was observed. However a significant variation between fever seasonality was observed during this study (p=0.000).Our results suggest that malaria remains the leading cause of fever in children and it was especially common in the under-5 age group. Further studies will be needed to better identify the different causes of fever in children in this health district.

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DEVELOPMENT OF FUNCTIONAL BOWEL DISORDERS AFTER TRAVEL IN DEPARTMENT OF DEFENSE BENEFICIARIES

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Post-infectious irritable bowel syndrome (IBS) has been associated with travelers' diarrhea (TD) in previous studies. We evaluated the association between TD and functional bowel disorders (FBD), based on the Rome IV criteria, in a prospective cohort of US Department of Defense (DoD) beneficiaries (TravMil), traveling to locations with risk of TD for ≤ 6.5 months between 2010-2019. 4787 US active duty servicemembers and adult civilian travelers were prospectively enrolled prior to travel or within 8 weeks following return. 1438 subjects completed a baseline FBD survey (documenting symptoms prior to travel), a post-travel survey (for symptoms and treatment during travel) and a 3-month follow-up FBD survey after return and were included in the analysis. The primary end point was new-onset FBD at 3 months post-travel, based on Rome IV criteria. The relative risk (RR) of FBD associated with TD was computed after adjusting for demographic and trip characteristics. The median age of enrollees was 45 years (IQR: 18-86y); 57% were male, 44% were active-duty personnel and 71% reported travel to a developing country within 5 years prior to enrollment. The median trip duration was 21 days (IQR: 13-61 days), 25% experienced TD and 9% used antibiotics. 15% of subjects reported FBD symptoms prior to travel. 10% (95%CI: 8-12%) reported new-onset FBD at 3 months post-travel. Functional diarrhea was the most common subset of FBD (38%) and 12% met criteria for IBS. TD (RR: 1.7 [95%CI: 1.2-2.6]), active-duty status (RR: 3.1 [95%CI:1.7-5.4]) and post-deployment enrollment (1.7 [95%CI:1.0-2.8]) were associated with new-onset FBD on multivariate analysis. The overall proportion of US DoD beneficiaries with FBD prior to and following travel in our cohort was lower than estimates for the US population (29-32%) possibly due to the older median age in our cohort. Our findings add to the existing post-infectious IBS literature by demonstrating an association between TD and FBD using the Rome IV criteria. Additional studies are needed to understand the increased risk of travel associated FBD in deployed servicemembers including the impact of TD severity and antibiotic use.

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EVALUATING THE IMPACT OF A LAO LANGUAGE MOBILE PHONE APPLICATION ON ADHERENCE TO ANTIMICROBIAL PRESCRIBING GUIDELINES IN LAO PDR

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Laos has one of the highest rates of antimicrobial usage among hospitalized patients in Asia. New antimicrobial prescribing guidelines were approved in 2020. An open cohort stepped-wedge cluster randomized 3-step controlled trial was conducted from 2021-2022 (16 months). The intervention was an antimicrobial prescribing guideline smartphone application with antimicrobial stewardship training at the time of introduction. The reference was a paper-based version of the same guidelines. Adherence with the guidelines was defined as prescriptions using the correct antimicrobial agent(s) and correct dose based on the provided guidelines. Primary outcome measurement was done by regular point prevalence surveys of hospital antimicrobial use (4-month intervals). A mixed-effects regression model, adjusting for the effect of time, clusters and possible confounders, was used to analyse the data. At month 0, 413/482 (86%; 82-87%-95%CI) of prescribers across six hospitals had access to paper-based guidelines. By the end of the study 382/498 (77%; 73-80%-95%CI) of prescribers had access to the intervention. Among inpatients, overall adherence to the guidelines was 17% (15-19%-95%CI; n=231/1,360) in the reference group and 26% (23-28%-95%CI; n=285/1,112) in the intervention groups (p<0.0001). Among outpatients, adherence was 22% (19-24%-95%CI; n= 263/1,212) and 23% (21-25%-95%CI; n=346/1,507) in the reference and intervention groups (p=0.433), respectively. The adjusted model showed that odds ratio (OR) for adherence to the guidelines in the intervention group compared to the reference group was 0.6 (0.36-1; 95%CI; p-value=0.06) among inpatients, and 0.9 (0.61-1.29; 95%CI; p-value=0.54) among outpatients. Adherence to the guidelines adherence was similar whether delivered in book format or by mobile phone application in Laos. While guidelines provide useful recommendations, adherence cannot be assumed, and the appropriate use of antimicrobials relies on multiple factors.

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VACCINE-INDUCED ANTIBODY LEVELS IN A PEDIATRIC POPULATION WITH WIDESPREAD ANTIBIOTIC USE

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Children in low- and middle-income countries (LMIC) frequently receive antibiotic treatment in their first year of life due to high rates of respiratory and diarrheal diseases. However, the impact of antibiotics on parenteral vaccine immunogenicity remains underexplored, especially in LMICs with high antibiotic use. Therefore, we conducted a retrospective cohort study using data from the Performance of Rotavirus and Oral Polio Vaccines in Developing Countries (PROVIDE) birth cohort study in Dhaka, Bangladesh. Antibiotic use was categorized based on duration of exposure and spectrum of activity. Vaccine-induced antibody levels against measles, pertussis toxin, pertussis pertactin, filamentous hemagglutinin, diphtheria toxoid, tetanus toxin, and *Haemophilus influenzae* type B (Hib) were measured at 53 weeks. Data from 582 evaluable infants were analyzed. Children in this cohort had high rates of antibiotic exposure, with a median of 80 days of use in the first year, 80% of which were broad-spectrum. Despite this, they were well-protected against measles, tetanus, and Hib, with 96%, 88%, and 91% respectively having antibody levels above protective thresholds. Neither duration nor spectrum of antibiotic exposure in the first 14 weeks of life significantly affected antibody titers at 53 weeks against pertussis, diphtheria, tetanus, or Hib, with two exceptions. We found lower anti-pertussis toxin titers in children with high broad-spectrum antibiotic exposure (>21 days) in the first 14 weeks of life (p = 0.049). Additionally, anti-measles titers in children with high broad-spectrum antibiotic exposure in the first 40 weeks of life were significantly higher than the low-exposure group (p = 0.015). Differences in measles and pertussis toxin antibodies between high- and low-exposure to broad-spectrum antibiotics were of limited clinical significance. Despite very high rates of antibiotic use in this cohort, no substantial impacts on vaccine-induced antibody titers were observed, suggesting the robustness of parenteral vaccine responses among children from LMIC with similar rates of antibiotic use.

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DISCORDANT DATING OF PREGNANCY BY LAST MENSTRUAL PERIOD VERSUS ULTRASOUND AND ASSOCIATED BIRTH OUTCOMES IN RURAL UGANDA

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Estimation of gestational age (GA) is most reliably achieved from the last menstrual period (LMP) confirmed by ultrasound (US) in early pregnancy. However, in resource-poor areas with limited access to US, pregnancy dating may rely only on LMP, which is often unknown. Inaccurate estimation of GA misinforms the true prevalence of population-level indicators such as preterm birth (PTB) and small-for-gestational-age (SGA). We evaluated the accuracy of estimated due date (EDD) via LMP (LMP-EDD) compared to Final EDD (where the LMP-EDD is corroborated by US) and compared the effect on the prevalence of PTB and SGA. In a cohort of 2757 pregnant women from Busia, Uganda enrolled in a randomized controlled trial evaluating intermittent preventive treatment of malaria in pregnancy, all participants received an US at the time of enrollment to confirm that GA was between 12-21 weeks. To determine the Final EDD, LMP-EDD was replaced with the US-determined EDD when the difference between the estimated GA was >7d (for GA <16 weeks) and >10 days (for GA between 16 and 20 weeks). The prevalence of PTB and SGA using LMP-EDD vs. Final EDD was compared among participants. Over half of the participants (56.8%) did not know their LMP and their GA was based solely on US. Among participants with known LMP, 253 (21.2%) had a change in EDD based on US. Overall, 7.6% of live births would have been classified as PTB if using LMP-EDD, compared to a PTB rate of 5.4% when using Final EDD (p=0.04). The overall rates of SGA were similar between the two methods (LMP-EDD 21.2% vs. Final EDD 22.4%, p=0.51). In the subset of patients with known LMP that were redated by US, the PTB rate was 16.0% vs. 3.5%, using LMP-EDD compared to Final EDD, respectively (p=0.01); the SGA rate was not significantly different (18.0% vs 23.6%, p=0.25). In summary, US was needed to determine the GA in the majority of our population. Use of LMP-EDD without US confirmation skews the true prevalence of PTB, an important maternal-child health metric. This study underscores the need for incorporation of US scans in antenatal care in low and middle-income countries.

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CLINICAL PRESENTATION, TREATMENT, AND OUTCOMES OF NEUROCYSTICERCOSIS AT AN ACADEMIC MEDICAL CENTER IN THE STATE OF FLORIDA, USA

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Neurocysticercosis (NCC) is a parasitic disease of the nervous system caused by the pork tapeworm, Taenia solium. Though NCC is the leading cause of seizures worldwide, it is under characterized in the US. In the US, NCC primarily occurs in patients who are immigrants and travelers to endemic countries. Characterizing the presentation, course, and outcomes of NCC patients will help clinicians improve diagnosis and treatment. A retrospective analysis was conducted from hospital records between 6/1/1993 until 6/1/2023 using ICD-9 and ICD-10 codes for NCC. Inclusion criteria for this study included those presenting to UF Health Shands Hospital (Gainesville, Florida) with asymptomatic or symptomatic NCC. Diagnostic criteria for NCC consisted of radiologic features, serologic evidence of T. solium infection, or pathological tissue confirmation. 34 patients met inclusion criteria. We collected epidemiological characteristics, hospitalization course, and clinical outcomes for each case. 97% of patients reported symptoms (seizures, neurologic deficits, headaches, hydrocephalus, nuchal rigidity, psychiatric disturbances, and altered mental status) prior to receiving an NCC diagnosis. 25% of patients presented with headaches, 20% presented with seizures, 15% presented with systemic symptoms such as fever, chills, and malaise, and 10% presented with CNS deficits such as cranial nerve deficits and tremors. 69% of patients had presented to another healthcare facility for these symptoms without receiving the correct diagnosis. 52% of patients' cysts were staged. Out of the 52% who were staged, 56% received incorrect medical management; these patients either received medications for inactive infection (18%) or did not receive proper medication for active infection (38%). 21% of patients were readmitted at least once for NCC symptoms or complications. Patients presenting with neurologic symptoms who have a history of travel to endemic areas need to be evaluated for neurocysticercosis. When patients are diagnosed with neurocysticercosis, it is essential that the stage of the infection is determined to properly treat the infection.

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IMPACT OF SULFADOXINE-PYRIMETHAMINE FOR MALARIA PREVENTION IN PREGNANCY ON THE RISK OF REPRODUCTIVE TRACT INFECTIONS: A RANDOMIZED CLINICAL TRIAL

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Pathogens responsible for treatable reproductive tract infections (RTIs), notably *Chlamydia trachomatis, Neisseria gonorrhoea*, and *Trichomonas vaginalis*, are estimated to cause >350 million infections annually and are associated with adverse birth outcomes, including abortion, stillbirth, preterm birth (PTB), low birth weight (LBW), small-for-gestational age (SGA), and neonatal death. Sulfadoxine-pyrimethamine (SP), the recommended drug for intermittent preventive treatment of malaria in pregnancy (IPTp), has activity against several bacterial pathogens, including *N. gonorrhea*, and in prior studies increasing doses of IPTp were associated with a decreasing risk of RTIs and adverse birth outcomes. However, there are limited data from randomized controlled trials (RCT) on the impact of IPTp-SP on RTIs and adverse birth outcomes. We are conducting a double-blinded RCT of monthly IPTp with SP vs dihydroartemisinin-piperaquine (DP) vs SP+DP (1:1:1) in HIV uninfected pregnant women residing in Busia District, Uganda. GeneXpert testing for RTIs (*C. trachomatis, N. gonorrhea, T. vaginalis, and Group B Streptoccus)* is performed on vaginal swabs collected during labor or within 28 days after delivery. To evaluate the impact of IPTp on the risk of adverse birth outcomes, we are performing a sub-study to evaluate relationships between IPTp arm, detection of RTIs, and adverse birth outcomes. Enrollment of 2757 women was completed between December 2020-December 2023. Based on preliminary findings through January 2024, 2192 women had delivered and the prevalence of RTIs at delivery was 6.0% for *C. trachomatis*, 2.6% for *N. gonorrhea*, 7.3% for *T. vaginalis*, and 9.7 % for Group B *Streptococcus*. The risk of a composite of adverse birth outcomes (abortion, stillbirth, LBW, PTB, SGA, or neonatal death) was 28.7%. Detection of *T. vaginalis*, but not the other studied pathogens, was associated with a significantly increased risk of having any adverse birth outcome (relative risk = 1.35, 95% CI 1.07-1.69, p=0.02). All women are expected to have delivered by August 2024, followed by unblinding, and unblinded results of the study will be presented.

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EPIDEMIOLOGY, CLINICAL PRESENTATION, AND MANAGEMENT OF SNAKEBITES IN GHANA: INSIGHTS FROM A RETROSPECTIVE STUDY AT A DISTRICT-LEVEL HOSPITAL

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Over 9,600 hospital visits due to snakebites are recorded annually in Ghana with a fatality rate of 3%. However, the epidemiology, clinical presentation, management, and outcomes have not been adequately studied. This retrospective observational study used clinical data on snakebites recorded from 2019 to 2023 at the Techiman Holy Family Hospital, a district-level facility in the Bono East Region of Ghana. The Ghana Health Service Ethics Review Committee approved the study protocol. Sociodemographic and clinical characteristics, as well as treatment and outcomes, were described. Data were obtained from clinical records of 587 snakebite victims. There were 366 (62.3%) male patients, with 50% being farmers. Most were bitten on the lower limb (81.2%), and presented with swelling 347 (63.8%), pain 342 (63.6%), and bleeding 126 (23.3%). Over one in five patients (22.3%) used a herbal remedy before reporting to the hospital. Initial whole blood clotting test (WBCT) was done for 480 patients and 111 (23.1%) of them had an abnormal result (greater than 20 minutes). A median of 5 vials each (IQR 2, 5) was used for the 430 patients (73.3%) who received antivenom. No anaphylaxis or other major side effects were recorded following antivenom administration. Other treatments included analgesia (87.5%), antibiotics (83.2%), anti-tetanus (70.3%), and steroids (59.3%). The commonest complications of the bites were cellulitis (39.2%), coagulopathy (17.9%), and anemia (6.6%), with a median hospital stay of 2 days (IQR 1, 4) and overall case-fatality of 2.4%. The study revealed a predominance of male patients, particularly farmers, highlighting the occupational risk in farming settings, a tendency for lower limb bites, and a high prevalence of hemotoxic envenoming. These can inform prevention efforts and appropriate antivenom stocking to address the specific characteristics of snakebite envenoming in the municipality and mitigate associated morbidity and mortality.

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MPOX INFECTION IN A POSTPARTUM PATIENT: A CASE REPORT FROM GHANA

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Monkeypox is a viral zoonotic disease caused by the monkeypox virus. The diagnosis can be easily mistaken for other differential diagnosis such as Chickenpox. In this paper, we discuss the case of a postpartum patient whose diagnosis of Monkeypox infection was missed on two occasions

before eventually being diagnosed and successfully managed remotely. A 42-year-old female had Caesarean section on account of severe pre-eclampsia and prolonged pregnancy. Three days after the surgery, she noticed a rash around the surgical wound which was misdiagnosed as a reaction due to adhesive allergy from the plaster. On discharge from the health facility, she noticed a spread of the similar rash to her face and reported back to the health facility where she was told she had developed Chickenpox and managed as an outpatient. Patient's condition however worsened over the next couple of days with the rash spreading to her arms, hands, legs, feet, and groin. She also subsequently developed low-grade fever, general malaise, fatigue, headache and vomited twice, leading to her coming to our emergency department. Significant examination findings included cervical and inguinal lymphadenopathy, and mostly papular skin rash with a few areas with vesicular skin eruptions. The labs were unremarkable. Her monkey-pox virus PCR swab result returned positive. Our health facility did not have in-patient isolation facilities. We decided to continue the management of the patient remotely after initial resuscitation, leveraging on telemedicine and scheduled out-patient visits. Through this innovative approach, patient recovered fully without the baby or any household member contracting the disease. This case presented clinical diagnostic problems. The first was with the location of the initial rash leading to the misdiagnosis of adhesive (plaster) allergy. The second was that Monkeypox was wrongly diagnosed as Chickenpox. This makes healthcare worker education very necessary, especially at the primary care level. The use of the telemedicine-based patient-centred care approach could help in the management of carefully selected patients in similar settings.

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TYPHOID CONJUGATE VACCINE DURATION OF IMMUNITY AND BOOSTER RESPONSE IN MALAWIAN CHILDREN

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A single dose of typhoid conjugate vaccine (TCV) given to children is safe, immunogenic, and efficacious in preventing typhoid fever for at least four years. A phase 3 trial of a Vi polysaccharide conjugated to a tetanus toxoid vaccine (Vi-TT) in Malawi, randomized children 1:1 to receive Vi-TT or meningococcal capsular group A conjugate vaccine. From this study population, we recruited children vaccinated at 9-11 months of age into a booster substudy to receive a first Vi-TT (1st-TCV) or booster (Booster-TCV) dose at approximately five years of age. Serum was collected before and 28 days after vaccination and tested for anti-Vi immunoglobulin (Ig) G and IgA antibodies by enzyme-linked immunosorbent assay (ELISA). Seroconversion was defined as ≥4-fold rise in antibody titers from day 0 to day 28 post-vaccination. We enrolled 136 children: 64 1st-TCV and 72 Booster-TCV. At baseline, a higher proportion of Booster-TCV (85.9% and 40.9%) compared to 1st-TCV children (26.6% and 3.1%) had detectable (≥7.4 ELISA Units (EU)/mL and ≥3.125 EU/mL) anti-Vi IgG and IgA titers, respectively. Geometric mean titers (GMT) rose significantly between day 0 and day 28 in both groups but were significantly higher in Booster-TCV children at 6794.2 EU/ml (95% CI 5738.2-8044.6) compared to 1st-TCV children at 2837.2 (2360.9-3409.6). Similar results were seen with IgA; 117.7 EU/ml (93.0-148.9) in Booster-TCV and 95.0 EU/ml (78.5-115.0) in 1st-TCV children. On day 28, all Booster-TCV children and all but one 1st-TCV child seroconverted for IgG. For IgA, a similar proportion of Booster-TCV [95.7% (88.0-99.1)] and 1st-TCV [98.4 (91.3-100.0)] children seroconverted at day 28. The geometric mean fold rise was lower in Booster-TCV [370.1 (289.4-473.4) and 56.7(44.1-73.0)] compared to 1st-TCV [(501.5 (373.5-673.4) and 42.7, (31.6-57.7)] children for both IgG and IgA, respectively, likely because 1st-TCV children started with lower titers. Our study shows a detectable Vi-TT immune response in most children at four years post-vaccination and a robust booster dose immune response at five years of age.

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SUCCESSFUL CHAGAS SCREENING PROGRAM IN OBSTETRIC PATIENTS IN A FEDERALLY QUALIFIED HEALTH CENTER IN NEW YORK

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Sun River Health (SRH) is the largest not-for-profit network of federally qualified health centers (FQHC) in NY State (NYS), with a visit volume of 250,000; 41% of patients were born outside of the USA and are predominantly from Central and South America. Chagas disease is underappreciated in the United States, reportable in only 8 states. Many providers are not familiar with the disease, epidemiology or the methods of screening and treatment. SRH began a formal screening program in our OB/GYN clinic in Brentwood, Long Island, in July 2023. A multidisciplinary team was engaged including nursing, infectious disease (ID), OB/Gyn, with strong support from administration. After intensive internal education, all patients seen in antenatal visits had country of birth recorded, and if born in endemic areas had Chagas serology performed. For those who tested positive, confirmatory testing was performed at the NYS Wadsworth Lab. Those who were confirmed positive, with a negative cardiology workup, were offered treatment post-delivery and after breast feeding. Babies of confirmed mothers, along with their siblings and spouses, were also tested. To date, 492 obstetric patients have been screened. Six patients were screened positive, 2 are confirmed, and 4 are pending confirmation. The ages of the women who screened positive ranged from 28 to 39 years. Four from El Salvador and 2 from Honduras. The 2 confirmed positive patients have begun treatment with benznidazole. One child has tested positive, but is awaiting confirmatory results. The success of this program is due to a multi-disciplinary group approach with OB/Gyn as a primary driver. Some of the challenges were the logistics of confirmatory testing and identifying patients for screening. Larger healthcare systems such as FQHCs serving these populations are perfectly positioned to develop screening programs to identify and treat those to with Chagas disease.

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IDENTIFYING BLOOD-BRAIN BARRIER SIGNATURES IN CEREBRAL MALARIA AND CENTRAL NERVOUS SYSTEM INFECTIONS TO INFORM TREATMENT TARGETS AND PATIENT STRATIFICATION

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Cerebral malaria (CM) is a leading cause of death and neurodevelopmental complications in African children. Post-mortem, in vivo retinal imaging, and magnetic resonance imaging studies have implicated blood-brain barrier (BBB) breakdown. BBB breakdown is driven by the adherence of *P. falciparum*-infected red blood cells to the endothelial surface of brain microvessels. Targeting cellular response pathways driving BBB breakdown in CM is key to improving patient outcomes, but the specific pathways involved are not well characterised. Existing models, while important, have limitations. Murine models of CM use a different parasite, and the pathology differs from human disease. In vitro BBB models, while manipulatable, are necessarily reductive. Therefore, it is important to identify their relevance. Post-mortem studies provide the only means to investigate the brain directly in human CM; however, investigating the cellular processes in the brain is complex. Rapid advances in spatial biology have enabled a step-change in

understanding such complex biological processes. We performed spatial transcriptomics and multiparameter imaging techniques on post-mortem brain tissue from fatal Malawian paediatric CM (n=51) and non-malaria central nervous system (CNS) infection cases (n=14). Histology, GeoMx Digital Spatial Profiling, and imaging mass cytometry (40-antibody panel) were used to characterise the cell interactions and phenotypes associated with BBB breakdown. Our data provides a spatially resolved atlas of cells in CM and CNS infection and a wealth of information about vascular and brain-associated changes. A focused analysis found that osteopontin and heme oxygenase-1 are significantly upregulated in vessels with BBB breakdown. These are linked to the downregulation of tight junction proteins. Notably, osteopontin has been associated with BBB breakdown in stroke patients. Additional experiments are in place to validate this dataset using orthogonal methods and in vitro mechanistic studies. Our data will help identify specific pathological CM endotypes and stratify patients to improve outcomes.

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EVALUATION OF A SCALABLE DESIGN FOR A PEDIATRIC TELEMEDICINE AND MEDICATION DELIVERY SERVICE: A PROSPECTIVE COHORT STUDY IN HAITI

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Early access to healthcare is essential to avert morbidity and mortality. A telemedicine and medication delivery service (TMDS) is an innovative solution to address this need, however pathways to scalability are unclear. Our objective was to evaluate a scalable design for a pediatric TMDS for low-resource settings that triages severe cases to hospital-level care, reserves in-person exams at households for moderate cases and provides virtual exams with medication delivery for mild cases.A prospective cohort study was conducted of pediatric patients (≤10 years) who were managed at the scalable TMDS (in-person exams reserved). Safety and feasibility metrics were compared to a prior TMDS mode in which all non-severe patients received both virtual and in-person exams (reference cohort). The primary outcome was rate of improvement (better/recovered) at 10-days. Among 1043 cases (41 severe; 1002 non-severe) enrolled at the scalable TMDS, 19% (190) of the non-severe cases received an in-person exam. Among the 382 cases (24 severe, 358 non-severe) enrolled in the reference cohort, 94% (338) of non-severe cases received an in-person exam. The rate of improvement at 10-days was similar between the scalable (97%, 897) and reference (95%, 329) modes. In the context of a five-fold reduction of in-person exams, the scalable TMDS mode that provides virtual exams with medication delivery for most mild cases had a non-inferior rate of improvement at 10-days. These findings provide a scalable pathway to improve healthcare access through a TMDS care model without compromising safety.

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QUALITY OF LIFE AND FATIGUE AFTER SEVEN YEARS OF CHIKUNGUNYA VIRUS INFECTION: RESULTS FROM A STUDY IN PIEDECUESTA, COLOMBIA

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Chikungunya virus (CHIKV) infection is associated with chronic sequelae whose burden has not been fully characterized. The study aimed to evaluate the quality of life (QoL) and the prevalence of fatigue in a cohort of adults exposed to CHIKV between 2014 and 2015 in Piedecuesta, Colombia. We evaluated 79 subjects (median age: 30 years, IQR: 21 years; women: 60.8%) with confirmed CHIKV infection (RT-qPCR or IgG/IgM ELISA) diagnosed during the outbreak (2014-2015) in Colombia. In 2022, patients completed the 36-item short form (SF-36) and the fatigue severity scale (FSS) surveys and underwent a physical examination that included the gait, arms, legs, and spine examination (GALS) conducted by trained physicians. A rheumatologist evaluated all patients with an abnormal, non-trauma-related GALS examination. We defined chronic fatigue (CF) as an FSS≥36 that persisted for >6 months. We assessed the association of QoL and CF with clinical outcomes by estimating age, sex, and comorbidities-adjusted OR (aOR) using multiple logistic regression. After a mean follow-up of 7.5 years, 11 patients (13.9%) were classified as cases of post-CHIK chronic inflammatory rheumatism (pCHIK-CIR), 32 (40.5%) as non-inflammatory pain likely degenerative (NIP-LD), and 36 (45.6%) as recovered from acute articular symptoms. Patients with pCHIK-CIR and NIP-LD had similar and significantly worse QoL (SF-36's physical and mental components) than those who recovered; however, CF's prevalence showed a gradient across groups, being significantly higher among pCHIK-CIR compared to recovered individuals: 54.6% (aOR=19.0, p<0.01), 25.0% (aOR=2.9, p=0.174) and, 8.6% (reference), respectively. Our results show that about one out of ten CHIKV infections develop chronic articular inflammatory sequelae. These are associated with worse QoL and a higher prevalence of CF. This profile might guide physicians in assessing the disease burden and differentiating pCHIK-CIR from NIP-LD.

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EXPLORING THE IMPACT OF HELMINTH CO-INFECTIONS ON SARS-COV-2 INFECTION DYNAMICS AND IMMUNE RESPONSE: A RETROSPECTIVE COHORT STUDY IN AN AFRICAN POPULATION

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The spectrum of clinical manifestations resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection varies widely. Despite the global halt of the COVID-19 pandemic, the reasons for Africa's comparatively limited exponential spread remain unclear. Helminth co-infections are suspected to have influenced the pandemic's trajectory in Africa. This study employs a retrospective cohort approach to investigate the interplay between SARS-CoV-2 and helminth infections. Blood plasma samples were analyzed from 104 participants using ELISA and Luminex assays, along with in vitro cell culture and stimulation. Our preliminary findings reveal an overall helminth seropositivity of 41.3% and a SARS-CoV-2 seropositivity of 52.9%, with a significant proportion co-infected. Interestingly, among asymptomatic SARS-CoV-2 infected individuals, the majority had helminth infections (61.5%, CI: 52.3 - 67.0). However, this proportion decreased as the severity of SARS-CoV-2 increased, suggesting a potential relationship between co-infection and milder symptoms. Coinfection and elevated levels of helminth-specific IgG were significantly linked to reduced odds of severe SARS-CoV-2 outcomes alongside decreased levels of SARS-CoV-2-specific IgA and IgG, as well as reduced neutralization potential against both wild type and variants. Moreover, individuals with co-infections showed altered cytokine expression

profiles favoring Th2 responses over Th1 and Th17 responses, whereas those with SARS-CoV-2 mono-infection tended to exhibit more Th1 and Th17 responses than Th2 responses. These initial findings indicate that while co-infection may influence adaptive immunity to SARS-CoV-2, it also helps to alleviate hyperinflammation linked to COVID-19 severity, ultimately enhancing overall health outcomes associated with SARS-CoV-2 infection.

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MULTIPLE PELVIC CONDYLOMATOUS MASSES IN AN AFRICAN CHILD

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Human herpes virus 8-associated malignancies cause significant mortality, mainly due to Kaposi Sarcoma (KS). While most patients with KS present with HIV infection, significant literature on the African endemic HIV-negative subtype is lacking. A twelve-year-old girl from North Ghana presented to a medical facility with rapidly increasing masses on the lateral lower pelvis. Physical examination revealed multiple fungating masses in the lateral side of the trunk suprapubic region, external genitalia, and generalized lymphadenopathy. The patient was negative for HIV antibody and VDRL. Biopsy of the pelvic mass was performed and sent to Labcorp. Histopathologic evaluation revealed a spindled cell vascular tumor positive for HHV8 immunohistochemical stain, consistent with KS, African endemic type. Adapalene, 0.1% cream, was prescribed, and the smallest 0.5 cm masses were entirely resolved after several weeks. Although HHV8 is the causative agent of Kaposi sarcoma and the most common cause of malignancy in HIV-positive individuals, the disease also occurs across sub-Saharan Africa in HIV-negative young adults and prepubescent children. This patient's disseminated lesions, generalized lymphadenopathy, and hepatomegaly suggest an aggressive form of endemic KS. While most cases of endemic KS have been described in Central and Southern Africa, her presentation in northern Ghana is somewhat unusual. While treatment for aggressive forms of KS with paclitaxel and liposomal doxorubicin is the first-line therapy, due to unaffordability, a third-generation retinoid was prescribed. However, retinoids have been successfully used to treat cutaneous KS. However, because of the aggressive and systemic nature of the patient's disease, it is unlikely that the patient will achieve remission from this drug alone. African Endemic KS is often a forgotten subtype that garners little attention and manifests with significant morbidity and mortality. It is hoped that governments can collaborate with pharmaceutical companies to make chemotherapeutic drugs available at low or no cost to treat this often fatal malignancy.

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NOT ALL SEVERE MALARIA CASES ARE SEVERE: IS IT TIME TO REDEFINE SEVERITY CRITERIA FOR MALARIA IN NON-ENDEMIC REGIONS?

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Management of malaria in non-endemic regions differs significantly from that in endemic regions. Despite this, the current definition of severe malaria in non-endemic areas follows WHO criteria, mainly targeting children in malaria-endemic areas, potentially misclassifying cases. We assessed the performance of a modified severe malaria classification criteria within our patient cohort. A retrospective cohort study of patients diagnosed and managed for malaria in a non-endemic hospital (2005-2023) was analyzed. Patients were classified into severe malaria (SM) and uncomplicated malaria (UM) according to WHO 2013 severity criteria with the exception of parasitemia. SM cases were re-classified into two new categories, named "very severe malaria" (VSM) and "less severe malaria" (LSM). A composite outcome called "life-threatening conditions", was defined, which integrated death and the need for life-saving interventions such as mechanical or non-mechanical ventilation, use of vasoactive drugs, hemodialysis and automated red blood cell exchange. Secondary outcomes included co-infections. The frequency of the outcomes was compared between groups (SM *vs.* UM and VSM *vs.* LSM). Among 506 malaria patients 176 (34.8%) presented with SM, according to WHO severity criteria. Regarding severity, 37(7.3%) patients developed a life-threatening condition, namely death (n=4) and/or the need for life-saving interventions (n=34). All fatalities and 33 of the 34 life-saving interventions occurred in the VSM group. Patients in LSM group did not develop any life-threatening conditions. As to co-infections, 28(5.5%) patients had a community-acquired co-infection, with no differences between groups (p=0.763). Severity criteria definitions would benefit from a review when assessing patients with malaria in non-endemic areas. Within the spectrum of severe malaria, patients reclassified as LSM have a low risk of developing a life-threatening condition, and could benefit from a less intensive monitorization unit and a restrictive use of empirical antibiotics.

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FIELD EVALUATION OF A NOVEL SEMI-QUANTITATIVE POINT-OF-CARE DIAGNOSTIC FOR G6PD DEFICIENCY IN INDONESIA

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The WHO recommends routine testing of G6PD activity to guide radical cure in patients with *Plasmodium vivax* malaria. Females can have intermediate G6PD enzyme activity, and to date, only complex quantitative diagnostics have been able to reliably identify them. The semi-quantitative G6PD diagnostic "One Step G6PD Test" (Humasis, RoK; "RDT") is a lateral flow assay that offers a simpler diagnostic alternative capable of distinguishing deficient, intermediate, and normal G6PD individuals. G6PD status of participants enrolled in Malinau and Nunukan Regencies and the capital Jakarta was assessed with the RDT, and their G6PD activity was measured in duplicate by reference spectrophotometry. The adjusted male median (AMM) of the spectrophotometry measurements was defined as 100% activity; 70% and 30% of the AMM were defined as thresholds for intermediate and deficient G6PD status, respectively. Results were compared to those derived from spectrophotometry at both of these clinically relevant thresholds. Of the 161 participants enrolled, 10 (6.2%) were G6PD deficient and 12 (7.5%) had intermediate G6PD activity by spectrophotometry. At the 30% threshold, the sensitivity of the RDT was 10.0% (95%CI: 0.3-44.5%) with a specificity of 99.3% (95%CI: 96.4-100.0%); the positive predictive value was 50.0% (95%CI: 1.3-98.7%) and the negative predictive value 94.3% (95%CI: 89.5-97.4%). The corresponding figures at the 70% threshold were 22.7% (95%CI: 7.8-45.4%), 100.0% (95%CI: 97.4-100.0%), 100.0% (95%CI: 47.8-100.0%) and 89.1% (95%CI: 83.1-93.5%), respectively. Although there is an urgent need for an easy-to-use, affordable, semi-quantitative point of care diagnostic for G6PD deficiency, the observed performance of the "One Step G6PD Test" in its current form was insufficient to guide antimalarial treatment.

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CHARACTERIZATION OF MORTALITY AMONG CHILDREN ADMITTED TO A RURAL MOZAMBICAN DISTRICT HOSPITAL: TWENTY-TWO YEARS OF CONTINUOUS HOSPITAL-BASED MORBIDITY SURVEILLANCE

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Hospitalized children in rural Sub-Saharan Africa often present an unacceptably high risk of mortality. Detailed descriptions of causes of death and in-hospital mortality trends provide valuable data to design targeted interventions for child mortality prevention. However, previous studies are often derived from unreliable and unspecific methods or focus solely on a particular disease. This study aimed to describe the main causes and trends of mortality across time, identifying risk factors independently associated to mortality during admission. Combining demographic and morbidity surveillance databases from the Manhiça district, Mozambique, admissions of children under 15 years to the Manhiça district Hospital from 2000 to 2021 were analysed. Over a total of 62200 paediatric hospital admissions, 2244 in-hospital deaths were identified (in hospital case fatality rate (CFR): 3.6%), with an additional 525 deaths within the first 7 days post-discharge (short-term mortality CFR: 4.45%) potentially linked to the same disease leading to the initial hospitalization. CFRs were significantly higher among neonates up to 28 days of age, and no clear decreasing trends were observed throughout the years. During our study period, malaria was the major contributor to overall mortality, closely followed by pneumonia. However, the proportion of deaths attributed to malaria declined, whereas conditions arising during the perinatal period increased. Variables related with respiratory distress, decreased consciousness status, malnutrition and diarrhea-associated symptomatology showed a higher prognostic value for death across all age groups and were found to be major independent risk factors for death. Other variables such as timing of admission (night or weekend admissions, or certain months during the cold season) also posed a higher risk of death for the admitted patient. This study highlights opportunities for clinicians and policy makers to target specific signs and symptoms, conditions, time periods, and geographical areas in measures aimed at improving child survival.

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ANTIBODY-OMICS REVEALS DISTINCT IMMUNOLOGICAL SIGNATURES IN LEPROSY PATIENTS AND THEIR HOUSEHOLD CONTACTS

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Leprosy diagnosis is often complex, requiring assessment of clinical and laboratory parameters. Lack of tests for an unequivocal early diagnosis has limited control and elimination efforts. Current antibody (Ab) tests (e.g. anti-LID-1 IgG, anti-PGL-1 IgM), offer limited and variable sensitivity. We have developed a multiplexed 'Ab-omics' platform for deep characterization of a diverse array of antigen-specific Abs (isotype, glycosylation, and Fc receptor binding). Applying the Ab-omics pipeline to sera from clinically confirmed leprosy patients, their household contacts (HHC) and endemic controls (EC) (n=92, from Minas Gerais, Brazil), using multiple M. leprae and other antigens uncovered distinct biomarkers indicative of leprosy. With a total of 221 measured features for each sample, LASSO-based feature selection identified an Ab signature, accurately distinguishing Leprosy patients and HHC (AuC>0.9). This included: IgA-PGL1, IgG3-PGL1, RCA-CFP10, FcR1-ML2567. Further we applied SLIDE, a novel interpretable machine learning method, to this high-dimensional dataset to identify latent factors that moves beyond individual biomarkers and provide insights into the pathophysiology of leprosy-infected patients as well as HHC and EC subjects. This identified modules with unique humoral signatures of active disease, including a module highlighting hallmark signatures of infection such as elevated IgG, IgG1, and IgM. However, we also captured previously uncharacterized humoral responses including elevated FcR binding and reduced sialylation and galactosylation in actively infected patients, helping distinguish them from HHCs. Furthermore, analysis of cytokines and chemokines obtained in culture stimulated with crude ML antigen demonstrated an inflammatory profile (IFN-g, TNF and IL-10) in leprosy patients. Overall, we unveil both novel biomarkers for Ab-based diagnostics and latent factors underlying the pathogenesis of Leprosy infection. Our results suggest selective antigen and Fc receptor targeting could be the key to early detection and controlling infection severity.

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DISSECTING THE DIAGNOSTIC PERFORMANCE OF THE ALERE FILARIASIS TEST STRIP FOR THE DETECTION OF ACTIVE *WUCHERERIA BANCROFTI* INFECTION AND TREATMENT SUCCESS

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Accurate and reliable diagnostic tools are critical in achieving the 2030 elimination targets for Lymphatic filariasis (LF), mostly caused by the *Wuchereria bancrofti* parasite. However, there are several concerns regarding the accuracy of the endpoint infection thresholds reported using the Alere Filariasis Test Strip (FTS), recommended for LF assessment surveys and treatment monitoring. This study sought to investigate the diagnostic performance, particularly sensitivity and specificity, of the FTS in providing precise endpoint infection thresholds. Plasma samples obtained from the same cohort of individuals (n = 143) with known adult worm and microfilariae (Mf) burdens at pre-treatment and 24 months post-treatment were used. The sensitivity of the FTS was evaluated in microfilaremic and amicrofilaremic subgroups of adult worm-infected individuals at both time points. Its specificity was assessed in those who cleared adult worm and Mf burdens two years after doxycycline macrofilaricidal treatment. Additionally, samples from 71 uninfected individuals living in the same endemic area were also analyzed for comparison. The FTS showed significantly greater sensitivity in detecting microfilaremic adult worm-infected individuals (pre-treatment = 100%; 24 months post-treatment = 95.8%) compared to their amicrofilaremic counterparts (pre-treatment = 65.8%; 24 months post-treatment = 52.2%). The specificity of the FTS in confirming treatment success among those who cleared both adult worm and Mf burdens at 24 months post-treatment was 73.0% (CI = 62.58-81.90). This was significantly lower compared to its specificity for uninfected individuals (95.8%, CI = 88.14-99.12). Overall, our findings reveal the subpar diagnostic performance of the FTS in detecting amicrofilaremic adult worm-infected individuals and confirming treatment success in individuals who clear adult worm and Mf two years after treatment. Hence, there is a need for alternative diagnostic approaches with improved performance characteristics, particularly in post-treatment contexts, to expedite the realization of the 2030 elimination targets for LF.

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COMPARATIVE ANALYSIS OF THE OV16 ENZYME LINKED IMMUNOSORBENT ASSAY AND THE OV16 RAPID DIAGNOSTIC TEST FOR THE MAPPING OF ONCHOCERCIASIS AND THE DISCONTINUATION OF MASS DRUG ADMINISTRATION

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Various tools have been evaluated for the diagnosis of onchocerciasis, including the standard diagnostic (SD) Bioline ELISA and the rapid diagnostic test (RDT), but their performance has been inconsistent. Sensitivity, specificity, and standardization of these tools are major challenges. We conducted a study to compare the sensitivity and specificity of the Ov16 ELISA and Ov16 RDT in detecting onchocerciasis infection in dried blood spots from individuals aged 1-10 years in two first-line villages in Central Cameroon. The Ov16 IgG4 ELISA kit and the Ov16 RDT were used to detect antibodies. Spearman correlation and kappa statistics were used to assess relationships and agreement between tests. A total of 158 samples (seroprevalence: 28.2%) were positive for Ov16 antibodies by ELISA and 104 (seroprevalence: 18.6%) by Ov16 RDT ($p<0.0001$). Median IgG4 levels were significantly higher in RDT-positive samples ($p<0.0001$). The agreement between the two tests was good, with high sensitivity (96.4%) and specificity (88.6%). Spearman correlation showed a positive correlation between RDT grade and antibody level, with the higher antibody rate observed in grade 2 and 3 tests ($r = 0.654$, $p<0.0001$). Although there was overall agreement between the Ov16 RDT and the Ov16 ELISA, with good concordance between the two tests, the Ov16 ELISA was able to detect more Onchocerca volvulus infections than the Ov16 RDT. Further studies in other populations and settings may be needed for a more thorough evaluation.

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FOCAL SPLEEN LESIONS IN LOIASIS: THE SPLOA PILOT STUDY IN GABON

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Infection with the filarial nematode *Loa loa*, has been associated with increased morbidity and mortality. A number of reports described the presence of spleen nodules, originating from degradation of microfilariae, in humans and animals infected with *L. loa*. The long-term consequences of this process on individuals chronically exposed to infection in terms of spleen function and possible link with excess mortality are unknown. The aim of this study was to evaluate the prevalence of focal spleen lesions, their evolution over time, and markers of spleen function, in individuals with *L. loa* infection living in highly endemic areas of Gabon. This was a cross-sectional study followed by a longitudinal study of subjects with spleen nodules. 216 participants from Ngounié and Moyen-Ogooué provinces of Gabon, reporting a history of eyeworm migration and/or Calabar swelling, were included. Participants were categorized into infected microfilaraemic with low (N=74) and high (N=10) microfilaraemia, and symptomatic amicrofilaraemic (N=132), based on evaluation of microfilaraemia by microscopy. Howell-Jolly bodies in erythrocytes, as indirect marker of spleen functional impairment, were not observed. On ultrasound, no evident signs of spleen fibrosis or hypotrophy were observed. Multiple spleen hypoechoic centimetric macronodules were observed in 3/216 participants (1.4%), all with patent *L. loa* infection (3.4% of microfilaraemics); macrondules disappeared at the 6-months follow-up examination in 2/3 individuals. Spleen hypoechoic micronodules, persisting at the 6-months follow-up, were detected in all 3/216 participants (1.4%), who became all amicrofilaraemic. Transitory spleen macronodules are present in a small but consistent proportion of individuals with patent loiasis, appearing a rather benign phenomenon in terms of impact on spleen morphology and function. Their occurrence should be taken into consideration to avoid misdiagnosis and mistreatment. Prevalence and significance of spleen micronodular ultrasound patterns in the general population would be also worth evaluating.

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ELIMINATION GOALS FOR ONCHOCERCIASIS CAN BE PROGRESSED FASTER BY INCORPORATING TREATMENT WITH REPURPOSED DRUGS THAT TARGET VARIOUS STAGES OF FILARIAL WORMS

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The Current Preventive Chemotherapy and Transmission Control strategy for onchocerciasis aims to interrupt transmission through annual or bi-annual mass drug administration with ivermectin (IVM). Without available macrofilaricides, however, the adult worms producing microfilariae will survive, underscoring the urgent need for developing macrofilaricides. Importantly, transmission model simulations indicate that the combined use of a hypothetical macrofilaricide (with ~60% efficacy) with IVM would substantially increase the probability of elimination compared with the independent use of each, highlighting a need for alternative integrated treatment regimens. Using phenotypic screenings of drugs approved for clinical use, we have identified several drugs that can be repurposed for use as therapeutic macrofilaricidal (targeting adult worms and/or embryos) as well as prophylactic drugs (targeting the establishment of early infections in the host that would have otherwise developed into adult fertile worms). We demonstrated that, 1) Nelfinavir (anti-HIV drug that targets aspartic proteases) significantly inhibited motility of *Brugia pahangi* female worms *in vitro* and reduced survival of adult worms as well as their fecundity *in vivo*; 2) Niclosamide and Rottlerin (autophagy inducing drugs) significantly reduced *Wolbachia* levels *in vitro* and *in vivo*, as well as embryogenesis and fecundity in treated female *B. pahangi* worms *in vivo*; and 3) Emodepside (repurposed macrofilaricide under clinical development), when used as a prophylactic drug, inhibits molting and motility of *O. volvulus* and *B. pahangi* early stages of the parasite *in vitro* with IC_{50}s in the nanomolar range. Our findings indicate that a major programmatic shift that incorporates integrated control strategies, aimed at reducing both the overall adult worm burden and transmission, is needed to achieve the 2030 WHO elimination of transmission goals for onchocerciasis.

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EVALUATION OF A NOVEL BIPLEX RAPID DIAGNOSTIC TEST FOR ANTIBODY RESPONSES TO *LOA LOA* AND *ONCHOCERCA VOLVULUS* INFECTIONS

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Loiasis, caused by the filarial worm *Loa loa*, affects approximately 10 million individuals. Clinical manifestations include Calabar swellings, eye-

worm, and less specific general symptoms. Loiasis presents a significant public health challenge because *L. loa*-infected individuals can develop serious adverse events after taking ivermectin, the drug used to combat onchocerciasis. In this context, alternative interventions and rigorous diagnostic approaches are needed. Diagnosing loiasis is challenging due to sporadic and non-specific clinical symptoms. The definitive diagnosis relies on identifying adult worms migrating beneath the conjunctiva, or microfilariae (embryos) in blood smears. However, "occult loiasis" (infection without blood microfilariae) is frequent. Serological rapid antibody diagnostic tests (ARTs) can provide an alternative diagnostic method. We compared a novel ART simultaneously targeting onchocerciasis (IgG4 to Ov-16 and OvOC3261, test line 1) and loiasis (IgG4 to L1-SXP-1, test line 2), called IgG4-SXP-1 biplex test, to the already established *Loa*-ART (all IgG isotypes to LI-SXP-1, called pan-IgG-SXP-1 test). Sensitivity was similar for both ARTs when using eye-worm or Calabar swelling history as references, but diagnostic performance varied based on microfilaremia levels and occult loiasis. Overall, IgG4-SXP-1 biplex test demonstrated a sensitivity of 84.1% and specificity of 47.6% for loiasis compared to the pan-IgG-SXP-1 test, leading to a Kappa coefficient estimated at 0.27 ± 0.03 for the qualitative results of the 2 ARTs. In the group that tested positive with the Pan-IgG test but negative with the IgG4-specific test, there was a lower prevalence of STH infection (p=0.008) and elevated eosinophilia (p<0.001) compared to the general tested population. The diagnostic agreement between the two ARTs was poor, suggesting that IgG and IgG4 antibody responses should be interpreted differently. The assessment of the innovative IgG4-SXP-1 biplex test, designed for onchocerciasis and loiasis, shows encouraging sensitivity but underscores the necessity for further in vitro assessment.

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RANDOMIZED, DOUBLE-BLIND TRIAL EVALUATING THE SAFETY AND EFFICACY OF A 3- OR 5-DAY COURSE OF LEVAMISOLE (2.5 MG/KG) IN SUBJECTS WITH *LOA LOA* MICROFILARAEMIA

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Onchocerciasis elimination programs are based on repeated mass administration of ivermectin to the entire population living in endemic areas, without prior diagnosis. However, these programs face challenges in loiasis co-endemic areas due to the risk of serious adverse reactions caused by ivermectin in individuals with high *Loa loa* microfilarial density (MFD). This research aims to evaluate a pre-treatment strategy based on levamisole (LEV) to reduce the *L. loa* MFD, enabling subsequent safe mass treatment with ivermectin in onchocerciasis-loiasis coendemic areas. This study represents the second trial of LEV in *L. loa*-infected subjects. In 2021, we conducted the first double-blind, randomized, placebo-controlled clinical trial in the Republic of Congo, evaluating the safety and efficacy of single doses (escalating dosages) of LEV on *L. loa* MFD. This trial demonstrated the safety of LEV in managing *L. loa* MFD and showed that a single dose of 2.5 mg/kg of LEV induced a transient but still insufficient reduction in MFD. The objective of the present trial is to evaluate the safety and efficacy of 3-day or 5-day regimens of LEV at 2.5 mg/kg. This trial is also a double-blind, randomized, placebo-controlled trial and will involve individuals with high *L. loa* MFD. It will be conducted from June 2024 in a rural area of Congo (Lékoumou department). A total of 99 subjects will be included in one of three study arms: 3 days of LEV (2.5 mg/kg), 5 days of LEV (2.5 mg/kg), or placebo. The goal is to recruit as many individuals as possible with at least 10,000 microfilariae/mL during the screening campaign, but all patients with microfilaremia can be included. Included individuals will be followed for 1 month (15 days of close follow-up for safety and 30 days to assess efficacy on *L. loa* MFD). The main evaluation criteria are assessment of adverse effects during the 15 days following treatment, and assessment of *L. loa* MFD reduction rates at one month.

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PROVIDING EVIDENCE ON THE STATUS OF TRANSMISSION OF ONCHOCERCIASIS IN FIVE COUNTIES IN LIBERIA

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In 2018, Liberia conducted its first programmatic Ov16 serological survey (pre-stop) to provide evidence on the status of transmission of Onchocerciasis in the Southwest Regions (five counties: Bomi, Cape Mount, Margibi, Grand Bassa and River Cess). These five counties had received 14th years of MDA with ivermectin. Specifically, the objective was to determine the village level sero-prevalence of Ov16 in children 5-9 years old. A target convenience sample size of 100 children from each of 30 frontline communities within 5km of a blackfly breeding site or onchocerciasis river basin was selected in line with WHO onchocerciasis technical subcommittee guidelines. All enrolled consented children were tested for Ov16 using RDT in the field, and DBS were collected to allow subsequent ELISA testing. Of children testing negative for rapid test, 10% was randomly selected for confirmatory testing using SD Ov16 ELISA (Abbott, South Korea). Out of the target sample size of 3,000, a sample size of 2,468 was achieved. 91 of these children tested positive for Ov16 via RDT in the field. Out of 30 communities tested with RDT, 19 communities had positive cases while 11 reported all negative tests. The overall seroprevalence rate of 3.7% (91/2432) was found in five counties (Bomi, Grand Bassa, Grand Cape Mount, Margibi and Rivercess) with rate of 3.7% (21/572) in onchocerciasis endemic county only. In addition, rates of 3.2% (10/314), 0.5% (3/595), 0.7% (3/455) was observed in onchocerciasis and lymphatic Filariasis co-endemic counties with a high rate of 10.9% (54/496), respectively. According to WHO, to proceed to a full stop MDA survey, the prevalence threshold for IUs to "pass" pre-stop is <2%. We realized only two counties have crossed this benchmark, onchocerciasis transmission is still ongoing in Rivercess county and there is a need for support to conduct similar testing in the remaining 10 counties.

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DEVELOPMENT OF A SIMPLE AND SENSITIVE SPLINTR LIGASE MEDIATED MICRORNA DETECTION METHOD FOR FILARIAL MIR71 AND BANTAM

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MicroRNAs (miRNA) are short (19-25 nt) non-coding RNAs that are found in an evolutionarily diverse assortment of organisms ranging from sponges to vertebrates, including filarial worms. Some miRNAs appear to be filarial-specific and differentially expressed in different stages of worm development. miR-71 is one of the most ubiquitous, conserved and highly expressed miRNAs in helminths, including *Brugia malayi*. It regulates multiple cellular processes and plays an important role in host-nematode interactions. It is found in extracellular vesicles secreted by filarial nematodes that could be internalized by host immune cells and regulate the host immune response. Even for the parasite such as *Onchocerca volvulus* that does not live in the bloodstream, circulating parasite-derived miR-71 has been found in human serum samples from infected human subjects, but not in uninfected ones, indicating that miRNA could serve as potential biomarkers. However, to detect the low levels of the filarial miRNA in human serum, a sensitive detection assay is essential for field application. Here we describe the development of an optimized SplintR ligase mediated microRNA detection method that uses a combined hybridization and ligation step of two DNA probes followed by sensitive qPCR detection for two filarial miRNAs: miR-71 and bantam. The assays showed higher sensitivity than other commercial miRNA detection methods and can specifically detect less than 100 copies of microRNA within 2 hours. Both microRNA can be detected in RNA extracted *Dirofilaria immitis* and *B. malayi*. Potential application was also demonstrated by detection of miRNA

in serum from infected host. This technique holds the promise of broad utilization as a miRNA detection tool in both scientific research and clinical settings.

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PERFORMANCE OF ELISAS BASED ON CHIMERIC PROTEINS TO DETECT ANTIBODY TO *ONCHOCERCA VOLVULUS* INFECTION

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WHO's target product profiles (TPP) for onchocerciasis outline stringent criteria, requiring tests intended for mass drug administration stopping decisions to have a sensitivity of ≥89% and a specificity of ≥99.8%. Achieving this specificity will require the use of multiple biomarkers. To identify *Onchocerca volvulus*-specific antigens to use in combination with Ov16, we utilized a serum epitope repertoire analysis (SERA) platform that employs a 12-amino acid peptide library display followed by next generation sequencing with proprietary informatics to screen unique reactivity to sera. 60 *O. volvulus* confirmed positive sera, 60 *O. volvulus* negative sera, and 60 *Wuchereria bancrofti* positive sera to eliminate cross-reactive epitopes were screened using SERA. Ninety-nine peptides were identified that showed reactivity for total IgG, IgG1, or IgG4 in positive *O. volvulus* specimens and no reactivity in negative or *W. bancrofti* specimen. These peptides underwent further screening using peptide arrays, with 24 epitopes exhibiting signal-to-noise (S/N) ratios ≥10. Candidate epitopes were mapped to specific proteins, synthesized as 24 amino acid biotinylated peptides, and screened in peptide ELISA against cross-reactors such as *W. bancrofti, Mansonella perstans,* and *Loa loa* pooled positive sera. We identified 19 peptides with S/N>10 and no reactivity against the cross-reactors. We created seven multi-epitope, chimeric (c) proteins using various peptide combinations, evaluated their antigenicity using the VaxiJen prediction program, and expressed them in an *E. coli* bacterial expression system. The most effective antigen combination (rOv16-rOv18c-rOv53c) demonstrated an improved sensitivity of 98% compared to the 89.5% sensitivity of rOv16 ELISA alone. None of these antigens alone or when used as combination was able to meet the WHO specificity requirements, and as such efforts are ongoing to identify additional biomarkers to meet the goal. Nevertheless, combining these antigens to detect IgG4 antibodies effectively met the minimum TPP sensitivity criteria for onchocerciasis mapping and stopping decisions.

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DEVELOPMENT OF A NEW RAPID DIAGNOSTIC TEST TO SUPPORT ONCHOCERCIASIS ELIMINATION

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Around 21 million people are estimated to have onchocerciasis (river blindness), a parasitic disease caused by the filarial nematode *Onchocerca volvulus* (Ov). Currently, the primary strategy for combating onchocerciasis is community-directed treatment with ivermectin (CDTI), requiring a minimum of 80% annual therapeutic coverage for 12-15 years. For onchocerciasis mapping and to know when and where CDTI could be stopped, highly sensitive and specific onchocerciasis diagnostic tests are needed. Rapid tests detecting Ov16 IgG4 antibodies in blood have been developed but showed diagnostic performances slightly lower than the 99.8% specificity as defined in the target product profiles generated by the WHO. To improve the existing Ov16 lateral flow immunoassay (LFA), the goal of this project is to achieve the targeted specificity performance by multiplexing immunogenic Ov antigens. First, we completed an *in silico* evaluation of 45 published Ov antigens using pairwise alignment on proteomes of helminths co-endemic with onchocerciasis. We selected 4 Ov candidate antigens (OVOC3261, OVOC10469, OvMCBL02 and LBE8) with ≤70% amino acid sequence identity over >70% of the total protein length with orthologs from related filarial and other helminth species. To further assess these candidate antigens, each antigen was separately immobilized on ELISA microplates, as well as on LFA membranes, and tested using plasma samples from patients with onchocerciasis, loiasis, mansonellosis and lymphatic filariasis along with healthy controls to confirm sensitivity, specificity, and absence of cross-reactivity with other helminths. For this purpose, we worked with partners in Africa to source a panel of clinical specimens to enable development and performance evaluation of the new onchocerciasis LFA. Then, prototyping of singleplex LFAs was performed in collaboration with DCN Dx to identify best mutual test conditions prior multiplexing. The next milestone of the project will focus on the feasibility, optimization, and clinical diagnostic performance evaluation of the prototype multiplex LFA to support WHO's goal of eliminating onchocerciasis.

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MAMMALIAN EXPRESSED OV16 ELISA PERFORMANCE ON GHANA PROGRAM SAMPLES IN COMPARISON TO ELUTED DRIED BLOOD SPOT ON OV16 RAPID DIAGNOSTIC TEST

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Onchocerciasis elimination programs are challenged by the lack of diagnostic tests that meet the WHO target product profile criteria for stopping mass drug administration (MDA). We developed a new Ov16 ELISA using a mammalian expressed Ov16 antigen (Ov16m ELISA) with improved assay performance, shorter time to result, and using standardized pre-coated and dried plates. Validation of the Ov16m ELISA showed excellent performance for precision (<15% CV), limit of detection, and stability. Using a validation panel of 314 samples, the Ov16m ELISA had sensitivity and specificity of 92.9% and 98.5%, respectively. Here we show data from an evaluation of the Ov16m ELISA using Ghana onchocerciasis program samples and compared with a current test used by programs, the eluted dried blood spot (DBS) on the SD Bioline Ov16 rapid diagnostic test (RDT). To validate the new ELISA 2,723 DBS samples were collected from participants aged 0-85 years in 4 districts in Northern Ghana where MDA has been ongoing for >15 years as part of a project to evaluate a 2% seroprevalence threshold for stopping MDA. All samples were tested by Ov16m ELISA at CDC and DBS RDT in Ghana. There were 57 positives by DBS RDT (2.1%) and 27 positives by Ov16m ELISA (1.0%). Of the 27 Ov16m ELISA positives, 21 were also positive by DBS RDT. The Ov16m ELISA showed 36.8% percent positive agreement and 99.8% percent negative agreement with the DBS RDT. In children aged 5-9 years (n = 2126) there were 30 positives by DBS RDT (1.4%) compared to 5 positives on the Ov16m ELISA (0.2%). Comparatively, in adults ≥20 years (n = 198) there were 20 positive by RDT (10.1%) compared to 19 positives (9.6%) on the Ov16m ELISA. The difference in positivity by the two tests could be due to Ov16m ELISA being either less sensitive or more specific than the DBS RDT. Because the DBS RDT has not undergone a rigorous validation, while the Ov16m ELISA's performance characteristics have been documented as part of a rigorous validation, the differences here may be due to the

Ov16m ELISA possessing a higher specificity. Comparing these and other upcoming assays using a defined panel of well-characterized specimens will be crucial.

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WHO LABORATORY CAPACITY REVIEW TOOL FOR ONCHOCERCIASIS

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The World Health Organization (WHO) NTD 2021-2030 road map has identified onchocerciasis (river blindness) as one of the diseases targeted for elimination. The road map also highlights critical areas necessary to achieve the onchocerciasis elimination targets, one of which is quality laboratory capacity to conduct testing for monitoring and evaluation (M&E) of programs and perform post-elimination surveillance. The WHO Onchocerciasis Laboratory Capacity Survey is an online data gathering tool developed to assess laboratory capabilities and capacities, with an emphasis on onchocerciasis elimination programs. The information collected from the survey will be used to identify a laboratory's strengths and needs. The survey tool was used to conduct an assessment of various general laboratory aspects, specifically their capacity to perform PCR testing of blackflies, one of the key elements needed to verify onchocerciasis elimination. The tool consists of 40 questions addressing areas including general laboratory facilities, testing capabilities, quality assurance, data management and test reporting, specimen shipping and receiving, training activities, and laboratory safety. Twenty-two institutions from 17 French and English-speaking onchocerciasis-endemic African countries were invited to participate in the survey. At the time of abstract submission, 17 institutions (77.3%) had completed the survey. Among respondents, 15 labs (88.2%) responded that they perform PCR and 15 (82.3%) perform PCR for onchocerciasis. Seven labs (52.9%) responded they currently have capacity for qPCR testing while seven labs (41.1%) perform qPCR testing for onchocerciasis. Fourteen labs (82.4%) indicated they performed human serology testing for onchocerciasis on over 1000 samples per year. The WHO Onchocerciasis Laboratory Capacity Survey compiles information electronically as quantifiable metrics that can be analyzed between/among countries to identify current status and gaps as well as to evaluate metrics over time to understand successful improvement in capacity/capability and identify needs for further investment and support.

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SAFETY OF A SINGLE DOSE OF MOXIDECTIN AND OF IVERMECTIN: FIRST RESULTS OF A LARGE STUDY IN INDIVIDUALS LIVING IN AN ONCHOCERCIASIS ENDEMIC AREA OF THE DEMOCRATIC REPUBLIC OF CONGO AND IN AN ONCHOCERCIASIS-LYMPHATIC FILARIASIS CO-ENDEMIC AREA IN CÔTE D'IVOIRE

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Community-directed treatment with ivermectin (IVM) over decades has controlled onchocerciasis as a public health problem in Africa and may have eliminated onchocerciasis in some areas, but alternative strategies are required for elimination across Africa. Moxidectin (MOX) reduces skin microfilariae levels (SmfL) more and for longer than IVM. MOX 8 mg is approved by the US Food and Drug Administration for treatment of onchocerciasis in patients ≥12 years old. MDGH is seeking regulatory approval for children 4 to 11 years old. A double-blind study is comparing the safety of a MOX and a 150 µg/kg IVM dose (MOX:IVM randomization ratio 4:1) in two locations: in onchocerciasis endemic areas in Ituri province of the Democratic Republic of Congo (DRC) and the onchocerciasis–lymphatic filariasis co-endemic Akoupé district of Côte D'Ivoire (CDI) where 400 mg albendazole is co-administered. Participants ≥8 years old received 8 mg MOX and those 4-7 years old 4 mg MOX. Individuals ≥12 years old with or without detectable SmfL (across 2 iliac crest snips), circulating filarial antigen (filarial test strip) or night microfilaremia were eligible. SmfL were not measured in children. All participants were assessed daily for adverse events (AEs) to 5 days after treatment and at Month 3. In DRC, 8026/8925 people screened were randomized and treated in this study, and 323 in a concurrent repeat-dose efficacy and safety study requiring ≥10 mf/mg skin for eligibility. Of the 7839 participants ≥12 years, 96% had undetectable SmfL; the remainder had between 0.1 and 34.8 mf/mg skin. In CDI, enrolment of children is ongoing. Of 4316 people ≥12 years screened, 4130 were randomized and treated: 93% had undetectable SmfL (the remainder had between 0.3 and 51.9 mf/mg skin) and 99% had undetectable night microfilaremia. To date, 5% of participants in DRC and 26% in CDI reported at least one AE. The types of AEs were similar to those in the Phase 2 and 3 studies, occurring primarily in the 5 days after treatment. In DRC and CDI, respectively, 96% and >99% of AEs were mild or moderate in severity. Details of the study design, participant population and safety results will be presented.

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FEASIBILITY OF A NOVEL ONCHOCERCIASIS RAPID DIAGNOSTIC TEST IN MARIDI, SOUTH SUDAN

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Point-of-care diagnostic tests are most indicated for confirming *Onchocerca volvulus* transmission in remote, resource-limited communities. In this regard, we conducted a serosurvey in Maridi (South Sudan) to determine the field feasibility and performance of a novel "Biplex A" rapid diagnostic test (RDT) developed by the company DDTD. In February 2023, children aged 3-9 years were recruited from five study sites situated at different distances from the Maridi Dam (blackfly breeding site). *O. volvulus* antibodies were detected with the prototype Biplex A RDT (detects antibodies to Ov16 and OvOC3261 at test line 1, and to Ov33.3 and OvOC10469 at test line 2), and the well-established Ov16 SD Bioline RDT using whole blood obtained by finger-pricking the participants. The feasibility and acceptability of the prototype Biplex A RDT were assessed, and the results of both tests were recorded. The Ov16 seroprevalence with the Ov16 RDT was 76/248 (30.6%), with the highest prevalence in children living closest to the Maridi Dam. Testing the children with the Biplex A RDT was found to be feasible and acceptable; additionally, testers reported its ease of use. Biplex A, test line 1, indicating a combined seroprevalence to Ov16 and OvOC3261, was positive in 84/239 (35.1%) of the children. Test line 2, reflecting seropositivity towards Ov33.3 and OvOC10469, was positive in 44/239 (18.4%) of the children. Both lines of the Biplex A RDT were simultaneously visible in 37/239 (15.5%) of the cases. In conclusion, the prototype Biplex A RDT was easy to use in the field, and its performance relative to the SD Bioline RDT was acceptable. Additional studies with skin snip test results, evaluating other types of this Biplex are currently being analysed. The high Ov16 seroprevalence suggests high ongoing *O. volvulus* transmission around the Maridi Dam. Therefore, strengthening the onchocerciasis elimination programme in Maridi is required.

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A ROBOTIC AI MICROSCOPE FOR AUTONOMOUS FILARIASIS QUANTIFICATION BASED ON SMARTPHONES AND OPTICAL MICROSCOPY

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Filariasis, a neglected tropical disease caused by roundworm infections, presents substantial health burdens in endemic regions worldwide. The accurate detection and quantification of filarial parasites is essential for providing timely access to treatment and effective disease management. Optical microscopy remains the gold standard method for filariasis diagnosis in blood samples, however, it suffers from low sensitivity, time-consuming procedures, and the need for skilled analysts at the point-of-care. In line with the WHO target product profile, we developed a prototype of a robotic AI system that automatically detects microfilariae in real time in blood smears, upgrading a conventional optical microscope and without need for internet connection. The components of the system, in addition to an optical microscope, are a mobile phone, securely attached to an eyepiece through a 3D printed adapter, and a mechanical system controlled by the smartphone app, which moves the sample in along the X and Y axis as well as adjusts the focus automatically along the Z axis. The smartphone app manages and controls the mechanical system, acquires images with the mobile camera, and analyzes images to detect microfilariae using an AI algorithm on the edge in real-time. The system is able to scan a blood smear with a 10x objective, digitize images, and run real time AI analysis at the same time in under 6 minutes. The AI model, which was previously validated on a clinical workflow, detects microfilariae with a precision and recall of 94% and 91%.
Additional field validations could contribute to optimizing the system. We envision a simple, scalable and easy to use device which works in low resource settings and is able to upgrade existing optical microscopes and transform them into AI driven microscopy diagnostic systems, contributing to reducing the diagnosis burden of disease.

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PREGNANCY, *ONCHOCERCA VOLVULUS* INFECTION AND IVERMECTIN USE: A CROSS-SECTIONAL STUDY

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Treatment with ivermectin (IVM) should not be given to pregnant women in onchocerciasis endemic areas according to World Health Organization guidelines as drug safety has yet to be assessed. Onchocerciasis infection during pregnancy might lead to parasite tolerance in the newborn and affect pregnancy outcomes. In our study we determined the proportion of pregnant women who were exposed to *Onchocerca volvulus*, who inadvertently took IVM and assessed the knowledge on IVM in relation to pregnancy. A hospital-based cross-sectional study was conducted in 2023 at Maridi hospital in Maridi County, an onchocerciasis endemic area in South Sudan. All pregnant or one-week *post-partum* women willing to participate were interviewed and tested with the Ov16 Bioline rapid diagnostic test (RDT). A total of 317 women aged between 14 and 44 years participated in the study [median age: 23, interquartile range (19-29 years]. Of 290 women who were tested, almost two out of three (62%) were Ov16 RDT positive and reported experiencing high levels of skin itching (40%). Seventeen percent of the women had never taken IVM, and 6% inadvertently took IVM during the last round of community-directed treatment in May 2023. Of the 16 women who took IVM during pregnancy, half of them knew that they were pregnant. Overall, knowledge on IVM and pregnancy was high, as 87% of the women knew that it was not advised to take IVM during pregnancy. Out of 248 women with children, 9 (3.6%) had children suffering from epilepsy; two of them had two children with epilepsy. No abnormalities were reported in the children of the women who inadvertently took IVM. Our results show that a high proportion of exposed pregnant women are missing out on IVM treatment, potentially affecting the pregnancy outcome and the life of the future offspring. We recommend that women should have access to IVM treatment *post-partum* in vaccination centers and that all women who inadvertently take IVM should be registered to further explore safety of IVM. In addition, a clinical trial evaluating the potential beneficial effect of treating *O. volvulus* infected pregnant women with IVM should be considered.

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PRE-CLINICAL DEVELOPMENT OF THE ANTI-WOLBACHIAL DRUG CORALLOPYRONIN A TO TREAT FILARIASES: END RUN TO PHASE 1 TRIAL

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The bacterial RNA polymerase inhibitor Corallopyronin A (CorA) is in late pre-clinical development to treat filariases. As an anti-wolbachial compound, it depletes the essential obligate intracellular *Wolbachia* symbionts of filarial nematodes, resulting in sterility and death of the worms. Our consortium has achieved the following significant milestones: 1) produced drug substance with >95% purity by heterologous production in *Myxococcus xanthus*, 2) received formal Scientific Advice from the German regulatory agency BfArM approving our proposed drug substance purity for toxicology studies, 3) upscaled upstream and downstream processes to industrial-scale, 4) developed oral formulations with increased CorA solubility and stability that are suitable for GLP pre-clinical studies and the phase 1 trial, 5) successfully completed non-GLP safety and toxicology studies with no relevant results that would halt development, 6) contracted a cGMP CMO to conduct a feasibility study and perform technical/engineering production runs of GMP material, and 7) expanded development to including difficult-to-treat *Staphylococcus aureus* and *Neisseria gonorrhoeae* infections. We have received support from the Global Health Innovative Technology Fund (GHIT) to complete the pre-clinical development: conduct PK/PD in *Dirofilaria immitis* infection, support a GLP toxicology study in dogs, produce GMP CorA and CorA standards, conduct a quantitative whole-body autoradiography study, perform CMC to further improve the oral formulations, and prepare the phase 1 trial planned for 2026. Successful completion of the phase 1 trial will derisk the project to continue development of CorA for registration.

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PERFORMANCE OF QUANTITATIVE PCR FOR THE DETECTION OF SOIL-TRANSMITTED HELMINTHS IN COMPARISON TO KATO-KATZ PRECEDING AND FOLLOWING COMMUNITY-WIDE MASS DRUG ADMINISTRATION IN TAMIL NADU, INDIA

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Accurate diagnostic tools to assess soil-transmitted helminth (STH) prevalence are critical for monitoring school-based and community deworming programs. Several studies have demonstrated that Kato-Katz is less sensitive in detecting STH than quantitative PCR (qPCR), especially at low intensity of infection. This secondary analysis, using data from the DeWorm3 India trial site in Tamil Nadu, seeks to assess the concordance of Kato-Katz and qPCR and compare intensity by both methods (eggs per gram of stool and cycle threshold [Ct]) using a large dataset of paired test results prior to and following multiple rounds of deworming. Stool samples were collected from randomly sampled participants at baseline (prior to mass drug administration [MDA]) and endline (following six rounds of MDA and two years without deworming) and tested for STH using Kato-Katz microscopy and qPCR. In total, 6,014 and 2,013 paired test results were available at baseline and endline, respectively, and nearly all infections observed were due to *N. americanus*. At baseline, the prevalence of *N. americanus* was 16.6% by Kato-Katz and 24.2% for qPCR (concordance was 90.8%) with most discordance due to samples that were only positive by qPCR (8.4%). The ratio of positivity, comparing qPCR to Kato-Katz, increased from 1.46 at baseline to 1.99 at endline, and concordance was 91.2% at endline. Among participants whose stool sample tested positive for *N. americanus* by qPCR, participants with moderate- (N=50) or heavy-intensity (N=26) hookworm infection by Kato-Katz had lower Ct distributions (median: 19.48, interquartile range [IQR]: 18.31-20.40 and median: 18.63, IQR: 17.47-18.97, respectively) compared to participants with light-intensity infection (N=1,028, median: 22.91, IQR: 21.05-24.96) and participants who did not test positive by Kato-Katz (N=668, median: 26.78, IQR: 25.50-28.38). These results demonstrate improved sensitivity of qPCR compared to Kato-Katz and suggest this difference is even more pronounced following deworming as prevalence and intensity decrease.

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STATUS OF SOIL TRANSMITTED HELMINTHIASIS AND THEIR RISK-FACTORS AMONG SCHOOL PUPILS AND NOMADIC -FULANIS IN SELECTED COMMUNITIES IN OSUN-STATE, SOUTHWEST, NIGERIA

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Soil transmitted helminthiasis (STHs) occur endemically in many rural communities of Nigeria with school aged children mostly affected. Though, there has been significant progress in STHs' control over the past decade through increased collaboration, country commitment, and donors support. However, these interventions did not cover the Nomadic Fulanis who continuously moves from one place to another with possible release of STHs eggs into the environment through their indiscriminate defecation. There is paucity of published data on prevalence, burdens and risk factors associated with STH infections among primary school pupils in Osun State. The study was carried out to assess the status of STHs among 200 primary school pupils and 100 children of the Nomadic Fulanis in three selected communities of Osun State, Southwest, Nigeria. Stool samples were collected and processed using filtration technique and examined microscopically. Intensity of infection was determined on positive samples using Kato Katz techniques. Questionnaire survey was administered to the participants to test their knowledge of STHs. 18.0% of the pupils compared to 87.6% of children of the Nomadic Fulanis were found to be infected with intensity of infection from 1 to 68520 (mean = 342.6) eggs/ 5g of faeces among the primary school pupils and from 30 to 96380 (mean = 963.8) eggs/ 5g of faeces among the children of the Nomadic Fulanis. 26 (13.0%) of 147 (73.5%) of the primary school pupils who rarely wash their hands after having contact with contaminated sites were found to be infected compared to 100 (100.0%) of Nomadic Fulani children. The STHs recovered in both groups include: *Ascaris lumbricoides*, *Ancylostoma duodenale Trichuris trichiura with T. trichiura* found only in children of the Nomadic Fulani. This research reveals that the children of the Nomadic Fulanis harbored high intensities of STHs and can be an absolute agent of the spread STHs. Including the children of the Nomadic Fulanis in the existing control measures could enhance eradication.

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EVALUATION OF *STRONGYLOIDES STERCORALIS* SS-IR RECOMBINANT ANTIGEN FOR DIAGNOSTIC AND SURVEILLANCE USING A BEAD-BASED IMMUNOASSAY

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Infection with the soil-transmitted helminth *Strongyloides stercoralis* is normally asymptomatic but can lead to a life-threatening hyperinfection syndrome in immunocompromised individuals. Serological testing for antibodies to *S. stercoralis* is the method of choice for diagnosis, but ELISAs for *S. stercoralis* lack reproducibility and specificity. There is an effort to modernize diagnostic testing at CDC by moving serological testing to a multiplex bead assay (MBA) platform. However, Ss-NIE, the best characterized recombinant antigen from *S. stercoralis*, suffers from variable results in the MBA. The antigen Ss-IR was therefore evaluated for use in the MBA. Ss-IR was coupled to microspheres at 5 concentrations in two different coupling buffers, then tested using 5 positive and 5 negative samples. The optimal coupling condition (i.e. the best signal-to-noise ratio between positives and negatives) was 1.5 µg antigen in 1X PBS (pH 7.2). To determine sensitivity and specificity of the assay, sera from individuals testing stool-PCR positive for *S. stercoralis* (n = 50) and from US based presumed negative individuals with no prior travel history (n = 185) were tested. The median fluorescence intensity (MFI) with background subtracted (MFI-bg) was determined for each specimen. A receiver operating characteristic (ROC) analysis set to maximize sensitivity and specificity calculated the cutoff to be an MFI-bg of 192, with a sensitivity of 90% (95% CI 78.64% to 95.65%) and a specificity of 99% (95% CI 96.14% to 99.81%), compared with a sensitivity of 84% (95% CI 71.49% to 91.66%) and specificity of 100% (95% CI 97.97% to 100.0) for the same specimens tested at the same time in the MBA for antibodies to Ss-NIE. To assess reproducibility, 10 positive and 10 negative samples were tested by two operators over a span of 10 days, using different critical reagents in the MBA process. The correlation coefficient (R-squared) was 0.976, indicating a robust assay with minimal variation between users and reagent lots. Overall, the Ss-IR antigen has a high sensitivity, specificity, and reproducibility, warranting more extensive validation for surveillance use.

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EUKARYOTIC ENTERIC PATHOGENS RELATIONSHIP WITH THE GUT FUNGAL COMMUNITY IN MALIAN CHILDREN

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The fungal gut microbiome (gut mycobiome) plays a role in protecting against certain dangerous microbes and regulating the immune system, but it could also be the cause of certain chronic diseases. However, the interaction between gut mycobiome and eukaryotic enteric pathogens (EEPs) is a less explored. To assess the relationship between EEPs and gut mycobiont, we conducted a case-control study among children in Bandiagara. Stool samples were collected from 296 Malian children. The presence of EEP was assessed by qPCR and the gut mycobiome was characterized by Illumina MiSeq™ rRNA ITS1 and ITS2 regions metabarcoding. The 100 (33.8%) children in whom no EEP was detected were considered as EEP negative; they were compared to: a) 196 (66.2%) children who had at least one EEP; b) 91 (30.7%) children who had only *Blastocystis*; c) 35 (11.8%) children who had only *Giardia intestinalis* in terms of stool consistency and mycobiome status. The results showed a significative difference in Shannon indice of negative EEP compared to positive EEP and to Shannon indice of *Giardia intestinalis* group. The Chao-1 indice of negative EEP was significatively decrease than that of positive EEP and *Giardia intestinalis*. Linear size effect discriminant analysis highlighted five species, including *Fusarium longipes* and *Penicillium caseilulvum*, which were relatively more abundant in children with at least one EEP whereas 28, including *Aspergillus sydowii* and *Microdochium colombiense* were more abundant in EEP negative. Regarding *Blastocystis* infected children, the abundance of *Fusarium*, *Pyxidiophora*, and *Stereum* genera was higher in infected children, whereas *Ogataea* and *Allocryptovalsa* were more abundant in EEP negative. Regarding *Giardia intestinalis*, *Sordariales* and *Mortierellales* abundance was higher in infected children, whereas *Agaricales* and *Capnodiales* abundance was higher in EEP negative. Overall, EEP significantly impact the global gut fungal community structure, but further studies are warranted to confirm our finding that taxa of the gut mycobiota are associated with susceptibility or resistance to specific EEP.

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PHARMACOPHORE APPROACH TO THE PREDICTION OF ACTIVATORS OF DAF-12 RECEPTOR TO DEACTIVATE AUTO-INFECTION LIFE CYCLE STAGE OF *STRONGYLOIDES STERCORALIS*

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Strongyloidiasis caused by infections with *Strongyloides stercoralis* affects over 600 million people globally, predominantly in the tropics. It is among the most neglected of all the NTDs. Infections are mainly asymptomatic and clinically silent and its symptoms include fever, gastrointestinal pain, anorexia, diarrhea and fatigue. Ivermectin is the current treatment drug with a cure rate of 88-96% against adult parasites but possible drug resistance has been reported. The life cycle alternates between free-living and parasitic stages involving autoinfection that leads to hyper infection and 90% mortality if left untreated. The overall goal of the study was to understand the mechanism of autoinfection and to devise strategies to prevent it in human infections using computational methods. To achieve this goal, activators of the abnormal Dauer Formation Protein 12 (DAF-12) receptor known to influence the transition between developmental arrest and growth to reproductive adults were predicted. Two *Caenorhabditis elegans* activators of DAF-12 and Dafachronic acid were used to generate a 3D chemical feature pharmacophore model using *LigandScout*. The validated model was screened against pre-filtered libraries containing 1871 and 4924 compounds in the EANPDB and NANPDB databases respectively. 179 and 69 compounds respectively, with fit scores above 66.59 were docked against the structure of the DAF-12 receptor to generate hits using Autodock Vina. Three compounds hispidol B, 3-O-(3'-acetoxy-2'-hydroxy-2' methylbutyryl) cuauthemone, and toonapubesin F with binding affinities of –10.8,-10.7, and –10.4 kcal/mol against DAF-12 receptor respectively were identified as potential candidates. Structural insights into the binding mechanisms were elucidated using LigPlot+ and Molecular Dynamics simulations. All three ligands passed the adsorption, distribution, metabolism, elimination, and toxicity (ADMET) tests. Our next step is to evaluate their efficacies in animal models e.g. in the Mongolian gerbil. Our findings open the avenues for combination therapy that also arrest auto infections against *S. stercoralis* infections

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EFFECT OF KNOWLEDGE, AWARENESS AND PARTICIPATION ON SUSTAINED REDUCTION OF SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG SCHOOL-AGE CHILDREN IN RIVERS STATE NIGERIA

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Preventive chemotherapy (PC) is an effective intervention strategy for the control and elimination of soil-transmitted helminthiasis (STH). Achieving high PC coverage in every treatment round is critical for attaining control and elimination goals. Sustained high levels of participation in every round of PC is crucial to achieving effective coverage, and individuals who do not accept PC are unlikely to participate in the intervention. To improve PC compliance, community sensitization and mobilization are conducted prior to each round, combining mutually reinforcing social and behavior change approaches like announcements by village announcers, radio jingles, word of mouth, posters, live radio and TV phone-in programs. During 7 years of PC in Rivers State, 1,493 parents of school-age children (5-14 years) were surveyed in sampled communities where PC was planned, to check awareness, knowledge and willingness to participate. Survey results showed 74% of respondents were aware of the deworming exercise, and 58% of respondents correctly mentioned intestinal worms/STH as the infection target. 87% of the parents were willing to have their children participate in the deworming exercise. The major reasons provided for not participating were lack of awareness (37%), already having dewormed their children at home (15%), or had not enrolled their children in school yet (9%). Only 6% of respondents expressed fear of/ lack of trust in the medicines. Following the 7 years of PC with consistently improving reported coverage, validated by 50% of the surveyed coverage, a 2023 prevalence survey showed a 71% relative reduction in STH prevalence in the state from baseline. A multivariable analysis showed statistically significantly increased odds of parent's willingness to send child(ren) for deworming associated with knowledge of the deworming treatment (OR: 4.164(P=0.006), 95%CI: 2.494 - 6.955) and awareness of the deworming exercise (OR: 1.002(P=0.006), 95%CI:1.000 - 1.003). Sound public awareness and sensitization around MDAs are valuable to achieving and sustaining high levels of treatment coverage to reduce the burden of disease.

6599

A TWO-PRONGED BIG DATA APPROACH TO CRITICALLY ANALYZE *STRONGYLOIDES STERCORALIS* INFECTIONS AMONG RURAL, IMPOVERISHED SOUTH CAROLINA RESIDENTS

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Strongyloides stercoralis, a soil-transmitted helminth, is known to persist throughout rural areas in the southeastern United States, but high-quality prevalence data is lacking.[1–3] This project aimed to (1) estimate the current prevalence of human *Strongyloides* infections, and (2) assess risk factors associated with *Strongyloides* infections among residents of South Carolina. To achieve this, two approaches were employed. First, to estimate prevalence, active surveillance was performed using *Strongyloides* serology testing via sampling of a subset of banked serum samples. Demographic, socioeconomic, and exposure data were collated from serum sample questionnaires. Positives were contacted and visited, during which an exposure survey, confirmatory testing, and offer of treatment were administered. Second, passive surveillance was conducted via electronic health records query for *Strongyloides* cases over a 5-year time period. Demographic, socioeconomic, risk factor, and health outcomes data were collected for all positive cases and two matched controls. Participant characteristics were compared between seropositive and seronegative groups, using ANOVA and Fisher's exact statistics. We tested a total of 1,572 serum samples, of which 77 (4.9%) were positive. Significant differences in race/ethnicity and level of education were noted between cases and controls. Geospatial analysis revealed the greatest hotspot to be in the northwest region of the state. Home visits are ongoing but so far 1/3 (10/30) of positives report no international travel in the past decade, while 1/2 (15/30) report regular time spent outdoors barefoot. Review of electronic health records revealed 26 patients diagnosed with *Strongyloides*, of which 6 (23.1%) had no travel history documented. Significant differences in race/ethnicity and place of birth were noted. In this study, we found a small but non-negligible prevalence of *Strongyloides* among residents of South Carolina. Further study will be needed to better characterize the burden and distribution of *Strongyloides* in South Carolina, which may inform future targeted public health interventions.

6600

APPLICATION OF QPCR TO DETERMINE COMMUNITY PREVALENCE OF *STRONGYLOIDES STERCORALIS* IN Y INDIA

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Strongyloides stercoralis, an intestinal nematode prevalent in the tropics and subtropics, infects ~370 million individuals globally. While most infections are asymptomatic, they can lead to severe disseminated infections in immunocompromised individuals. While most national programs focusing on soil-transmitted helminth infections do not include drugs active against *Strongyloides*, the WHO NTD roadmap 2030 recommends targeted deworming of school-aged children with ivermectin if prevalence >10% and emphasizes the need for precise estimates of burden and sensitive diagnostics. In this study, we leveraged stool samples collected at baseline of a cluster randomized trial on community-wide deworming (DeWorm3) to determine prevalence of S. stercoralis by qPCR in India. The study site included rural (Timiri) and tribal (Jawadhu hills) blocks in Tamil Nadu, and samples tested (n=6091) from an age-stratified cohort of pre-school-aged and school-aged children (PSAC, SAC) and adults (15+ years). Age and cluster-weighted prevalence of *S. stercoralis* was 4.4% (95% CI: 3.9-5.0%), with a higher prevalence in the rural block (4.9%, 4.2-5.6%) than the tribal block (2.96%, 2.0-4.3%). Adults had more infections (5.5%, 4.8-6.3%) than PSAC (0.6%, 0.3-1.4%) and SAC (0.4%, 0.2-0.9%). Older age (mOR=10.1, 95% CI: 4.2-24.3), belonging to farming households (mOR=1.4, 1.02-2.04), and middle socio-economic strata (mOR=1.9, 1.1-3.6) were associated with increased odds of *S. stercoralis* infection. Female gender (mOR=0.6, 0.4-0.8), belonging to households with females possessing higher secondary education (mOR=0.6, 0.3-0.9), and access to handwashing facilities (mOR=0.5, 0.3-0.9) were protective. The weighted prevalence of *N. americanus* in the same community was 29.6% by qPCR. While ecological niche models suggest that hookworm prevalence would be predictive of *Strongyloides*, our findings indicate a lower prevalence of *Strongyloides* by qPCR. A combination of molecular and serological diagnostic approaches may be needed to accurately estimate the burden of *Strongyloides* to help plan and prioritize appropriate interventions for control.

6601

IMPACT OF PREVENTIVE CHEMOTHERAPY ON THE STATUS OF SOIL-TRANSMITTED HELMINTHIASIS ACROSS THREE IMPLEMENTATION UNITS IN ONDO STATE, NIGERIA

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Routine epidemiological data are invaluable for tracking the progression of preventive chemotherapy (PC), optimising resource allocation, and addressing emerging needs for the elimination of soil-transmitted helminthiasis. This study was conducted to assess the prevalence, intensity, and WASH conditions in the three local government areas (LGAs) of Ese-Odo, Irele, and Ile-Oluji in Ondo State, Nigeria. Stool samples were collected from 2,093 children aged 5-14 years across 45 schools and analysed using Kato-Katz techniques. Standardised questionnaires were also used to collect information on access to WASH resources. Parasitological findings reveal significant decline in aggregated prevalence estimates across the three LGAs. In Ese-Odo, prevalence was 25.8% (95% CI: 23.0, 29.0) versus 39% at baseline (d = -34%, p=0.00). Also, in Irele, the aggregated prevalence estimate was 9.7% (95% CI: 7.6, 12.0) versus 51.3% at baseline (d= -81%, p =0.00). In Ile-Oluji, the aggregated prevalence was 6.4% (95% CI: 4.6, 8.7) versus 23% at baseline (d=-72.2%, p =0.00). *Ascaris lumbricoides* was the most prevalent STH across all three IUs, with rates of 25.5%, 9.4%, and 6.4% in Ese-Odo, Irele, and Ile-Oluiji, respectively, followed by *Trichuris trichiura* in Ese-Odo (2.7%) and Irele (0.4%), whereas hookworm infection was only observed in Irele (0.7%). Most infected individuals exhibited low infection intensity in Ese-Odo (91.0%), Irele (96.8%) and Ile-Oluiji (100%). Prevalence rates did not vary significantly by sex or age category across the three IUs ($p < 0.05$). However, WASH data revealed deplorable access to improved sanitation (17.7%, 54.9%, and 58.2%, $p<0.05$), improved water sources (24.5%, 66.1%, and 69.8%, $p<0.05$), and handwashing facilities (9.0%, 39.6%, and 25.4%) across Ese-Odo, Irele, and Ile-Oluiji, respectively. Open defaecation was practiced by 54.2%, 36.3%, and 34.3% of participants recruited in Ese-Odo, Irele, and Ile-Oluji, respectively. These findings show significant progress in STH elimination in the three IUs with PC but call for more efforts in the provision and usage of WASH facilities.

6602

RESISTANCE OF SOIL TRANSMITTED HELMINTHS TO SINGLE DOSE ALBENDAZOLE AND RESULTS OF COMBINED THERAPY WITH ALBENDAZOLE AND IVERMECTIN IN CHILDREN AGED 2 TO 11 YEARS IN THE PERUVIAN AMAZON

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In countries where soil- transmitted helminth (STH) infections are endemic deworming programs are crucial for reducing morbidity. However, the growing concern over increasing resistance to benzimidazoles requires continuous monitoring of treatment efficacy. In this observational study conducted in Peru, we evaluated the clinical efficacy of a single dose of 400 mg albendazole in children aged 2 to 11 years. Our aims were to assess clinical resistance to albendazole at 20 days post-treatment and to investigate reinfection with STH four months after treatment. We enrolled 426 participants, among whom 52.3% were infected with at least one STH, specifically, 33.8% were positive for Ascaris (41.8% light, 50.8% moderate, and 7.4% heavy), 34.5% were positive for Trichuris (75.2% light, 22.5% moderate, and 2.3% heavy), and 1.1% were positive for hookworm species (100% light). Additional stool samples were collected and examined at 20 days, 90 days, and 130 days after the initial treatment. At 20 days post-administration of albendazole, the cure rate (CR) for Ascaris was 80.1% (95% CI: 73.5-86.7), with an egg reduction rate (ERR) of 70.8% (95% CI: 57.8-88.7). For Trichuris, the CR was 27.1% (95% CI: 20.0-34.3), with an ERR of 29.8% (95% CI: -1.40-57.5). Among participants with a positive stool sample indicating persistent or recurrent Trichuris infections, treatment with combined therapy of albendazole (400 mg) and ivermectin at 600 µg/dose increased the overall CR for Trichuris to 75.2% (95% CI: 67.3-83.2%) with an ERR of 84.2% (95% CI: 61.3-93.8%). Albendazole administration alone for the control of STH showed high rates of treatment failure, particularly for Trichuris. However, combined single doses of albendazole and ivermectin appeared to improve efficacy.

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IDENTIFICATION OF NOVEL BIOMARKERS FOR SEROSURVEILLANCE OF HUMAN HOOKWORM INFECTIONS

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Hookworm, a blood-feeding, soil-transmitted helminth parasite, infects about 500 million people globally, including pregnant women and children. This Neglected Tropical Disease (NTD) is prevalent in sub-Saharan Africa, Asia, and parts of South America. The World Health Organization (WHO) recommends Mass Drug Administration (MDA) of benzimidazole anthelmintics to combat morbidity, while for diagnosis, it suggests Kato-Katz thick smear, a labor-intensive method, lacking sensitivity. PCR-based tests are more accurate but require well-equipped labs and are rarely used in endemic regions due to resource limitations. Addressing these challenges, the WHO Target Product Profile emphasizes the need for improved surveillance tools with higher sensitivity. As for other NTDs, integrating serosurveillance into monitoring efforts can facilitate decision-making for MDA programs. To this end, we sought to identify sensitive and specific hookworm biomarkers for use in an ELISA for serosurveillance. We screened ~11,000 peptides for IgG reactivity on a high-density microarray, generated from 34 hookworm proteins identified through LC-MS/MS analysis of hookworm Excretory/Secretory and L3 soluble extracts, along with a bioinformatics analysis and literature search. Further down-selection of peptides from the microarray was based on fluorescence intensity and signal to noise ratio. Six peptides, combined in a single mixture, were ultimately selected for final screening by ELISA on hookworm positive (Kato-Katz thick smear, n=109) and negative (non-endemic U.S., n=224) sera, yielding a sensitivity of 86% and specificity of 92%, with an AUC of 0.95 and p-value <0.0001. Serum samples from other STH infections including *Ascaris* sp. (n=3), *Trichuris* sp. (n=1) and *Strongyloides* sp. (n=5) were negative on the ELISA. In conclusion, we have identified, for the first time, highly sensitive and specific hookworm biomarkers, demonstrating promising potential for serosurveillance as a new tool to improve monitoring of MDA programs in endemic regions

6604

SOIL-TRANSMITTED HELMINTHS (STHS) IDENTIFIED IN ENVIRONMENTAL SAMPLES (SOIL AND FECAL MATTER) COLLECTED FROM SOME PRIMARY SCHOOLS IN GHANA

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Soil-transmitted helminths (STHs) are common parasitic infections that present a notable risk to the health and development of school-aged children, especially in the tropics. This study aimed to investigate the diversity of STHs in soil and faecal samples were collected from selected primary schools. A survey was conducted across 24 primary schools; each school was divided into 5 locations (playgrounds, school fields, canteens, cafeterias, and walkways). 100g of soil samples (50g each) were collected from 2 points (20 meters away) in each location. Fecal matter of stray animals was collected for analysis, where found. Thus, a total of 240 soil and 20 fecal samples were collected from different school locations; and analyzed using the flotation technique. Microscopic examination of soil samples revealed the following organisms: Ascaris lumbricoides (55; 22.9%), Strongyloides spp (13; 5.4%), Schistosoma spp. (8; 3.3%), Fasciola spp. (8; 3.3%), Hookworm (7; 2.9%) Hymenolepis spp. (6; 2.5%), Trichuris trichiura (4; 1.7%), Diphyllobothrium spp (2; 0.8%) and Taenia (1; 0.4%). The playgrounds recorded the highest positivity rate (22; 9.2%), while school fields and canteens recorded the lowest positivity rate of 5.8% (14) each. Ten (50%) out of the 20 faecal samples were found to contain STHs with Ascaris lumbricoides (25%) mostly observed. The results suggest a significant presence of STHs in the schools' environment, emphasizing the immediate need for specific public health actions. Initiatives such as deworming programs, advocating for better hygiene and sanitation practices within schools, and increasing awareness are crucial measures in mitigating health impacts associated with STHs.

6605

SEROPREVALENCE AND ASSOCIATED FACTORS OF *STRONGYLOIDES STERCORALIS* INFECTION AMONG AT-RISK POPULATION IN NORTHERN TAIWAN

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Many case reports of strongyloidiasis from Taiwan have been published in the literature over the years, with a high rate of mortality. Despite its health impact, the prevalence of *Strongyloides stercoralis* infection (SSI) have not been systematically investigated in Taiwan. We conducted a prospective serological survey at National Taiwan University Hospital (NTUH), NTUH Hsin-Chu Branch, and NTUH Biomedical Park Branch. Two different ELISAs were used to detect *Strongyloides* IgG. Individuals were eligible for enrollment if they had a history of eosinophilia, soil-contact activities, immunocompromising medical conditions, or clinical manifestations that could be attributable to strongyloidiasis. We defined seropositive, indeterminate, and seronegative as having both ELISAs positive, either ELISA positive, or both ELISAs negative, respectively. Factors associated with seropositivity were assessed in a multivariable model. between 2021 and 2023, 453 participants were enrolled. The mean age was 62.8 years (range 22 to 99) and 33.3% were female. Comorbid conditions were common, including 37.7% with chronic kidney diseases (stage 3 or higher), 33.6% with diabetes mellitus, 27.4% with chronic airway diseases, 16.3% with malignancy, 14.8% with autoimmune diseases, 59.2% with steroid exposure, and 15.2% were transplant candidates. Among all participants, seropositivity of SSI was 4.2%, while indeterminate serostatus was observed in 12.8%. In multivariable models, participants born after 1960 were less likely to be seropositive compared to those born before 1945 (adjusted odds ratio [aOR] 0.184, 95% CI 0.047 - 0.592), while mainlanders and indigenous populations were more likely to be seropositive (aOR 4.333, 95% CI 1.405 - 12.838). Six-month mortality was higher among seropositive participants (36.8% versus 11.2% among those who were seronegative, p-value = 0.004). Our seroepidemiological survey shows that SSI is still prevalent in Taiwan, at least among at-risk populations. Ongoing efforts are needed to expand SSI screening to different regions of Taiwan and identify proper confirmation tests.

6606

HIGH PREVALENCE OF INTESTINAL PARASITES AMONG ADULTS LIVING IN 36 VILLAGES IN NORTHERN GABON AND RELATIONSHIP WITH BODY MASS INDEX : CROSS-SECTIONAL STUDY

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Intestinal parasitic infections (IPIs) are widespread worldwide and can constitute a public health problem. These parasitoses are mainly studied in school-aged children due to their impact on growth retardation, cognitive development, anemia, etc. However, since 2015, certain studies carried out in Gabon have shown that the population at risk of IPIs consists of adults. No studies have focused solely on this neglected population and the impact of intestinal parasites on nutritional status. To fill this gap, a prospective cross-sectional study was carried out in rural areas of northern Gabon. This study was part of the clinical trial on the treatment of hypermicrofilaremic loiasis: PHYLECOG. Adults aged at least 18 years were included after signing informed consent and sociodemographic, clinical and lifestyle data were recorded on a paper case report form. Weight and height were measured and used to determine body mass index (BMI). For the diagnosis of IPIs, a stool sample was collected to perform merthiolate-iodine-formaldehyde staining and concentration, Kato-Katz and parasite culture. A total of 1,363 subjects were included. The proportion of IPIs in adults was 53.8% with 23.4% helminths, 52.6% protozoa and 24.0% protozoa+helminths. An unbalanced nutritional state based on BMI calculation was found in 47.1% of the study population: 25.7% overweight, 17.4% obese and 4.0 underweight. Age- and sex-adjusted odds ratios showed that populations with IPIs had twice the risk of being thin compared to populations with normal BMI (aOR = 2.2, [95% CI : 1.1-4.2], p = 0.02). These results showed the importance of including adult populations aged over 15 years in the national campaign to combat IPI and constitute an important parasitic reservoir in both urban and rural areas.

6607

THE OCCURRENCE OF CROSS-HOST SOIL TRANSMITTED HELMINTH (*ASCARIS*, *TRICHURIS* AND *ANCYLOSTOMA SPP.*) INFECTIONS IN HUMANS AND DOMESTIC/ LIVESTOCK ANIMALS: A SYSTEMATIC REVIEW

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The role of zoonotic soil transmitted helminth (STH) species such as *Ancylostoma ceylanicum*, *Ancylostoma caninum*, *Ancylostoma baziliense*, *Ascaris suum*, *Trichuris suis* and *Trichuris vulpis*, are increasingly acknowledged as potential sources of human infection. However, the extent of transmission in humans remains poorly understood due to reliance on morphological diagnostics, which hinders accurate species identification. This systematic review compiled data on the occurrence of cross-host STH infections (i.e., the occurrence of zoonotic STH in humans and/or

human STH in domestic/livestock animals). Following PRISMA guidelines, studies published in PubMed, Medline, and Web of Science were searched from inception to October 2023. Inclusion criteria encompassed studies identifying evidence of cross-host infections confirmed through molecular methods, and published in English. Exclusion criteria included experimental and wildlife studies, studies that did not find cross-host infections and those without the availability of full-texts. AXIS and Joanna Briggs Institute critical appraisal tools were used for bias assessment of studies. The protocol is registered with PROSPERO (CRD42024519067). A total of 3873 titles and abstracts were screened; 45 studies were included. *Ancylostoma ceylanicum* was the commonest zoonotic STH species, reported mostly from studies in Southeast Asia. Other zoonotic STH such as *Ancylostoma caninum*, *Ancylostoma braziliense*, *Trichuris vulpis* and *Ascaris suum* were also reported. The presence of *Trichuris trichiura*, *Necator americanus*, *Ancylostoma duodenale*, and *Ascaris lumbricoides* in dogs, cats, and pigs were also reported. The findings underscore the need for epidemiological investigations of humans and animals in sympatric environment, using molecular tools, to better understand transmission dynamics and estimate the risk of zoonotic STH infections.

6608

ENVIRONMENTAL SURVEILLANCE TOOLS FOR MONITORING COMMUNITY-LEVEL SOIL-TRANSMITTED HELMINTH PREVALENCE

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Soil-transmitted helminths (STH) are one of the most prevalent infections world-wide and current recommendations from the WHO include targeted deworming and improvements in water, sanitation and hygiene. Elimination of STH typically requires improved infrastructure due to environmental reservoirs. Current surveillance strategies for STH focus on identifying eggs in stool samples via microscopy, which is expensive and exhibits poor sensitivity and specificity especially in settings with low intensity infections. Wastewater epidemiology is a prominent surveillance tool used to detect pathogen circulation and potential reservoirs of disease, but sampling strategies for settings lacking networked sanitation are not well developed. Here, we deploy environmental surveillance strategies in India and Benin where STH are endemic (around 20% human infection prevalence of any STH in both countries). Our group has optimized DNA extractions from large quantities of soil and non-networked wastewater. We use multi-parallel qPCR assays to detect STH DNA in soil collected from high foot traffic locations and three types of wastewater samples in Comè, Benin and Timiri in Tamil Nadu, India. We report detection of STH in soil (India n=95, Benin n=125) and wastewater (India n=61, Benin n=68) with a detection frequency across all sample types of 37% in India and 24% in Benin. We evaluate which sample locations and types allow for more sensitive detection of STH DNA. We determine that wastewater sediment (India 63%, Benin 18%) samples outperform wastewater Moore swabs (India 37%, Benin 6%) and, in India, wastewater grab samples (India 27%, Benin 18%). Wastewater sediment (63%) and soil from markets (50%) had the highest detection frequency in India while soil from open defecation fields (37%) and community water taps (40%) had the highest detection frequency in Benin. We expand our methods to include other enteric pathogens using multiplexed qPCR for wastewater samples. Our results are useful for designing sampling strategies for environmental and wastewater surveillance in settings without networked sanitation across a wide range of enteric pathogens.

6609

TARGET MOLECULES OF *BACILLUS THURINGIENSIS* CRYSTAL PROTEINS AND ANTHELMINTHIC COMPOUNDS IN *CAENORHABDITIS ELEGANS*

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Bacillus thuringiensis (Bt) produces a variety of crystal (Cry) proteins during sporulation. Cry proteins have been used as agricultural pesticides against insects for decades. Our lab has pioneered work on Cry proteins, e.g., Cry5Ba, active against nematodes, and these are being developed for use against gastrointestinal nematode (GIN) parasites. The related Cry proteins, CryH16 and CryH18, have been under the development as anthelminthics against GINs as well. To understand how these Cry proteins worked we screened for mutants resistant to these proteins and have found 2 rare alleles. Both are conditional mutants. Whole genomic sequencing was used to identify the bre-6 gene, which mutants to CryH16/18 resistance, and it was found to encode a gene involved in transcriptional regulation of a key intracellular pathway. RNAi, extrachromosomal complementation, RNAi knockdown and the Crispr gene editing experiments confirmed that the gene is required for the resistance to CryH16 and CryH18. *bre-6(ye123)* animals have significant fitness costs, suggesting resistance via this mechanism is difficult. In addition to Cry proteins, we have discovered new compounds that have anthelmintic activity against *A ceylanicum* and *Trichuris muris* as part of a 30,000+ compounds high-throughput screen against parasitic nematodes. We have found several new families of compounds highly effective *in vivo* against hookworms but the mechanism of action is unknown. To address this, we obtained two mutant *Caenorhabditis elegans* strains resistant to one class of compounds using forward genetic screens. Mapping and cloning is underway. Uncovering the mechanism of action of these compounds is important for medicinal chemistry and improving activity of this class of compound for eventual clinical deployment.

6610

CHARACTERIZING GENETIC DIVERSITY AND POPULATION STRUCTURE OF HUMAN HOOKWORMS USING WHOLE GENOME DATA FROM ACCESSIBLE SAMPLE TYPES

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Human hookworms infect >500 million individuals worldwide and targeted treatment through Mass Drug Administration (MDA) of anthelmintic drugs reaches hundreds of millions of people every year. Using genomic data to understand how parasite populations are structured, and how that structure changes through time and in response to treatment campaigns, is a novel approach to measure the impact of global health programs. Larvae are the ideal sample type for hookworm genomic studies as they are both more accessible from natural populations than adults and easier to manipulate than eggs; however, the amount of genomic DNA (gDNA) extracted from individual larvae is insufficient for whole genome sequencing. We explore the use of whole genome amplification (WGA) of third-stage hookworm larvae to generate complete genomic data from individual specimens. To first ensure that WGA does not systematically bias next-generation sequencing (NGS) datasets, we validated our approach using adult worms. Genomic DNA extracted from individual adults was serially diluted tenfold (10^{-1} to 10^{-4}) and dilutions were amplified prior to library preparation. Following sequencing, genome breadth at 10x depth of coverage (DOC) varied from 93.8% in undiluted samples to 15.15% in the lowest dilution. Quality-controlled NGS data were aligned to a reference genome and single nucleotide polymorphisms (SNPs) were called to measure false discovery rate and genotype concordance between amplified dilutions and unamplified gDNA sequenced from the same individual. Following validation, gDNA was extracted from individual larvae. Successful

extractions were confirmed with qPCR and used for WGA and NGS. Breadth of coverage ranged from 67.96-92.92%, indicating that the majority of the genome of individual larvae can be sequenced to >10x DOC using this approach. To assess genetic differences between individuals, SNP datasets were analyzed using discriminant analysis of principal components (DAPC), STRUCTURE, and RAxML. Moving forward, this approach can be used to characterize hookworm population structure and diversity in natural populations.

6611

PREVALENCE AND RISK FACTORS OF SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG SCHOOL CHILDREN IN BIOKO NORTE PROVINCE, EQUATORIAL GUINEA

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Soil-transmitted helminths (STHs) are intestinal worms that affect more than a quarter of the world's population, causing significant health problems. In Equatorial Guinea, STHs remain a major public health issue, with *Ascaris lumbricoides, Trichuris trichiura, and Ancylostoma duodenale* being the most common species. The health impact of STH infections is directly related to the worm burden, with severe infections contributing to anemia, malnutrition, stunting, and low birth weight. This study aims to investigate the prevalence of STHs and associated risk factors among school children in Bioko Norte Province, Equatorial Guinea. The research will also evaluate the effectiveness of current prevention and control measures. A community-based cross-sectional study will be conducted in Bioko Norte Province from May to September 2024. A total of 250 school children aged 1-15 years will be recruited using a multistage sampling technique. The study will analyze data on clinical and laboratory findings of study participants to assess the prevalence of STHs in different schools, identify risk factors associated with their transmission, and evaluate the effectiveness of implemented control strategies. The study will provide up-to-date data on the prevalence of STH infections among school children in Bioko Norte Province. Risk factors associated with STH transmission, such as socioeconomic status, hygiene practices, and environmental conditions, will be identified. The effectiveness of current prevention and control measures will be evaluated, and recommendations for improvement will be proposed. The findings of this study will contribute to a better understanding of the epidemiology of soil-transmitted helminthiases in Equatorial Guinea. The results will inform public health authorities and guide the development of targeted interventions to reduce the incidence of STH infections and improve the quality of life of affected populations.

6612

INOCULUM DEPENDENT ANEMIA AND HUMORAL IMMUNE RESPONSES IN HAMSTERS INFECTED WITH A FIELD-ADAPTED STRAIN OF *NECATOR AMERICANUS*

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Laboratory passage of an African strain of *Necator americanus* hookworms has been sustained through 15 passages in outbred golden Syrian hamsters using infectious third-stage larvae (L3) cultivated from human study subjects in Beposo, Ghana. Patent infections have been sustained by subcutaneous infection of weanling hamsters provided *ad libitum* drinking water containing dexamethasone. Here we present the results of a study in which animals were infected with 200 or 400 *N. americanus* L3 and followed for 91 days to characterize pathology and parasite-specific humoral immune responses. When compared to uninfected controls, infected hamsters developed anemia in a dose-dependent manner, with mean blood hemoglobin levels reduced by approximately 21% in the 200 L3 group ($P = 0.08$) and by 55% in the 400 L3 group ($P = 0.004$) at day 42 postinfection. Mean blood hemoglobin levels remained depressed in infected animals for the remainder of the observation period; in the 400 L3 group the reduction was profound and significant, ranging from 45.3% to 58.1% ($P < 0.05$ at all time points). At the time of sacrifice mean +/- SEM intestinal worm burdens were found to be 5.4 +/- 1.8 in the 200 L3 group and 14.2 +/- 2.5 in the 400 L3 group. Intestinal worm burdens were found to be highly correlated with final blood hemoglobin levels ($r^2 = 0.8995$, $P < 0.0001$). Analysis of hookworm-specific humoral immune responses exhibited robust serum IgG responses to soluble L3 extract and adult excretory-secretory (ES) antigens. ES-specific secretory IgA responses were also detected in soluble intestinal flush and soluble fecal extracts prepared from infected animals at the time of sacrifice. These results provide further support for the utility of the hamster *N. americanus* model for the evaluation of hookworm pathogenesis, immune responses, diagnostics and vaccination.

6613

GUT DYSBIOSIS IN MATERNAL HELMINTH INFECTION

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Intestinal helminth infections may alter the bacterial composition of the host gut microbiome. The infant gut microbiome is thought to be established through vertical transfer during birth or with breastfeeding. The effect of maternal helminth infection on gut microbiome composition, with implications for establishment of the infant gut microbiome, has yet to be investigated. To address this, a cohort of 400 pregnant women in Leyte, Philippines were enrolled during the second trimester and evaluated by Kato-Katz for helminth infections. Women with hookworm, *Schistosoma japonicum*, *Trichiura trichuris*, *Ascaris lumbricoides*, or coinfection were matched to uninfected controls. Of these 154 women, 16S rRNA was sequenced using Oxford Nanopore and long reads were mapped using Emu and the Ribosomal Database Project. Differentially abundant taxa were determined using ZicoSeq followed by linear model hypothesis testing. At 32 weeks gestation, women infected with hookworm, *S. japonicum*, *T. trichuris*, and *A. lumbricoides*, were found to have significantly increased abundance of *Enterococcus hirae* when compared to uninfected controls. Overgrowth of *Enterococcus spp.* have been associated with colon cancer and can lead to bacteremia. Women with hookworm, *S. japonicum*, and *T. trichuris* were also found to have significantly decreased abundance of *Bacteroides galacturonicus*. *Bacteroides spp.* are a commensal species of the gut, providing protection from pathogens and supplying nutrients to other commensals. These findings suggest that helminth infection leads to dysbiosis of the gastrointestinal tract. This is the first study to investigate the gut microbiome of pregnant women harboring helminth infections, which has potential implications for the early infant gut microbiome. Future work will investigate the gut microbiomes in children born to women with helminth infection.

6614

DISENTANGLING THE COVARYING EFFECTS OF MOTOR DEVELOPMENT AND WEANING FROM BREAST MILK ON INTESTINAL PARASITE INFECTIONS AMONG CHILDREN AGED 0-2 YEARS IN NORTHERN COASTAL ECUADOR

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Intestinal parasite infections (IPI) contribute significantly to child morbidity, particularly in settings with poor sanitation, and have harmful effects on growth and development. Incidence of IPI is low during the first year of life, even in high-burden settings, before rising rapidly. Breastfeeding protects against IPIs by enhancing development of the immune system and microbiome, and weaning is hypothesized to cause the rise in IPIs after 1 year. But children experience many concurrent changes during this period, such as learning to walk independently, which increase contact with the environment and may lead to increased ingestion of parasites. We aimed to disentangle the influence of weaning and increased motor development on IPIs among children in the ECoMiD birth cohort conducted in coastal Ecuador. A total of 1,503 stool samples were collected from 465 children during quarterly visits between ages 3-24 months. IPIs were determined by microscopy. In an age-adjusted regression model, breastfeeding was not associated with IPI, while children who could walk independently had a 2.75-fold higher prevalence of any IPI compared to children who could not yet crawl. However, all children over 12 months were able to crawl and few children under 12 months could walk independently; thus, residual confounding by age might still explain the association. To reduce confounding, we fit stratified models restricted to ages at which breastfeeding or motor development had substantial variation. Among 12-month-olds, breastfeeding was not associated with IPI, while children who could walk independently had 42% fewer infections compared to those who could crawl only (PR = 0.58, 95% CI 0.31, 1.08). Among 15-24-month-olds, children who partially breastfed had 63% more helminth infections but 34% fewer protozoa infections compared to fully weaned children. For highly correlated variables, combined models can mask or invert associations present within finer strata. Breastfeeding's converse associations with helminth and protozoa infections among older children suggest diverse transmission pathways that should be distinguished in studies of IPIs.

6615

HIV MORTALITY TRENDS AMONG THE UNITED STATES POPULATION, FROM 1999-2023: A CDC WONDER DATABASE STUDY

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Despite the progress made in managing HIV, the mortality trends among the general population in the United States remain understudied. This lack of information hampers the ability to implement evidence-based interventions at community levels. Our aim was to analyze the trends in HIV-related mortality among US residents by demographic characteristics such as age, gender, race/ethnicity, urbanization, and US Census Regions. State-wide Age-Adjusted Mortality Rates (AAMR) and county-wide data were subsequently analyzed. We abstracted national mortality data from the multiple cause of death files in the CDC-WONDER Database. The ICD-10 codes (B20-B24) were used to identify HIV deaths from 1999-2023. Trends in age-adjusted mortality rate (AAMR) were assessed using Joinpoint regression analysis. Results were expressed as annual percentage changes (APC), average annual percentage changes (AAPC), and 95% confidence intervals (CI). Between 1999 and 2023, a total of 271,568 HIV-infected patients died within the US (AAMR=3.4 per 100,000; 95% CI: 3.3-3.5). Overall mortality trends decreased at an annual rate of -4.66% (95% CI: -4.96, -4.43) from 1999-2023 across the entire population. Specifically, the mortality trends increased among males (from the year 2018-2021), age groups 65-74 and 75-84 (overall), Non-Hispanic American Indian or Alaskan natives (from 2017-2023), across all regions (during 2018-2021), and increased slightly from 2017-2019 onwards across the urbanization divide. States in the top 90th percentile included: the District of Columbia, Florida, Maryland, Louisiana, New York, and Georgia. Union County and Miami-Dade County are highly affected within the state of Florida. Maryland showed a slight increase in trend in recent years, while Mississippi showed the slowest decline overall. HIV mortality among the US population has decreased overall from 1999 to 2023, but with varying demographic and geographic trends. These trends highlight the need for enhanced public health surveillance to better understand the scope of HIV mortality and to identify high-risk demographic and regional subgroups for targeted interventions.

6616

T CELL RECEPTOR REPERTOIRE ANALYSIS REVEALS A DISTINCT PHENOTYPE OF *MYCOBACTERIUM TUBERCULOSIS* (MTB) SPECIFIC T CELL FUNCTION IN PEOPLE LIVING WITH HIV (PLHIV)

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People living with HIV (HIV) have an increased risk of developing lower respiratory tract infections, such as tuberculosis (TB), due to compromised Mtb-specific T cell function. However, the impact of HIV on Mtb-specific T cell receptor (TCR) in the alveolar T cells is incompletely described. Our study aimed to assess the effect of HIV and antiretroviral therapy (ART) on Mtb antigen-specific T-cell receptor (TCR) diversity and clonality. Peripheral blood and bronchoalveolar lavage (BAL) samples were collected from PLHIV on long-term ART and HIV-uninfected adults recruited at Queen Elizabeth Central Hospital, Blantyre Malawi and analysed using flow cytometry and bulk sequencing. Notably, Mtb-specific TCR repertoires in HIV-uninfected individuals showed increased clonality and diversity compared to PLHIV in both the airway and blood. ART was associated with the restoration of the repertoire clonality in PLHIV. Additionally, lower frequencies of Mtb-specific CD4 IFN-γ-producing cells were observed in both blood and airway in PLWH compared to HIV-uninfected individuals (P=0.003 and P= 0.013 respectively). Significant alterations in TCR Vβ expressions were noted in CD4+ T-cells in PLHIV compared to healthy controls. Vβ1, Vβ7.2, and Vβ23 were higher ($p < 0.05$), while Vβ9 and Vβ18 were lower in blood and airway in PLHIV than in HIV uninfected individuals. In CD8 T cells, no significant differences were found in TCR Vβ specificities in the blood. However, in the lung, Vβ5.1, Vβ16, and Vβ17 were increased, while Vβ14 was decreased in PLHIV. The elevated TCR Vβ in the lung & blood in PLHIV suggests their potential involvement in HIV immune response whilst depletion of certain TCR Vβ clones may indicate HIV-induced alteration in the repertoire. Together, these findings suggest a more restricted TCR repertoire in PLHIV with alterations in certain TCR families, potentially impacting antigen recognition and decreasing protection against infections, including TB. Identifying key TCR chains associated with cytokine production may offer targets for vaccine development, improving outcomes for PLHIV and reducing the risk of TB and other infections.

6617

THE PREVALENCE OF CRYPTOCOCCAL ANTIGENEMIA AMONG PATIENTS WITH ADVANCED HIV DISEASES IN SOUTHWEST AND NORTHCENTRAL NIGERIA

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Cryptococcal meningitis (CM) is a serious opportunistic infection that is a major cause of morbidity and mortality in people living with HIV (PLHIV) with advanced disease. Nigeria ranks first in the global burden of cryptococcal meningitis with an estimated annual incidence of 27,100 accounting for 18% of the global incidence of CM. In this study, we determined the prevalence and risk factors for cryptococcal antigenemia in adult people living with HIV (PLHIV) to advocate for the implementation of routine CM screening before ART commencement with support from US-CDC through PEPFAR funding. A multicenter retrospective study of AHD package of care implementation in 334 treatment sites across APIN-supported states in Nigeria. People who present with advanced HIV who were screened for cryptococcal infection between October 2022 and September 2023 were assessed. Data was exported from the facility register into Excel and was analysed using SPSS version 23 Chicago, IL. Logistic regression was conducted to identify risk factors for cryptococcal antigenemia. 7618 was identified as AHD either by CD4<200 cells/μL or clinical stage 3-4. 6933 (91%) had access to CM screening using the Immy Cryptococcal antigen (CrAg) kit. 180(2.6%) were positive for Immy serum cryptococcal antigen. 74(41%) had lumbar puncture and CSF Cryptococcal antigen screening. 27(36%) was positive for CSF CrAg. Cryptococcal antigenemia is higher in treatment-experienced individuals who are failing treatment and those returning to care than those who are treatment-naive. Other risks of cryptococcal antigenemia include lower CD4 cell count <100 cells/mm^3, prolonged immunosuppression, poverty and occupation. Cryptococcal meningitis still poses a great challenge in the global battle to end HIV as an epidemic in 2030. Unsuppressed clients and those with CD4 <100 cells/mm3 possess a higher risk of cryptococcal antigenemia. There is a need to consistently screen all newly diagnosed HIV clients, Clients returning to care and patients with unsuppressed viral load for >1 year of treatment for cryptococcal infection to reduce cryptococcal-related AIDS death.

6618

THREE NOVEL EPIGENETIC-MODIFYING COMPOUNDS IDENTIFIED AS HIV LATENCY-REVERSING AGENTS IN GHANA

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The persistence of latent reservoirs has hindered HIV cure. These reservoirs serve as the source of viral rebound when ART is interrupted. One potential strategy for an HIV cure involves reversing viral latency using small molecules known as latency-reversing agents (LRAs). A critical mechanism by which HIV remains latent during ART involves modifications to the chromatin surrounding the virus. We hypothesized that epigenetic-modifying compounds might effectively serve as LRAsWe utilized the JLAT 10.6 cell line to screen 150 epigenetic compounds. Positive hits were further screened in various J.LAT clones (6.3, 8.4, 15.4). A primary cell latency model was used to identify lead compounds, which were then screened in a macrophage cell line (THP-1 55.2). Lead compounds were validated using RT-qPCR and intracellular HIV p24 staining. The lead compounds were further screened in CD4+ T cells of four individuals living with HIV on suppressive ART.We identified five positive hits (MC1568, Abexinostat, Pracinostat, EPZ2015666, CXC6258-HCL) from the J.LAT 10.6 cell culture system with GFP-positive cells (20-91%). Among the various J.LAT clones (6.3, 8.4, and 15.4). The primary latency model screening revealed three lead compounds (MC1568, Abexinostat, and Pracinostat) that significantly induced GFP positive cells (30-80%) in the macrophage cell model screening. The lead compounds significantly increased HIV gag expression (10-19-fold) and induced intracellular HIV p24 production (43-94%). Importantly, in four individuals on suppressive ART (the lead compounds caused a significant increase (6 to 19-fold) in intracellular HIV-1 transcript levels.We have successfully established for the first time in Ghana, a medium- to high-throughput drug screening system for HIV latency reversal. We have pinpointed three novel LRAs (MC1568, Abexinostat, and Pracinostat). These compounds effectively reactivated latent HIV-1 in vitro and induced HIV expression ex vivo. Our findings suggest that these LRAs hold promise for reactivating latent HIV in individuals living with the virus.

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HIV SCREENING ON NEUROSURGICAL PATIENTS IN SRI LANKA; INSIGHT TOWARDS WHEN TO DO IT

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HIV/AIDS is gaining an increasing interest in Sri Lanka as the incidence is growing up. Cerebral Infections and lymphomas are well recognized neurosurgical complications of HIV/AIDS. Currently screening for HIV infection is not routinely carried out on these patients unless the clinical picture suggests the possibility of HIV infection. The objective of this study is to evaluate the extent of HIV/AIDS related neurosurgical disease spectrum in Sri Lanka. HIV status of the sexually active patients who underwent neurosurgical interventions for HIV/AIDS related cerebral pathology over 3 years were evaluated using standards laboratory diagnostics. This was done as a part of the clinical management of the patients and data related to patient's identity was not included in the study. 59 patients (26 females and 33 males, age between 24 to 58 years) have undergone neurosurgical interventions (aspiration, biopsy, excision, debulking) for HIV/AIDS related cerebral pathology. Bacterial abscess, fungal abscess, tuberculous lesions, Toxoplasmosis and lymphoma were the pathology among 26, 04, 08, 09 and 12 patients respectively. HIV infection was diagnosed in one patient with bacterial abscess (3.8%), one patient with fungal abscess (25%) and three patients with toxoplasmosis (33%). No HIV was detected in patients with tuberculosis and lymphomas. HIV/AIDS is unlikely to be a significant predisposing factor for cerebral tuberculosis and lymphomas, but it is a definite predisposing factor for fungal infections and toxoplasmosis of the brain. Therefore, routine screening for HIV status among patients with cerebral fungal infections and toxoplasmosis is recommended for Sri Lankan population.

6620

IMPACT OF MHV-68'S HEPATOTROPISM ON A SUBSEQUENT LIVER INFECTION BY MALARIA PARASITES

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Concurrent infections by gammaherpesviruses, such as Epstein-Barr virus (EBV), and *Plasmodium* parasites, the causative agents of malaria, are highly prevalent in the sub-Saharan region and are etiologically linked to several malignancies. Host-mediated interactions between these pathogens thus appear inevitable, and may impact either infection and/or disease progression.During the clinically silent but obligatory liver stage of *Plasmodium* infection of its mammalian host, parasites multiply within hepatocytes before egressing into the bloodstream, ultimately leading to

the onset of malaria symptoms. Although hepatomegaly and mild hepatitis are common EBV-related hepatic manifestations, the consequences of the viral hepatotropism on a subsequent liver-stage infection by *Plasmodium* remain underinvestigated. We established a mouse co-infection model employing murine gammaherpesvirus-68 (MHV68) and rodent *P. berghei* parasites as surrogates for their human-infective counterparts, to investigate their crosstalk in the livers of C57BL/6 mice. We showed that an early latent infection by MHV68 markedly inhibits a subsequent liver infection by *P. berghei*, suggesting that MHV68 alters the liver environment and influences *Plasmodium*'s ability to establish a hepatic infection. Our results also show that infection by MHV68 prior to *P. berghei* inoculation significantly decreases malaria severity and associated mortality. Our characterization of the liver's pathological and immunological responses to MHV68 infection revealed noticeable virus-associated alterations in hepatic morphology and immunological microenvironment, with a pronounced increase of specific cytotoxic T cell populations. Our findings unveil a previously unknown effect of gammaherpesvirus infections on the liver microenvironment, which may shape the host's response to subsequent infections by malaria parasites. These findings may not only influence the clinical management of these diseases in malaria-endemic regions, but also impact the efficacy of whole-sporozoite and pre-erythrocytic vaccination against malaria in EBV-infected patients.

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RESPIRATORY VIRUSES AND BACTERIA CARRIAGE AMONG PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN ACCRA, GHANA

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Respiratory infections are particularly prominent among individuals with compromised immune systems, representing the most common opportunistic infections. While these infections are typically self-limiting, they pose significant risks to immunocompromised individuals, especially those living with human immunodeficiency virus (PLHIV). Despite the substantial burden of respiratory infections in the sub-Saharan region, there is a scarcity of data on this specific issue among PLHIV.To address this gap, a cross-sectional study was carried out among 240 PLHIV on antiretroviral therapy in three hospitals; Korle Bu Teaching Hospital, Lekma Hospital and University of Ghana Hospital in the Greater Accra region of Ghana from January to May 2023. Participants underwent confirmation of their HIV status, determination of HIV serotype, and measurement of plasma viral load. Nasopharyngeal and oropharyngeal swab samples were collected for respiratory virus and bacteria screening using Real Time Polymerase Chain Reaction (RT-PCR) and Culture and Sensitivity testing, respectively.Among the enrolled participants, 32% tested positive for at least one viral respiratory pathogen, while 28% harboured at least one respiratory bacterium. The predominant virus was NL63, detected in 52 participants, while Staphylococcus aureus was the prevalent bacterium in 38 participants. Notably, the highest occurrence was observed between NL63 and Staphylococcus aureus. The study also highlighted substantial resistance patterns, particularly against Trimethoprim/Sulfamethoxazole, tetracycline, cephalosporins, ampicillin, chloramphenicol, and ampillicin-clavulanate for various bacterial species.The findings indicated a higher detection rate of respiratory viruses compared to bacteria in the respiratory tracts of PLHIV. However, the prevalence of respiratory virus/bacteria-associated occurrences did not demonstrate significant associations with HIV viral load or symptoms. Additionally, the assessment of antimicrobial resistance among nasal bacterial isolates indicated an overall high resistance pattern.

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PLACENTAL AND CONGENITAL MALARIA IN HIV POSITIVE PREGNANT WOMEN AND HIV EXPOSED NEONATES IN ABUJA NIGERIA

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HIV and Malaria are two of the greatest medical challenges facing Sub-Saharan Africa today, and despite this, there is minimal data on the interaction between these two infections in the highest risk group for both infections in Nigeria, sub-Saharan Africa. Placental and congenital malaria was assessed in HIV^+ pregnant women on antiretrovirals visiting 4 hospitals in Abuja Nigeria, between 2017 - 2020 to bring out the possible interaction of these infections and the birth outcomes. Informed and duly signed consents were obtained from the relevant agencies as well as from the participants. Venous blood samples (2mls) were collected from the peripheral blood of consenting near-term pregnant women and used to confirm the HIV status, CD4 cells, PCV and malaria parasitemia pre-delivery. Post delivery, 1ml blood sample respectively was collected from the incision made between the maternal and fetal surface of the placenta, and from Cord blood immediately after separation of placenta from the neonate. Parasitological examination was through microscopy and RDT. The neonatal anthropometric parameters were measured and noted. A total of 237 pregnant women participated in this study; 116(48.94%) HIV^+ while 121(51.05%) were HIV^-. The PCV levels of the HIV^+ participants pre-delivery were ≤32 in 60(51.72%) and ≥33% in 56 (48.27%) respectively. The CD4 cell counts of the HIV^+ participants pre-delivery had 700-799 cells range in 85 (73.27%) and 31 (26.72%) had ≥800 cells. Peripheral malaria was seen in 84 (72.41%) of the HIV+ participants and post-delivery placental malaria in 76 (65.52%) out of whom (45 (59.21%) were primigravids, 27 (35.53%) were secundigravids while 4(5.26%) were multigravids). Congenital malaria was observed in 60(51.72%) of the neonates exposed to HIV with 28 (24.14%) weighing between 2.5 - 3.0kg and, 46(39.66%) weighed between 3.1 - 3.5kg. Congenital malaria in HIV exposed neonates should be given urgent attention especially as malaria prevention is much less effective pregnant women living with HIV.

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THE IMPACT OF HEPATITIS B CO-INFECTION ON T-CELL RESPONSES IN VIROLOGICALLY SUPPRESSED HUMAN IMMUNODEFICIENCY VIRUS PATIENTS ON ANTIRETROVIRAL THERAPY IN GHANA

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Antiretroviral therapy can suppress HIV in many patients however, people living with HIV (PLWH) are still prone to other infections, even when virologically suppressed. Among PLWH in Africa, 15% are co-infected with Hepatitis B virus. Co-infections complicate disease progression and lead to higher mortality rates in HIV but their impact on T-cell responses is not well understood. Since HIV/HBV co-infection results in over-activation of the immune system, due to residual viral production, we assessed the differences in T cell responses in HIV/HBV co-infected patients and mono-infected controls. We screened 390 archived samples from PLWH for HBV and selected HIV/HBV co-infected samples for this study. Archived peripheral blood mononuclear cells from thirty-one (31) HIV/HBV-coinfected individuals, were stimulated with PMA and ionomycin, stained for activation and exhaustion markers (CD25, CD38, CD69, HLA-DR, CTLA4, PD-1) cytokines (IL-2, IFN-γ, TNF-α) and measured by flow cytometry. Levels of these markers from HIV/HBV co-infected patients were compared with thirty one (31) paired HIV mono-infected, twenty five (25) HBV mono-

infected, and six (6) healthy non-HIV controls. The prevalence of HBV/HIV was 7.9%. We found higher levels of CD69, CTLA4, and HLA-DR in HIV mono-infected and HBV mono-infected individuals compared to the other groups. We also found higher levels of CD25, CD69, and CTLA4 in HIV/HBV co-infected and HBV mono-infected individuals compared to the other groups. The healthy non-HIV controls had higher CD69 levels. No significant differences were observed in the expression levels of immune activation and exhaustion markers or cytokines between HIV/HBV co-infected and HIV mono-infected individuals. However, lower expression levels of IL2 and TNFα were observed in the HIV/HBV co-infected compared to the mono-infected individuals. Immune activation and exhaustion markers were highly expressed even in virologically suppressed HIV-1 pateints, an indication of ongoing residual viral production.

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EXPLORING HISTOPLASMOSIS IN NON-ENDEMIC AREAS: COMPARATIVE ANALYSIS OF CLINICAL FEATURES, RISK FACTORS, AND OUTCOME OF HISTOPLASMOSIS IN HIV-POSITIVE AND HIV-NEGATIVE COHORTS IN WESTERN INDIA

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Histoplasmosis, caused by the *Histoplasma capsulatum*, is a significant public health concern predominantly in regions where it is endemic. While it is endemic in certain regions of the world, it is considered rare in India. It is more common along the Gangetic belt, however, sporadic cases have increasingly been reported in western India, suggesting a wider than recognized distribution. Disseminated histoplasmosis is of particular concern it often mimicks tuberculosis. This prospective study evaluated the clinical features, treatment, and outcomes of disseminated histoplasmosis in Western India, comparing HIV and Non- HIV cohorts. The study was conducted between January 2022 - December 2023 in Infectious diseases division, AIIMS Jodhpur. Patients aged >18 years with clinically suspected disseminated histoplasmosis were screened using a urinary lateral flow test. Other samples such as Blood, biopsy etc, were collected for confirmatory tests from patients. Demographic data, comorbidities, symptoms, antifungals & outcomes were recorded. A total of 112 patients were recruited, of which 38 confirmed cases were included. The mean age for the HIV group was significantly younger than HIV-negative group (p=0.0042) & was predominantly male patients. Fever & cough was significantly more prevalent in the HIV group compared to the Non-HIV group.Detection of urinary Histoplasma antigen was notably higher in the HIV group compared to the Non-HIV group (p=0.0554). Biopsy confirmation rates were significantly higher in the Non-HIV group (47.37% vs 22.22%) compared to the HIV group. The detection of histoplasmosis from bone marrow samples in HIV vs Non-HIV patients (22.22% vs 5.26%). The mortality rate was relatively low (11.11% vs 10.53%).The findings demonstrate a notably higher prevalence of histoplasmosis among the HIV cohort, & a lower mean age compared to the non-HIV group. HIV patients had a higher rate of positive bone marrow biopsies, possibly due to more frequent disseminated infections. Despite similar mortality rates across groups, we advocate for targeted interventions to enhance outcomes.

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UNVEILING THE NEXUS: PREVALENCE AND ATTRIBUTES OF TUBERCULOSIS POSITIVITY AMONG PEOPLE LIVING WITH HIV IN BANGLADESH

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Tuberculosis (TB) poses a significant threat to individuals living with HIV/AIDS (PLHIVs) globally. Unfortunately, it is also a pressing concern for TB control efforts in Bangladesh. Due to low prevalence rate of HIV/AIDS in Bangladesh, its impact on national TB control program has not been studied adequately. Therefore, it is utmost necessity to understand the prevalence and potential factors contributing to TB positivity among PLHIVs in the country. In this context, we conducted a cross-sectional study to obtain necessary data from the Infectious Disease Hospital, the largest Anti-retroviral therapy (ART) center in Bangladesh. The data of the PLHIVs on ART recorded between January to December 2023 had been included. The prevalence of TB among PLHIVs in Bangladesh was found 8.7%. Among the 813 PLHIVs included, males constituted 67.4%, females 31.1%, and transgenders 1.2%, with the majority falling within the 30-39 age group (38.3%). Notably, the risk of TB development was higher among male PLHIVs, those whose HIV has progressed to advanced stage (WHO stages 3 and 4 with CD4 cell count<200 cells/mm3), and individuals with a family history of TB. In addition, TB testing using Gene-Xpert was conducted on 38.2% of PLHIVs, which yielded 9.3% TB positivity rate, considered to be very high. TB-positive PLHIVs were significantly older (p=0.002*) than younger counterparts (≤40 years) (55.2% vs. 44.8%, p=0.008*). Moreover, clients of sex workers and Men who have Sex with Men (MSMs) demonstrated higher TB positivity rates (44.8% and 17.2% respectively, p=0.0001*) compared to other groups. Our study findings provide valuable insights for policymakers and health managers grappling with the dual burdens of HIV and TB in Bangladesh. The identification of specific risk groups and demographic trends underscores the urgency of targeted interventions to effective mitigation of the national HIV and TB burdens.

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AGEING AND FRIALTY: THE CASE OF HIV-POSITIVE AND HIV-NEGATIVE INDIVIDUALS IN ASUTIFI-SOUTH DISTRICT AND TECHIAMAN MUNICIPALITY IN AHAFO AND BONO REGIONS OF GHANA

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Frailty remains a critical problem associated with age, which can be further aggravated with infections such as HIV infection. The dearth of indepth knowledge on frailty among Ghanaians especially in persons living with HIV, informed our decision to investigate the prevalence and factors associated with frailty among older adults with or without HIV infection in Ghana. This was a case control study conducted from January 2020 to December 2020. A total of 181 elderly persons were recruited into this study. Sociodemographic and lifestyle data were obtained with a well-structured questionnaire. Blood samples were obtained to determin the HIV-status of individuals whose HIV-status was unknown. Frailty was assessed by the Frailty Phenotype Tool. Statistical values with $p < 0.05$ was considered statistically significant. Of the 181 participants, 42.5% (n=77) were known HIV positive individuals on antiretroviral therapy whereas 57.5% of participants of this study were HIV-negative. Whilst the overall prevalence of frailty was 15.5% (n=28), the prevalence of frailty among HIV-negative adults was 12.5% (n=13) and 19.5% (n=15) for the HIV-positive adults. Occupation ($p = 0.020$), age ($p = 0.049$), smoking status ($p = 0.029$**)**, and not having multiple sex partners ($p = 0.031$) were associated with frailty among older HIV-negative adults. Frailty is more common among elderly persons with HIV-infection than those without HIV-infection, with nearly 2 out of 10 elderly persons with HIV being frail. No significant association was observed between frailty status and the socio-demographics and lifestyle characteristics among the HIV-positive participants. We conclude that, frailty is common among Ghanaian older adults and it is a bigger problem in the elderly living with HIV-infection.

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TATTOOING, CHRONIC DIARRHEA AND ANEMIA - A CLINICAL TRIAD OF HIV INFECTION

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Tattooing has rarely been documented as a mode of transmission in HIV infection. HIV wasting is the involuntary weight loss of more than 10% of an individual's body weight while having diarrhea or weakness, and fever for more than 30 days. Anemia is a predictor of poor prognosis in individuals with HIV independent of the CD4 count. This triad is rarely seen in HIV.A male in his 30s, bank manager by profession, who recently tested positive for antibodies to HIV 1, presented with watery diarrhea, fever and significant weight loss for 6 months. Deranged kidney function also indicated acute kidney injury. Further workup showed low CD4 counts (71/µL) and high HIV viral load, making the patient immunocompromised. The presence of anemia (Hemoglobin-5.5g/dL) increased the complexity of this case. It was confirmed to be autoimmune hemolytic anemia (AIHA) based on findings of hemolysis (LDH-510.0U/L), reticulocytosis (4.12%), and a positive direct antiglobulin test (DAT). Initially, the patient was stabilized with intravenous fluids, and metabolic acidosis and hypokalemia were corrected. Adding co-trimoxazole and nitazoxanide led to clinical improvement of the patient's diarrhea. HAART was initiated for the HIV infection/AIDS CDC Stage 3 on Day 12 of admission. Prednisolone was prescribed for AIHA, and blood transfusion was required because of a decline in hemoglobin levels in the blood.Transmission of HIV through tattooing calls for stricter regulations on tattooing while ensuring proper hygiene, use of sterile equipment, and proper disposal after the procedure, especially in developing countries. It should also be ensured that only those individuals with a valid license perform tattooing. Chronic diarrhea, attributed to HIV enteropathy or opportunistic infections leading to malabsorption, could have contributed significantly to the waste in this patient. Prevention or reversal of weight loss can be done by intensive nutritional rehabilitation. Anemia in HIV is mostly anemia of chronic disease, while AIHA is rarely seen as in this patient. When this triad of tattooing, wasting and AIHA is present, one should suspect HIV infection.

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OPTIMIZING SEROLOGICAL DIAGNOSIS OF TOXOPLASMOSIS: HETEROLOGOUS EXPRESSION OF GRA1 PROTEIN OF TOXOPLASMA GONDII IN E. COLI AS A KEY ANTIGEN IN CHRONIC INFECTION

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Toxoplasma gondii (TG), a protozoan parasite, typically induces mild infections in immunocompetent hosts but may cause severe complications in immunosuppressed individuals, such as those with HIV, by reactivating latent infections, leading to potentially acute and fatal neurotoxoplasmosis. Differentiating between the IgM antibodies, acute infection (tachyzoites), and IgG antibodies, as well as chronic infection (bradyzoites), is crucial in these patients. However, the sensitivity and specificity of many commercial serological assays are compromised by their reliance on total lysate antigens, which include a broad spectrum of parasite proteins. Diagnostics using recombinant antigens from the MICs, ROPs, and GRAs protein families have shown variable results, highlighting the need for enhanced precision in toxoplasmosis diagnostics. In response to this problem, we focus on the GRA1 protein, which is predominantly expressed in tachyzoites and known for its high immunogenicity as a principal antigen. We produced the recombinant GRA1 protein (rGRA1) using an *E. coli* expression system. Our first results showed the specificity of rGRA1 with sera pools from HIV patients; the first had six IgG-positive serums, and the other had ten IgG-negative. The Western Blot analysis showed a distinct and intense 25 kDa band corresponding to the GRA1 protein in IgG-positive samples, absent in IgG-negative samples. These results validate the use of our rGRA1 protein for diagnostic purposes and suggest its potential to significantly improve the diagnosis of chronic toxoplasmosis among immunocompromised patients.

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DETERMINANTS OF HEALTH AFFECTING THE CARE CASCADE OF VULNERABLE PEOPLE LIVING WITH HIV IN SENEGAL

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HIV infection poses a global health challenge, with significant implications for countries worldwide, including Senegal where it remains a pressing social issue. Today, the global goal in the fight against HIV/AIDS infection is to achieve UNAIDS' 95-95-95: 95% of people aware of their status, 95% of diagnosed individuals treated, and 95% on treatment achieving viral suppression. High lost-to-follow-up rates, especially among women, hinder progress. In Senegal, women's vulnerability to HIV care is exacerbated by factors like gender inequality that restrict their control over their sexual and reproductive health, hindering safer sexual practices. Addressing these issues is crucial to reducing HIV incidence and improving women's well-being. This study focuses on understanding social determinants (SDHs) of health affecting the HIV care cascade in Senegal's vulnerable populations, namely women. This cross-sectional descriptive pilot led by prominent researchers from Senegal and Canada, aims to address the gap in HIV care and management for vulnerable groups. The project is carried out at Dakar's Dalal Jam Hospital with data on women diagnosed seropositive and followed up since 2007. The analysis strategy employs descriptive methods to investigate SDHs of HIV care cascade in Senegal's vulnerable populations. It encompasses trend analysis and potential associations with SDH factors. Data will be described using means (standard deviations), or medians (1st quartile-4th quartile) for quantitative variables, and frequencies with confidence intervals for categorical variables. The findings, set to be shared with key stakeholders in May 2024, will reveal insights into the relationship between SDHs and HIV care continuums. The anticipated outcomes will be crucial in designing tailored care programs, enhancing HIV care, well-being, and social equality, thereby improving patient follow-up. In sum, this research not only aims to contribute to achieving the UNAIDS targets in Senegal but also offers a model that may applied in similar contexts globally, thus advancing the fight against the HIV epidemic and empowering vulnerable women.

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UNVEILING A BROADER STI SPECTRUM: THE ADVANTAGES OF MULTIPLEX PCR FOR TRANSGENDER WOMEN'S HEALTH

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Background Transgender women (TGW) are highly vulnerable to sexually transmitted infections (STI). In Colombia exist a lack of research on STI prevalence and are few data on the utility of multiple pathogen testing in samples from the sites of sexual exposure. We conducted a transversal study in Cali, Colombia to assess STI frequency and etiology in TGW comparing dual and multiplex PCR-diagnostic methods across various sample types.Methods TGW were enrolled from the community. Oropharyngeal and anorectal swabs were obtained and pooled for each patient, and urine was collected. All the samples were tested using a dual assay for Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG), and

a multiplex assay for CT, NG, Mycoplasma genitalium (MG), Mycoplasma hominis (MH), Ureaplasma urealyticum (UU), Trichomonas vaginalis (TV), Haemophilus ducreyi (HD), Treponema pallidum (TP), Herpes simplex 1 (HS1) and Herpes simplex 2 (HS2). Data were collected in Redcap for descriptive analysis.Results Between May and October 2023, samples from 50 TGW were collected. From the pooled samples 10/50 (20%) were positive for CT only, 8/50 (16%) for NG only and 5/50 (10%) for the two bacteria, by both methods. Among samples with CT/NG detection, 17/23 (74%) were positive for one to four additional pathogens by the multiplex assay: 11/23 (48%) UU, 24/23 (17%) TV and MG, 9/23 (39%) MH, 2/23 (9%) TP and 1/23 (4%) HS2. None of the urine samples were positive for CT/NG. Among samples negative for CT/NG, 15/27 (53%) were positive for one to three different pathogens: 5/27 (18%) MH and UU, 4/27 (15%) TV, 3/27 (11%) TP and 1/27 (4%) HS1 and HS2. Only 25/38 (66%) of the participants with STI diagnosis were symptomatic.Conclusions There is an extreme burden of STI in TGW in Cali, Colombia. Molecular methods for STI diagnosis are not available in the routine of care. The multiplex assay facilitated the diagnosis of additional pathogens in the same samples used for the dual assay, detecting asymptomatic infections, and having the potential to impact treatment decisions. These findings emphasize the need for expanded STI screening and advanced diagnostics in TGW populations.

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NEURODEVELOPMENTAL OUTCOMES IN UGANDAN PERINATALLY-INFECTED CHILDREN WITH HIV AT PRESCHOOL AGE WHO ARE NOT IMMUNE-COMPROMISED

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Neurodevelopmental delays have been well documented in children living with HIV, especially in impoverished settings host to many risk factors. The present exploratory study compares a cohort of immunologically stable Ugandan preschool-age children living with HIV (prior to antiretroviral treatment initiation), to a comparable cohort of non-exposed or infected children matched for age and living situation. We hypothesize that immunologically stable perinatally infected Ugandan children living with HIV (CLWHIV) in early childhood will be neurodevelopmentally comparable to non-infected children, even in the absence of early ART intervention. To test this hypothesis a cohort of CLWHIV (12 boys, 12 girls; mean age 4.6 yrs, SD 0.77) were compared to demographically similar non-exposed/non-infected children (14 boys, 17 girls; mean age 4.8 yrs, SD 0.78) using the Mullen Scales of Early Learning (MSEL) and the Color Object Association Test (COAT), an experimental measure for object placement immediate recall and learning. CLHIV children were immunologically stable in that all but one child was at WHO stage 0 or 1 and children included in this study had CD4% levels above 20 (mean 29.0 (SD 7.4). After adjusting for socio-economic status (SES), gender, age, and quality of caregiving (HOME scale), the HIV cohort was significantly lower than their non-infected counterparts on overall MSEL cognitive performance ($p<0.05$). MSEL differences were especially apparent on receptive language and expressive language. These groups differed on overall learning outcomes with the COAT assessment ($p<0.05$). MSEL and COAT performance was not related to immunology status (CD4, CD4%, viral load), although they were strongly correlated with SES and HOME environment. We conclude that immunologically stable CLWHIV may be at risk neurodevelopmentally for delays or deficits when compared to the non-infected counterparts. These deficits may be the direct result of the disease itself, as well as from the effects of environmental risk factors precipitating both risk for HIV in an impoverished urban Ugandan family and compromising caregiving in affected households.

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INTEGRATING SMOKING CESSATION INTO HIV CARE SETTINGS: A SYSTEMATIC REVIEW OF THE EVIDENCE BASE ON INTERVENTION EFFECTIVENESS AND COST-EFFECTIVENESS

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Tobacco smoking is a leading risk factor for non-communicable diseases. The prevalence of smoking among patients with HIV is significantly higher than in the general population, and smokers with HIV are more vulnerable to smoking- and HIV-related co-morbidities. The majority of patients and smokers with HIV live in low- and middle-income countries (LMICs), stressing the need for effective and cost-effective smoking cessation services for this vulnerable population in resource-constrained settings. This study systematically reviewed the published literature on the effectiveness and cost-effectiveness of smoking cessation interventions for smokers with HIV. Searches were conducted on four different databases (PubMed, Cochrane, Scopus, Web of Science) in December 2023. Only interventional and quasi-experimental studies assessing the effectiveness and cost-effectiveness of smoking cessation interventions for HIV-infected smokers were included. Of the 4,408 citation hits**,** only 24 studies met the eligibility criteria. All of the included studies were conducted in high-income countries, and the review identified no cost or cost-effectiveness studies. Smoking cessation interventions varied by type of treatment (behavioral, pharmacotherapy), treatment duration and intensity, and type of provider across studies. The included studies had low to moderate risk of bias. The findings of this review further showed that there was a considerable variability across studies in terms of their design and measurement of outcomes, which limited our ability to compare and generalize the findings of the studies. This systematic review provides the most up-to-date evidence on the effectiveness of smoking cessation interventions among smokers with HIV and reveals two critical gaps in the published literature. First, there is a lack of cost and cost-effective evidence on smoking cessation interventions for smokers with HIV, and second, none of the included intervention studies were conducted in LMIC settings.

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COST ANALYSIS OF SMOKING CESSATION INTERVENTIONS FOR SMOKERS WITH HIV IN HIV OUTPATIENT CLINIC SETTINGS IN VIETNAM

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Smoking prevalence is greater in smokers with HIV compared to the general population and smokers with HIV have a higher risk of developing HIV- and non-HIV-related illnesses than non-smokers with HIV. There is, however, a lack of studies on the effectiveness and cost-effectiveness of smoking cessation interventions for this vulnerable population, particularly in low- and middle-income country (LMIC) settings. We conducted a prospective costing study of three different smoking cessation interventions targeted at smokers with HIV and utilized an activity-based, micro-costing approach in our analysis. The costing study was nested within a randomized controlled trial in Vietnam (VQuit), which aimed to assess the effectiveness and cost-effectiveness of the three interventions in HIV outpatient clinic settings: (1)

Ask, Advise, and Assist and Refer to Vietnam National Smoker's Quitline (3As+R); (2) 3As and six in-person intensive Counselling sessions and text messages (3As+C); and (3) 3As+C and Nicotine replacement therapy (3As+C+N). Costs from the provider's perspective included the recurrent costs of the interventions, including personnel, overheads, materials and supplies, as well the capital costs of equipment. From the patient's perspective, we included direct non-medical and indirect costs incurred by patients due to their participation in the interventions. Our preliminary analysis showed that the total cost per smoker was US$38 for 3As+R, $179 for 3As+C, and $284.2 for 3As+C+N. These costs are likely to be overestimates due to the intensive technical and financial support provided for the implementation of these interventions in research setting and hence are conservative estimates. To our knowledge, this is the first cost analysis of smoking cessation interventions for smokers with HIV in an LMIC setting.

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LEPROSY, PARASITIC CO-INFECTION, AND FOOD INSECURITY: A CROSS-SECTIONAL STUDY IN MINAS GERAIS, BRAZIL

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According to epidemiologic and immunologic evidence, undernutrition and co-infection with helminths may be risk factors for Hansen's disease (HD) due to suppression of cell-mediated immunity. We examined associations of food insecurity, HD, and parasitic infection through antibody reactivity and self-reported infection history. Persons aged ≥3 years in 4 municipalities of eastern Minas Gerais, Brazil (n = 1,313) were tested for antibodies against *M. leprae* (LID-1, a marker of infection), *S. mansoni* (SEA), and *S. stercoralis* (NIE) via a multiplexed bead assay. Descriptive analyses and multivariable logistic regression were performed to assess associations of food insecurity with infection. Of the participants, 94(7.2%) were anti-LID-1+, 153(11.6%) were anti-SEA+, and 69(5.3%) were anti-NIE+. Seventy-two (5.5%) reported a history of HD, fifty-four of whom reported past parasitic infection. Compared to participants without history of infection, participants who reported both HD and a parasite were more likely to report running out of food without money to purchase more (aOR = 2.24, 95% CI 1.20, 4.20); running out of money for a healthy, varied diet (aOR = 2.54, 95% CI 1.38, 4.68); and reducing meal size due to lack of money (aOR = 2.67, 95% CI 1.43, 4.98), adjusting for sex. Participants with a history of HD and roundworms were more likely to experience the same metrics of food insecurity, respectively (aOR = 2.94, 95% CI 1.43, 6.07; aOR = 2.97, 95% CI 1.40, 6.28; aOR = 3.12, 95% CI 1.53, 6.36), than participants without a history of either infection. Though not statistically significant, anti-LID-1+/anti-SEA+ (n = 9) and anti-LID-1+/anti-NIE+ (n = 7) participants were observed to be more likely to reduce the size of meals due to lack of money (OR = 1.79, 95% CI 0.44, 7.24; OR = 1.64, 95% CI 0.34, 7.88) compared to LID-1 mono-infected persons. HD mono-infection history was not significantly associated with the food insecurity metrics. In conclusion, food insecurity was observed as more common among participants with multiple infections. Further investigation is needed to discern if food insecurity is a consequence of infection or a predisposing factor.

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CO-INFECTION DYNAMICS: PREVALENCE AND DEMOGRAPHIC INSIGHTS OF HEPATITIS B AND C AMONG HIV PATIENTS

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The prevalence and demographic characteristics associated with co-infection of hepatitis B (HBV) and hepatitis C (HCV) among individuals living with HIV were investigated. Despite significant advancements in antiretroviral therapy (ART), co-infections with viral hepatitis remain a major concern due to overlapping routes of transmission and shared risk factors. Co-infection hastens viral replication, fosters the advancement of chronic liver conditions, and presents hurdles for antiviral treatment. Understanding the prevalence rates and demographic profiles of co-infection is crucial for informing targeted prevention strategies and optimizing clinical management protocols. The Co-Infection Dynamics was studied using the Rapid Test Detection (RTD) strips, Enzyme-Linked Immunosorbent Assay (ELISA) and Polymerase Chain Reaction (PCR) method. Non-HIV volunteers in the same area served as control. A total of four hundred (400) subjects were involved in the study using the Stratified Random Sampling method; two hundred (200) from the district hospital for HIV patients and two hundred (200) from the non-HIV volunteers within the study area. The overall prevalence of hepatitis in the district hospital using RTD was 4% and 6% respectively for HBV and HCV as against 20% for both when the PCR method was used. Young adults within the age group 25-35 had the highest prevalence of HIV/HBV while the age ranging 45-55 had the highest prevalence of HIV/HCV. Co-infection of either HIV/HBV or HIV/HCV was higher among the participants who ignorant, civil servants, public servants, petty traders and international business men. Health literacy should be advocated to control these infections.

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DEVELOPMENT OF A CHAGAS DISEASE SEROLOGIC SCREENING PROGRAM WITHIN AN ACADEMIC PUBLIC SAFETYNET HOSPITAL IN CALIFORNIA

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Undertesting and inappropriate testing for Chagas disease (CD) is widespread among clinical populations with risk factors in California, predominantly Latin American immigrants. Towards the goal of increasing recommended risk-based screening and developing research cohorts, we identified two clinics at San Francisco General Hospital (SFGH) with expected increased morbidity from CD: Heart Failure Clinic and HIV Clinic. Employing an interdisciplinary team of laboratory medicine, cardiology, and infectious disease specialists, we performed process mapping for CD clinical screening. We additionally evaluated clinic staff understanding of CD using a brief knowledge and attitudes survey. These assessment tools identified variable provider knowledge of risk factors for CD and indications for clinical screening and confirmatory testing. To address provider knowledge gaps, we facilitated expert presentations to SFGH internal medicine, cardiology, and infectious disease clinicians and provided a targeted educational intervention to clinic staff. To address limited understanding of the CD diagnostic algorithm—which required provider familiarity with confirmatory testing requirements and patient presentation for two blood draws—we developed an in-house tandem serology testing algorithm. Using an automated ELISA platform, two distinct commercial serologic assays are run in parallel on a single serum sample for integrated diagnosis and confirmation of chronic Chagas disease, with a streamlined process for send out to CDC in case of discordance. To address results misinterpretation, we developed interpretive result comments for the battery of CD serology tests with accompanying recommendations for next steps and references to clinical recommendations. Towards development of high-quality CD research cohorts, we designed a secure database and workflow

for prospective collection of remnant clinical specimens and review of patient data under IRB-approved protocols. These interventions represent targeted responses to a CD diagnostic needs assessment through development of a novel clinical testing and research program.

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PRELIMINARY VALIDATION OF *ACANTHAMOEBA* PCR IN A UK PARASITOLOGY REFERENCE LABORATORY

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Free-living amoebae (FLA) of the genus *Acanthamoeba* may cause keratitis (AK) and, more rarely, granulomatous amoebic encephalitis (GAE). The parasitology reference laboratory at the Hospital for Tropical Diseases, London, uses the published multiplex qPCR assay from Qvarnstrom *et al.* (2006) for central nervous system (CNS) FLA diagnostics. In order to evaluate the sensitivity of this assay and establish its utility for AK (currently diagnosed within HSL by *in vitro* culture), a series of positive *Acanthamoeba* cultures from clinical isolates were evaluated. Here, we describe the preliminary testing and validation of several *Acanthamoeba* PCR tests in our laboratory. Two previously published PCR primer sets were assessed, along with three primer sets designed in-house (AcCOX 1, 2 and 6). Primer annealing temperatures were tested, followed by serial dilutions of control *Acanthamoeba* DNA. Quantitative PCR (qPCR) was then performed on these serial dilutions, as well as six clinical isolates of *Acanthamoeba* extracted in duplicate directly from cells resuspended in PBS and cells immobilised on a dry cotton swab. These extracts were tested using (1) the Riviere and Qvarnstrom primers with SYBR Green and (2) the standard triplex Qvarnstrom assay using a fluorescent probe. The Riviere and Qvarnstrom primers had the highest analytical limit of detection (dilution of $2.5x10^{-4}$) in standard and qPCR assays. The Qvarnstrom assay detected 6/6 clinical isolates, whereas the Riviere assay detected 5/6 and yielded less DNA per reaction. Results suggest that use of the Qvarnstrom qPCR in our laboratory is valid, and that it performs better than the Riviere qPCR. SYBR Green qPCR gave comparable results to the published multiplex assay, may be more cost-effective than fluorophore-labelled probes. The literature suggests that the Riviere assay only detects genotype T4 isolates, and the negative sample had an atypical melt temperature with Qvarnstrom primer SYBR Green PCR. Next steps will be sequencing the discordant clinical isolate to confirm its genotype, and comparing qPCR with culture on AK clinical samples.

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EVALUATION OF ANTIGENIC REGIONS OF GRA7 FOR THE DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC PHASES OF TOXOPLASMOSIS

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Toxoplasma gondii, an opportunistic intracellular parasite, infects approximately one-third of the global population and can cause severe or even fatal conditions, particularly in immunocompromised individuals. Accurate and early diagnosis is essential to facilitate prompt treatment and prevent disease progression. Conventional diagnostic methods, relying on natural antigens, often lack the specificity required to differentiate between the acute and chronic phases of toxoplasmosis. This challenge is critical in HIV/AIDS patients, where the infection stage dictates the therapeutic approach. In pursuit of precise differential diagnosis, we investigated the potential of recombinant proteins, specifically dense granule proteins (GRA), with an emphasis on GRA7, known for its high immunogenicity in both tachyzoites and bradyzoites. Serological evaluations of GRA7 have demonstrated its capacity to detect anti-*T. gondii* antibodies, exhibiting enhanced sensitivity in detecting acute infections. Further comparative studies on *T. gondii* proteins, SAG2, MIC 1 and GRA8, revealed variable antigenic reactivities, highlighting the necessity of extensive assays. To address these challenges, we employed bioinformatics tools to predict antigenic epitopes of GRA7, enhancing our understanding of its interaction with the host immune system. Our detailed bioinformatic analysis utilizing the IEDB Analysis Resource, Ellipro and ABCpred, identified three linear epitopes of GRA7. Notably, two of these epitopes are part of a larger discontinuous or conformational epitope. Antigenicity levels of these epitopes were quantified using VaxiJen 2.0, with threshold scores exceeding 0.5, indicating significant antigenic potential. This study underscores the complexity of GRA7 and its diagnostic capabilities, revealing distinct reactivities of identified epitopes against sera from acute and chronic toxoplasmosis cases in HIV/AIDS patients. These findings suggest a promising avenue for the development of more targeted diagnostic tests, currently under further evaluation.

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FIRST DOCUMENTED DETECTION OF *TRYPANOSOMA CRUZI* IN *PARATRIATOMA HIRSUTA*

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We present the first documented detection of *Trypanosoma cruzi* in *Paratriatoma hirsuta*. Entomologists within the Entomological Science Division, US Army Public Health Command, West, collected kissing bug samples and submitted them to their collaborators at the Department of Defense Food Analysis and Diagnostic Laboratory at Fort Sam Houston, Texas. Each sample was speciated by the entomology laboratory, accessioned, and submitted for molecular analysis. Sample processing was performed using the automated QIACube HT instrument with the QIAamp 96 QIACube HT Kit. Initial *T. cruzi* PCR screen analysis was performed using two assays: CRUZI 1-3 and 32F, 148R, 71P LNA probe. Six presumptive positive *T. cruzi* samples were identified. These samples were re-analyzed using a novel kinetoplast PCR/Sanger sequencing assay based on published validated targets. Traditional PCR amplicon was submitted to an external laboratory for sequencing. Analysis of the Sanger sequence data for a unique 20 base pair region confirmed *T. cruzi* identification in each of the *P. hirsuta* samples. To the best of our knowledge, this is the first documented detection of *T. cruzi* in *P. hirsuta*. This finding may help inform Chagas disease preventive measures in geographic areas populated by *P. hirsuta* vectors.

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EXPLOITING THE HUMAN AND ANIMAL HOST INTERACTION WITH *TRYPANOSOMA BRUCEI GAMBIENSE* FOR RAPID DIAGNOSTIC TEST DEVELOPMENT

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Trypanosoma brucei gambiense is an extracellular, single-celled parasite causing fatal human African trypanosomiasis (HAT) due to neurological

involvement. Ghana and Democratic Republic of Congo (DRC) are among the 38 countries affected by Tsetse fly invasion (or infestation) and Trypanosomiasis on the African continent. More than 90% of the total land area of Ghana and DRC are infested with tsetse fly hindering productivity. Tools for early diagnosis of latent *T. b. gambiense* Human African Trypanosomiasis (gHAT) are not available and existing methods have low sensitivity, are not rapid, are costly and require sophisticated equipment and skilled personnel to perform. Early detection and insecticide treatment of domestic animals hold promise for current control strategies. Plasma cytokines have been reported as potential biomarkers of *T. b. rhodesiense* HAT infection and treatment. The study will identify host plasma biomarkers as potential agents for early diagnosis of latent gHAT in Ghana and DRC. Venous blood samples from people living in gHAT endemic area in DRC and non-endemic areas in Ghana will be analysed for the prevalence of gHAT using SD BIOLINE HAT RDT kits and confirm using nested PCR. T-cell functionality in gHAT will be assessed by relevant cytokine biomarkers in plasma and cell culture supernatant of *T. b. gambiense*-infected individuals using Magpix or Luminex 200 analyzer in a multiplex immunoassay. Appropriate controls will be included in all assays. Demographic and other relevant data will be collected. Prevalence of gHAT and other infecting parasite species in humans will be reported. Correlations between participants' gHAT status and demographic data will be reported. Potential host biomarker in culture supernatants, plasma and cell surface activation marker will be known. The predictive biomarkers for early detection of latent *T. b. gambiense* will be reported.

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EVALUATION OF THE ELISA TECHNIQUE USING SAG1 AND TOTAL ANTIGEN TO DETECT IGG ANTIBODIES AGAINST *TOXOPLASMA GONDII* IN HEALTHY AND HIGH-RISK HUMAN SERUMS

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Toxoplasma gondii is an obligate intracellular protozoan parasite that infects humans, domestic and wild warm-blooded animals. This parasite produces a generally asymptomatic primary infection; however, it can be hazardous in immunosuppressed hosts and cases of vertical transmission(mother-fetus) during gestation. The ELISA test is commonly used to diagnose toxoplasmosis, which can identify immunoglobulins. This test is relatively simple and is available in commercial kits with its execution protocol, usually using total lysed antigens. However, the recombinant antigens could be highly beneficial in this application. The present study aimed to evaluate the ELISA technique using recombinant SAG 1 and total antigen (TLA) of *T. gondii* in 33 serums from the human population at risk and in 42 serums from a healthy population. The results concerning tail frequency found with recombinant SAG 1 antigen in the high-risk population was 96.96% (32/33), while in the healthy population, it was 19.04% (8/42). With the total antigen (TLA), the frequency of IgG anti-*T.gondii* antibodies were 96.96% (32/33) in the population at risk as opposed to 7.14% (3/42) in the healthy population. The frequency found in the healthy population using SAG 1 and TLA was lower than the average reported worldwide; however, TLA was detected more than twice as often as SAG 1 in the healthy population. The frequency of anti-*Toxoplasma gondii* IgG antibodies found in both populations with TLA and SAG 1 was equal, with no significant difference between the antigens. The use of recombinant proteins for the immunodiagnosis of *T. gondii* is a crucial contribution because no studies have been carried out on the population at risk in Peru.

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PROLIFERATING PARASITES- INCREASES IN THE IDENTIFICATION OF CUTANEOUS LEISHMANIASIS CASES IN NEW YORK STATE

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Classically described as a tropical disease, leishmaniasis cases are increasingly being diagnosed in non-endemic areas. This is especially true within New York State, USA where travel of residents and surges in human migration have brought substantial increases in the number of parasitic diseases identified. When cutaneous leishmaniasis is suspected, traditional methods of *Leishmania* detection have relied on microscopy and specialized culture techniques. These tests require highly trained staff and are typically available only at reference laboratories. To provide a less labor intensive and more sensitive assay for *Leishmania* detection and identification, the Wadsworth Center Parasitology Laboratory developed molecular-based assays. We first perform a real-time PCR assay (Clemons et al., 2021) to detect the amino acid permease 3 gene (AAP3) and the 70-kDa heat shock protein (HSP70). *Leishmania* spp. are further identified to the species or complex level by sequencing of the internal transcribed spacer 2 (ITS2) region of the ribosomal RNA gene. In just the first quarter of 2024 the laboratory reported 11 positive specimens compared with only 7 in all of 2023. Cases are largely linked to recent migration through South and Central American countries, which is consistent with a majority of the specimens containing *L. (V.) panamensis* or *L. (V.) braziliensis.* Overall *Leishmania* species identified by the laboratory to date using molecular detection and sequencing include *L. donovani* complex, *L. (V.) braziliensis, L. (V.) panamensis, L. tropica and L. major.* Leishmaniasis cases are not currently tracked in the United States. However, given changes in migration patterns and climate it is important to raise awareness for healthcare providers in non-endemic areas and provide species identification to inform treatment decisions.

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EVALUATING THE KNOWLEDGE, ATTITUDES, AND PRACTICES OF CHAGAS DISEASE AMONG HEALTH PROFESSIONALS IN SOUTH FLORIDA, USA

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Chagas Disease (CD) is a vector-borne illness caused by the parasite Trypanosoma cruzi. The confluence of immigration/travel from endemic areas, limited blood bank data, and the presence of the disease vector or epidemiological factors has created a potential for CD cases in the Southern United States, including the State of Florida, with an estimated >18,000 people living with CD. Given this potential risk, we identified South Florida as an important region in the state to track CD. Prior research has highlighted a notable deficiency in awareness of CD in the US, with no studies conducted in Florida, or South Florida across medical specialties of interest or in practices where patients may present with classic acute or chronic clinical findings of CD. Thus, this IRB exempt cross-sectional study utilizes an online 25 question survey measuring demographic information (e.g. specialty of medicine), knowledge, attitudes, and practices (KAP) among health care professionals (physicians, medical residents, nurse practitioners & physician assistants) in South Florida. Responses are evaluated using statistical evaluations. Our current survey responses showcase significant differences in KAP from N=51 health professionals (a majority of physicians) across N=19 sub-specialties (a majority from family medicine, pediatrics, & internal medicine) with varying years of experience,

ethnicity, region of medical training, and types of medical setting. Many respondents do not feel very confident in their CD practices (92.16% Wilson 95% CI 81.5%-96.9%), are unable to completely identify the modes of transmission/epidemiology for CD (100% 93.0%-100.0%), believe CD is misdiagnosed (92.16% 81.5%-96.9%), underdiagnosed (62.75% 49.0%-74.7%), or that more training is needed in the state (88.24% 76.6%-94.5%). Specialists (17.65% 9.6%-30.3%) within family medicine, pediatrics, cardiology, and infectious disease have even confirmed a diagnosis of CD. Our pilot study aids awareness and management of CD and informs future steps for research, education, community outreach, and training across health professions on this neglected tropical disease.

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APPLICATION OF RKMP11 BASED ELISA FOR DIAGNOSIS OF CUTANEOUS LEISHMANIASIS CAUSED BY *LEISHMANIA DONOVANI*

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Serology-based diagnostic tools for leishmaniasis can vary in terms of sensitivity, specificity & reliability. The KMP-11 antigen has been studied primarily as a potential vaccine candidate antigen against leishmaniasis. Sri Lanka predominantly reports cutaneous leishmaniasis (CL) caused by *Leishmania donovani*. This study aimed to compare the efficacy of recombinant KMP-11 antigens prepared from *L. donovani* and *L. infantum*, along with crude *L. donovani* antigen, in detecting CL infections in Sri Lanka using enzyme-linked immunosorbent assays (ELISA). An optimized indirect ELISA was employed to determine the cut-off values, sensitivities & specificities for the three selected antigens. The cut-off value for each test was determined using a receiver operating characteristic (ROC) curve based on the absorbance values of sera from 21 CL patients confirmed by microscopy & 21 healthy individuals from non-endemic areas. The cut-off values for KMP-11 antigens were 0.169 for *L. donovani* and 0.162 for *L. infantum*, with sensitivities of 95.2% and 79.2% and specificities of 100% and 71.4%, respectively. The cut-off for crude *L. donovani* antigen was 0.150, with a sensitivity of 98.0% and specificity of 90.3%. A positivity of 95.2% (95% CI: 87.1-100) was observed for ELISA based on KMP-11 for *L. donovani* in comparison with 81.0% (95% CI: 71.6- 90.4) for KMP-11 of *L. infantum* and 100% for crude antigen. All antigens yielded negative results for non-endemic healthy controls. Crude antigen showed the highest sensitivity, while the recombinant KMP-11 antigen for *L. donovani* displayed comparable performance in the detection of CL infections. Further validation, including a larger cohort from different settings reporting CL due to *L. donovani*, is needed to assess its potential for use as a candidate diagnostic biomarker.

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IDENTIFICATION OF ANTIBODY BIOMARKERS TO DIFFERENTIATE POST KALA AZAR DERMAL LEISHMANIASIS FROM LEPROSY

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Post Kala Azar Dermal Leishmaniasis (PKDL) is a complication of visceral leishmaniasis with skin lesions that can be difficult to differentiate from leprosy. Because treatment decisions differ between these diseases and an accurate diagnosis is imperative for proper patient care, we are seeking to develop improved test that can rapidly identify the infectious agent. We used the serum epitope repertoire analysis (SERA) platform that combines a bacterial display library technology, next-generation sequencing, and bioinformatics to identify antibody binding epitopes specific to a disease state. For epitope discovery, we used sera from patients with confirmed visceral leishmaniasis (n=40), cutaneous leishmaniasis (n=25), or leprosy (n=30); and patients negative for leishmaniasis (29) or leprosy (n=30). For validation, we used a panel that included sera from the same patient categories (66 visceral leishmaniasis positive sera, 24 cutaneous leishmaniasis sera, 30 leishmaniasis negative sera, 16 defined positive leprosy sera, 28 defined negative leprosy sera), as well as sera from 31 leprosy contacts. SERA screening identified 15 epitope motifs that uniquely reacted with sera from leishmania patients. These epitopes mapped to Histone H2A, an uncharacterized protein with 33 repeats, Histone H2A.1/2, and a J domain-containing domain. SERA screening also identified 14 epitope motifs that uniquely reacted with sera from leprosy patients. These epitopes mapped to putative secreted p60-family protein, Ag85A, Ag85B, UvrABC system protein A, and MTB12. We followed up with peptide array by testing 1,127 peptides (from SERA targets and *in-silico* analysis) and expressed 31 candidate proteins. Four proteins of *L. donovani* and 4 proteins of *M. leprae* differentiated significantly. We conducted large expression of these proteins and developed ELISAs. The next step is validation of these antigens.

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COMPARATIVE EVALUATION OF FOUR MOLECULAR DIAGNOSTIC TESTS FOR THE DETECTION AND IDENTIFICATION OF CUTANEOUS *LEISHMANIA* PARASITES

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Cutaneous Leishmaniases (CL) are a group of diseases considered as the most NTDs. In Tunisia and many countries in MENA region CL present a complex epidemiological situation with the proven implication of at least 3 *Leishmania (L.)* species (*L. infantum, L. major, L. tropica*) with diverse clinical presentations. *L.* species identification is essential for etiological diagnosis, patient's management and surveillance. PCR based assays are the most accurate diagnostic tests for CL because of their higher sensitivity and specificity. The aim of this study is to compare the performances of different PCR based assays we developed for simultaneous *L.* species detection & identification to improve the diagnostic accuracy of generic tests. A total of 91 cutaneous samples collected during routine diagnosis at the Parasitology department of the Farhat Hached UH were used to assess and compare the performances of 4 molecular tests: 2 conventional tests (a genus-specific PCR Lei-70, PCR RFLP ITS1 which profiles are used to identify species) and 2 tests we recently developed (PCR HRM assay, Multiplex PCR assay coupled to Lateral Flow DNA chromatography (Mx PCR LF)) which concomitantly detect & identify the *L.* species. Among the 91 samples, 54 were revealed (+) by at least 1 of the molecular tests. Considering the Direct Examination as the gold standard method, the sensitivities of detection of the PCR Lei-70, PCR ITS1, PCR HRM and Mx PCR assay were 92%, 80%, 88% and 82%, respectively. PCR Lei-70, PCR HRM & Mx PCR LF assays showed similar specificities (95%) while PCR ITS1 showed a specificity of 92%. *L.* species identification was possible with RFLP ITS1, Mx PCR LF and PCR HRM methods. Of 43 PCR^+, RFLP ITS1 identified 39 and PCR HRM 35; Mx PCR LF identified 45 out of 46 PCR^+. This latter was the most performant in terms of species identification. Identity was congruent with the 3 molecular tests, but ambiguities mainly seen with PCR RFLP ITS1 and PCR HRM were resolved with the Mx PCR LF. According to these results, the Mx PCR LF holds promise for accurate simultaneous detection & identification of *L.* parasites in clinical samples that could be used to improve CL diagnosis in health centres

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PHAGE DISPLAY IMMUNOPRECIPITATION SEQUENCING (PHIP-SEQ) FOR THE IDENTIFICATION OF *TRYPANOSOMA CRUZI* ANTIGENS WITH DIAGNOSTIC POTENTIAL

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Trypanasoma cruzi infection, also known as Chagas disease, is predominantly diagnosed in the chronic phase, requiring confirmation by two distinct IgG serology assays. In the United States, few serological diagnostics are cleared for detecting anti-*T. cruzi* antibodies. Performance evaluations of these tests have shown variable test performance between assays and infected populations throughout endemic regions of the Americas. We hypothesized that using the next-generation technology of phage display immunoprecipitation sequencing (PhIP-Seq), which presents linear peptide fragments across an entire genome within a library of bacteriophages for immunoprecipitation with plasma, will elucidate better antigen targets for laboratory diagnostics. The advantage of PhIP-Seq is that it allows for the antibody profile assessment of each individual without pooling specimens. Our phage library spans the entire *T. cruzi* genome (CL Brener) composed of 228,127 peptide fragments, each being a 47-mer with 19-residue overlap. This *T. cruzi* phage library was immunoprecipitated using plasma samples with confirmed blood donor testing (n=90; 64 seropositive, 26 seronegative), including donors from Mexico, Central and South America. The phage library underwent two rounds of selection before sequencing to identify antigenic peptides. Sequencing reads were normalized, and a z-score was calculated for each peptide within a sample, compared to seronegative controls. To orthogonally validate our findings, we used a mass-univariate generalized linear model. We identified 15 peptide fragments with a z-score ≥4 in 57/64 seropositive samples (≥90% PPA), and in 0 seronegative samples; including microtubule-association proteins (MAPs), surface-antigen (CA-2), 60S ribosomal proteins L23a, and trans-sialidase proteins. One trans-sialidase peptide fragment had a z-score ≥4 in all seropositive samples. These analyses show insight into antigenic peptides that could be easily translated into an immunoassay format. Future steps will validate in larger, real-world infected populations to evaluate test performance to commercial diagnostics.

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PRODUCTION AND EVALUATION OF LB6H RECOMBINANT ANTIGEN PRODUCED IN BRAZIL TO DIAGNOSE AMERICAN TEGUMENTARY LEISHMANIASIS

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American tegumentary leishmaniases (ATL) have a wide distribution, with an estimated annual incidence of between 600,000 and 1 million new cases, mainly in tropical and subtropical countries. The clinical-epidemiological aspects are fundamental, but laboratory exam data are needed to confirm the diagnosis, mainly due to the varied clinical aspects that are not pathognomonic. A recombinant antigen (rLb6H), identified during the screening of a genomic expression library of *L. (V.) braziliensis* (MHOM/BR/75/M2903) with serum from a patient infected by *L. braziliensis* with mucosal leishmaniasis at the Access to Advanced Health Institute—AAHI, Seattle, USA and was evaluated (2017) and validated (2022) on an ELISA platform for ATL diagnosis, with promising results. This study aimed to produce the rLb6H in Brazil and evaluate its performance on the ELISA platform to diagnose ATL infection. The rLb6H sequence was optimized and analyzed using bioinformatics. The pET24a(+) containing the Lb6H gene was transformed into *E. coli* of the SHuffle T7 Express strain. The induction was conducted at different times and temperatures to evaluate the best condition for protein expression. SDS-PAGE analysis showed that the Lb6H protein presented a band of 76.2 kDa. After lysis, the pellet containing the Lb6H protein was solubilized in a buffer with 8 M urea, and the protein was purified by affinity chromatography on a histidine column. The protein was quantified by using a BCA Protein Assay after dialyzing. After ELISA standardization, 176 serum samples from Brazilian regions were assayed: 93 from ATL patients, diagnosed by direct identification of *Leishmania* infection or PCR, and 83 controls considered healthy by their assessment and clinical exam. The rLb6H-ELISA performance was based on the Receiver Operating Characteristic curve results. In samples from ATL patients, rLb6H-ELISA sensitivity (CI 95%) was 95.6 % (89.1%-98.3%), and the specificity was 96.4% (89.9%-99.0%). Our preliminary evaluation results corroborate previous results, showing that rLb6H produced in Brazil is valuable for possible future use in the routine serological diagnosis of ATL.

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EVALUATION OF THE CROSS-REACTIVITY OF THE RK28 ANTIGEN USED IN THE SEROLOGICAL DIAGNOSIS OF HUMAN VISCERAL LEISHMANIASIS

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Advances in VL diagnosis were driven by the development of lateral flow immunochromatographic tests based on the rK39 antigen, facilitating access to diagnosis and presenting high sensitivity and specificity. On the other hand, the low accuracy observed in East Africa led to the development of rK28, which, although it has high sensitivity, has demonstrated low specificity in regions where other infectious diseases coexist. The present work aimed to evaluate the cross-reactivity of the rK28 antigen compared to rK39 (produced by Access to Advanced Health Institute - AAHI, Seattle, USA), employing samples from patients with malaria from different locations in Brazil. The panel used was composed of serum samples from patients with positive thick blood smear and positive serology (ELISA with MSP1-19) for *Plasmodium falciparum* or *P. vivax*: 55 from patients diagnosed in São Paulo Municipality (15 with *P. vivax* and 40 with *P. falciparum*), and 48 from the State of Pará (*P. vivax*). The samples were tested with rK39 and rK28 antigens on the ELISA platform. In São Paulo, a positivity rate of 40.0% (24.9%-56.7%) was obtained with ELISA-rK28 and 2.5% (0.1%-13.2%) with ELISA-rK39, in *P. falciparum* samples, and 20.0% (4.3%-48.1%) with ELISA-rK28 and 6.7% (0.2%-31.9%) with ELISA-rK39, in *P. vivax*. In samples from Pará (*P. vivax*), positivity was 16.7% (4.5%-30.2%) with ELISA-rK28 and 2.1% (0.1%-11.1%) with ELISA-rK39. Although the coexistence of malaria and visceral leishmaniasis in the patients' places of origin cannot be excluded, the significant difference in positivity between the antigens (Fisher exact test, p=0.0001) indicates the occurrence of cross-reactivity between rK28 and the patients' antibodies with *falciparum* malaria. In the case of patients with *P. vivax*, there was no significant difference between both antigens in the samples from São Paulo (Fisher exact test, p=0.5977), although in Pará, the positivity was significantly higher with rK28 (Fisher exact test, p=0.0305).

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VALIDATION OF A WHOLE BLOOD *TRYPANOSOMA CRUZI* QUANTITATIVE RT-PCR ASSAY ACROSS A RELEVANT RANGE OF PARASITEMIA

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Detecting acute or reactivated Chagas disease is important in immunocompromised patients, commonly in the setting of organ transplant and HIV co-infection. The US CDC is the only lab accessible to all US

healthcare providers that provides clinical PCR testing. It is expected that new requirements for donor screening will increase the volume of testing that may necessitate more widespread implementation of quantitative PCR (qPCR) assays for Chagas disease. Our study seeks to adapt published PCR primers and probes (minicircle and satellite DNA) to a standard curve of clinically relevant parasite concentrations. Additionally, we aim to evaluate the analytical sensitivity of SYBR green reporter (all amplified DNA) to TaqMan probe (sequence-specific amplification products) to determine if SYBR green may provide more sensitive detection. We will evaluate limits of detection (LoD) and quantification (LoQ) in multiple *T. cruzi* strains relevant to human infection (Dm28c (TcI), Y(TcII), and CL Brenner(VI)). The relevant range of LoQ was determined to be ~0.05-500,000 parasite equivalents per mL (Peq/mL) based on published research in immunocompromised populations. LoQ was determined along an 8-point standard curve with linearity r^2 >0.90 and a cycle threshold (Ct) coefficient of variance <10% for each concentration run in triplicate. We have evaluated 3 technical replicates for minicircle primers with Dm28C DNA, demonstrating acceptable linearity and intra-assay precision by SYBR green and TaqMan methods. SYBR green demonstrated increased analytical sensitivity by lower Ct values at all points across the quantitative range with an average Ct difference of 2.4. These findings suggest that TaqMan probe sequences may not be present in all kDNA amplicons. This may be of limited clinical significance given both are detectable across this range of clinically relevant parasite concentrations. These preliminary findings demonstrate that a whole blood qPCR method quantifying parasitemia can be achieved. Further studies are planned to evaluate whether the observed increase in analytical sensitivity by SYBR is applicable to LoD.

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THE RELATION BETWEEN RECOMBINANT PROTEIN GRA1 AND SEVERITY INDICATORS IN PATIENTS WITH TOXOPLASMOSIS AND HIV/AIDS CO-INFECTION

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Toxoplasmosis is a critical opportunistic infection in patients with HIV/AIDS, which faces important challenges in its diagnosis and treatment. In this context, recombinant proteins offer significant advantages in terms of sensitivity and specificity. The GRA1 protein, secreted by *T. gondii,* is key in the life cycle of the parasite and essential for maintaining the parasitophorous vacuole, allowing persistence in the host. It has been established that GRA1 can be a valuable marker for the detection of recent infections of toxoplasmosis. This study investigates the relationship between the serological response in Western blot towards the recombinant protein GRA1 produced in *E.coli* and the immunological markers CD4+, CD8+ and the CD4+/CD8+ ratio, exploring its potential as a biomarker of severity in advanced stages of HIV infection. The results showed that 80.7% of the patients (46/57) were positive for IgG and 31.6% (18/57) for IgM. Mean CD4+ lymphocytes of 63 (27-136) cells/mm3 were recorded. , CD8+ of 764 (385-984) cells/mm3, and a CD4+/CD8+ index of 0.08 (0.04-0.17). The mean log viral load was 4.7 ± 1.0 log10 RNA copies. In addition, three relevant clinical cases are detailed with positive IgM and negative IgG values, indicating a high probability of recent toxoplasmosis infection. The first case describes a patient with severe neurological compromise and altered consciousness (total Glasgow Scale = 9), who did not improve with cotrimoxazole treatment and died after recruitment. The second case involves a patient with myelopathy from the level T10 and disorientation (total Glasgow Scale = 14), who was also positive for HTLV-1. The third case reports a patient with mild IgM positivity, CD4+ in 70 cells/mm3 and symptoms of altered consciousness (total Glasgow Scale = 13), together with a brain tomography compatible with cerebral toxoplasmosis, treated with cotrimoxazole. This antigen has the potential to predict cases of acute infection and reactivation of toxoplasmosis in patients with HIV. Future studies should validate the sensitivity and specificity of GRA1, comparing it with standard tests and increasing the number of samples analyzed.

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DEVELOPMENT OF ISOTHERMAL AND CRISPR-BASED DIAGNOSTICS FOR THE DETECTION OF *BABESIA* PARASITES

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Human babesiosis is caused by infection of the red blood cells with *Babesia* species parasites and can result in severe disease and even death, especially in immunocompromised or asplenic individuals. In the USA there are ~2,000 cases of human babesiosis annually, primarily caused by *B. microti*, however, due to underdiagnosis the true number of infections has been estimated to be up to 10-fold higher. The number of cases of babesiosis is likely to continue increasing due to the expanding range of the ticks that transmit infection. Further, babesiosis can be transmitted by blood transfusion, although testing is now in place in endemic states. Diagnosis is currently based on the presence of parasites in a blood smear or by PCR which require trained technicians and specialized equipment. Here, we investigate and compare the utility of recombinase polymerase amplification (RPA) and Cas12 or Cas13-based CRISPR assays as a simple isothermal method for the detection of *B. microti* and *B. divergens* nucleic acid. We further investigate the sensitivity and specificity of each assay from different sample types, including lysed whole blood and purified nucleic acids. These methods offer the potential of a simple point-of-care diagnostic with the sensitivity and specificity of PCR and the ability to multiplex for the detection of other tickborne pathogens in the future.

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TOXOPLASMA GONDII IN TERTIARY HOSPITAL, EASTERN SAUDI ARABIA: ROLE OF SEROLOGY AND MOLECULAR DIAGNOSIS AND INSIGHT INTO PREDICTIVE RISK FACTORS

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Toxoplasmosis is a potentially life-threatening disease that necessitates accurate diagnosis for treatment, prevention of transmission, and unfavorable consequences. This study is to determine the serological and molecular prevalence of *Toxoplasma gondii* in sera of clinically suspected cases and estimate potential risk factors for the occurrence of Toxoplasmosis. *Toxoplasma*-specific IgG and IgM were detected in 22.4% (32 cases) and 4.2% (6 cases), respectively. 529 bp-repeat elements PCR (RE-PCR) detected *Toxoplasma* DNA in 33.6% (48 cases), and B1-nPCR detected *Toxoplasma* DNA in 23.7% (34 cases) of the study population. All positive cases by the B1-nPCR were also positive by direct RE-PCR, and none of the negative cases by B1-nPCR were positive by direct RE-PCR. RE-PCR revealed a perfect sensitivity (100%) and 87.16% specificity compared to B1-nPCR with substantial agreement. The serological test showed limited sensitivity and moderate specificity with a slight agreement between the serology test and B1-nPCR results. Age distribution of positive

cases showed a peak in the 25-40 years age group. Among patient characteristics (demographic, clinical, and laboratory data and lifestyle habits), patients with chronic diseases, a history of adverse neonatal consequences, pregnant women who had intrauterine growth restriction/ premature rupture of membranes, handled undercooked meat, routinely ate from restaurants were at higher risk of having *Toxoplasma*. In positive *Toxoplasma* patients, there was a statistically significant increase in the risk of neonatal consequences among individuals with chronic diseases. Routine hand washing was a protective habit against toxoplasmosis. The study results emphasized the advantage of using PCR tests coupled with routine serological tests for diagnosing toxoplasmosis in clinically suspected cases, thus helping improve national guidelines for *Toxoplasma* screening.

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CHARACTERIZATION OF LEISHMANIASIS IN THE TOURIST CORRIDOR OF THE AMAZONAS REGION, PERU

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Cutaneous leishmaniasis (CL) is endemic in the region of Amazonas and represents a major public health challenge. In 2023, 314 cases of CL were reported, compared to 284 cases in 2022. It is worth noting that most of the cases were reported in the tourist corridor of "Alto Utcubamba" which includes the provinces of Luya and Chachapoyas. However, a high number of underreported cases is suspected due to the social stigma, the lack of health coverage, and an apparent resistance to the treatment. In this study, we analyzed 24 samples collected in the provinces of Chachapoyas and Luya during 2022 and 2023. Samples were diagnosed as positive to *Leishmania* through a direct smear examination and cultured on blood agar, followed by a FRET-based real-time PCR technique targeting the MPI and 6PGD genes. Results showed 12 positive specimens for *L. (V.) braziliensis* and 11 for *L. (V.) peruviana*; however, one sample was undetermined. The majority of the patients reported u*lcers in the lower limbs with raised edges and a granular bottom*. According to the epidemiological information, most of the patients (10/24) belonged to the ≥ 60 age group with agriculture as their main occupation. Although most of the samples were properly characterized, the difficulty in the identification of one of the samples could be attributed to genetically complex strains, including hybrid. Moreover, *Leishmania* strains, resulting from genetic exchanges, are suggested to cause more severe clinical symptoms and an increase transmissibility. On the other hand, it is important to highlight that some species within the *L. braziliensis* complex, such as *L. (V) braziliensis*, can cause metastasis to destructive mucosal lesions after healing the initial skin lesion. In addition, reports suggest that this species is more virulent because it can cause mucocutaneous leishmaniasis, therefore, it is important to characterize and properly identify the *Leishmania* species circulating in the area, to have a better idea of the prognosis of the disease.

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ASSOCIATION BETWEEN IMMUNE PROFILE AND CHAGAS DISEASE PROGRESSION IN NATURALLY INFECTED RHESUS MACAQUES

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Chagas Disease is caused by the protozoan parasite *Trypanosoma cruzi*; clinical presentation ranges from asymptomatic to severe cardiac and/ or digestive damage. Previous studies in naturally infected macaques indicated a role for parasite strain composition in disease progression, suggesting differences in immune response between "controller" and "progressor" macaques. In this study, we used RNA-sequence data to analyze Major Histocompatibility Complex (MHC) genes, immunoglobulin (Ig) subclasses, and Ig and T-cell Receptor (TCR) repertoires in eighteen naturally infected macaques and nine uninfected macaques to test for differences in the breadth of the immune response associated with disease progression and parasite strain diversity. MHC molecules are responsible for binding foreign epitopes to induce adaptive immune responses via antigen presentation. The TCR complex is found on the surface of T lymphocytes, and reflects the diversity of antigens presented via MHC molecules during infection. Similarly, IgG diversity can also inform on the differentiation of B cells as a response to infection. Different MHC alleles were observed between the uninfected and infected macaques, with several alleles unique to the progressors. The proportion of Ig subclasses showed limited differences associated with infection. On the other hand, analysis of the Ig repertoire indicated that infection was associated with an increase in IgG diversity together with the expansion of selected IgGs, and this was more pronounced in controller macaques compared to progressors. TCR repertoire was also affected by infection with the expansion of several TCRs, but differences between controller and progressor macaques were minimal. These results provide evidence that MHC genes may play a role in host genetic susceptibility, and that differences in IgG and TCR repertoires may be associated with Chagas disease progression. A better understanding of these processes is needed to improve understanding of disease risk and patient care.

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MOLECULAR EPIDEMIOLOGY OF *TRYPANOSOMA CRUZI* IN EL SALVADOR ELUCIDATED BY MULTI-LOCUS SEQUENCE TYPING USING THIRTEEN HOUSE-KEEPING GENES.

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One of the important factors in controlling infectious diseases is the precise targeting of the foci on which we apply our limited resources. El Salvador, located in the Central America, is endemic of Chagas disease with newly diagnosed patients every year to date. Chagas disease is a zoonotic disease caused by the infection of a single-celled parasite called *Trypanosoma cruzi*. The transmission of *T. cruzi* to humans in this region mainly occurs through contact with blood-sucking triatomine bugs called *Triatoma dimidiata*, locally known as 'chinche'. Although endemic for a long time, little is known about the characteristics of *T. cruzi* lineages circulating in this country. This study focused on illustrating the current distribution of *T. cruzi* lineages in El Salvador by genetically analyzing 145 *T. cruzi* samples from *T. dimidiata* collected from throughout the country. The results of DTU classification showed homogenous genetic characteristics in the country – 99.3% resulted in *T. cruzi* lineage I (TcI). Further analysis based on the sequence data of thirteen housekeeping gene fragments revealed the twelve novel sequence types, which consisted of two major groups based

on phylogenetic analysis. These results suggested persistent area-limited transmission of *T. cruzi*, which may serve as an important insight for the disease control strategy in this region.

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CO-INFECTIONS OF *LEISHMANIA DONOVANI* AND *LEISHMANIA MAJOR* IN BLOOD OF PATIENTS WITH VISCERAL LEISHMANIASIS FROM GARISSA COUNTY, NORTHERN KENYA

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Leishmaniasis is endemic in many countries, including Kenya. Globally, around 350 million people are at risk of contracting the disease. Despite an increased frequency of visceral leishmaniasis (VL) outbreaks in Northern Kenya (Garissa county) in recent years, there is little data on the genetic structure and epidemiology of *Leishmania* parasites in the region. This study investigated the inter-species diversity and evolutionary relationships of *Leishmania* parasites collected from Northern Kenya (Garissa County) during the 2019 - 2022 visceral leishmaniasis outbreak. A total of 286 blood samples collected from patients suspected of having VL at Garissa Referral County Hospital between 2019 and 2022 were analyzed. *Leishmania* parasites were screened at genus and species level by quantitative real-time PCR (qRT-PCR). To characterize the parasites genotypes, amplicons of Hsp70 (~2000nt) and ITS (1,400nt) genes generated through conventional PCR were fragmented into suitable library sizes, sequenced and analyzed using phylogenetic tools. To deconvolute unexpected observation of mixed infections of *L. donovani* and *L. major*, we designed a deep sequencing assay targeting un-fragmented 350nt region of ITS1 gene. Sequencing was performed on the Illumina MiSeq platform. Sequences were analyzed using the ngs mapper pipeline and Dada2 in R. By qRT-PCR, 128/286 (45%) blood specimens tested positive for *Leishmania* at the genus level. Upon speciation, 48/128 (17%) had mono-infections of *L. donovani*, 2/128 (1%) had mono-infections of *L. major* while 78/128 (27%) had co-infections of *L. donovani* and *L. major*. On sequencing the PCR amplicon libraries, 86/128 Hsp70 and 79/128 ITS gene sequences clustered with *L. donovani* complex. On sequencing the full 350nt ITS fragments, mixed infection of *L. donovani* and *L. major* were detected. This study reveals the complex nature of *Leishmania* epidemiology in Kenya. It also sheds light on the possible inter-species interaction that may have significant implications on diagnosis and pharmaco-therapy.

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EVIDENCE FOR VERTICAL TRANSMISSION OF GENETICALLY DIVERSE *TYRPANOSOMA CRUZI* IN A NATURAL RODENT RESERVOIR POPULATION

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Chagas disease, caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*), poses a significant health threat in the Americas with 6-8 million people infected by the parasite and 75 million at risk of contracting the disease. While Chagas disease is vector-borne, vertical transmission has played an increasingly significant role in disease transmission. Across Latin America, the monitoring of blood and organ donations coupled with vector control programs has led to vertical transmission becoming the main transmission pathway for spread amongst humans. Studies have found that a high diversity of *T. cruzi* DTUs (Discrete Typing Units) can circulate within human populations, and also that individuals of other mammalian hosts can have high *T. cruzi* DTU diversity. It is less clear how *T. cruzi* prevalence and diversity is sustained in non-human mammals. We hypothesized that vertical transmission may also be a pathway for sustaining pathogen reservoirs and DTU genetic diversity in other mammals, namely urban rodent reservoirs. Leveraging a previous study in New Orleans (LA, USA), we examined 10 *T. cruzi* PCR positive pregnant rodents (Norway rats, black rats, and house mice) and 66 embryos. Fifteen of the 66 (22.7%) embryos were positive for *T. cruzi* by PCR. Genotyping PCR of the *T. cruzi* mini-exon gene and deep sequencing were performed to characterize the DTU structure, demonstrating infections with multiple DTUs such as TcI, TcII and TcV. These findings indicate that vertical transmission in rodent populations can potentially sustain *T. cruzi* infection and multiclonality in urban areas where vector populations might be small or absent. Given the increasing importance of vertical transmission, it would be prudent to conduct further investigations to better characterize the transmission pathway and understand what impact vertical transmission could have on *T. cruzi* prevalence and diversity in other natural reservoir populations. For example, combining diagnostic and genotyping assays with genomic estimates of relatedness among *T. cruzi*-positive hosts could shed further light on vertical transmission in natural populations.

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GENOME ANALYSIS OF *TRYPANOSOMA CRUZI* FIELD ISOLATES OFFERS THE OPPORTUNITY TO STUDY THE EFFECT OF INFECTION CONTEXT ON PARASITE GENETIC DIVERSITY

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Trypanosoma cruzi is the causative agent of Chagas disease, a neglected parasitic disease that kills 10,000 people each year. Despite the disease's high public heath burden, there has been very little investigation into the parasite's genome, especially in parasite strains infecting human patients. Here, we describe short read whole genome sequencing and assembly of 15 clinically isolated T. cruzi samples from different relevant infection contexts: mothers at time of delivery, patients with Chagasic cardiomyopathy, and patients co-infected with HIV. We have produced gene level assemblies for each sample and resolve multiple putative single copy genes. We observe variable allele frequency at these single copy loci and demonstrate that, even after successive passage in culture, the parasite isolates maintain clonal complexity, and can distinguish heterozygous haplotypes of divergent clones within a single infection. This represents the first comparison of whole genomes from such a wide array of clinical contexts. These results demonstrate the feasibility of large scale *T. cruzi* whole genome studies using even low sample inputs and allows additional investigation of complex parasite infection to uncover genetic features driving clinical manifestation of disease.

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ACCEPTABILITY AND IMPACT OF THE MAGIC GLASSES LOWER MEKONG, A CARTOON-BASED EDUCATION PACKAGE TARGETING SOIL-TRANSMITTED HELMINTHS AND OPISTHORCHIASIS VIVERRINI IN THE LOWER MEKONG BASIN

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Helminth infections caused by soil-transmitted helminths and the liver fluke, *Opisthorchis viverrini*, are a major public health concern in the Lower Mekong Basin, impacting health, educational, and socioeconomic outcomes. Infections, often beginning in childhood, are associated with anaemia, malnutrition, cognitive deficit, and in chronic cases of *Opisthorchis viverrini*, cholangiocarcinoma. The primary control strategy for helminthiases is mass drug administration, however this does not prevent reinfection. Therefore, additional strategies aimed at improving sanitation and hygiene and safe eating practices, are needed. Children have been identified as an

important target group for health intervention, with several studies reporting high incidence of helminthiases in pre- and school-aged children. The "Magic Glasses" is a novel cartoon-based helminth education intervention for schoolchildren, that has demonstrated success with improving schoolchildren's knowledge, attitudes and practices surrounding soil-transmitted helminths, in China, the Philippines and Vietnam. A cluster-randomised trial will be conducted to evaluate the acceptability and impact of a new "Magic Glasses" intervention, targeting schoolchildren in the Lower Mekong Basin, including Cambodia, Thailand and Lao PDR. This study will be the first "Magic Glasses" intervention to target multiple countries, and to address *Opisthorchis viverrini* (in addition to soil-transmitted helminths).I will present our findings from the Lower Mekong study, and their implications for a scaling up protocol of the "Magic Glasses" in the Lower Mekong Basin.

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USING PHOTOVOICE AS A COMMUNITY BASED PARTICIPATORY RESEARCH TOOL FOR CHANGING SANITATION AND HYGIENE BEHAVIOURS IN TAABO, COTE D'IVOIRE

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In Côte d'Ivoire, observable efforts have been made by the government and its partners against NTDs, but this does not contribute in the long term results in efforts to control the disease. Those efforts being jeopardised by the absence of participatory community-based programmes. In contribution to correct that gap, a research program on Community Health Education (CHE) has been designed and implemented alongside chemotherapy and Community Led Total Sanitation (CLTS). TThe objective of this paper is: to show how photovoice, a community based participatory research tool, can be used to change behaviours of communities regarding hygiene and sanitation. This study was based on qualitative approach. Disposable cameras were entrusted to 4 peoples in each of the four selected villages (respecting the criteria of age and sex) to provide pictures on hygiene and sanitation. Pictures generated were discussed during FGDs. The activities were completed with one-on-one interviews with 18 key informants. Photos show les informations, feelings, and realitises of the communities. photovoice were used to explore local perceptions and practices around hygiene, sanitation related to health. The findings illustrate that photovoice was an effective participatory art-based tools for understanding behaviours, creating awareness, arouse action among communities, and engaging with local leaders at the hygiene and sanitation-health nexus.

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IMPACT OF COMMUNITY PARTICIPATORY APPROACHES IN ENHANCING ACCESS TO MASS DRUG ADMINISTRATION FOR TRACHOMA IN A PASTORAL CONFLICT AREA OF KENYA

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Trachoma, a neglected tropical disease (NTD) is the leading infectious cause of blindness in sub-Saharan Africa. The disease is caused by the bacterium *Chlamydia trachomatis*. In Kenya, trachoma is endemic in 12 out of the 47 counties. In Baringo county, eight rounds of mass drug administration (MDA) have been implemented. Treatment coverage has remaining consistently low in Loyamorok ward of Baringo County, ranging from 62% in 2012, 56.6% in 2020 and 67.6% in 2021.Successful implementation of MDA programmes for NTDs requires community engagement strategies to reach out the local communities. This study sought to identify barriers of community participation and access to MDA in Loyamorok ward, develop and test strategies to be recommended for improved uptake during subsequent MDA. The study adopted a pre-intervention, intervention and post intervention phase design without control groups. Household surveys were conducted during pre-intervention and post intervention phases. Community barriers to MDA access and participation were identified, strategies for improving MDA uptake were developed and tested using participatory approaches prior to the 2023 MDA. Power and gender dynamics, insecurity, terrain and accessibility, ineffective teams and unsupervised swallowing of drugs during MDA campaigns were the barriers identified during the pre-intervention phase. Effective stakeholder's engagement, enhanced social mobilization, community awareness creation for trachoma, effective planning and execution, implementation monitoring of MDA campaigns were the strategies developed and tested during intervention phase. Knowledge about the causes of trachoma increased from 46.9% during the pre-intervention phase to 65.5% during the post intervention phase. The overall MDA coverage in the area increased from 67.6% in the previous MDA to 87% during the 2023 MDA thus meeting the WHO threshold of 80%. The strategies identified, verified and tested by the stakeholders in Loyamorok ward prior to the 2023 MDA had a positive significant impact on MDA treatment coverage.

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SUPPORTING LYMPHATIC FILARIASIS MORBIDITY MANAGEMENT AND DISABILITY PREVENTION (MMDP) ACTIVITIES IN WEST AFRICA: CASE STUDY FROM NIGERIA AND SIERRA LEONE

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According to the World Health Organization (WHO), neglected tropical diseases (NTDs) affect more than 1 billion people globally. Among these an estimated 882 million people in 44 countries are at risk of Lymphatic Filariasis (LF) and require preventive chemotherapy. Lymphatic filariasis (LF) is a parasitic disease caused by nematodes (roundworms) that are transmitted through the bites of infected mosquitos. Left untreated, adult worms disrupt the lymphatic system and result in fluid retention leading to lymphedema, elephantiasis, and hydrocele. These often painful and disfiguring conditions lead to impairments, reduced economic productivity and discrimination. Morbidity management and disability prevention (MMDP) is an important aspect of the Global Program to Eliminate Lymphatic Filariasis (GPELF). In Africa the burden of LF morbidity remains high due to several factors, among these are lack of timely treatment, stigma, and a higher prevalence of the disease manifesting among economically impoverished populations. Despite the availability of WHO minimum package of care for LF morbidity to countries, LF morbidity management interventions continue to receive low attention from national NTD programs. In this case study, we present secondary data analysis of implementing partners supporting MMDP programs between 2020 and 2023 in Nigeria and Sierra Leone. The analysis focuses on the programmatic and financial reports of LF MMDP activities from five supported implementing partners. We found that the burden of morbidity is inadequately understood, the LF MMDP program is often delayed until endemic implementing units complete five effective rounds of Mass Drug Administration (MDA), there is a shortage of human resources, and services are concentrated in urban areas. Furthermore, the national LF program tends to prioritize assessments over morbidity management, and the cost of providing care to individuals affected remains high, averaging $150 per patient, as of 2023.
We note a need for national NTD programs to address challenges highlighted above to integrate the program into the public health system.

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ASSESSING THE CAPACITY OF HEALTH FACILITIES TO DIAGNOSE, TREAT, AND MANAGE VISCERAL LEISHMANIASIS: EVIDENCE FROM TIATY, BARINGO COUNTY, KENYA

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Visceral Leishmaniasis (VL) is a significant threat in Kenya, with 1,573 cases reported in 2022. However, funding for VL within the Ministry of Health is limited. The Kenyan Strategic Plan for VL (2021-2025) aims to enhance healthcare workers' capacity and establish more testing and treatment centers, yet there is no systematic tracking of health facilities offering VL services. This research evaluates health facilities' capacity in managing VL and explores patient experiences in accessing VL health services in Tiaty, amidst challenges of poverty and limited healthcare access. The study adopts mixed methods. Health facility surveys were dispersed across health facilities in Tiaty sub-county, covering 8 level 2-4 facilities from January-April 2024. Household questionnaires and focus group discussions were conducted in 5 village clusters with the highest VL case reports in Tiaty. Furthermore, surveys were administered at the VL treatment center to patients completing VL treatment until May 2024 to assess their experiences. Observations highlight that level 2&3 health facilities lack resources for diagnosing and treating VL, resulting in patient referrals to level 4 hospitals. Approximately 62.5% of facilities fall under the level 2 category, with 75% are managed by the government. 75% of health personnel has received training for VL, yet diagnostic services (rK39 test) are only available in 50% of facilities, and treatment services are provided in just 12.5% facilities. These challenges are exacerbated by supply chain issues, leading to shortages of diagnostic kits and treatment materials in the facilities that offer the services. Villages with high VL cases are located, on average, 13.63 km away from local health centers, negatively impacting health-seeking behavior. 124 household surveys conducted in March 2024 highlighted transportation costs and distance as significant barriers to healthcare access. Despite these challenges, respondents view health services as somewhat effective, highlighting the need for increased staffing and improved facilities closer to communities to improve VL diagnosis, treatment, and management.

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ASSESSING COMMUNITY DRUG DISTRIBUTORS PERFORMANCE IN GHANA; A GENDER BASED APPROACH

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According to a gender equity and social inclusion (GESI) assessment conducted in 2019 in Ghana men and women indicated that female community drug distributors (CDDs) express themselves very well, are reliable, patient, take more time to explain NTDs and their effects, why take MDA medicines, MDA drug potential side effects and what to do if they occurred. Female CDDs meet their targets and have impressive record-keeping abilities. These findings were disputed and the recommendation to conduct a gender specific assessment of CDDs performance. The main objective of this study was to assess performance differences in male and female CDDs in completion of registers during MDA for Lymphatic Filariasis and Onchocerciasis. Bole, Kwahu East and Sunyani West Districts were randomly selected to represent three Lymphatic Filariasis and Onchocerciasis endemic districts in Ghana whose CDDs were assessed during the study. Based on the total number of CDDs used in the immediate past MDA for the three selected regions a total sample size of 317 CDDs was estimated and adopted for the assessment. This sample size was proportionally allocated to the three selected districts based on their total CDDs in the previous MDA. In each sub district in depth interviews were conducted for 10% of all selected CDDs with a structured questionnaire on Kobo collect software. All Data from the assessment and in-depth interviews was captured and cleaned with MS excel. Basic descriptive statistics were run in MS excel and further analysis done using SPSS version 21. There were differences in the mean percentage scores for the various areas assessed in the registers and the overall assessment for Female and Male CDDs. These differences were not statistically significant. Mean percentage scores for all CDDs across districts showed statistically significant differences. Mean percentage scores for male CDDs across districts showed statistically significant differences. Mean percentage scores for female CDDs across districts showed statistically significant differences. More advocacy is needed in engaging both gender equally in conducting and supporting their communities with MDA.

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MIXED INFECTIONS OF SOIL TRANSMITTED HELMINTHS AND *SCHISTOSOMA MANSONI* AMONG SCHOOL STUDENTS IN KAKAMEGA COUNTY, KENYA

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Soil-transmitted helminth (STH) and schistosome infections are a major public health concern affecting mainly School-aged children in poor resource areas. Mass drug administration (MDA) has proven to be an effective approach to reduce worm burden. However, there are cases of recurrent infections in areas where Mass drug administration is not supported by water, sanitation and hygiene (WASH) activities. This Cross-sectional study aimed at assessing the prevalence of soil transmitted helminths and *Schistosoma mansoni* among school aged children in Kakamega County, Kenya. Stool Samples were collected from 278 school aged children from five primary schools within, Lurambi sub-County. Data on risk factors associated with Soil transmitted helminthes and *S. mansoni* infections was obtained using a structured questionnaires. Stool samples were examined for eggs of STHs and S. mansoni using quantitative Kato-Katz technique. The data obtained was analysed using Pearson Chi-square test and multivariate logistic regression analysis. The overall prevalence of intestinal parasite infection was 14.4 % (n=278). Ascaris lumbricoides had the highest prevalence at 11.5%, followed by S. mansoni at 2.1%, whereas Hookworm and *Trichuris trichiura* had the least prevalence of 0.4% each. Highest prevalence of STH was recorded in rural primary school at 8.3% and a mean intensity of 3396 epg. Poor hygiene such as not washing hands/fruits and vegetables before eating (OR: 3.529; CI: 1.0539-11.8175; P-value ≤0.05: OR: 2.3129; CI: 1.831-4.1691; p-value≤ 0.005) were the major risk factors to STH infections. There is still high prevalence of mixed infections with intestinal worms. There is need to intensify utilization of WASH activities to complement the School deworming programmes for successful control of soil transmitted helminthes.

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RISK FACTORS AND ULTRASOUND ASPECTS ASSOCIATED WITH UROGENITAL SCHISTOSOMIASIS AMONG PRIMARY SCHOOL CHILDREN IN MALI WEST AFRICA

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Urogenital schistosomiasis is endemic in Mali and is a major cause of serious morbidity in large parts of the world. This disease is responsible for many socio-economic and public health issues. This study aimed to investigate the impact of the disease on morbidity and to describe demographic and socioeconomic factors about the status of children with

urogenital schistosomiasis in Mali. We conducted a cross-sectional study in November 2021 of 971 children aged 6 to 14 years selected at random from six schools in three districts in the Kayes Region of Mali. Demographic and socioeconomic data were collected on survey forms. Clinical data were collected following a medical consultation. Hematuria was systematically searched for through the use of strips. The search for *Schistosoma haematobium (Sh)* eggs in urine was done via the filtration method. The urinary tract was examined by ultrasound. Associations between each of these variables and disease infection were tested using multivariate logistic regression. The overall prevalence of urinary schistosomiasis detected was 50.2%. The average intensity of infection was 36 eggs/10 ml of urine. The associated risk factors for urogenital schistosomiasis showed that children who bathed used the river/pond as a domestic water source, and who habitually urinated in the river/pond were more affected (P<0.05). Children with farming parents were most affected (P=0.032). The collection of clinical signs revealed that boys had more pollakiuria (58.6%) and dysuria (46.4%) than girls. Ultrasound data showed that focal lesion rates were recorded in all villages with the lowest rate in Diakalel (56.1%). Ultrasound and parasitological findings showed that irregularity and thickening were strongly associated with urinary schistosomiasis (P<0.0001). *Sh* infection was still endemic in the study site despite more than a decade of mass treatment with praziquantel. However, the high percentage of symptoms associated with high intensity reinforces the idea that further studies in terms of schistosomiasis-related morbidity are still needed.

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TREATMENT COVERAGE ACHIEVED UNDER TWO ENHANCED MASS DRUG ADMINISTRATION REGIMENS FOR TRACHOMA IN THE REPUBLIC OF SOUTH SUDAN: ENHANCING THE A IN SAFE (ETAS) TRIAL RESULTS

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The 2022 Enhancing the 'A' in SAFE (ETAS) trial (NCT05634759) evaluated the cost, feasibility, and acceptability of enhanced mass drug administration (MDA) treatments for trachoma in the Republic of South Sudan. Thirty communities in trachoma endemic Kapoeta North County were randomized 1:1 to 2 treatment arms, and an electronic census was conducted in all enrolled communities. The first arm (triple dose) entailed a community-wide MDA, followed by 2 rounds of treatment aimed at children ages 6 months to 9 years, 2 weeks and 4 weeks later. The second arm (biannual) consisted of 2 community-wide MDA campaigns separated by 6 months. The aim of this report is to detail the MDA coverage achieved in the study arms. The triple dose arm included 17,626 participants, including 8,644 (49.0%) children ages 6 months to 9 years. The biannual treatment arm included 16,974 participants, including 7,852 (46.3%) children. In the triple dose arm, 7,390 (85.5%) children were treated during community-wide MDA, and 6,101 (70.6%) and 6,615 (76.5%) received treatment in the second and third child-only rounds. Coverage among children at the community-level in this arm varied from 50.0-95.5% across all rounds. In the biannual arm, 5,583 (74.5%) and 6,354 (80.9%) children were treated during the 2 MDA rounds with a community-level coverage range of 70.1-95.2% across all rounds. Cumulatively in the triple dose arm, 7,959 (92.1%) children received at least 1 dose of MDA (from any round), 6,632 (76.7%) received at least 2 doses, and 5,515 (63.8%) received all 3 doses. In the biannual arm, 7,465 (95.1%) children received at least 1 dose of MDA, and 4,742 (60.4%) received both doses. Families moving to farms and families with cattle most often missed treatment. This trial demonstrated that both treatment regimens achieved similar per-protocol coverage, triple dose (63.8%) and biannual (60.4%), and in both arms over 90% of children received at least 1 dose. Work is needed to improve coverage across each round of treatment, particularly among mobile families, and to determine whether the cost and effort required by these enhanced regimens result in trachoma reductions.

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EFFECTIVENESS OF COMMUNITY HEALTH EDUCATION ON VISCERAL LEISHMANIASIS IN IMPROVING KNOWLEDGE, PRACTICE AND HEALTH SEEKING BEHAVIOR IN TIATY, KENYA

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This project seeks to examine the effectiveness of community health education on visceral leishmaniasis (VL or kala-azar) in improving knowledge, practice and health seeking behavior in Tiaty East and West sub-counties, Baringo county Kenya. A World Health Organization meeting in January 2023 in Nairobi reached a consensus on elimination of VL as a public health problem among East African countries which is now the global disease foci. Kenya's Ministry of Health VL strategic plan stresses health education interventions in community settings. Education is the first step to preventing the occurrence of a disease: knowing what the disease is, how to identify it, where to seek treatment, or how it is transmitted. It is therefore important to assess the efficacy of health education interventions in promoting behavioral changes. However, there is limited research in Kenya where a scoping review of studies in the country found limited research on prevention (less than 4%). We therefore conducted a study in nine villages within Tiaty, where a local nonprofit, African Centre for Community Investment in Health has conducted health education on kala-azar at least twice in the last 10 years. Nine enumerators were used to collect information through the household questionnaires within these villages; each enumerator visited two villages except for one who only visited one. Participants were chosen on the basis of whether they were aware of Kala-azar. Preliminary results of the 184 participants show that 183 are aware of Kala-azar and 171 have implemented some prevention measures for kala-azar after receiving health education. Based on the preliminary results, current health education on Kala-azar has been effective in increasing knowledge of the signs, symptoms and treatments for Kala-azar and promoting better health behaviors.

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SOCIO-ECONOMIC PROFILE OF NEVER TREATED INDIVIDUALS DURING MASS DRUG ADMINISTRATION TARGETING ONCHOCERCIASIS IN HARD-TO-REACH AREAS OF MALI: A CROSS-SECTIONAL STUDY

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Onchocerciasis operational transmission zone (KA05) failed the last pre-stop survey assessment. After decades of mass drug administration (MDA) implementation in KA05, the never treated population (NT) may

contribute to ongoing transmission. This study sought to understand the demographic and socio-economic profile of individuals never treated during MDA for onchocerciasis. A cross-sectional survey was conducted in the KA05 zone, combining three health districts (HDs): Sagabari, Kita, and Kenieba. The study involved participants aged 18 years and above. validated questionnaire including history of MDA participation, individual characteristics, housing conditions, income and material goods was used to collect data. Based on these characteristics, we adopted a multiple correspondence analysis and a hierarchical ascending classification approach to classify NT. We used these profiles to conduct a multilevel logistic regression approach (individual, household, and health districts) to estimate factors associated with never-treatment. We obtained 3 profiles according to socio-economic (SES) characteristics. Profile 1 (reference group for regression) has the highest SES status in terms of facilities and access to toilets while Profile 3, has the lowest standard of living. Younger age (less than 33 years) and Profile 2 were two characteristics significantly associated with increased likelihood of being NT, with respectively, adjusted ORs (aOR (95% CI)) of 2.77 (2.03 to 3.81) and 4.48 (2.23 to 9.30). The difference between profile 3 and profile 1 (reference) regarding the risk of never treatment was not statistically significant (aOR = 1.18 (95% CI 0.62 to 2.28)). Never treatment during MDA targeting onchocerciasis in hard-to-reach areas of Mali is associated with younger age and profile 2 (midlevel SES status). Further research is needed to understand the underlying factors driving these associations and to develop tailored interventions to improve access to treatment, especially in areas with lower living standards.

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SOCIO-ECONOMIC IMPACT OF 24-MONTH LYMPHEDEMA MANAGEMENT IN AFFECTED PERSONS IN MALI: CROSS-SECTIONAL STUDY

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Lymphedema is a disfiguring complication of lymphatic filariasis that prevents affected individuals from carrying out their activities, contributing to low productivity and social exclusion. During a trial implemented for 24 months (LEDoxy), local hygiene measures improved the quality of life of lymphedema patients. The aim of this study was to assess the socio-economic impact of regular local care based on the hygiene package used during the clinical trial among participants up to 16 months after the trial completion. We conducted a mixed method study with a before-and-after approach in the health districts of Kolondieba and Kolokani from August to December 2021. Quantitative data were collected using a questionnaire through Kobotoolbox platforms. For qualitative data, we used a pre-established interview guide to conduct in-depth interviews and focus group discussions. Quantitative data were analyzed using SPSS V25.0. Fisher's exact test and Student's t-test were used to compare proportions and means, respectively. We performed a thematic analysis approach to analyze qualitative data using Quirkos V2. We investigated 196 lymphedema patients with a median age of 56 years, and a sex ration of 0.15. We observed a reduction in the monthly frequency of acute filarial attacks from 90.8% (178/196) before the trial to 43.9%, (86/196) after the trial ($p<10^{-3}$). Additionally, the average cost of managing acute filarial attacks significantly decreased from US$20 before the trial to US$6, 16 months after the trial ($p<10^{-3}$) per acute attack. Patients reported that the hygiene program reduced social isolation and stigma and improved their ability to work. A patient stated "*We had difficulty walking, but thanks to the LEDoxy study, I can now walk long distances and participate in community activities*". Local hygiene care of affected limb appears to be an effective intervention for reducing the monthly frequency of acute filarial attacks among lymphedema patients, leading to cost savings in managing acute attacks. Further explorations are needed to assess the sustainability and long-term impact of this hygiene-based care.

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SUSTAINABILITY OF LYMPHEDEMA HYGIENE-BASED SELF-CARE WITHIN LEDOXY PATIENTS MORE THAN TWO YEARS AFTER THE CLINICAL TRIAL IN RURAL AREAS, MALI: A CROSS-SECTIONAL STUDY

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The LEDoxy clinical trial comparing doxycycline plus local hygiene to placebo plus local hygiene on filarial lymphedema management did not confirm the expected ability of doxycycline to reverse or halt the progression the condition. All trial participants received repeated training in hygiene practices of WHO's Essential Package of Care for lymphedema and were provided with hygiene kits over the 24-month trial period. The current study investigated the sustainability and barriers to self-care more than 2 years after the trial completion. A mixed-method study was conducted in the Kolondieba and Kolokani health districts from December 2023 to March 2024. All LEDoxy participants with stages 1-3 lymphedema were invited to participate in this study. Data were collected through questionnaire administration using REDCap platform and analyzed using SPSS 26.0 and NVIVO 14. Additionally, individual in-depth interviews (IDI) were conducted to understand patients' behaviors and experiences regarding lymphedema self-management. Overall, 165 lymphedema patients from LEDoxy were included in the survey. Regarding the sustainability of limb hygiene, 93 (41.9%) patients washed their affected limbs on the day of the survey, 67 (30.2%) the day before, 18 (8.1%) more than two days before, while 44 (19.8%) reported a more distant occurrence. The main difficulties mentioned by participants in maintaining regular hygiene care were lack of financial resources (40.6%), lack of support (4.2%), lack of time (5.5%) and pain during washing (5.5%). Most patients believed that participating in agricultural activities will make affected limbs dirty. Avoiding farming resulted in people believing the LE patient was reluctant to work. Findings show

the sustained impact of high quality training and supervision on routine LE management. Although patients reported barriers to self-management, they were largely able to sustain regular care the two years since the research study. These findings can inform the design of sustainable and well-adapted national self-care programs as part of the morbidity management and disability prevention program in LF elimination.

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MONITORING THE IMPACT OF COMMUNITY-BASED DEWORMING ON SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHIASIS AMONG SCHOOL-AGE CHILDREN IN WESTERN KENYA: MIDTERM RESULLTS

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The progress of Kenya's National Breaking Transmission Strategy for interruption of transmission (IoT) for schistosomiasis (SCH) and soil-transmitted helminthiasis (STH) in 4 Kakamega, Bungoma, Vihiga and Trans Nzoia counties of western Kenya (2021-2025) is evaluated through a monitoring and evaluation framework that involves the periodic collection of parasitological data. The midterm evaluation used data from surveys conducted at baseline (689 schools; 41045 School Aged Children (SAC)), 1st sentinel survey (34 schools; 2039 SAC) and at midterm (56 schools; 2804 SAC) after 2 rounds of community-wide MDA, between 2021 and 2023 in wards under MDA . Stool was randomly collected from school-age children in selected schools and examined for SCH and STH infections using Kato-Katz. Prevalence and mean intensity of each helminth species and their 95% confidence intervals (CIs) were calculated. The overall prevalence of *Schistosoma mansoni* was 10.9% (95% CI: 10.3-11.5%), 5.8% (95% CI: 4.9-6.9%) and 4.9% (95% CI: 3.8-6.3%) at baseline, 1st sentinel site survey and at midterm, respectively, with a relative reduction (RR) of 55% ($Z = 11.5$, $P < 0.001$) between baseline and midterm. Overall, 8.1% (95% CI: 7.9-8.4%), 13.5% (95% CI: 12.1-15.1%) and 5.5% (95% CI: 4.7-6.4%) of the children were infected with any STH species at baseline, 1st sentinel site survey and midterm, with a RR of 32.1% ($Z = 4.7$, $P < 0.01$) between baseline and midterm. The mean intensity of *S. mansoni* was 125 epg (114-136) at baseline and 102 epg (77 - 127) at midterm, with a RR of 18.4%. The proportion of Wards with <1% HI *S. mansoni* infections among SAC increased 1.8-fold from baseline to midterm, while Wards with <2% M&HI STH infections increased 1.4-fold. Both the overall prevalence and prevalence of Medium & High Intensity SCH and STH infections reduced at mid-term, but prevalence of infection increased in a few Wards suggesting ongoing transmission. Scaling up of other strategies including behavior change and communication, WASH interventions and snail control to augment MDA coupled with effective treatment coverage will be required to sustain the gains and accelerate the efforts towards IoT.

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ASSESSMENT OF KNOWLEDGE, ATTITUDES, PRACTICES AND FACTORS CONTRIBUTING TOWARDS ONGOING TRACHOMA TRANSMISSION AND MASS DRUG ADMINISTRATION (MDA) COVERAGE IN UGANDA

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Moroto and Nabilatuk districts have persistent and recrudescent trachoma, respectively. Past survey failure investigations and Coverage Evaluation Surveys suggest that, while overall MDA coverage is high, there are certain communities and groups that may be more likely to miss MDA. To better understand how these groups and communities may be contributing to ongoing transmission, the study team undertook an assessment to explore the trachoma knowledge attitudes and practice (KAP) among female farmers, male kraal leaders, youth, and village health teams (VHTs) in select communities. Study communities were purposely selected based on historically low coverage or high number of cases of TF, together with other identified social or geographic risk factors. Eight focus group discussions were undertaken and a trachoma KAP questionnaire was administered to 123 individuals living in sample communities and who had missed the most recent MDA. Limited knowledge of trachoma and trachoma prevention was exhibited by female farmers, VHTs, and youth. Many respondents reported rarely undertaking key prevention practices such as washing faces of children at least twice a day; and cleaning children's noses or eyes with a cloth or towel and with water. Instead, respondents reported poor practices such as washing children's faces with saliva and/or with hands or fingers. The findings suggest limited knowledge on the causes and prevention of trachoma, and poor practices towards water, sanitation, and hygiene improvements (WASH), facial cleanliness and seeking trachoma related information to be serious problems, especially among female farmers, youths, and VHTs. It is possible that the low trachoma KAP in these communities may be contributing to ongoing transmission in Moroto and Nabilatuk. Tailored interventions to improve trachoma KAP should be designed for these communities, particularly for women, youth, and VHTs. These include involvement of fellow women, youth and VHT influencers during sensitization and mobilization through local groups that bring them together and enhanced capacity building of VHTs, women and youth leaders.

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TREATMENT COVERAGE FOLLOWING AN ENHANCED MASS DRUG ADMINISTRATION STRATEGY FOR TRACHOMA IN AMHARA REGION, ETHIOPIA: THE CHILD MDA PILOT STUDY

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In Ethiopia's Amhara region, annual mass drug administration (MDA) has been implemented for trachoma since 2007. Despite nearly 15 years of MDA intervention, some districts in the region continue to have persistently high trachoma. Recently, the Ministry of Health of Ethiopia recommended piloting an enhanced treatment strategy encompassing a standard annual MDA, followed by an additional round targeted to children ages 6 months to 9 years (within one month of the initial treatment). In Amhara, two pilot districts, Lasta and Wadilla, in North Wollo zone, received the enhanced MDA strategy. The aim of this study was to determine the self-reported MDA coverage for both rounds of treatment in these districts. MDA coverage surveys were conducted in July 2023, three weeks after the second MDA round, and employed a multistage cluster-randomized sampling design to select participants. Trained data recorders asked respondents if they were offered and swallowed the MDA medications. Sixty clusters comprised of 4,948 individuals from 1,799 households (899 in Lasta, 900 in Wadilla) were surveyed, including 1,651 children ages 1-9 years. The overall self-reported treatment coverage for the community-wide MDA was 82.5% (CI: 73.6 - 88.8%) in Lasta and 77.9% (CI: 67.9 - 85.4%) in Wadilla. During this first round of community-wide MDA, 84.7% (CI: 70.2 - 92.9%) of children from Lasta and 86.9% (CI: 74.9 - 93.6%) of children

from Wadilla received treatment. For the second MDA round targeted only to children, 82.0% (CI: 69.0 - 90.4%) of children from Lasta and 83.1% (CI: 72.8 - 90.1%) of children from Wadilla reported receiving treatment. Of the children surveyed, 82.1% received both rounds of treatment, 12.0% received only one round, and 5.8% did not participate in either MDA. The most common reason individuals reported for not receiving treatment was due to traveling during MDA distribution. This study demonstrated that the additional round of child targeted MDA had an acceptable level of coverage (>80%), which is promising for the feasibility of this strategy and provides important information for the scale-up of enhanced MDA for trachoma throughout Ethiopia.

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SAMPLING AND SITE SELECTION STRATEGIES FOR LYMPHATIC FILARIASIS TRANSMISSION ASSESSMENT SURVEYS IN AREAS WITH HIGH SECURITY CHALLENGES: THE BURKINA FASO EXPERIENCE

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Burkina Faso is one of 35 countries in the World Health Organization (WHO) African region that is endemic for lymphatic filariasis (LF). In June 2000, all health districts (HDs) were classified as endemic, with antigenemia prevalences ranging from 2% to 74%. However, since 2016, Burkina Faso has faced security challenges in some regions, negatively impacting the pursuit of certain LF elimination activities. As a result, several transmission assessment surveys (TAS) have been delayed since 2019 due to insecurity. This is the case for TAS2 surveys in four evaluation units (EUs) in four HDs, and TAS3 surveys in 14 EUs in 14 HDs. In addition, some HDs recently eligible for pre-TAS or TAS are facing security challenges that make it difficult to conduct surveys using the classic methodology recommended by the WHO. This is due to the inaccessibility of localities and major population displacement. The WHO recommends that the National Neglected Tropical Diseases Program document best practices for implementing surveys in areas with high security challenges. In Burkina Faso, participatory approaches were used to assess feasibility, site selection and sampling for pre-TAS and TAS and to develop resilient implementation strategies based on local health workers. Excel forms were used to collect information on security risk and decision algorithm applied to identify eligible sites for the survey. The decision criteria include proportion of target population present, sites where displaced populations are located, the ability to conduct surveys using local actors, and population size. These criteria are reviewed by all the stakeholders at a regional scoping meeting. These sampling strategies were successfully used for pre-TAS and TAS1 surveys in 2023. In 2024, TAS surveys will be conducted in eight EUs across eight HDs using the same approach. However, continuous monitoring of the security situation prior to the start of the surveys is necessary. In addition, special attention should be given to areas that have been excluded due to risk as part of post-stop transmission monitoring.

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THE CONTROL AND ELIMINATION OF NEGLECTED TROPICAL DISEASES IN MALI: A SUCCESS STORY

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In Mali, neglected tropical diseases (NTDs) are a major public health problem. Baseline mapping in 2004 showed an average lymphatic filariasis (LF) prevalence of 7.07%. Schistosomiasis (SCH) and soil transmitted helminths (STH) surveys from 2004 - 2005 found an average prevalence of 36.1% and 6.3%, respectively. A 1996-1997 trachoma baseline survey found an active trachoma (TF/TI) average prevalence of 34.9% among children <10 years old and trachomatous trichiasis average prevalence of 2.51% in women >14 years old. The 1974 mapping of river basins in the south and south-east regions showed onchocerciasis (OV) prevalence reaching as high as 84% in one village. From 2005 to 2018, six to 12 mass drug administration (MDA) rounds against LF and STH were conducted, with an average programmatic coverage of 83.5%. For SCH, six to thirteen MDA rounds were carried out, with an average (school-based) coverage of 90%. For trachoma, three to six MDA rounds were carried out, with an average coverage of 85.6%. Over the past 40 years, more than twenty rounds of OV MDA were carried out, with an average coverage of 83.9%. Other strategies implemented include morbidity management, vector control, dissemination of awareness-raising messages, WASH interventions, and capacity-building. Despite over a decade of insecurity, sociopolitical instability, and health crises, Mali is close to achieving its NTD control and elimination objectives. Since 2020, all endemic districts (75/75) have met the criteria to stop LF MDA. In 2021, WHO STH experts confirmed STH is no longer a public health problem. In April 2023, Mali became the 17th country validated by the WHO as having eliminated trachoma as a public health problem. There are two NTDs still being treated by MDA. A SCH data review in 2023 showed that of 1,643 health areas, 16% no longer need MDA, 37% had a prevalence <10% and 18% had a high prevalence >50%. All OV-endemic districts except one (33/34) have done stop MDA surveys (results pending). This progress is the result of strong commitments by health authorities, partnership, and the use of innovative strategies to conduct NTD activities in the challenging operating context.

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PRE-STOP OV MDA IN 32 FIRST-LINE VILLAGES IN FOUR OPERATIONAL TRANSMISSION ZONES IN GUINEA

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Onchocerciasis is a major neglected tropical disease in Guinea. Between 1985 and 2005, onchocerciasis mapping was conducted using the Rapid Epidemiological Mapping of Onchocerciasis (REMO)/skin snip method, supported by the Onchocerciasis Control Program (OCP) in West Africa and later by the African Program for Onchocerciasis Control (APOC). Twenty-four endemic districts were classified as follows: hypo-endemic (nodule prevalence < 20% or microfilariae (mf) prevalence < 40%) in 15

districts; meso-endemic (nodule prevalence 20-39% or mf prevalence ≥ 40% and < 60%) in one district; or hyper-endemic (nodule prevalence ≥ 30% / mf prevalence ≥ 60%) in eight districts. After more than 28 years of annual ivermectin distribution, a pre-stop treatment survey is necessary to determine if these areas can proceed to the stop-MDA survey. A total of 63 first-line villages across four pre-determined operational transmission zones (OTZ) were selected, covering all endemic river basins. The first phase of the survey was conducted in 32 first-line villages. One hundred children aged 5-9 years old per village were selected and dried blood spot (DBS) samples were collected from each child and analyzed using the OV16 rapid diagnostic test (RDT) in the national laboratory. A total of 3,199 children aged 5 to 9 were sampled in 32 villages near *Simulium* breeding sites, (44%) were female. Analysis of the samples revealed that most villages surveyed had zero positive cases and only 8 of the 32 villages surveyed had 2 or more positive cases, with percentages ranging from 2% to 12%. These 8 villages were mostly located in OTZ2 (the forest region) and a few localities near the border with Sierra Leone. Preliminary results indicate that the OTZs may need to be redefined and that some OTZs may qualify for the full stop-MDA survey, pending on the results of the remaining pre-stop villages.

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A FOLLOW-UP STUDY IN 2024: SCHISTOSOMIASIS IMPACT ASSESSMENT IN EIGHT DISTRICTS FOLLOWING A DECADE OF MASS DRUG ADMINISTRATION

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The National Neglected Tropical Disease Program in Sierra Leone conducted schistosomiasis (SCH) baseline mapping in all 16 health districts (HDs) between 2008 and 2009. They were categorized as follows: low (≥1 and <10%) prevalence in five HDs; moderate (≥10 and <50%) in five HDs; and high (≥50%) in four HDs. The intestinal species *Schistosoma mansoni* was identified in nine HDs and the urogenital species, *S. haematobium*, was endemic in three (of those nine) HDs. In 2009, annual mass drug administration (MDA) at the district level started by targeting school-aged children (SAC) in six (three high and three moderate) endemic HDs and scaled up in 2010 to include all SAC and at-risk adults in the nine highly or moderately endemic HDs. The five low endemic HDs have received no MDA to date. A subsequent SCH/STH impact assessment was conducted in 2022 in the nine high/moderate HDs to assess the impact of multiple rounds of treatment. In May 2023, a SCH data review evaluated the 2022 SCH impact assessment results, resulting in a revised chiefdom (sub-district) treatment strategy based on updated prevalence estimates. The revised strategy targets either SAC only or community-wide MDA as determined by the new prevalence data. The data review highlighted data gaps in 53 chiefdoms across eight HDs and thus the need to supplement the 2022 survey. A follow-up survey was conducted in 2024 to address these gaps. Results from both surveys indicate a significant reduction in both prevalence and intensity of SCH infection compared to baseline. However, pockets of persistent infection were identified. Survey results from 2022-2024 showed an overall prevalence of 15.4% for *S. mansoni, 5*.4% for *S. haematobium* (haematuria), and 4.5% (urine filtration). Overall, the nine HDs were re-categorized as follows: low prevalence in one HD; moderate in eight HDs; and no high HDs. Over a decade of MDA in Sierra Leone led to a significant reduction in any SCH infection, from an average prevalence of 42.2% at baseline to 19.1% in 2024.

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FIX-DOSING IVERMECTIN REGIMENS IN MASS DRUG ADMINISTRATION ACTIVITIES. IS IT TIME TO LEAVE THE DOSING POLE BEHIND?

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Ivermectin (IVM) is a critical tool for the control of different Neglected Tropical Diseases. In mass drug administration (MDA) campaigns it is dosed adjusted to body height. Dosing IVM by weight or height has operational disadvantages. In this study we explored alternative dosing regimens for MDA campaigns. To carry out the analysis individual participant anthropometry data of children aged 5 to 15 years was used. 9638 children were included from previous soil-transmitted helminths (STH) clinical trials from endemic areas in Latin-America and Sub-Saharan Africa. The dose in µg/Kg of IVM for each child according to their weight was calculated using four different dosing regimens: 1) Weight-adjusted dose for 200 µg/Kg; 3 mg for children from 15 to 24 kg; 6 mg for 25 to 35 Kg; 9 mg for 36 to 50 Kg; 12 mg for 51 to 65 Kg and 15 mg for 66 to 79 Kg. 2) Height - adjusted dose (WHO dosing pole): 3 mg for 90 to 119 cm; 6 mg for 120 to 139; 9 mg for 140 to 159 cm; and 12 mg above 159 cm. 3) Fixed-dose of 9 mg. 4) Fixed-dose of 18 mg. The proportion of children with correct dose (200 to 600 µg/Kg), above the recommended dose (> 600 µg/Kg) or underdose (< 200 µg/Kg) with each dosing regimen was calculated. Results showed the Fixed-dose IVM 9 mg achieved a higher proportion of correct doses (86%) compared to weight-based (35%) and height-based (66%) regimens, with significantly lower underdosing (4% vs. 55% and 33%, respectively). No children received doses above recommended levels with Fixed-dose of IVM 9 mg or other regimens. Subgroup analysis revealed 87 % correct dosing with Fixed-dose 9 mg for children aged 5 to 13 years old and 93 % with Fixed-dose 18 mg for children aged 14 and 15 years old. The proportion receiving above the recommended dose was 10 % with Fixed-dose 18 mg in children aged 14 and 15 years old. In conclusion implementing a fixed dose IVM regimen based on age would achieve a high proportion of adequate doses, reducing the proportion of underdosing and with little risk of exceeding the recommended dose. Added to the operational advantages of using a single formulation for the entire school population.

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SOIL-TRANSMITTED HELMINTH TRANSMISSION DYNAMICS AND OPTIMAL CONTROL

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Soil-transmitted helminth infections are among the most prevalent neglected tropical diseases, particularly in impoverished regions. These infections affect over 1.5 billion people (about 24% of the global population) and are most common in school-aged children. The diseases impair physical and mental growth in children, thwart educational advancement, and hinder economic development. Soil-transmitted helminth infections are caused by a group of parasitic worms primarily transmitted via soil contaminated with feces from infected individuals. Here, to assess transmission dynamics of helminth infection through the soil in school-aged children, we use a model-inference approach to estimate a key epidemiologic parameter, i.e. the rate at which parasitic worms in the soil infect human population. Further, to explore effective intervention strategies for controlling the spread of these infections, optimal control theory is applied. A dynamic model-inference approach is applied in conjunction with epidemiological data from

the most affected countries in Sub-Saharan Africa and Asia to estimate the rate at which parasitic worms in the soil infect human population. Pontryagian's maximum principle is used to formulate the optimal control problem, where two time-varying control variables are incorporated: the rate of hygiene consciousness through public health education in the susceptible class and the rate of hygiene consciousness in the infectious class. Application of the confirmed system to actual case data is underway and estimates of infection transmissibility to humans and recommendations for optimal control will be reported. The main findings aid in understanding soil-transmitted helminth dynamics and can help guide future public health planning. The disease burden can be significantly reduced or eliminated in affected regions by implementing optimal control measures.

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STRENGTHENING TRACHOMA CONTROL PROGRAMS THROUGH THE INTEGRATION OF LATERAL FLOW ASSAYS FOR SEROLOGICAL MONITORING: A DISTRICT-LEVEL STUDY FROM AMHARA, ETHIOPIA

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Trachoma Control Programs conduct trachoma impact surveys (TIS) to monitor programmatic impact using the field-graded clinical sign trachomatous inflammation–follicular (TF). Recently, programs have begun to collect complementary indicators alongside TF, such as antibody responses to the Pgp3 antigen, to estimate population-level exposure to *Chlamydia trachomatis* (*Ct*). Serological monitoring has been used by the Program in Amhara, Ethiopia, since 2017. Due to the infrastructure needed to perform assays, the Program has relied on an external laboratory in the United States to analyze their samples, which presents logistical challenges and delays. A newly developed lateral flow assay (LFA) is a promising alternative to other serological tests due to its ease of use, high sensitivity (92.6%, CI: 86.4 - 96.2%) and specificity (100%, CI: 94.1 - 100%) compared to the multiplex bead assay, and low laboratory infrastructure needs. In January 2024, the Program in Amhara facilitated a remote LFA training for 3 experienced laboratory personnel at the Trachoma Molecular Laboratory at the Amhara Public Health Institute. The training was held over 3 days and concluded with a competency exam, which all participants passed and were certified. Following certification, participants analyzed dried blood spot samples from a 2023 TIS in Tach Gaynt, a district with considerable trachoma (28.6% TF) despite 14 years of interventions. A total of 2,441/2,539 (96.1%) samples were assayed by the laboratory personnel over 12 working days. They demonstrated high capability to perform LFA, with only 4 (0.2%) invalid samples upon first run, all of which were valid upon retesting. Seropositivity in children ages 1-5 years was 19.9% (CI: 16.2 - 24.2%), which is consistent with Tach Gaynt's high TF prevalence. Individuals ages ≥15 years had high seropositivity (85.7%, CI: 83.8 - 87.4%), indicative of cumulative *Ct* infections from living in endemic areas. The quality of these results and speed at which the samples were analyzed underscore the potential of LFA as a viable option for in-country serological monitoring for Ethiopia and other trachoma endemic countries.

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THE LEISHMANIASES IN ETHIOPIA: A SCOPING REVIEW TO DETERMINE THE SCOPE OF RESEARCH AND REMAINING GAPS

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The leishmaniases are among the group of neglected tropical diseases that cause significant morbidity and mortality. There are mainly two broad categories of the disease: the visceral form, which is deadly, and the cutaneous form, which is disfiguring and stigmatizing. Currently, the East Africa region has the highest visceral leishmaniasis (VL) burden in the world. Ethiopia is one of the East African countries affected by the disease and showed commitment as part of the 2023 Nairobi Declaration for the elimination of VL by 2030. In this endeavor, it is important to identify the scope of existing research, study the available evidence, and identify gaps in research that need priority. This review aims to examine the body of literature on the leishmaniases in Ethiopia and identify remaining research gaps. This scoping review is reported following PRISMA-ScR. The following databases were searched without date restrictions: PubMed, Embase via Embase.com, Web of Science Core Collection, Cochrane CENTRAL, Global Index Medicus, ClinicalTrials.gov, the Pan African Clinical Trials Registry, and PROSPERO. Locally published gray literature will be identified by team members familiar with the Ethiopian setting. Each abstract and full-text will be dually and blindly screened with conflicts resolved by a third reviewer. Included articles must contain an in-depth discussion of the leishmaniases in Ethiopia. Data extracted will consist of study themes, study types, categories, and sub-categories each defined in a comprehensive and previously published codebook developed by this team, with adaptations made to account for the Ethiopia context. There were 8,698 records included in the abstract screen and the full text screen is ongoing. This study will be completed by August 2024 and was registered in OSF on March 2nd, 2024. We plan to disseminate our findings to the appropriate stakeholders in Ethiopia and globally.

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STAKEHOLDER PERSPECTIVES ON THE FEASIBILITY AND ACCEPTABILITY OF A FIXED DOSE COMBINATION OF IVERMECTIN AND ALBENDAZOLE IN GHANA

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The multi-disciplinary and multi-institutional EDCTP & Swiss government funded project - STOP2030 - seeks to 1) provide an effective treatment against all five species of soil-transmitted helminths, and 2) implement complementary research and activities supporting decisions on potential adoption and scaling up of the fixed-dose combination (FDC) of co-formulated ivermectin (IVM) and albendazole (ALB). A strength of this consortium is the inclusion of a social-science analyses supporting implementation of clinical, regulatory and programmatic developments. Among the complementary planned studies, Kenya and Ghana will explore the acceptability, feasibility and adherence of the FDC of IVM and ALB. As a key component of acceptability evaluation, Ghana Health Service conducted a formative study to explore stakeholders' opinions and perceptions regarding the current management of STH in Ghana, their views on the proposed FDC of IVM and ALB in MDA programs against STH, and the contextual and systemic factors likely to influence the feasibility and acceptability of FDC. The research team conducted 32 key

informant interviews with NTD programme managers at national, regional and district levels, regional and district school health education programme coordinators and schoolteachers, and six focus group discussions with parents of school children in three districts. This analysis highlights challenges (such as availability of adequate logistics for delivery of drugs, community education and sensitization on school deworming) with the current management of STH in Ghana, as well as contextual factors (such as perceptions regarding safety of drugs, and procedures for reporting and managing drug reactions) with implications for the feasibility and acceptability of FDC of IVM and ALB. Findings of this formative study will inform the design of a study that explores the acceptability, feasibility, and adherence of a FDC of IVM and ALB for the control of STH. The results of this formative study, the eventual larger study and the wider STOP2030 project will generate evidence to inform STH control efforts in Ghana, Kenya and beyond.

6685

SUCCESSES TACKLING PERSISTENCE AND RECRUDESCENCE OF TRACHOMA: KAJIADO COUNTY, KENYA

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Trachoma surveys in Kajiado County, Kenya, in 2020 identified a problem of trachoma persistence and recrudescence. Kajiado County is primarily made up of nomadic Maasai communities, who often cross the border to Tanzania and have poor access to adequate water and sanitation, compounded by animal husbandry practices that facilitate *Musca sorbens* (vector for trachoma) breeding. Sightsavers in collaboration with the Kenya MoH, KEMRI and CDC worked to confirm and understand the causes of on-going or recrudescent transmission. Evidence-based programmatic adaptations were made to address the causes and a rigorous monitoring and evaluation framework was put in place to monitor progress (and adapt as necessary) towards elimination targets. Efforts were made to better understand underlying transmission dynamics through enhanced trachoma impact surveys (TIS) adding on testing for *Chlamydia trachomatis (Ct)* infection and anti-*Ct* antibodies (TIS+) in 2021, 2022 and 2024. There has been a clear reduction ($p<0.001$) in *Ct* infection from 6.2%, 3.3% and 2.6% in 2021 to 0.8%, 0.8% and 0.1% in 2024 amongst children 1-5 years in Kajiado West, Central and South sub-counties respectively. Similarly, there is a reduction in clinical indicators (trachomatous inflammation—follicular, TF) from 13.8%, 18.0% and 8.1% in 2021 down to 6.6%, 8.0% and 5.2% in Kajiado West, Central and South, respectively. This has been complemented by an evaluation of anti-*Ct* antibody prevalence data and seroconversion rates over time. The presentation will also outline the key outcome indicators measured as part of the programme performance, including improved real-time reporting of mass drug administration (MDA) coverage and innovative community drug distributor tracking tools, validated through coverage evaluation surveys. Despite this significant progress, geospatial analysis has identified areas with high re-infection rates, six months after MDA. On-going challenges in this area will be outlined, along with plans to protect the significant gains made in tackling persistence and recrudescence of trachoma in Kajiado County, Kenya.

6686

UNRAVELING CHEMOKINE AND CYTOKINE NETWORKS IN PBMCS CULTURED FROM INDIVIDUALS WITH LEPROSY AND HOUSEHOLD CONTACTS, STRATIFIED BY OPERATIONAL CLASSIFICATION

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Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* infectionthat affects the skin, peripheral nerves and nasal mucosa presenting a wide range ofclinical manifestations. Identifying immunological biomarkers applicable as complementarydiagnostic tools for these subgroups as well as to detect subclinical leprosy in householdcontacts would be advantageous. Blood samples (257 individuals, Governador Valadares, Brazil) were collected and tested for immunological assays. Chemokines (CXCL8, CCL2, CXCL9, CCL5,and CXCL10) and cytokines (IL-6, TNF, IFN-ϒ, IL-17, IL-4, IL-10, and IL-2) present in cell culturesupernatants were assessed utilizing the CBA method. Analysis was performed using theFACSVerse, and data were processed through FCAP Array software. Quantitative results wereexpressed in pg/mL, derived from standard curves. Subsequently, integrative networks wereconstructed based on spearman correlations among soluble mediators subsequent to theassessment of the chemokine and cytokine profiles in PBMC cultures from diverse cohorts.Results revealed that the *M. leprae*-stimuli led to a decrease in the number of correlationsbetween soluble mediators as compared to Unstimulated culture (EC = 68 → 62; HHC = 56 → 50and L = 46 → 42). Additionally, when subdivided groups (HHCPB, HHCMB, LPB, and LMB) analyses were performed, an increase in correlations occurred in all groups except for HHCMB when *M. leprae* stimulated the culture. Color map analysis further illustrated that thephenomenon of downregulation was universally observed in the total number of correlations,in the intra-cluster connectivity as well as in the analysis of single patterns of most solublemediators. These findings underscore the intricate interplay of chemokines and cytokines in theimmunological landscape of leprosy. Their complex interactions, modulated by diseaseprogression and antigenic stimuli, unveil the importance of immune responses in leprosypathology, helping elucidate valuable insights into the disease's immunopathogenesis.

6687

THE POTENTIAL GEOGRAPHICAL DISTRIBUTION OF HANTAVIRUS RODENT HOSTS IN NORTH AMERICA

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The main way that hantaviruses infect people is through contact with rodent hosts that are infected. These viruses are noteworthy for their zoonotic potential and importance to public health. This study creates a detailed model of 15 hantavirus rodent hosts (that were documented with positive hantavirus from the National Ecological Observatory Network (NEON)) in North America. We used available geospatial data from the Global Biodiversity Information Facility (GBIF). The modeling methodology predicts the spatial distribution of hantavirus rodent hosts across several ecosystems in North America by utilizing sophisticated machine learning techniques, such as Ecological Niche Modelling (ENM). The models are more accurate and ecologically relevant when MERRAclim environmental data are included. The findings of this investigation shed light on potential hotspots of hantavirus rodent hosts, which advances our knowledge of the spatial epidemiology of hantaviruses. Additionally, the modeling approach provides a useful tool for comparing and answering the question of why

more hantavirus cases have occurred in the western United States than in other areas across the country. We provided sets of maps where we highlighted the geographic distribution of each species, a richness map for all 15 species across North America, and a richness map for the most important hosts with high hantavirus prevalence to be compared with a map of human cases on the State level from CDC. The findings of this study have implications for public health planning, enabling more targeted surveillance and intervention strategies to mitigate the risk of hantavirus transmission in North America, especially in the United States where the number of incidents has increased in recent years.

6688

THE ROLE OF LANDSCAPE CHARACTERISTICS IN THE TRANSMISSION OF VECTOR-BORNE DISEASES: CASE STUDY OF PLAGUE

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Plague caused by *Yersinia pestis* infection is a virulent vector-borne disease. Despite advances in plague control globally in past decades, Madagascar accounted for 80.5% of the worldwide cases from 2013 to 2018 by WHO. Landscape characteristics may affect the population dispersal of its hosts and vectors and hence the distribution of *Y. pestis*. The identification of spatial patterns of genetic structure of *Y. pestis* is a key factor to understand the dynamics of transmission and spread of the disease. The aim of this study is to examine geographic genetic patterns of *Y. pestis* from small mammal reservoirs and humans in three active plague foci across the central highlands of Madagascar where human plague is reported every year. These areas are separated by high altitudes and distances between 5km to 30km. *Y. pestis* DNAs from rat spleens and human buboes from 2019 to 2022 were extracted and genotyped using single nucleotide polymorphism (SNP) analysis. The North American strain CO92 was used as a reference and *Y. pestis* from 2007 was used to look at population dynamics over time. *Y. pestis* isolates from 23 humans and from 4 rats were analyzed. Two groups y and t were identified using a set of 249 SNPs previously identified. Isolates from humans and rats in the same locality had similar genomic and there was a relationship between genetic and geographic distance. Each group had been persisting over 15 years in these localities. This study highlights the presence of spatial genetic structure of *Y. pestis* at local scales suggesting efficient circulation at smaller geographic scales. Landscapes play a major role in the maintain of plague because of the movement of rodent and their fleas in the short distances in mountainous areas. The characteristics of the micro and macro peridomestic landscape may explain patterns of local transmission of plague. Understanding pathogen population dynamics provides insight into how, where, and when transmission occurs and can inform control decision making.

6689

UTILIZING A ONE HEALTH APPROACH TO RIFT VALLEY FEVER VIRUS LABORATORY AND FIELD INVESTIGATIONS

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The WHO attributes 700,000 deaths each year to vector-borne diseases. Communities living in certain geographic regions or within lower socioeconomic sectors are disproportionately at risk for VBD. Furthermore, the changing climate is rapidly reshaping vector boundaries. Therefore, an integrative approach that considers socioecological dynamics, vector biology, vector control, public health, agriculture, disease kinetics, and other sectors is necessary to reduce the global burden of VBD. We examine the transmission of a high consequence pathogen, Rift Valley fever virus (RVFV), both in the lab and the field to answer the questions: How do ecological factors like temperature impact RVFV transmission in competent mosquito vectors? and What are the risk perceptions of local stakeholders and community members regarding RVFV? To elucidate the effects temperature on virus dissemination and transstadial persistence in naturally infected mosquito vectors: laboratory colony mosquitoes were provided a RVFV-infected blood meal, placed at experimental temperatures (18°C, 28°C and 32°C), monitored for oviposition, survivorship, feeding-rate, and viremia. Oviposition is reduced at 18°C, blood feeding rates and survivorship are reduced at 32°C, indicating a temperature-dependent reduction in vector capacity. Evidence of RVFV vertical transmission in mosquitoes is shown. To further understand RVFV burden of disease, a multinational, transdisciplinary collaboration is underway in endemic regions of Tanzania. The project includes surveillance of humans, livestock, and mosquitoes in vaccine deployment regions, and an investigation of RVF knowledge, attitudes, and practices (KAP) of local stakeholders. Preliminary results of KAP, specifically, risk perceptions and behaviors for RFV will be presented. Ecological factors, such as temperature, can alter vectorial capacity and disease kinetics; whereas social factors, such as individual perceptions and behaviors could limit or exacerbate risk for VBD. Overall, this research will describe the applications of One Health framework to a VBD of global public health concern.

6690

FINANCING, OPERATIONALIZING, AND IMPLEMENTING REGIONAL ONE HEALTH COORDINATION IN SOUTHEAST ASIA

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Regional One Health coordination is a promising strategy for addressing shared global health priorities by avoiding duplication and maximizing synergies. Developing coordination mechanisms is urgently needed in Southeast Asia, a recognized hotspot for new zoonoses with the potential to spread globally. The objective of this piece is to identify priority action items for financing, operationalizing, and implementing regional One Health coordination in Southeast Asia. In December 2023, we conducted a 1.5-day workshop to convene 34 experts from government, national research institutes, universities, and international organizations across seven countries in Southeast Asia. This workshop focuses on exchanging experiences in and generating ideas for One Health investment, operationalization, and implementation. Based on their collective experiences, participants agreed on the following 12 action items: 1) leverage existing and emerging funding sources; 2) encourage domestic resource mobilization; 3) cultivate private-public partnerships; 4) develop business cases for One Health; 5) establish a One Health centre for Southeast Asia; 6) develop data governance frameworks; 7) formalize national coordination mechanisms; 8) strengthen engagement in social sciences; 9) strengthen engagement with diverse dimensions of One Health; 10) integrate One Health into national and local frameworks; 11) take stock of past and current initiatives; and, 12) invest in the One Health workforce. The outlined action items serve as ideas for resourcing, operationalizing, and implementing regional One Health coordination in Southeast Asia, with relevance to other regions that are tackling parallel One Health challenges of zoonoses, antimicrobial resistance, and food safety.

6691

UNVEILING ZOONOTIC EXTRAINTESTINAL *E. COLI* BURDEN IN LMICS: A STUDY IN NIGERIA

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The Global Burden of Disease studies estimated that *E. coli* was associated with nearly 1 million deaths globally in 2019, with 80% occurring in low- and middle-income countries (LMICs). 94% of *E. coli* deaths were caused by infections out of the gastrointestinal tract. Previous research underscored the prevalence of foodborne zoonotic strains of *E. coli* in extraintestinal infections in the United States. However, research in LMICs is limited, where factors such as extensive human-animal interaction and inadequate Water, Sanitation, and Hygiene (WASH) conditions may elevate the risk. To understand the burden of zoonotic extraintestinal *E. coli* infections in LMICs, we conducted a study in Nigeria, a West African nation. We analyzed Whole Genome Sequencing data of 122 *E. coli* isolates from humans extraintestinal infections (e. g. bloodstream and urinary tract infections) and included 520 food-animal isolates from Africa as context. We applied a Bayesian latent class model that leverages 17 host-associated (either human or meat) mobile genetic elements to generate probabilistic predictions of the underlying host of the *E coli* isolates, thereby identifying putative spillover strains. The model identified 24.7% of the human extraintestinal *E. coli* infections as food-animal zoonotic. This proportion is significantly higher than previous estimations in the United States, where 8% and 18% of isolates from Arizona and California, respectively, were predicted to be foodborne zoonotic. Our findings indicate that approximately one in four extraintestinal *E. coli* infections in Nigeria may originate from food-animals. Analysis of host-associate elements patterns and major sequence types of zoonotic *E. coli* highlighted geographic variations between African and American isolates. Collecting and analyzing isolates from underexplored regions are imperative to understand the pathogen transmission from food-animals to humans.

6692

ALTERATION OF THE MURINE GUT MICROBIOTA MEDIATES ANTIDEPRESSANT EFFECT OF *MALLOTUS OPPOSITIFOLIUS* EXTRACT

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Major depressive disorder (MDD) is one of the leading causes of disability globally. The treatment of MDD remains an uphill task, but the gut microbiota has been posited as a potential target for the treatment of MDD. We investigated the effect of the hydroethanolic leaf extract of *Mallotus oppositifolius* (MOE) on the gut microbiota of mice and how this contributes to the extract's known antidepressant-like effect. A 7-week chronic unpredictable mild stress (CUMS) procedure was employed in seven (7) groups of mice to induce depression. Oral drug or extract treatment began from the third (3rd) week with MOE (10, 30, 100 mg/kg) and two reference drug groups, fluoxetine (12 mg/kg) and minocycline (40 mg/kg), which have known influence on the gut microbiota. The sixth and seventh groups were the vehicle stressed (VEH-S) and vehicle non-stressed groups (VEH-NS) respectively. Changes in depressive-like behaviours were assessed using sucrose preference test while the forced swimming (FST) test was used to assess sustained antidepressant-effect after treatment discontinuation. Changes in prefrontal cortex (PFC) and hippocampal serotonin (5-HT) levels were also evaluated using enzyme-linked immunosorbent assay (ELISA). The effect of treatment on the profile of the gut microbiota of the various groups was elucidated using 16S rRNA Oxford Nanopore sequencing. MOE and reference drugs reversed the depression-associated reduction in sucrose preference when compared to VEH-S. MOE (with peak effect at 30 mg/kg) reduced immobility while increasing swimming and climbing behaviours in the FST. In addition, MOE reversed CUMS-induced reduction of 5-HT concentration in PFC and hippocampus. The behavioural effects of MOE were associated with shifts in the gut microbiota of CUMS-exposed mice by modifying the relative abundances of depression-related taxa such as Lactobacilli, Desulfovibrio, Parabacteroides. The study has provided seminal evidence that the hydroethanolic leaf extract of *M. oppositifolius* ameliorates CUMS-induced depressive symptoms by modulating the levels of gut microbiota constituents and increasing brain 5-HT levels.

6693

CUSTOMERS' WILLINGNESS-TO-PAY FOR POULTRY FROM BIOSECURE LIVE BIRD MARKETS IN DHAKA, BANGLADESH

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Bangladesh is a known hotspot for avian influenza circulation. Live bird markets (LBMs) are particularly risky, highlighting the critical need to enhance biosecurity measures. Despite this, little is known about consumers' willingness-to-pay (WTP) for purchasing poultry products from hygienic and biosecure LBMs. This study aimed to examine the WTP of customers to buy poultry from a biosecure LBM in Bangladesh. A total of 600 customers from 60 LBMs in Dhaka, Bangladesh were selected using stratified random sampling and surveyed in June and July, 2023. A set of 17 attributes related to infrastructure, biosecurity practices, and institutional responsibilities to create a biosecure LBM were identified before the survey. The survey asked participants to score each attribute with a 5-point Likert scale according to perceived importance, and state how much they would be willing to pay for those attributes. Washable walkways in LBMs and a regular water supply ranked highest among infrastructure attributes, while separating sick poultry from healthy ones and arranging for separate disposal of dead chickens were most important biosecurity measures. Regular monitoring by market and city corporation authorities ranked highest among institutional attributes. The majority (73%, 439/600) of the customers were willing to pay extra for chicken from an improved biosecure LBM. They were willing to pay BDT 13 (USD 0.12) more per kilogram (kg) for broiler, BDT 17 (USD 0.16) more for *Deshi (Gallus gallus domesticus)*, and BDT 14 (USD 0.13) more for *Sonali* (a cross-breed chicken, similar phenotypic appearance to *deshi* chicken) chicken. Of the customers willing to pay more, 85% (375/439) reported consuming the same amount of chicken at their stated increased price. LBM customers were willing to pay 3-7% more per kg of chicken from a clean and biosecure market. The finding may motivate LBMs stakeholders to improve biosecurity, as customers are willing to pay extra money. Customers' preferences for biosecure LBMs could inform government decision-making on investments and policies for improving LBMs to reduce the risk of spillover of pathogens with pandemic potential.

6694

DISENTANGLING THE EFFECTS OF FINE-SCALE MOBILITY ON LEPTOSPIRAL INFECTION USING GPS TELEMETRY DATA

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Human movement significantly influences the transmission dynamics of infectious diseases, particularly those with strong environmental drivers like leptospirosis, a zoonotic bacterial infection associated with mud and water contact. The use of GPS loggers allows a large amount of telemetry data to be collected. Telemetry data offers insights into fine-scale interactions with environmental risk factors, especially useful in complex settings like urban informal settlements. This is crucial in understanding where environmental exposure to leptospirosis occurs, an epidemiological question that remains unclear. In this study, we aimed to characterise people's movements through urban marginalised communities in Salvador, Brazil, quantifying their interactions with three environmental risk factors: domestic rubbish piles, open sewers and a local stream. Our analysis focused on identifying differences in movement patterns between genders, age and leptospirosis antibody status. We used step-selection functions, a spatio-temporal point process model used in animal movement ecology, to estimate selection coefficients. These represent the likelihood of an individual choosing to move in the direction of a specific environmental factor. With 130 participants across four matched study areas wearing GPS loggers for 24 to 48 hours, we recorded locations every 35 seconds during daytime active hours, segmented into morning, midday, afternoon, and evening. We found women were more likely to move closer to the central stream in their community and further away from open sewers than men. This study showcases a novel approach to analysing human telemetry data in infectious disease epidemiology, providing insights crucial for targeted intervention strategies.

6695

A SCOPING REVIEW ON CONTROL STRATEGIES FOR *ECHINOCOCCUS GRANULOSUS*

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Cystic echinococcosis caused by the tapeworm *Echinococcus granulosus (EG)* is a significant public health concern due to its widespread distribution and impact on human health. Cystic echinococcosis is a neglected disease; therefore, it does not receive enough funding and research and programs evaluating interventions are scarce. Our objective was to identify the scientific rationale, objectives, and efficacy of various interventions aimed at reducing, controlling, or eliminating EG in animals and humans, providing a comprehensive overview of the current status of EG interventions worldwide. We mapped all available evidence on interventions for EG up to December 2022. We screened major databases and categorized papers based on type of study, biological mechanism of control, and target populations. We characterized intervention's efficacy and safety outcomes, and associated barriers/facilitators. We assessed study quality. Out of 6080 potentially relevant studies, 40 were deemed appropriate for analysis and included in our review. Ten of these studies reported interventions in humans, 18 in animals, and 12 in animals and humans. Human interventions focused primarily on preventive education aimed at increasing knowledge and awareness. Half of the animal interventions targeted only dogs and the other half targeted dogs and sheep. Interventions involving praziquantel comprised 72% of all interventions. Only two studies focused on sheep vaccination. Among interventions focused on both humans and animals, we found a variety of approaches including education, mass screening, dog population control, slaughterhouse control and surveillance, and praziquantel treatment. The efficacy was varied and will be discussed. The overall quality of the studies was low. Available evidence suggests that interventions with multiple components aimed at animals and humans could achieve EG control. However higher quality evidence is needed. Our study reveals research gaps that need to be addressed to inform future interventions and control programs. Further evidence is needed to assess the sustainability of control measures.

6696

IMPACT OF ANGOLAN ROUSETTE BAT (*MYONYCTERIS ANGOLENSIS*) FORAGING SITE CONSISTENCY ON SPILLOVER POTENTIAL IN THE MOUNT ELGON REGION OF UGANDA

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Angolan rousette bats (*Myonycteris angolensis*) are a potential reservoir for viruses that could be of importance to public health. Our preliminary data suggest these bats host paramyxoviruses and rhabdoviruses. While many bat-associated spillover events are deduced to have occurred at the cave interface, many could not have occurred at caves, and thus must have transpired in locations bats use in the night, likely for foraging. Understanding the consistency of bat nightly foraging behavior across different seasons will illuminate habitat features that are most important to bats, and thus should be targeted for prediction and prevention of viral spillover. In this study, we used GPS tracking to ascertain foraging sites of the frugivorous *M. angolensis* within the Mount Elgon region of Uganda. Through geospatial analysis applications, we tested whether these foraging sites were significantly associated with particular landscape features. GPS data were acquired by suturing GPS units onto bats and taking fixes during periods of high activity over the course of five days in both January (dry season) and May (wet season) of 2023. Using kernel density algorithms to determine foraging hotspots from the distribution of GPS points, our preliminary data suggest foraging hotspots are significantly closer to rivers/streams and protected areas and significantly further from human settlements than would be expected if their distribution was random. Using multi-night data, it was evident that specific foraging locations were visited by multiple bats from the colony, as well as by the same bats over consecutive nights. Foraging ranges were fairly consistent in protected forested areas across seasons, but different foraging locations were identified in populated agricultural sites in wet versus dry seasons. Foraging sites were more variable and more frequently included human settlements during the dry season when endemic fruits are less readily available. These results suggest a seasonal component to resource stress and an associated impact of seasonality on potential for viral spillover due to changes in bat foraging site selection.

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DIVERSE MICROBES HABITING MEDICINAL HERBAL PREPARATIONS EXHIBIT VARIED RESISTANCE TO ESSENTIAL ANTIBIOTICS

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The use of herbal medicine is on ascendency worldwide. This study sought to assess the microbial and heavy metal quality of herbal medicines in the Kumasi Metropolis. Twenty commercially available herbal medicines were sampled from wholesale pharmacies in the metropolis, serially diluted and inoculated on various culture media for microbial growth and count using the pour plate technique. Bacterial isolates were identified by MALDIToF MS, and their Antibiotic Sensitivity patterns determined using the Kirby Buer disc diffusion method, employing breakpoints from the EUCAST guidelines. The samples were digested by the Triple Acid Digestion technique and concentrations of Cadmium, Arsenic and Lead assessed using the MP-AES. All samples were contaminated. Total Aerobic Microbial Counts of $5x10^2$ to $2.38x10^6$ CFU/mL and Total Yeast and Mould Counts of $6.6x10^2$ to $1.71x10^6$ CFU/mL were observed with 45% and 80% of products exceeding the European Pharmacopeia threshold for aerobic count and yeast and mould count, respectively. 87 bacterial isolates comprising 27 species were identified. *Bacillus pumilus* was the predorminant bacterial species (26.13%). *Bacillus cereus* (9.09%), *Pantoea septica, Mixta calida* and *Klebsiella oxycota* were among the least (1.14%). 26 fungal isolates. *Aspergillus* spp. was the most prevalent (46.15%). *Phialophora* spp. and *Fusarium* spp. were the least (1.78%). All bacteria subjected to the Antibiotic Sensitivity Tests exhibited resistance to at least one class of antibiotics. 29 *Enterobacteriaceae* were resistant to ampicillin (10 µg), 46 *Bacillaceae*, resistant to ciprofloxacin (5 µg) and 6 *Pseudomonades*, resistant to ticarcillin (75 µg) and Aztreonam (30 µg). 5 isolates were multidrug resistant. 5% and 40% of products exceeded WHO's daily limits for lead (10mg/kg) and arsenic(5mg/kg), respectively. The presence of a vast array of resistant microorganisms and toxic heavy metals indicates potential contamination of herbal preparations in the Kumasi metropolis. Regulatory authorities should ensure quality assurance for manufacture of herbal medicines is properly enforced.

6698

A ONE HEALTH APPROACH TO TACKLE PLAGUE OUTBREAKS IN DEMOCRATIC REPUBLIC OF THE CONGO: THREE YEARS OF ONGOING EPIDEMICS.

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Plague is a neglected zoonosis, caused by the flea-borne bacterium *Yersinia pestis*, with mortality rates of around 65% for bubonic plague and around 100% for pulmonary plague if the infection is left untreated. The Ituri endemic plague focus, also known as the Lake Albert focus (6000 km2), is the oldest known focus in Africa. Since 2000, the number of suspect plague cases and outbreak sites has been increasing in range and scope with 9265 suspect cases and 510 deaths (CFR=5.5%). As we all know, a local risk can become global, and ignoring the spread of plague in one of the world's most active hotspots exposes DR Congo and its neighbors to a transnational risk. Moreover, plague outbreaks are unpredictable calling for increased in-country preparedness, detection and response capacities. In the last 20 years, the average annual number of suspect plague cases was 421.1±11.9 (median 155), and the average weekly number of suspected cases was 7.4±21.7 (median 3 cases per week). Between 2021 and 2024, the Rethy health zone alone located in Djugu Territory, has reported 881 cases of human plague. The primary route of infection is likely flea-borne transmission, with domesticated guinea pigs and black rats being significant amplifiers; sylvatic carriers are yet to be identified. Most cases remained classified as suspect due to the absence of confirmatory diagnostic, active surveillance, and funding. However, recent collaborations have allowed for molecular and microbiological *Y.pestis*diagnostics at INRB Goma. Of 55 buboes samples tested, 29 were positive, and 3 full genomes have been generated. To prevent future outbreaks, logistical and technical support have recently focused on public awareness and education in household sanitation and rat consumption risks, free case management, chemoprophylaxis for contact cases, and vector control.

6699

SETTING THE PLATFORM FOR THE ELIMINATION OF STRONGYLOIDIASIS IN AUSTRALIA

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Strongyloidiasis is a neglected tropical diseases caused primarily by infection with the roundworm *Strongyloides stercoralis*. While the majority of infections are so-called 'asymptomatic', it can have deadly consequences in cases of immune-compromise leading to hyperinfection and disseminated strongyloidiasis which, untreated, is almost universally fatal. Infections occur globally, although there is little to no surveillance performed, thus the true burden of disease is unknown. While more recently included in the Soil-Transmitted Helminths (STH) by the WHO, traditional diagnostics and treatments for STH are ineffective against *Strongyloides*, further underscoring the urgency of addressing this issue. Estimates based on published literature suggest there may be 600 million infections worldwide, with the majority of these infections occurring in South East Asia (SEA) and the Pacific.While Australia has a low country-wide prevalence, prevalence in endemic communities, particularly in Northern Australia, can be over 30%, and as high as 60%. There is also the added complication of HTLV-I, which is co-endemic in Australia and may be a trigger for more severe disease, and the potential for a zoonotic reservoir in dogs. It is our central thesis that strongyloidiasis is a zoonotic neglected tropical disease of public health importance in Australia and that an integrated interdisciplinary "One Health" approach is required for its elimination. Here we will present an overview of strongyloidiasis in Australia and outline an elimination program we are developing for implementation in remote communities in Northern Australia.

6700

EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS IN PATIENTS WITH INFLUENZA LIKE ILLNESS IN THE GAMBIA: RESULTS FROM A NEWLY IMPLEMENTED SENTINEL SURVEILLANCE PROGRAM

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Respiratory syncytial virus (RSV) is a major cause of acute respiratory infections in children worldwide and can cause high mortality, especially in developing countries. The Gambia, experiences a high burden of respiratory illnesses among pediatric populations, yet there is limited data on the epidemiology and clinical characteristics of RSV infections. Here, we present results of a newly implemented sentinel surveillance program in two hospitals in the Gambia with a focus on epidemiological and clinical characteristics of RSV infection. From January to December 2023, nasopharyngeal samples were collected from outpatient with influenza-like

illness in two referral hospitals. Clinical and socio-demographic data were obtained using a standardized questionnaire. Collected samples together with the clinical forms were sent to the National Public Health Laboratory (NPHL) on a weekly basis through the Sample Referral Network. Once in the laboratory, samples were tested by targeting 3 respiratory pathogens, including RSV, SARS-CoV2 and influenza A/B viruses using a multiplex RT-PCR. Overall, 148 respiratory specimens were received and analyzed at the NPHL during this pilot phase. Among enrolled patients, 79 (53.4%) were males, 67 (45.3%) were infants aged under 1 year and children above 5 years of age represented 35.1% of all patients. RSV was detected in 14.2%, among which RSV type A was confirmed in 38.1% and RSV type B in 61.9%. RSV detection rates in the different age groups varied significantly with infants aged ≤11 months accounting for 66.7% of positive patients. The highest detection rate of RSV was noted in August (38.1%), which coincide with the rainy season in the Gambia. The most frequently observed symptoms among patients with confirmed RSV infection were cough (90.5%), fever (80.9%) and Dyspnea (52.4%). In summary, our findings from the newly implemented sentinel surveillance program reveal a relatively high prevalence of RSV infection among pediatric patients in the Gambia with co-circulation of both type of RSV. Enhanced surveillance of Severe acute respiratory illnesses in pediatric inpatients in needed.

6701

GENETIC DIVERSITY AND MUTATIONAL PROFILES OF SARS-COV-2 VIRUS IN ADDIS ABABA, ETHIOPIA (2020 TO 2022)

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The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a significant impact on global health and economies. The purpose of this study was to limit the sample area to Addis Ababa and analyze the genetic diversity and mutational profiles of SARS-CoV-2 viruses from 2020 to 2022. SARS-CoV-2 genome sequences were retrieved from the Global Initiative on Sharing All Influenza Data (GISAID) database as of July 19, 2023 only samples collected in Addis Ababa, Ethiopia. A total of 451 high-quality, complete genome sequences were selected for analysis. Nextclade (version 2.14.0) command line pipeline and Pangolin were used for viral genome clade assignment, mutation calling, phylogenetic placement, and lineage designation. The analysis revealed a diverse range of SARS-CoV-2 genetic variants in Addis Ababa, with the Delta variant (66.1%) identified as the predominant strain (Clade 21J: 61.9%, 21I: 1.8% and 21A: 2.4; Pangolin: AY.120: 40.4%, B.1.617.2: 15.5% and others: 10.2%), followed by the Omicron (20.2%) variant (Clade21K: 18.8%, BA.1.1: 11.8). There were a shift from diverse early variants (A, B.1, B.1.480, Alpha, and Beta) to Delta dominance in mid-2021, followed by Omicron's supremacy from late 2021 to mid-2022. A total of 14093 amino acid substitutions were identified (average of 31.2 mutation per sequence). The average substitution rate of amino acids was larger in Omicron variants (45.1) than in Delta variant (30.6). There were four most frequent amino acid substitutions (D614G, T478K, P314L and T3255I) shared between Delta and Omicron variants. Addis Ababa's SARS-CoV-2 landscape transitioned from diverse early variants to Delta dominance in mid-2021, followed by Omicron's predominance from late 2021 to mid-2022. Higher substitution rates in Omicron compared to Delta suggest continued adaptation and emphasize the need for ongoing surveillance and targeted interventions.

6702

RISK FACTORS ASSOCIATED WITH COVID-19 IN-HOSPITAL MORTALITY IN PANAMA

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from China in December 2019 and raised serious concerns worldwide. SARS-CoV-2 was transmitted across Panama in a short period followed by the announcement of the first imported case on March 8th, 2020. This retrospective cohort study aims to examine the epidemiological, clinical, laboratory, medical treatment, and clinical outcomes of patients hospitalized in the Santo Tomas Hospital of Panama City from May 18th, 2020, to November 19th, 2021. A total of 1,526 patients were identified to be SARS-CoV-2 positive through RT-PCR presenting the following characteristics: mean age 54.86 ± 16.60; 61.2% males, 81.4% Panamanians, and 20.2% belonging to the White race/ethnicity. In-hospital mortality was 27.4%. All patients were classified as mild [338(22.2%)], moderate [785(51.4%)], and severe [403(26.4%)] cases, and 331 (21.7%) received invasive ventilation. Hypertension [627(41.1%)] and Diabetes mellitus [425(27.9%)] were the most frequent comorbidities. Laboratory indicators, such as CRP and AST were significantly higher in cases with fatal outcomes. The most frequent acute complications were pneumonia [1,264(82.8%)], acute respiratory distress syndrome [541(35.5%)], and cardiovascular disease [46(3.0%)]. Older age was the risk factor most strongly associated with a fatal outcome (e.g. Age of >75 years vs 18-45 years: odds ratio [OR], 25.7; 95 CI, 13.3, 51.2), followed by exposure to invasive ventilation ([OR] 17.3; 95 CI, 10.8, 28.2), presenting septic shock as an acute complication ([OR] 11.8; 95 CI, 3.55, 47.1) and presenting comorbidities, such as Chronic Kidney Disease ([OR] 5.65; CI, 2.22, 15.1), or HIV ([OR] 3.84; 95 CI, 1.61, 8.92). Additionally, being of Non-white race/ethnicity was a risk factor for death: Mestizo ([OR] 2.02; 1.11, 3.71), Trigueño ([OR] 1.93; 1.16, 3.23). Medical management with non-steroidal anti-inflammatory drugs (OR, 0.67; 95% CI, 0.45, 0.99) was associated with a decreased probability of death. Further collaborative studies are needed to validate our findings with similar studies in other countries of the region.

6703

PULMONARY FUNGAL INFECTIONS AND TUBERCULOSIS CO INFECTION IN YAOUNDE, CAMEROON

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Infectious diseases of the respiratory tract are known as respiratory tract infections and are the leading cause of death among all infectious diseases. The objective of our study was to identify the association between Tuberculosis and pulmonary fungal infections in YaoundeWe carried out a transverse and descriptive study from February to June 2021, at the Jamot hospital in Yaounde. A macroscopic, microscopic, fungal culture of the sample (sputum and broncho alveolar liquid) was carried out and a germ tube test, fungal sensitivity test as well as specie identification using the ID 32 C gallery was carried out on the positive cultures as well as microscopy and loop-mediated isothermal amplification done on the samples for *Mycobacterium tuberculosis* identification. Statistical analysis was carried out using the R version 3.6.1 software. The mean was calculated with the aid of the Kruskal Wallis rank sum test. 300 patients participated in this study. They had mean age ±standard deviation of 41.59 ± 17.5 years and extremities of 1 and 91years. The male /female ratio was 2:1. Fungal infection was positive in 127 patients (42.33 %), and Tuberculosis

71 (23.7%). Fungal-TB Co-infection was 46.5%. There is a statistically significant association between Tuberculosis and pulmonary fungal infection.

6704

HOUSEHOLD CONTACT TUBERCULOSIS SCREENING EXPERIENCE AND PREDICTORS OF TUBERCULOSIS DISEASE DIAGNOSIS IN RURAL TANZANIA

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One third of people with TB disease (PWTB) remain undiagnosed, experiencing prolonged illnesses before diagnosis. To close this gap, the World Health Organization and national guidelines recommend TB screening for all household contacts (HHCs) of index PWTB. HHC TB screening experiences vary between countries, and between rural and urban parts within the same country. Therefore, we aimed to characterize the HHC TB screening and explore predictors of TB disease diagnosis among HHCs in Rural Tanzania. We used data from a prospectively enrolled cohort of index PWTB and their HHCs in Haydom, Tanzania. We describe the testing recommended as part of HHC TB screening and use a multivariate regression model to explore predictors of TB disease diagnosis. The cohort enrolled 120 index PWTB with 398 HHCs. 261 HHCs (66%) from 85 households completed TB screening with sputum and chest x-ray recommended for 121 (46%) and 3 (1%) HHCs respectively. 18 HHCs (4.5%) were diagnosed with TB disease, 14 of them with no sputum or CXR recommended. HHCs with TB symptoms and HHCs of index PWTB with pulmonary TB or HIV were more likely to be diagnosed with TB. Only 10 HHCs completed six-months of daily isoniazid TPT out of 61 HHCs who started TPT (16.3%) and 79 HHCs who were eligible (12.7%). The recommended sputum and imaging studies to complete HHC TB screening and short TPT regimens have suboptimal penetration in this rural high-burden setting. Innovative testing and coverage modalities are needed to bridge the gap.

6705

DETERMINATION OF THE LIMIT OF DETECTION OF HETERORESISTANCE OF *MYCOBACTERIUM TUBERCULOSIS* IN TUBERCULOSIS PATIENTS BY NANOPORE SEQUENCING TECHNIQUE FROM GENOMIC DNA AND GENE REGIONS IN SPUTUM SAMPLES AND PRIMARY CULTURES COMPARED TO THE AGAR PROPORTIONS METHOD

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Heteroresistance in *Mycobacterium tuberculosis* involves the coexistence of resistant and susceptible bacterial subpopulations, potentially leading to inaccuracies in resistance profiling and the emergence of drug-resistant phenotypes. This study aims to detect heteroresistance in *M. tuberculosis* by analyzing direct sputum samples, encompassing both genomic DNA and amplicons, alongside primary cultures. We employed targeted next-generation sequencing (tNGS) and whole genome sequencing (WGS) techniques, comparing our findings against to the gold-standard agar proportion method. DNA yields from sputum varied significantly, ranging from 105 ng to 3.9 µg, underscoring the necessity for optimized DNA extraction and library preparation methodologies. DNA was extracted from saponin-treated sputum to enrich *Mycobacterium* populations, followed by cell lysis using Fastprep. The lysates underwent purification using a dual approach: a non-kit based method utilizing phenol-chloroform and AMPure beads, and a kit-based method. DNA integrity was subsequently assessed via TapeStation. Libraries for sequencing were prepared using Rapid Barcoding and Ligation kits, suitable for both genomic DNA and amplicons. Sequencing metrics will be evaluated using MinKNOW UI software.The non-kit-based extraction yielded significantly higher DNA concentrations (1.2-17 µg) compared to the kit-based method (1-6.7 µg) ($p < 0.05$), with both methods achieving high-quality DNA, as indicated by A260/A280 and A260/A230 ratios (1.7-2.21). DNA integrity index (DIN) values ranged from 1.7 to 6.7, with no significant differences between methods. Regarding DNA integrity, the kit-based method produced longer fragments (13-20 kb), as opposed to the shorter fragments (6-8.5 kb) typical of the non-kit-based method ($p < 0.05$). Nevertheless, both methods generated fragments as short as 400 bp, characteristic of degraded sputum samples. Based on these outcomes, we recommend the non-kit-based method for applications requiring high DNA concentrations, whereas the kit-based method is preferable for obtaining longer DNA fragments.

6706

PRELIMINARY COMPARISON OF ILLUMINA MISEQ AND OXFORD NANOPORE TECHNOLOGIES MINION SEQUENCING METHODS FOR CHARACTERIZATION OF *KLEBSIELLA PNEUMONIAE* ISOLATES

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Klebsiella pneumoniae (KP) is a significant contributor to healthcare-associated infections globally and a leading gram-negative bacterial cause of invasive disease. The burden on healthcare systems may rise due to antimicrobial resistance (AMR) to third generation cephalosporins and carbapenems. Illumina whole-genome sequencing (WGS) is commonly used for KP genomic surveillance. While Illumina sequencing yields high accuracy sequences, the short reads result in fragmented genome assemblies that hinder the contextualization of AMR genes to transmissible elements. It is also costly and requires advanced laboratory infrastructure. In contrast, Oxford Nanopore Technologies (ONT) MinION is suitable for low-resource settings due to its portability and affordability. Its long-read sequences improve resolution of structural variations and generate nearly complete genome assemblies but with lower sequence accuracy. We compared the performance of Illumina and ONT WGS results to characterize key genomic features across 10 KP isolates. Illumina reads were generated with the Illumina DNA prep kit and MiSeq paired end sequencing, then assembled with SPAdes. ONT reads were generated with the Rapid Barcoding kit and R9.4.1 flow cells, basecalled using Guppy, assembled with Flye, and polished using Medaka. Sequence types (STs), K (capsular polysaccharide) and O (lipopolysaccharide) antigen loci, AMR elements, and virulence factors, were extracted using KP-specific genomic tools Kleborate. Results showed 100% concordance in STs, O antigen loci, and virulence factors between Illumina and ONT assemblies. However, discordance was observed in AMR profile of 1 of 10 (10%) isolates and K antigen loci for 3 of 10 (30%) isolates due to missing genes in ONT assemblies. In conclusion, preliminary results suggest that ONT still struggles with base-call errors, potentially affecting the identification of clinically significant features, notably K typing, critical for genomic surveillance. Nevertheless, continual improvements to its basecalling tool and analysis algorithms may enhance its utility for public health genomic surveillance.

6707

RESPIRATORY SYNCYTIAL VIRUS-INDUCED METABOLITES REGULATE MITOCHONDRIAL HETEROGENEITY THROUGH LUNG-BRAIN AXIS

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Respiratory syncytial virus (RSV) infection established the involvement of metabolites in brain function. This metabolite is an important anti-

inflammatory hormone secreted through the hypothalamic-pituitary-adrenal (HPA) axis. This study is designed to make a follow up studies on our biological pathway of the lung-brain axis, where we found metabolomics and pathological changes in the lungs and brain of mice infected with RSV. The method involved are cell culture and passage (HT-22 cells), CCK-8 analysis, Cell total RNA extraction and qRT-PCR, Western blots and metabolomics analysis. RSV infection induced up-regulation of 16 metabolites in the lung was observed. Twelve up-regulated metabolites were selected their effects were observed on cell proliferation and IL-1β secretion in lipopolysaccharide (LPS)-induced neuronal injury model. The results showed that propanoic acid promoted the proliferation of LPS-treated neurons and inhibited the production of reactive oxygen species (ROS) and the secretion of IL-1β and IL-4. Spermine inhibited the proliferation of LPS-treated neurons and the secretion of IL-1β. Glutaric acid inhibited the proliferation of LPS-treated neurons and promoted the production of ROS and the secretion of IL-1β, IL-6 and IFN-γ. Moreover, propanoic acid inhibited the expression of Drp1 protein and mRNA, and promoted the expression of Mfn2 protein and mRNA. Spermine and glutaric acid promoted the expression of Drp1 mRNA and protein, and inhibited the expression of Mfn2 mRNA and protein. MDIVI-1 treatment inhibited Drp1 expression and promoted Mfn2 expression, thus reversing spermine- and glutaric acid-induced effects. **Conclusion**: This study deciphered possible mechanisms of mitochondrial dynamics imbalance in nerve cells that are driven by spermine and glutaric acid to promote mitochondrial heterogeneity in HT-22 nerve cells.

6708

IMPROVED TUBERCULOSIS DETECTION BY PARTIAL AMPLICON CAPTURE AND RECONSTRUCTION OF PLAMID DNA FRAGMENTS DEGRADED IN URINE

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Tuberculosis (TB) diagnosis remains a significant challenge. Gold standard culture tests and other common methods such as smear microscopy or the GeneXpert® MTB/RIF PCR assay require sputum samples. However, sputum is often difficult to produce for children and individuals infected with HIV. Urine is an ideal patient sample because it is easily collected in large volumes. There are several WHO approved TB diagnostics that detect proteins in urine but suffer from poor analytical sensitivity. Prior work in the field suggests that TB cell free DNA (cfDNA) is present in urine. However, urine-based assays that target DNA are hindered by dilute concentrations and the presence of DNases that degrade cfDNA into fragments too short to detect by traditional PCR methods. We have developed a novel method to capture and detect small TB DNA fragments from 1 mL urine samples. Synthetic DNA, complementary to the TB biomarker IS6110 gene, was functionalized with dual biotin and used in urine as a fragment capture strand. The bound fragments are extracted by biotin binding to streptavidin coated magnetic beads. The capture strands subsequently act as a template for DNA polymerase to reconstruct the fragments into full length amplicons for detection by commercial PCR kits. This method was evaluated by capturing and detecting known, short synthetic DNA targets spiked into urine. However, we further developed a surrogate clinical sample by spiking a plasmid vector containing full length IS6110 into urine to degraded naturally. This test method represents what occurs in patient samples by incorporating random DNA cleavage in urine and can replicate different clinical circumstances such as the time DNA is exposed to nucleases, poor sample handling, and EDTA preservation. Using this method, we were able to detect as few as 100 copies of fragmented IS6110 DNA in pooled human urine. This method has the potential to improve the sensitivity of urine based TB diagnostics so that children and HIV positive individuals can be tested using a more easily obtained sample specimen without compromising analytical sensitivity.

6709

RISK OF SARS-COV-2 INFECTION AMONG HOSPITAL-BASED HEALTHCARE WORKERS IN THAILAND AT THE MYANMAR BORDER MARCH-JULY 2022

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The risk of Coronavirus 2019 (COVID-19) infection was investigated during the Omicron wave in 2022 among healthcare workers (HCWs) in a hospital-based setting in Thailand, near Myanmar border. Bivariate and multivariate regression analyses measured the descriptive self-reported adherence to general infection prevention and control (IPC) measures, the risk and factors associated with COVID-19 infection. Among 300 eligible HCWs, 289 (96.3%) provided written informed consent and participated in the study. The median age was 41 years (interquartile range [IQR] 28-48), and 84.1% were female. Of those, 274 HCWs participated in the daily reporting and 27 (9.9%) tested positive for SARS-CoV-2. In the bivariate analysis, nurse assistants (NAs), work locations at the inpatient department (IPD), COVID-19 ward, and acute respiratory infection clinic were associated with increased risk of infection. In the multivariable analysis, working at IPD and COVID ward assignments remained significantly associated with an increased risk of infection, with adjusted RRs of 2.37 (95% CI 1.09-5.15, *p=0.030*) and 5.97 (95% CI 1.32-26.9, *p=0.020*), respectively. NAs were associated with a 3.87 times higher risk of COVID-19 infection (95% CI 0.96-15.6, *p=0.058*), compared to individuals with job titles other than physicians, nurses, and patient caregivers. NAs found high risk of infection, likely due to their frequent and prolong contact with patients and potentially be got COVID-19 infection. It remains unclear whether COVID-19 infection among HCWs was due primarily to exposures during patient care, cross-transmission between HCWs during other activities, or widespread transmission by asymptomatic patients and HCWs. Our findings suggest that HCW's knowledge and attitudes (e.g., disagreeing that caring for COVID-19 patients is stigmatizing, fear of becoming infected), implementing effective IPC strategies, and practicing preventive behaviors are key components of prevention. The importance of prompt detection of COVID-19 and identification of gaps in IPC are an opportunity for improvement the prevention among HCWs in a hospital along the border.

6710

HEALTHCARE FACILITY-BASED INTENSIFIED TUBERCULOSIS CASE DETECTION IN ETHIOPIA: OPPORTUNITIES AND CHALLENGES

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Ethiopia is one of tuberculosis (TB)-burden countries with an estimated incidence rate of 164 cases per 100,000 people. Limited healthcare access, low community awareness, inadequate diagnostic infrastructure, and limited screening efforts are major challenges for TB control in Ethiopia. The objective of this study was to evaluate the effectiveness and challenges of facility-based intensified TB case detection in selected health facilities in Ethiopia. The study was conducted in nine health facilities (four hospitals and five health centers) in southwest Ethiopia. Patients and their companions age 18 years and older visiting outpatient units of these facilities were assessed with cough screening tool. Participants with a cough of 14 days or longer (chronic cough) were evaluated as presumptive TB cases with TB symptom screening and sputum GeneXpert examination. Patients already on treatment as confirmed or presumptive TB cases were excluded. A total of 76,988 participants (42,047 patients and 34,941

companions) were included in the survey. Overall, 10,436 (13.6%) reported having a recent cough, of which 2,742 (3.6%) (2,216 patients and 526 companions) had a chronic cough. Among patients with chronic cough, only 1,565 (70.6%) were screened by the treating physician as presumptive TB cases. On the other hand, among the 526 companions with chronic cough, 438 (83.3%) were not willing to be evaluated as presumptive TB cases. In total, 1669 participants were tested with sputum GeneXpert, while the remaining were not tested either because they were unwilling or they had a dry cough. *Mycobacterium tuberculosis* was detected in 76 (4.6%) cases tested with GeneXpert, two of which were among companions. Facility-based TB symptom screening has the potential to improve TB case detection in Ethiopia. However, the lack of a clear strategy at healthcare facilities, along with inadequate level of awareness among patients and healthcare providers, are major hinderances. Improving the capacity of healthcare providers and enhancing health systems for TB screening are essential steps towards advancing the TB elimination agenda.

6711

PROTEOMIC ANALYSIS REVEALS MOLECULAR PATHWAYS UNDERLYING ACUTE KIDNEY INJURY IN COVID-19

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Acute kidney injury (AKI) is a severe complication observed in many patients hospitalized with COVID-19. To understand the molecular mechanisms driving AKI in the setting of COVID-19, proteomic analysis was performed utilizing an aptamer-based technology (SomaScan™) on plasma collected from COVID-19 patients who developed AKI (n=17, 42.5%) during hospitalization and those who did not (n=23). There were 125 differentially expressed proteins (DEPs, $P<0.05$), with 74 over-expressed and 51 under-expressed proteins in AKI. Enrichment analysis using MetaCore™ revealed significant enhancement of the Classical Complement (FDR=1.895e-9), Alternative Complement (FDR=1.895e-9), and Lectin-induced Complement (FDR=2.235e-8) Pathways in AKI. Complement system activation can occur directly due to interactions between SARS-CoV-2 and the lectin pathway, as well as through secondary mechanisms such as endothelial injury and cytokine release syndrome. This can contribute to inflammation, tissue damage, and endothelial dysfunction, potentially leading to AKI. Additionally, the dataset showed enrichment of the Blood Coagulation Pathway (FDR=2.729e-5), supporting previous associations between COVID-19 and a hypercoagulable state, which can lead to AKI by impeding renal blood flow and causing ischemia. Furthermore, dysregulation of the Angiotensin System Maturation Pathway (FDR=2.826e-7) was associated with AKI. Dysregulation of the renin-angiotensin-aldosterone system (RAAS) by angiotensin may further be exacerbated by the direct effects of SARS-CoV-2 on ACE2 receptors and secondary inflammatory responses. Overactivation of RAAS can also contribute to AKI by impairing renal perfusion and function. Overall, activation of the complement pathways, coagulation pathway, and angiotensin system in COVID-19 patients with AKI suggests a multifaceted process that involves immune-mediated inflammation, vascular dysfunction, and thrombotic complications. Understanding the molecular mechanisms is crucial for identifying therapeutic targets to mitigate AKI and improve outcomes in COVID-19 patients.

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ELEVATED PERIPHERAL BLOOD SARS-COV-2 VIRAL LOADS ARE ASSOCIATED WITH THE DEVELOPMENT OF ACUTE KIDNEY INJURY IN COVID-19 PATIENTS

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Acute kidney disease (AKI) is prevalent among COVID-19 patients and is associated with poor clinical outcomes. We previously showed that elevated SARS-CoV-2 viral loads (VLs), particularly in peripheral blood (PB), are an important predictor of severe COVID-19. Here, we examine the relationship between SARS-CoV-2 VLs and the development of AKI in a cohort of hospitalized COVID-19 patients (n= 475) recruited between 4/2020-12/2021 at the University of New Mexico Hospital. Patient demographics, laboratory measures, comorbidities, and major clinical events were collected throughout hospitalization. To ascertain if patients developed AKI, baseline serum creatinine was retrospectively adjusted to the median serum creatinine level. A ratio of >1.5 from peak creatinine to baseline was classified as AKI. SARS-CoV-2 VL dynamics were investigated in the upper respiratory tract (URT) and PB on days 0-3, 6, 9, and 14 by RT-qPCR using the CDC-recommended panel of N1 and RNase P primers and probes. The incidence rate of AKI in the cohort was 29.3% (n=139) with 82.7% (n=115) of these individuals admitted to the ICU and/or died during hospitalization. AKI was more prevalent in patients who were male ($P=0.002$), between 45-64 years ($P=0.037$) and had hypertension ($P=0.032$). Patients who developed AKI had significantly higher URT and PB VLs on the initial sampling days and cumulatively across two weeks. Logistic regression modeling revealed that being male [Odds Ratio (OR)=1.776, $P=0.09$] and higher PB mean VL (OR=1.255 $P=8.10\times10^{-4}$) were predictors of AKI. Mortality across hospitalization was associated with having AKI (OR=6.66, $P=3.02\times10^{-10}$), being male (OR=2.260, $P=0.011$), infected with the Delta variant (OR=0.475, $P=0.038$), higher URT mean VL (OR=1.186, $P=0.005$), and higher PB mean VL (OR=1.717, $P=5.73\times10^{-9}$). These results identify viral load, especially in peripheral blood, as an important predictor for the development of AKI and death. Therapeutic interventions that reduce SARS-CoV-2 in the bloodstream, while also not exacerbating renal impairment, could play a crucial role in improving patient outcomes.

6713

TRENDS IN RESPIRATORY DISEASES DEATHS BEFORE AND DURING THE COVID PANDEMIC BETWEEN 2010 AND 2021 IN KOMBEWA SUBCOUNTY OF KENYA

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The emergence and rapid evolution of novel infectious pathogens alongside conditions that favor transmission amid rising population, redolent of higher risk of these infection warrant intensified surveillance. This study evaluated the causes of mortality in the Kombewa sub-county, focusing on respiratory infections. The Kombewa Health Demographic Surveillance System collected data on causes of mortality among this population between 2011 and 2021. This was performed using surveys using questionnaires, structural question, and answer sessions, verbal autopsies, and a review of health records to establish causes of death in the region. Demographic information for each participant was collected, and data was archived in an access database and analyzed in the SPSS analysis tool V27. Of 11,209 deaths, 7477 were from known causes, while 3732 were from unknown causes. Respiratory diseases were the main known cause of death at 1351 (17.9%), followed by HIV (14.7%), malaria (10.9%), lifestyle diseases (stroke, hypertension, diabetes, and heart disease) at 775 (10.4%), diarrheal

diseases 557 (7.4%) and other varied causes at 31.4%. Their median age was 57 (interquartile range (IQR) = 27-76 years). Acute respiratory infections, including pneumonia, accounted for 59.1% of the mortality cases, followed by TB with 28.6%. The analysis showed a significant association between age and the cause of death (*p-value* =0.000), however, there was no significant variation in the cause of death between the two periods.. Despite being a malaria-endemic region, respiratory infections were the main cause of death, depicting an increased threat of this infection in the wake of emerging and reemerging respiratory disease pathogens.

6714

CHANGES IN THE RESPIRATORY PATHOGENS TREND IN SEVERE ACUTE RESPIRATORY INFECTION CASES PRE- AND POST-COVID-19 PANDEMIC IN THE KINGDOM OF JORDAN, 2018-2023

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Detection rates of respiratory pathogens and hospitalization due to respiratory infections were globally influenced by COVID-19 pandemic. In the kingdom of Jordan, a retrospective analysis of the severe acute respiratory surveillance (SARI) data collected from 2018 and 2023, confirmed the pandemic impact on the severe respiratory infections. SARI hospitalized cases increased significantly from 1785 cases pre-pandemic to 5353 cases during the COVID-19 pandemic, to more than 6150 cases post-pandemic. The detection rates of respiratory viruses such as influenza, respiratory syncytial virus (RSV) and rhinovirus(RV), as well as bacteria such as *Bordetella* have been influenced by the pandemic. The first COVID-19case in the kingdom of Jordan was reported in March 2020. During the first 3 months of 2020, there were regular reports of influenza A cases, but as described globally, influenza detection rates dropped to0% in the following months of 2020, until it was detected again in 2021. The percent positivity of influenza A varied: 3.9% (2018), 10% (2019), 3.3% (2020), 0.8% (2021), 4.2% (2022), and 7.7% (2023). The two lineages of influenza B, Victoria and Yamagata, were co-circulating in 2018 with percent positivity of 1.5% and 0.9%, respectively. In 2019 only B/Yamagata lineage was circulating (0.8%), while in2020 only B/Victoria lineage was circulating (1.4%). No influenza B was reported in the kingdom of Jordan in 2021, while in 2022 and 2023 only B/Yamagata lineage was detected with percent positivity of (0.3% and 2.8%, respectively). In 2018, the detection rate of RSV reached 13.6%. However, during the pandemic, RSV detection dropped to 0.5% in 2020 and 2.5% in 2021. Following the pandemic, it increased again to 10.5% in 2022. *Bordetella* cases were reported with percent positivity of 1% in 2023.Our data show that substantial variations in the detection rates of respiratory pathogens were recorded in the kingdom of Jordan between 2018 and 2023. These results highlight the dynamic impact of theCOVID-19 pandemic on respiratory health surveillance in Jordan, emphasizing the need for adaptation to changing patterns.

6715

IL-26 DIFFERENTIALLY AFFECTS THE INFLAMMATORY RESPONSE OF HUMAN MACROPHAGES TO MYCOBACTERIUM TUBERCULOSIS WHOLE CELL LYSATES

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IL-26, a proinflammatory cytokine with antimicrobial properties, contributes to host defense against intracellular Mycobacterium tuberculosis (Mtb) and Mycobacterium leprae, reducing bacteria viability even when they are localized inside macrophages. IL-26 can induce autophagy as well as fusion of phagosomes containing bacilli with lysosomal compartments. Interleukin-26 also activates macrophages and facilitates killing of Mtb. We aimed to evaluate the effect of monomeric and dimeric forms of IL-26 in the response of human macrophages to Mtb whole cell lysate containing proteins, lipids and carbohydrates present within the bacterial cell.Human monocytic cell line THP1 which harbor two reporter systems for NF-kB and IRF, were transformed into macrophages with phorbol myristate. Cells were then treated with monomeric and dimeric forms of human IL-26, and then stimulated with Mtb whole cell lysates from various lineages for 24 hours. We observed an increase in NF-kB activation when cells had been treated with IL-26. The effect was more evident in the response to Mtb lysates from strain CDC 1551 in cells treated with IL-26 dimer, and to lysates from HN 878 in cells treated with IL-26 monomer. No changes in IRF activation were observed after treatment with IL-26 nor stimulation with the lysates.IL-26 skews macrophage polarization towards an M1 phenotype by activating NF-κB pathway. IL-26 is a member of the IL-10 cytokine family with, and induces IL-10, an M2 polarization marker. IL-26 induces neutrophil mobilization and accumulation in the lung which is associated with granuloma disruption in active tuberculosis (TB). The lack of IRF activation, which would lead to production of Type I IFNS associated with active TB, may be due to an absence of PAMPS signaling by live mycobacteria from the phagosomal compartment. An aberrant immune response to Mtb ligands from certain lineages may be mediated by IL-26 in human macrophages.

6716

MAPPING UNDIAGNOSED TUBERCULOSIS PREVALENCE IN SUB SAHARA AFRICA: GEOSPATIAL META-ANALYSIS

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The high burden of undiagnosed tuberculosis (TB) in the community poses a significant challenge for TB control in sub-Saharan Africa (SSA). Interest is increasing in predictive risk mapping for undiagnosed tuberculosis, particularly to scale up early diagnosis and treatment. However, broad geographical analyses are scarce in SSA. We aimed to predict the spatial distribution of undiagnosed TB, including the number of infected people, across SSA. We systematically searched PubMed, CINHAL, Scopus, and PROQUEST from inception to February 20, 2024, for community-based surveys on TB. We extracted data on the prevalence of undiagnosed TB from the surveys and geospatial covariates were obtained from publicly available sources. Bayesian geostatistical model was used to align the data in space and estimate the spatial variation of undiagnosed TB at regional, national, and sub-national levels. Within a Bayesian framework, a logistic regression model was fitted using both fixed covariate effects and spatial random effects to identify drivers of spatial distribution of undiagnosed TB. We identified 66 studies that referenced 233 unique geographical locations from 17 countries. The geospatial analysis showed the mean prevalence of undiagnosed TB ranged from 0.91% in Rwanda to 2.5% in South Africa. It is also estimated there were 0.72 (95% CrI: 0.58 to 1.42) million undetected TB cases in the 17 countries. Substantial national, regional, and local-level variations in the prevalence of undiagnosed TB were also observed. Population density (β: -0.068, 95% CrI: -0.129 to -0.066) was negatively associated with the spatial distribution of undiagnosed TB, while the distance to the nearest health facility (β: 0.332, 95% CrI: 0.273 to 0.482) showed positive association. These findings imply that implementing targeted interventions, such as active case-finding and improving access to health facilities in the identified high-risk areas, could alleviate the burden of undiagnosed TB in SSA. However, additional data collection is necessary to draw further conclusions regarding the prevalence in countries where data is lacking.

6717

DEVELOPMENT OF A NOVEL CELL-FREE CULTURE SYSTEM FOR *IN VITRO* SCREENING OF NEW ANTI-SCHISTOSOMAL MOLECULES USING PURE AND HYBRID *SCHISTOSOMA HAEMATOBIUM*

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Schistosomiasis is a worldwide parasitic disease, with 90% of infections occurring in sub-Saharan Africa. The currently available and effective preventive chemotherapy is praziquantel (PZQ). Despite efforts to control and eliminate the disease, it persists in certain regions, particularly in West Africa. The aim of the present work is i) identify the genetic profile of cercariae emitted by snails collected in the Kayes region of Mali; ii) optimize the transformation of *Schistosoma haematobium* cercariae into newly transformed schistosomules (NTS) and into pulmonary, early and late hepatic and adult stages in long-term in vitro culture; iii) evaluate the efficacy of the schistosomicidal activities of two medicinal plants (*Euphorbia hirta and Tamarindus indica*) on *S. haematobium* and its hybrids. Cercaria were obtained by exposing infested snails collected in the Kayes region to sunlight. PCR was used to determine the species (pure or hybrid) of cercariae. The extracts (*Euphorbia hirta and Tamarindus Indica*) were screened before testing their anti-schistosomal activities on NTS previously cultured on: Dulbecco's Modified Eagle Medium (DMEM) and Roswell Park Memorial Institute medium (RPMI). To these media, we added 20% human serum to test the most appropriate conditions for NTS culture. Molecular identification showed that cultivated cercariae were pure *S. curassoni* and hybrids (*S. curassoni x S. haematobium*). We succeeded in transforming 90% of the NTS (45 NTS/50 cercariae). Cultivation of pure and hybrid parasites revealed that parasites develop respectively into adult worms on complete RPMI medium with 20% human serum, and into early liver stages (LiS) on DMEM medium with 20% human serum after 14 days of cultivation. Screening of both plants showed their richness in secondary metabolites, with higher yields for aqueous extracts. Both extracts at a concentration of 500 µg/mL killed NTS at 72 hours post-exposure as also observed for the reference PZQ control.

6718

IDENTIFYING PLATFORMS FOR OPTIMAL DELIVERY OF A NOVEL PEDIATRIC PRAZIQUANTEL FORMULATION FOR SCHISTOSOMIASIS TREATMENT IN HARD-TO-REACH AREAS AND POPULATIONS IN KENYA - WHAT ARE THE KEY CONTEXTUAL FACTORS?

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A new formulation of praziquantel, arpraziquantel (arPZQ), has been developed for preschool-aged children (PSAC) to fill the treatment gap for this age group in schistosomiasis control and elimination programs. There is now a priority to ensure that the drug reaches all at-risk PSAC in endemic areas, including hard-to-reach areas and populations. This study aimed to determine schistosomiasis treatment-related contextual factors among fishing communities and island populations in the Lake Victoria region (Homa Bay County) in Kenya, and to identify a suitable platform to deliver arPZQ. We conducted a qualitative study using unstructured observations, two case study interviews with parents/caregivers living with disability caring for children ≤5 years,18 focus group discussions (FGDs) with parents/caregivers of children ≤5 years (each with 8-10 participants), and 14 key informant interviews (KIIs) with various government agencies. The data were analyzed using thematic analysis. The results revealed awareness of schistosomiasis among community members but limited knowledge of transmission risk factors. Lake water and open defecation were the main predisposing factors to infection. We observed poor health-seeking behavior in the community due to inaccessibility of quality healthcare services, resulting from health system level, population level, and geographic barriers. Despite these barriers, community members reported positive experiences with previous PZQ mass drug administration (MDAs) and other innovative healthcare programs, and expressed willingness to participate in future MDAs, including with arPZQ. Door-to-door distribution approach by community health volunteers was proposed by parents and key informants as the most feasible platform for community sensitization, mobilization, and arPZQ delivery. To achieve high arPZQ treatment coverage for all at-risk PSAC, and promote ownership and sustainability of the program, the door-to-door approach is the most promising platform to deliver treatment and public health promotion in marginalized hard-to-reach settings in the Lake Victoria Region of Kenya.

6719

LIVER ULTRASOUND FINDINGS BEFORE AND AFTER PRAZIQUANTEL TREATMENT IN UGANDAN PRESCHOOL AGE CHILDREN FROM THE PRAZIQUANTEL IN PRESCHOOLERS (PIP) TRIAL

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Periportal fibrosis is a recognised late-stage manifestation of chronic infection with *Schistosoma mansoni.* Ultrasound changes consistent with schistosomiasis-related morbidity are frequently shown in school age children in endemic areas, with evidence of partial reversibility when treated with Praziquantel (PZQ), the only drug available for the treatment of schistosomiasis. Little is known about the prevalence of periportal fibrosis in preschool age children (PSAC) in endemic areas, or reversibility of ultrasound changes with PZQ treatment. As part of a phase II clinical trial comparing different dosing regimens of PZQ in children age 12-47 months infected with *S. mansoni* in Lake Albert, Uganda ("praziquantel in preschoolers" (PIP) trial), we present results assessing liver ultrasound (US) findings at baseline and at 12 months. Standard ultrasound measures were recorded as per the WHO Niamey Protocol. Children participating in the trial were randomised to receive either (1) 40 mg/kg PZQ at baseline and placebo at 6 months, (2) 40 mg/kg PZQ at baseline and 40 mg/kg PZQ at 6 months, (3) 80 mg/kg PZQ at baseline and placebo at 6 months, or (4) 80 mg/kg PZQ at baseline and 80 mg/kg PZQ at 6 months. Of 283 PSAC seen at both baseline and 12 months, 25 (8.8%) had Image Pattern B with a 'starry sky' appearance at baseline, reducing to 12 (4.2%) at 12 months (p=0.01). 5/283 (1.8%) children had established fibrosis (Image Pattern C) at baseline, and 1/283 (0.3%) had this appearance at 12 months (p=0.22). At baseline 114/283 (40.2%) of PSAC had evidence of periportal thickening as evidenced by abnormally thickened second order portal branches. This reduced significantly to 42/283 (14.8%) at 12 months (p=0.001). Cross-sectional regression analysis of ultrasound results at 12 months showed no significant difference across treatment groups. Incipient schistosomiasis related liver morbidity was detected in the preschool age population enrolled in the PIP trial. There was evidence of susbtantial reversibility of these changes with early praziquantel treatment, with no significant difference based on treatment dose or frequency.

6720

THE IMPACT OF A NEW RAPID DIAGNOSTIC TEST FOR SCHOOL-BASED PREVALENCE MAPPING AND MONITORING AND EVALUATION OF SCHISTOSOMIASIS: A MODELLING STUDY

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In endemic communities where the prevalence of Schistosoma species infection is ≥ 10%, the World Health Organization (WHO) recommends mass drug administration (MDA) with praziquantel. WHO sampling determines infection prevalence through district-level surveys in school-aged-children (SAC). Recently, the Schistosomiasis Oversampling Study (SOS) has advocated for precision mapping—a two-phase sampling strategy—that would target treatment to the sub-district level. A novel circulating anodic antigen rapid diagnostic test (CAA-RDT) could replace the standard tools for mapping (Kato-Katz and urine-filtration microscopy) to better support precision-mapping and thus more efficient drug distribution. We modeled the ability of a CAA-RDT to correctly classify sub-districts with prevalence above or below 10%, and the associated survey costs, across a range of test sensitivities (60-100%) and specificities (95-100%), district prevalence distributions, and sampling strategies (WHO, SOS) for schistosomiasis mapping or monitoring and evaluation (M&E). We then compared these outcomes to those of Kato-Katz and urine-filtration. High specificity was a key determinant of CAA-RDT performance—with a 97% specificity correctly classifying at least 80% of sub-districts across prevalence settings. A test with 100% specificity and 85% sensitivity correctly classified the most sub-districts (87%) through the SOS sampling strategy. The estimated CAA-RDT cost/SAC was always less than Kato-Katz for prevalence mapping under both sampling strategies—$13.23 (WHO) and $24.98 (SOS phase 1 and 2) for Kato-Katz, versus $12.14 and $19.94 for the CAA-RDT. The cost savings are even greater in settings with both *S. mansoni* and *S. haematobium*, which require Kato-Katz and urine filtration, or for M&E which requires two days of sampling for microscopy. The CAA-RDT could be a valuable diagnostic tool for determining schistosomiasis prevalence and supporting M&E to achieve the WHO target to eliminate schistosomiasis as a public health problem in 78 countries by 2030.

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ASSESSMENT OF ALBENDAZOLE SUSCEPTIBILITY IN *FASCIOLA HEPATICA* EGGS FROM ENDEMIC REGIONS OF THE PERUVIAN HIGHLANDS

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Triclabendazole is the main chemotherapy for the control of fascioliasis around the world. However, albendazole (ABZ) is also indicated for *Fasciola hepatica* infections older than twelve weeks. The frequent use of ABZ has led to increasing resistance in Latin America. The present work describes the susceptibility to ABZ in *F. hepatica* from three endemic regions of the Peruvian highlands, assessed using the Eggs Development Inhibition Test. Adult *F. hepatica* were collected from five naturally infected cattle in each of the main abattoirs from Cajamarca, Junín, and Cusco in Peru. The parasites were maintained for one hour in RPMI medium at 37 °C to allow them to oviposit. Aliquots were pooled for each study area constituting a final concentration of 200 eggs/mL with five repetitions per treatment group. Eggs were incubated in darkness at 25 °C for 12 h with ABZ at 0.5 nmol/mL. Untreated eggs served as controls and were incubated with methanol (1%) under the same conditions. All eggs were then carefully washed to facilitate drug removal and kept in the dark at 25 °C for 15 days. After this period, the eggs were exposed to artificial light (1000 lm) to stimulate hatching of the miracidia. The proportions of hatched/developed and undeveloped eggs were evaluated using an optical microscope. For each repetition, between 100-150 eggs were observed and the ovicidal activity was expressed as a percentage. Data are shown as the mean of five repetitions. The unexposed control egg groups had a mean development rate ≥70%. In the Cajamarca collection the ovicidal activity of ABZ was 79.4%, in Junín 97.5% and in Cusco 97.0%. In conclusion, the susceptibility of eggs exposed to ABZ suggests this drug may be an alternative for the treatment of adult *F. hepatica*.

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SYNTHESIS AND ANTISCHISTOSOMAL STRUCTURE-ACTIVITY RELATIONSHIP PROFILING OF *N*-PYRIDAZIN-3-YLBENZAMIDES

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Schistosomiasis is a neglected tropical disease and the second most fatal tropical disease after malaria. By 2021, there were 240 million cases worldwide with 700 million people at risk and 280,000 deaths per annum. *Schistosoma mansoni* and *S. haematobium* species are endemic in Zambia. The drug exclusively remains praziquantel (PZQ), which has been used for over 40 years. This study was based on the structure-activity relationship (SAR) exploration results on Medicines for Malaria Venture's MMV687807 and subsequent SAR explorations e.g. MK1-11. The study introduced an *N*-pyridazin-3-yl heterocyclic ring in lieu of the *N*-phenyl carbocyclic ring thereby editing the *N*-phenylbenzamide (*N*-PhBA) scaffold of MMV687807, MK1-11, etc to the *N*-pyridazin-3-ylbenzamides (*N*-PdzBAs) seeing that *N*-PhBA hits were experimentally found poorly soluble. Six target compounds were successfully synthesized by carbodiimide-mediated amide coupling to the required purity i.e. ≥ 95% cut-off. LC-MS was used as the ultimate criterion of purity and to profile retention time (t_R) while UV-VIS, IR, ^{1}H and ^{13}C-NMR spectroscopy were used for characterization. Compared to the *N*-PhBA hits, *N*-PdzBAs showed much lower potency on *S. mansoni* adult worms and newly transformed schistosomula (NTS) but favourably lower cytotoxicity, better solubility and hydrophilicity. One candidate at 100 µg/mL even at highest dosage only showed 48.33% dead in 72 hrs activity on NTS which was still below the ≥ 50% activity threshold. In addition, other pharmacokinetic properties - measured by both algebraic and *in silico* methods - were found to be better compared to the *N*-PhBAs and calculated solubility (*S*) usually favourably way above the ≥ 100 µM cut-off.

6723

DETECTION OF *SCHISTOSOMA HAEMATOBIUM* CELL-FREE DNA IN URINE SAMPLES STORED ON FILTER PAPERS TO IMPROVE THE DIAGNOSTIC OF URINARY SCHISTOSOMIASIS

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In area under decades of Mass drug administration of Praziquantel, the urine filtration test (UF) currently used to diagnose urinary schistosomiasis lacks sensitivity. As the disease prevalence decreases and the process of elimination is approaching, developing diagnostic tools that could be used to validate the disease elimination, to monitor and evaluate control programs, and also to ensure post-elimination monitoring is becoming essential. This study aimed to improve the diagnosis of urinary

schistosomiasis by detecting cell-free DNA in urine samples stored on filter papers. Urine samples were collected from school-aged children and UF was used to search for *Schistosoma haematobium* eggs. For this study, 119 and 54 urine samples with and without *S. haematobium eggs* were filtered and stored for up to 5 months on Whatman filter papers. DNA was extracted from these filter papers at different time points using cetyl-trimethyl-ammonium bromide (CTAB) and chelex-based method as well as DNA extraction kit. The capacity of filter papers to store *S. haematobium* DNA for several months and the performance of different DNA extraction methods were assessed by PCR. After 3 weeks, 3 and 5 months of storing urine samples on filter paper, specific DNA fragments of *S. haematobium* were amplified on all the 119 (100%) DNA extracts from urine samples found with schistosome eggs; showing that *S. haematobium* cell-free DNA stored on whatman filter paper for up to five months remain detectable with molecular tools. Out of the 54 samples negative by UF, 27 and 23 samples respectively extracted with chelex and CTAB -based method amplified after 3 months of urine storage on filter paper, thus showing the capacity of the molecular tools to detect infections missed by UF. A sensitivity of 100% was recorded for detecting *S. haematobium* DNA in urine samples stored on filter paper. The chelex DNA extraction method appeared less time consuming, cost-effective and easy to perform. It can therefore be used to extract schistosome DNA in urine samples stored on filter paper for molecular diagnostic of urinary schistosomiasis during the elimination and post elimination monitoring.

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FACTORS INFLUENCING THE RESOLUTION OF FEMALE GENITAL SCHISTOSOMIASIS: A LONGITUDINAL STUDY FROM RURAL MADAGASCAR

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Female genital schistosomiasis (FGS) is the chronic manifestation of *Schistosoma haematobium* infection. Complications include infertility, ectopic pregnancy, and increased risk of HIV acquisition, while the association with HPV infection remains unclear. Schistosomiasis is highly endemic in Madagascar.The objective of this study is to assess the rate of resolution and the factors associated with lesion regression following treatment with praziquantel (PZQ) in women of reproductive age.Enrolment of women in this longitudinal study started in 2021 with a 4-year follow-up with scheduled visits at 12-month intervals (12 +/- 3 months). Follow up will be completed in 2024. The study is implemented at three Primary Health Care Centers (PHCCs) in the rural district of Maravoay. Women were invited to participate in FGS screening by colposcopy (CLP). Each woman screened positive for FGS is offered 40mg/kg praziquantel treatment. FGS diagnosis is confirmed through a blind assessment of CLP images by two specialists. Cervical vaginal lavages (CVLs) are collected to assess the role of sexually transmitted infections, such as HPV. Data collected at recruitment were analyzed to estimate the baseline prevalence of the disease.By February 2024, 1,073 women underwent CLP and CVLs were collected at least once. Specifically, 551 women underwent CLP once, 429 had one baseline and one follow up visit, and 93 had two follow up visits. Among 500 women enrolled in 2021, 302 had a final FGS diagnosis: FGS prevalence was 62.6% (189, 95% CI: 56.9-68.1), and 26.5% (80, 95% CI: 21.6-31.8) of women with FGS were also infected with HPV. Our preliminary data show that Madagascar has a high prevalence of FGS among women of reproductive health. The cohort established in this study will contribute to clarify the role of PZQ treatment in this complicated form of schistosomiasis, informing the clinical management of FGS and the development of targeted public health interventions.

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ACCURATE DETECTION OF FEMALE GENITAL SCHISTOSOMIASIS - A NEGLECTED GYNECOLOGICAL TROPICAL DISEASE

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Schistosomiasis is second to malaria as the most devastating tropical parasitic disease in the world. Two main species of Schistosomes, *Schistosoma mansoni*, and *S. haematobium* are predominantly distributed in sub-Saharan Africa, South America, East Asia, and the Middle East. 56 million women are infected with *S. haematobium*, the causative parasite of Female Genital Schistosomiasis (FGS). Schistosomes primarily affect the urinary and intestinal tract, but in FGS parasite eggs can travel and deposit on other tissues such as the female reproductive system resulting in inflammation, causing mechanical blockage, scar tissue, and destruction of anatomical structures. Three-quarters of girls and women with *S. haematobium* infection have FGS making it Africa's most common gynecologic condition. FGS is responsible for up to a three- to four-fold increase in horizontal transmission of HIV/AIDS and likely acts as a cofactor. This study aims to determine FGS infection from field-collected human urine samples from the endemic African country Tanzania via a sensitive and specific molecular approach called loop-mediated isothermal amplification (LAMP). A total of 66 filtered urine samples collected from Tanzania were evaluated via LAMP by amplifying the cell-free species-specific repeat DNA fragment and compared against the PCR amplification. All urine samples were collected after 7-8 days of praziquantel treatment. We have determined the positivity of 14 of 66 urine samples from females with an age range of 17-97 years. All 14 of the samples are LAMP positive, whereas only 4 are PCR positive. LAMP detected *S. haematobium* responsible for FGS from different age groups of females with high sensitivity and specificity. This diagnostic method can be used along with the detection of lessons as hallmark pathophysiology of FGS to develop comprehensive detection and control strategies for FGS in the future.

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DEVELOPING A SIMPLE POINT-OF-CARE LATERAL FLOW ASSAY FOR DETECTION OF *FASCIOLA HEPATICA* DNA IN CLINICAL AND ENVIRONMENTAL SAMPLES

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Fascioliasis is infection with the liver fluke *Fasciola hepatica*. Lack of data about distribution and burden of fascioliasis in endemic regions is associated with the poor performance of currently available diagnostic methods. Therefore, there is an urgent need to improve the diagnostic of Fascioliasis in endemic areas. Molecular diagnostic methods as real time PCR (RT-qPCR) can detect *Fasciola* DNA in clinical and environmental samples with a high sensitivity and specificity. However, RT-qPCR require expensive equipment, highly trained personnel, and reliable power which may be lacking in endemic locations. In these settings, the ideal diagnostic method for resource constrained areas should be accurate, low cost, portable, and easy to perform and interpret. Lateral flow assays (LFAs) are paper-based point-of-care (POC) diagnostic tools that are widely used because of their low cost, ease of use, and rapid format. We have developed the first rapid PCR-based test to detect Fh DNA in lateral flow (LF) strips. For this assay we have developed a PCR-primers that produce Fh dual-labeled PCR amplicons that can be detected in lateral flow strips. To demonstrate the feasibility to detect Fh in low resource setting, we have used a portable miniPCR equipment. We validated detection of DNA of

F. hepatica (Fh) with miniPCR in LF strips using clinical and environmental samples. Our experiments demonstrated that Fh-miniPCR-LF assay has high sensitivity and specificity (comparable to standard RTqPCR assay) and the assay can be performed in less than 1 hr. To validate the new assay, we used clinical samples obtained from an endemic area. Our results showed 100% correlation with qPCR results to distinguish positive and negative samples. In addition, in this work we described a simple and inexpensive DNA extraction method that can be used in combination with the miniPCR to detect *Fasciola* in remote areas. Therefore, our results will be useful to improve diagnosis of *Fasciola* and also to develop similar strategies for detection of other parasitic infections in remote areas.

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ENHANCING DETECTION AND MONITORING OF SCHISTOSOMIASIS USING FLOW, A URINE-BASED ANALYTE PRE-CONCENTRATION TECHNOLOGY

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Diagnosis of schistosome infection at the point-of-care using a parasite antigen would improve sensitivity of current testing methods, which use urine and stool microscopy, to both increase access to testing and further efforts toward elimination of schistosomiasis. Salus Discovery has developed a new technology, termed Flow, that expands upon the operational concepts of lateral flow assays (LFAs) by enabling pre-concentration of analytes from 20 mL of urine into 100 µL (i.e., up to 200-fold pre-concentration) prior to detection on an LFA. Importantly, Flow can be performed by minimally trained field workers as it requires < 1 min of hands-on time, no pipetting or centrifugation, and can be either read visually or scanned by a portable reader. One schistosome target of interest, the circulating anodic antigen (CAA), is detectable in serum and urine for all major human schistosome species but testing for it still requires time-consuming and resource-intensive sample preparation and/or pre-concentration so is currently limited to being performed in a laboratory. Our team has recently sought to adapt our Flow technology for POC diagnosis of schistosomiasis using CAA quantified in bio-banked urine samples collected from 30 individuals in an *Schistosoma haematobium* endemic region in north-western Tanzania. Results from this recently published limited clinical study with a prototype (i.e., non-optimized) Flow device indicate that the assay will achieve sensitivity and specificity as targeted in the WHO target product profile (TPP). We've since optimized the Flow device and are currently evaluating its performance using fresh urine samples collected from over 100 individuals in the same *S. haematobium*-endemic region in Tanzania. Participant positivity is determined by quantitative laboratory-based serum and urine CAA testing and results are being compared to urine egg counts. We expect to complete all field testing by June 2024 and will be able to present the results for the performance of the optimized Flow device at the ASTMH conference in November 2024.

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RISK FACTORS FOR SCHISTOSOMIASIS CURE FAILURE/ REINFECTION AMONG PRE-SCHOOL-AGED CHILDREN 12 MONTHS AFTER TREATMENT IN UGANDA

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Schistosomiasis is caused by blood flukes called Schistosoma and poses significant health risks, especially for young children. Transmission occurs via contact with contaminated fresh water. Praziquantel (PZQ) is an effective treatment, but in highly endemic regions like the Lake Albert region of Uganda, both cure failure and reinfection following PZQ are common. There are limited data on PZQ cure failure/reinfection rates among preschool-aged children (PSAC). Various factors such as genetics, environment, water contact frequency, and socio-economic conditions may contribute to cure failure/reinfection. A secondary analysis of the Praziquantel in Pre-Schoolers (PIP) trial data was conducted, involving children aged 12-47 months positive for S. mansoni at baseline. Schistosomiasis infection was assessed via stool Kato-Katz (KK) microscopy at baseline, Week 4 and 12 months post-PZQ. Children received either 40 mg/kg or 80 mg/kg PZQ at baseline and received either a repeat dose or placebo after 6 months. Cure failure/reinfection was determined by the proportion of children positive by KK 12 months post-baseline treatment. After adjusting for treatment arm, logistic regression showed that odds of cure failure/reinfection was higher among children aged 2.1-3 (OR=2.8, CI 1.45, 5.55 p=0.002) and >3years(OR=3.1 CI1.6,5.73 p=0.001) and with more frequent visits to Lake Albert (OR= 3.3 CI 1.89, 5.9 p=<0.001). Those with better educated parents had lower odds of cure failure/reinfection at 12 months (OR=0.37, CI 0.23, 0.56 p=<0.001). Malaria or HIV co-infection, anemia, feeding practices, and latrine type showed no significant relationship with cure failure/reinfection risk. As PSAC grow, contact with contaminated water sources increases, emphasizing the importance of clean water and latrine access to reduce reinfection risk. Targeted interventions are crucial for schistosomiasis control in PSAC. Findings for how Treatment impacts reinfection risk by 12 months post PZQ will be published separately.

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INVESTIGATING THE PREVALENCE, INTENSITY, AND CONTRIBUTING FACTORS OF *SCHISTOSOMA MANSONI* INFECTION IN ALMATA DISTRICT, TIGRAY, NORTHERN ETHIOPIA

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Intestinal schsitosomiasis caused by *Schistosoma mansoni* continues to be a significant public health problem in Ethiopia. Hence, this study aimed to investigate the prevalence, intensity and contributing factors of *S.mansoni* infection in Almata district, Tigrai, Northern Ethiopia. A community based cross sectional study design was employed and 1762 participants were enrolled from five clusters in Alama district. Questionnaire was used to assess socio-demographic and other risk factors. Stool sample was collected and examined using Katho katz technique to investigate eggs of *S.mansoni* and determine intensity of infection. The data were analyzed using SPSS version 25. The survey included 941 (53.4%) females and 821 (46.6%) males. Participants' ages varied from 5-80 years, with a median age of 25 years (IQR=27). In this study, the overall prevalence of S.*mansoni* among study participants was 379 (21.5%) and males were predominantly infected, 204 (11.6%), than their female counter parts with statistically significant difference (χ^2= 10.146, P-value=0.001). The proportion of infection was higher among participants lying in the age groups 10-14 and 20-29 years accounting for 7.4% and 3.3% of the infection, respectively. The mean egg count among the infected study participants was 146.82 eggs per gram of feces (epg) + (243.17 SD), and majority 249 (65.7%) had

light (1-99 epg) followed by 106 (28.0%) moderate (100-499 epg) infection. The overall intensity of *S.mansoni* infection was higher among males (180 EPG) than females (108.2 EPG). Factors such as being in Waja cluster (AOR:8.9; 95% CI, 3.5-23.2; P< 0.001); lying in the age groups 10-14 (AOR:6.0, 95% CI: 3.1-11.7, P<0.001), 15-19 (AOR:5.8, 95% CI:2.8-12.2, P<0.001), and 20-29 (AOR:3.5, 95% CI:1.8-6.8; P<0.001) years old; having direct contact with water while crossing (AOR: 2.4, 95% CI: 1.5-3.8, P<0.001); and swimming (AOR: 1.4, 95% CI: 1.01-2.0, P=0.035) were shown to be significantly associated with *S.mansoni* infection. This study indicated that there is a notable burden of the disease in the area and implementing public health interventions are recommended.

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NOVEL INTERVENTION STRATEGIES FOR SCHISTOSOMIASIS ELIMINATION

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Elimination of schistosomiasis as a public health problem by 2030 is a declared goal of the WHO. Pemba Island, Tanzania, achieved this goal in 2017 and now proceeds towards transmission interruption. The existing spatial heterogeneity of *Schistosoma haematobium* infections calls for targeted interventions. In the SchistoBreak project, implemented from 2020-2024, new adaptive intervention approaches were investigated for their contribution to elimination. In low prevalence areas, a new schistosomiasis surveillance-response approach, including test-treat-track-test-treat (5T) and snail control activities, was assessed for its sensitivity and potential to prevent recrudescence. In hotspot areas, the impact of a multidisciplinary intervention package, consisting of mass drug administration, behavior change communication, and snail control measures was investigated. Annual school- and household-based cross-sectional surveys were conducted to monitor *S. haematobium* prevalence and infection intensities, schistosomiasis-related knowledge, attitudes and practices, and economic status. Each year, more than 6000 individuals were surveyed. The 5T strategy was very useful to identify and treat infected individuals. Across the 3 years of implementation, the surveillance-response approach showed a sensitivity of 43% and the low prevalence levels were mostly maintained. In hotspots, prevalences were significantly reduced in schoolchildren and showed a decreasing trend in the community in Year 1 and 3, but slightly increased in Year 2. Hotspot areas were hallmarked by a large number of poor and rural households, and waterbodies containing *Bulinus*. Behavior change communication significantly improved knowledge and attitude scores of exposed schoolchildren. The overall prevalence remained ~1% across all years, with heavy intensities ≤0.3%. The novel adaptive intervention approaches did not result in interruption of transmission within 3 years. Yet, important insights and evidence were generated that can inform control program decisions and the development of schistosomiasis elimination guidelines.

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SOCIO-ENVIRONMENTAL FACTORS AFFECTING THE RISK OF HUMAN FASCIOLIASIS IN CENTRAL VIETNAM

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Fascioliasis, infected by consuming contaminated vegetables and water with *Fasciola* parasites, has caused public health concerns in Central Vietnam, which accounts for 93% of the national prevalence of the disease. Scant attention, however, has been paid to the influences of socio-environmental factors on the infection risk. To bridge the research gap, a cross-sectional survey was conducted in 2023, involving 2,500 participants from 10 communes in four Central Vietnam provinces for ELISA-based blood test for infection status. A subset of these participants was also invited for questionnaire surveys to understand their knowledge about fascioliasis, eating and living habits, and practice to prevent the infection. Household locations were collected using smart phones with Global Positioning Systems capabilities to analyze possible environmental influences of land uses, derived from the Sentinel-2 remote sensing products, on infection risk. The results showed that the associated social risk factors were gender as female (OR=2.395, 95% CI: 1.78-3.22), occupation as farmer (OR=7.57, 95% CI: 2.24-25.59), eating raw vegetable (OR=1.80, 95% CI: 1.20-2.69), and drinking unboiled water (OR=2.935, 95% CI: 2.19-3.93). Importantly, participants with higher knowledge scores did not effectively implement preventive practices. Geospatial analysis of environmental factors showed that individuals' homes surrounded by forest might be less susceptible to infection. Nevertheless, association with water was not consistent across all areas, with some closer to waterbodies more likely to be infected. This study underscores the need for tailored intervention measures that consider specific socio-environmental characteristics of each area, to develop effective risk mitigation plans for foodborne trematode infection.

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DIET OF SCHISTOSOME VECTORS INFLUENCES INFECTION OUTCOMES

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Schistosome parasites cause chronic infections in their vector hosts, freshwater snails, and continually produce infectious cercariae throughout the snail's life. The resource-intensive nature of this relationship suggests that snail diet could greatly impact the disease dynamics of the system. Enhanced nutrition could favor snail immunity, or could favor establishment and reproduction of the parasite. Our study aimed to determine the effect of diet on: (1) snail susceptibility to infection and (2) cercaria production. We fed *Biomphalaria sudanica* snails either a strict lettuce (low nutrient) or pellet (high nutrient) diet for two generations before exposing them to *Schistosoma mansoni*. We used two parasite strains, one that is incompatible and another that is compatible with the snails. When exposed to incompatible parasites, diet did not affect snail susceptibility, as few snails were infected overall. When challenged with the compatible parasites, snails fed the high nutrient diet were more susceptible to infection than their low nutrient fed counterparts. The high nutrient fed snails also produced more cercariae than low nutrient fed snails, but this advantage was lost after the initial assessment at 8 weeks. To determine how diet effects cercariae production post-infection, infected snails were either kept on their initial diet or switched to the other diet. This experiment showed that snails switched from a low to high nutrient diet produced more cercariae than those remaining on the low nutrient diet and similar numbers to those remaining on the high nutrient diet. Unexpectedly, the high to low nutrient group initially produced more cercariae relative to controls, but the pattern reversed after initial assessment. This study showed that resources can impact the susceptibility of the vector snail and the reproductive capacity of intramolluscan schistosomes, with higher nutrients favoring parasite establishment and reproduction, highlighting the plasticity of susceptibility phenotypes. This data can aid predictions of how future environmental changes and resource availability may impact schistosomiasis transmission.

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FACTORS ASSOCIATED WITH NATURAL INFECTION BY *FASCIOLA HEPATICA* IN THE MAIN DAIRY BASIN OF CAJAMARCA IN NORTHERN PERU

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Cajamarca is an important region of Peru for dairy production. Dairy animals in this area are often affected by fascioliasis caused by *Fasciola hepatica*. Fascioliasis negatively affects the productivity parameters of livestock. This study aimed to estimate the prevalence of natural *F. hepatica* infection in cattle and determine animal husbandry factors associated with the infection. Fecal samples from cattle in farms in the Cajamarca Region, Peru were collected between March 2023 and March 2024. Animals were raised in extensive rearing conditions. Cattle demographics and wellbeing using a score based on body condition (5 points maximum) were evaluated. Samples were analyzed using the simple sedimentation technique for differential egg counting. 606 cattle from 97 farms were included in the study. The prevalence of *F. hepatica* infection was 27.7% ($I.C._{95\%}$ 24.1 - 31.3%) (168/606). The mean intensity of infection was 6.1 (S.D. 9.9) eggs per gram (e.p.g.) of stool and 84.5% had infection intensities ≤10 e.p.g. which are considered low. Most *F. hepatica* positive animals were female (75%), adults (51.8%), and had a wellbeing score between 2.5 and 3 points (86.3%). The most common breed was creole (41.1%). There was no statistically significant association between *Fasciola* infection status and demographic/wellbeing score characteristics. The chronic infection of cattle by *F. hepatica* at the low intensity encountered did not appear to affect the general condition of the animals or be influenced by the other variables analyzed.

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ENVIRONMENTAL DNA OF SCHISTOSOME PARASITES REVEALS POSSIBILITY OF WIDENING THE SNAIL VECTOR SPECTRUM IN ENDEMIC AREAS UNDER CLIMATE CHANGE CONDITIONS IN NIGERIA

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Climate change has a significant impact on schistosomiasis, leading to changes in cercariae shedding patterns, changes in the range of definitive hosts for schistosome species, and an increase in the number of countries at risk. Therefore, it's important to broaden the range of techniques used to find possible sites of transmission for schistosomiasis surveillance in endemic communities. This includes detecting parasite and schistosome environmental DNA (eDNA). In October and December of 2023, and February 2024 seven locations in Asamu, Ile-tun tun, Alagbon, and Eleyele in Southwest Ibadan, Oyo State, Nigeria, were sampled for schistosome snail intermediate hosts, *Bulinus* and *Biomphalaria* species. Snails were examined morphologically with a stereomicroscope and molecularly by qPCR. Water samples were also analysed by qPCR for eDNA of snail vectors *Bulinus* and B*iomphalaria*, and *Schistosoma spp*: *haematobium* and *mansoni.* Ct values were determined for each sample and the ultimate DNA quantity of the target samples ascertained. A total of 268 snails and 7 water samples were collected from the study sites. Microscopic morphological analyses revealed the presence of *Bulinus* (5) and *Biomphalaria (3)* species, with the majority being *Radix natalensis* (*Lymneae natalensis*), *Melanoides tuberculate, Indoplanorbis exustus, Physa acuta* and *Aplexia waterloti.* Standard cercarial shedding was negative. Water samples from the sites were negative for the eDNA of *Bulinus* and *Biomphalaria* species but were positive for *Schistosoma haematobium* and *S. mansoni*. The qPCR amplification success for parasites in the snail samples was 79% and 89.5%, respectively. The other snails from the sites were positive for schistosome spp. DNA, indicating the snails may be vectors. *Lymnea natalensis* from Asamu (100-120%) had the highest amount of *S. mansoni* DNA , while *Aplexa waterloti* had the highest amount of *S. haematobium* (>100%). These data correspond to similar reports from some African countries, of deviations from schistosome normal cercarial shedding pattern and snail host spectrum. Our data can be used to develop schistosomiasis monitoring in endemic areas.

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SUITABLE COMMUNICATION STRATEGIES PRIOR TO THE INTRODUCTION OF A NOVEL PEDIATRIC TREATMENT OPTION < SCHISTOSOMIASIS IN KENYA

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Approximately 50 million preschool-age children (PSAC) in Africa need treatment for schistosomiasis but are excluded due to lack of a suitable child-friendly medication. The Pediatric Praziquantel Consortium has developed arpraziquantel, a novel paediatric treatment option for PSAC. In advance of its roll-out, we conducted a social science study to inform implementation. We conducted a cross-sectional study in four villages in two purposively selected Kenyan counties: Homa Bay and Kwale. We conducted 17 in-depth interviews with community opinion leaders, 21 parents/guardians of PSAC and 28 healthcare workers. Ten focus group discussions were held with parents/guardians of PSAC and seven with community health volunteers (CHVs). The aim was to gather information on preferred sources of information about the new drug prior to pilot roll-out. Thematic data analysis was performed. Participants indicated that their traditionally prefered methods of receiving information on treatment programmes for other diseases for PSAC were CHVs, health facilities, radio, road shows and community meetings. Caregivers appreciated those platforms and stated they would, in addition, like to receive information about the PSAC schistosomiasis medication through village leaders, schools, and religious gatherings. Messages to participants during sensitization should include information on the disease effects, signs and symptoms, myths and misconceptions, how to administer the new drug, it's safety and possible side effects. Participants preferred sensitization, shortly before and during the intervention. Our results demonstrate that community members obtain health information concerning their children from multiple sources. To reach audiences with preferences for different information sources and message formulations, we recommend designing a sensitization strategy that employ a variety of channels. Emphasis on key messaging about the drug's safety is needed to build trust in advance of its roll-out

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ENDEMIC COUNTRY LABORATORY QUALIFICATION OF *SCHISTOSOMA HAEMATOBIUM* ANTIBODY BIOMARKERS IN KENYA

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In response to the World Health Organization's 2021-2030 Roadmap for Neglected Tropical Diseases emphasis on the need for improved

diagnostic tests, we explored several strategies to identify recombinant antigens suitable for *Schistosoma haematobium*-specific antibody tests. We utilized serum epitope repertoire analysis (SERA), a platform that uses a 12-amino acid peptide library display followed by next generation sequencing with proprietary informatics to screen unique reactivity to sera. We identified two candidate diagnostic peptides. One peptide mapped to *S. haematobium* saposin (SAP)-1 protein. Because the Sh_SAP1 protein sequence is short, we used the whole protein sequence without its signal peptide to express the protein. The other peptide mapped to a hypothetical protein which was not suitable for expressing as a whole protein. Instead, we created a synthetic protein consisting of four repeats of the peptide sequence (rSh_quadruplet). The rSh_SAP1 ELISA, which detects specific IgG1 antibody, had a sensitivity 85% and a specificity of 97%. The rSh_quadruplet ELISA, which detects specific IgG4 antibody, had a sensitivity of 81% and a specificity of 96%. Further evaluation of the ELISAs was done using a different sample set (50 egg positive persons and 52 controls) in Kisumu, Kenya, an endemic country laboratory. The ELISAs conducted in Kisumu mirrored the results from CDC Atlanta labs, meeting or closely approaching the sensitivity and specificity targets of the WHO schistosomiasis target product profile for interruption of transmission and surveillance. We also evaluated samples from 37 individuals at baseline, 6 months, and 12 months after praziquantel treatment using the rSh-quadruplet ELISA, anticipating IgG4 responses would be most likely to decline. Serum samples from participants who were *S. haematobium* egg positive at baseline had lower specific IgG4 antibody levels after 12 months ($p < 0.0001$), although some samples showed an increase at 6 months, followed by a decrease after 12 months. These antigens have the potential to fulfill unmet programmatic needs for schistosomiasis programs.

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ETIOLOGY OF ANEMIA IN THE CONTEXT OF *SCHISTOSOMA MANSONI* INFECTION AMONG PRE-SCHOOL AGED CHILDREN FROM LAKE ALBERT, UGANDA

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There is a significant global burden of disease due to anemia among young children. Among older children and adults, schistosomiasis has been shown to cause both iron deficiency anemia (IDA) and non-iron deficiency anemia (NIDA), the latter largely due to anemia of inflammation, yet this has not been studied in young children. In this study, 345 Ugandan children aged 12 to 48 months infected with egg patent *Schistosoma mansoni* were recruited from villages along Lake Albert, Uganda. Infection intensity was determined by Kato Katz quantifying egg counts per gram of stool (EPG). WHO age-adjusted cutoffs for hemoglobin (< 11 g/dL) were used to determine the presence of anemia. Among anemic children, serum ferritin levels were used to classify children as having IDA (≤ 30 ng/mL) or NIDA (> 30 ng/mL). CRP was measured as a non-specific marker of inflammation. We employed multivariate regression models to assess the relationship between S. *mansoni* infection intensity and anemia etiology. Overall, 23.5% of children had IDA and 32.5% had NIDA. Higher continuous *S. mansoni* EPG was associated with higher odds of IDA (OR 1.36, 95% CI 1.12-1.65, p=0.002) and NIDA (OR 1.23, 95% CI 1.03-1.46, p=0.019) compared to no anemia, after adjusting for age, sex, SES, and malaria. CRP was significantly higher among individuals with NIDA (5.0 mg/L) compared to both no anemia and IDA (0.7 and 1.5 mg/L respectively, $p < 0.0001$). Occult blood loss in stool was significantly more common among children with IDA compared to no anemia (42.1% v. 20.7%, p=0.003). Anemia in pre-school aged children with schistosomiasis is due to both IDA with occult blood loss and NIDA with ongoing immune activation and systemic inflammation. Despite the fact that the WHO recommends including children ages 1-4 in mass drug administration (MDA) campaigns, most are still excluded due to a) limited dissemination of this recommendation, b) lack of widely available pediatric formulation, and c) provision of school rather than community based MDA, missing pre-school aged children. Efforts should be made to better include this vulnerable age group to mitigate morbidity.

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TCBS POSITIVE VIBRIO SPECIES IN WATER SAMPLES OF PRE-URBAN AND PERI-URBAN MAPUTO, MOZAMBIQUE

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Despite Maputo's exponential expansion in the last few decades, Mozambique's capital still experiences challenges providing clean water and stable housing to thousands of inhabitants lining its periurban neighborhoods. We performed an observational cross-sectional analysis of data from periurban residential areas of Maputo in spring 2014, prior to the implementation of the Maputo Urban Transformation Project. It was hypothesized that water samples would exhibit increased risk for bacterial contamination, including diseases with epidemic risk such as Vibrio cholerae. Water runoff samples from informal settlements (n=89) were collected in the 25 de Junho A and Inhagoia neighborhoods of Maputo, with locations informally geotagged and labeled by location type (residential runoff, agricultural runoff, piped water), point-of-care pH and oxidation reduction potential, and thiosulfate-citrate-bile salts-sucrose (TCBS) agar growth. A total of 33 samples (37%) were TCBS positive, with positive specimens seen in all three location types including piped drinking water. Spatial analysis was performed using ArcGIS in order to map cluster and outlier cases, as well as hot and cold spots for positive specimens. A cluster of 25 specimens was described as a hot spot with 99% confidence, proximal within a simultaneous distance of 0.3km to an Infulene River wastewater treatment placement as well as a central factory for a local 2M beer brewing company. These studies suggest that Vibrio species and other gram-negative coliform bacteria remain endemic and prevalent in Maputo informal settlement housing. As risk amplifiers such as natural disasters place Maputo's settlements at risk for outbreaks of enteric disease, future studies should assess point-prevalence sites of Vibrio cholerae. These studies could consider high-risk zones such as clusters near industrial sites, as well as water, sanitation, and hygiene interventions that can accompany the Urban Transformation Project's changes.

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WATER QUALITY AND OCCURRENCE OF ENTERIC BACTERIA AND VIRUSES IN ASIPA RIVER, OYO STATE, WESTERN NIGERIA

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Epidemiological evidence substantiates the fatality rates associated with poor Water, Sanitation, and Hygiene (WaSH) practices, in developing nations like Nigeria. The investigation aimed to evaluate the water quality and distribution of enteric bacteria and viruses in Asipa River in Oyo, Nigeria. This study assessed the Knowledge Attitude Practices and Beliefs (KAPBs) of the residents' utilization of Asipa River, investigated the physicochemical characteristics, identified the genotypic variants of enteric organisms isolated, and evaluated the impact of Zinc Oxide Nanoparticles (ZnO-np) treatment on water samples. Six hundred structured questionnaires were utilized to evaluate the KAPBs. Standard procedures were employed to determine the water samples' physicochemical characteristics, total and thermotolerant coliforms. Polymerase Chain Reaction and Sanger sequencing were employed for molecular identification, while ZnO-np

treatment was conducted using established protocols. Results revealed 26.4% of the participants observed sewage disposal within the river, 51.8% utilized the river for domestic and irrigation activities, and 60.2% reported diarrhea from the associated use of the river. The concentrations of dissolved oxygen and chemical oxygen demand (mg/L) varied between 1.2 and 6.4 and 30 and 75, respectively, beyond the limitations set by the World Health Organization. The total and thermotolerant coliform counts (CFU/100mL) ranged from 5.0 x 10^2 to 1.3 x 10^4, and 2.0 x 10^2 to 8.5 x 10^3, respectively. Forty-three bacteria were confirmed and sequences were deposited at the National Centre for Biotechnology Information, USA, and assigned accession numbers. Distribution of enteric viruses reported Sapovirus, Human rotavirus, and Astroviruses presence in 44%, 22%, and 33% respectively in the water samples. ZnO-np treated water significantly reduced in physicochemical parameters ($p<0.05$). Conclusively, Asipa River is contaminated with enteric bacteria and viruses that are of public health significance requiring treatment, implementation, and monitoring for regulatory compliance.

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LATRINE AVAILABILITY AND UTILIZATION ASSESSMENT IN PRIMARY SCHOOLS OF MERHABETE, ETHIOPIA: A MIXED METHOD STUDY

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While the vast majority of previously trachoma-endemic districts have been controlled in the past two decades, a few hot spots remain. Merhabete District in Ethiopia still has active disease (TF) prevalence ranging from 30-50% in children. As hygiene and sanitation are thought to play major roles in transmission, we assessed latrine availability and utilization at primary schools in the district. A simple random sample of 20 schools was chosen in the Kebele Elimination of Trachoma for Ocular Health (KETFO) study catchment area. At each school, two students, two teachers, and one school principal participated, for a sample size of 100. In-depth interviews were conducted to identify factors that influence latrine utilization. Latrines at each school were observed for availability and utilization with a checklist. Qualitative and quantitative data were analyzed in ATLAS.ti 24 and SPSS, respectively. Among the 20 schools, one, nine, and 10 had zero, one, and two latrines, respectively. In schools with latrines, 79% (15/19) had improved pit latrines, 53% (10/19) had latrines that needed maintenance, and 45% (9/20) had piped water. 47% (9/19) of latrine pits were covered in feces, and 74% (14/19) had feces present outside of the toilet around the latrine compound. The overall latrine utilization at schools was 26% (5/19). 68% (58/85) of participants said that latrine use reduces communicable diseases: trachoma (68%) and diarrhea (59%) were the most frequently cited. Challenges faced in latrine utilization were absence of functioning toilets, inadequate toilets, water shortage, and lack of knowledge on toilet use. Solutions proposed included providing water and soap to the schools through community contributions, building and renovating appropriate toilets through partner mobilization, raising awareness on latrine utilization, and hiring toilet cleaners and school guards. In the study area, the utilization of latrines at schools is influenced by multiple factors including absence of functioning toilets. Stakeholders including MOE and MOH should collaborate to provide appropriate hygiene facilities and raise knowledge about toilet use.

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INTERACTIONS BETWEEN WATER, SANITATION, AND HYGIENE (WASH) AND MOSQUITO DYNAMICS IN WESTERN KENYA: IMPLICATIONS FOR DIARRHEAL AND MALARIA DISEASES

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Despite the implementation of Water, Sanitation, and Hygiene (WASH) and malaria vector control programs, diarrheal illness and malaria are the leading causes of morbidity and mortality among children under 5 years in Kenya. Since the transmission of diarrhea and malaria may interact with each other through outdoor latrines, we conducted a novel study on integrating WASH practices with mosquito dynamics. Our aim was to evaluate the risk posed by the use of outdoor latrines on diarrheal illness and malaria in a malaria-endemic area of western Kenya. The specific aims were to 1) explore factors associated with outdoor latrine use during the daytime, at night, and early morning, 2) examine the impact of latrine use behaviors on the risks of diarrheal and malaria diseases, and 3) explore factors influencing the abundance of adult *Anopheles* mosquitoes in latrines and houses. We conducted cross-sectional population-based surveys and malaria tests for individuals aged 4 years or older (n=531). Additionally, monthly mosquito sampling was carried out in paired houses (n=50) and outdoor latrines (n=50) using Prokopack aspirators from July 2023 to March 2024. Latrines were more frequently used by adults than children, for defecation than urination, and during the daytime and early morning than at night. A generalized linear mixed models (GLMMs) showed that individuals who felt safe between houses and latrines used latrines more at night than those who did not (urination: aOR=6.65, 95%CI: 1.95, 22.69; defecation: aOR= 5.00, 95%CI: 2.33, 10.71). No association was observed between latrine use and diarrheal or malaria diseases (diarrhea: aOR=0.77, 95%CI: 0.38, 1.57; malaria: aOR= 1.42, 95%CI: 0.74, 2.75). The negative binomial GLMMs showed that pit latrines, having bath space, and iron walls increased abundance of *An. gambiae s.l.* in latrines compared to ventilated improved pit latrines, non-bath space and brick/cement. Only pit latrines increased the abundance of *An. funestus s.l*. No significant factors were associated with the abundance of *Anopheles* mosquitoes inside houses. Further studies will be necessary to achieve a comprehensive understanding.

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HOUSEHOLD RISK FACTORS ASSOCIATED WITH HOSPITALIZED DIARRHEAL PATIENTS IN ULAANBAATAR, MONGOLIA

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Diarrheal disease is common in Mongolia yet risk factors for infection and hospitalization are not well understood. This study examined hospitalized diarrheal patients (n=120) at the National Center for Communicable Diseases (NCCD) in Ulaanbaatar. From February 2017 to January 2018, medical staff administered a questionnaire to patients or caregivers. Patients were largely from Tov province, including Ulaanbaatar (n=115; 95.8%), female (n=62; 51.7%) and male (n=58; 48.3%), and aged ≤ 1 year to 27 years. Prior illness duration was primarily 2-4 days (n=79; 65.8%). Symptoms included headache (n=28; 23.3%), fatigue (n=12; 10%), nausea (n=11; 9.2%), abdominal cramps (n=19; 15.8%), weight loss (n= 95; 79.2%), vomiting (n=18; 15%), fever (n=99; 82.5%), and diarrhea (n=117; 97.5%). Patient were using antibiotics (n=88; 73.3%), antiparasitic drugs

(n=93; 77.5%) and/or home remedies (n= 55; 45.8%). Housing included ger/yurt (n= 38; 31.7%), house (n=38; 31.7%), and apartment (n=44; 36.7%). Household animal ownership was not common (n=14; 11.7%). Most households used piped water (n=45; 37.5%), well water (n=31; 25.8%), tanker truck (n=14; 11.7%), or a combination of drinking water sources. Sanitation varied between flush/pour flush toilet (n=31; 25.8%), pit latrine w/slab (n=47; 39.2%), pit latrine w/o slab (n=1; 0.8%), composting/biotoilet (n=3; 2.5%), bucket/container (n=5; 4.2%), bury (n=3; 2.5%), or multiple services. One household also used open defecation (n=1; 0.8%). Reported handwashing differed by activity with 18.3% (n=22) of patients or caregivers washing hands before cooking, 22.5% (n=27) before feeding a child, 54.2% (n=65) before eating, 3.3% (n=4) after animal contact, and 26.7% (n=32) after bathroom visit. Households reported consumption of raw or undercooked meat (n=21; 17.5%), unpasteurized milk/milk products (n=22; 18.3%), unwashed/raw vegetables (n=7; 5.8%), and unwashed/raw fruit (n=20; 16.7%). Recognizing risk factors for diarrheal disease, particularly in children, can lead to prevention efforts to reduce hospitalization and household illness.

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MERCURY LEVELS IN HAIR OF PREGNANT WOMEN IN TUMBES, PERU: A CROSS-SECTIONAL STUDY

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Mercury, a potent toxicant posing serious risks to human health, particularly for pregnant women and young children, is widely present in the environment due to artisanal and small-scale gold mining (ASGM). The Puyango-Tumbes River, the main source of freshwater for the Tumbes region of Peru, is known to be contaminated with Hg from ASGM sites upstream in Ecuador. This study aimed to characterize hair total mercury (THg) concentrations among 148 pregnant women across 24 communities in Tumbes. Through purposeful sampling, we classified communities into three exposure risk zones. The Puyango-Tumbes watershed group included communities located within 5 km of the Puyango-Tumbes River, where river water is used for irrigation and freshwater fish consumption is common. The Coast group included a Pacific Coast fishing district approximately 30 km from the Puyango-Tumbes River mouth, where there is potential mercury exposure from seafood. The Zarumilla group comprised non-coastal communities in a different watershed unaffected by mining. The mean THg concentration was 2.08 µg/g ± 1.36, with 45% of participants (67/148) exceeding exposure limits (> 2.0 µg/g). The median THg level was 1.84, with an interquartile range (IQR) from 1.01 to 2.83. Median THg levels varied significantly among regions, with the Puyango-Tumbes River group showing the highest levels (2.72 µg/g; IQR 1.66, 3.55) compared to Zarumilla (1.61 µg/g; IQR 0.67, 2.63; p = 0.001) and to the Coast (1.71 µg/g; IQR 1.13, 2.50; p = 0.01), suggesting a higher probability of mercury exposure for pregnant women residing near the Puyango-Tumbes River. This association remained significant after controlling for potential confounding factors. Our findings underscore the importance of identifying high-risk regional populations and ensuring continuous biomonitoring of the Puyango-Tumbes River watershed.

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A MECHANISTIC MODELING APPROACH TO ASSESSING THE SENSITIVITY OF OUTCOMES OF WATER, SANITATION, AND HYGIENE INTERVENTIONS TO LOCAL CONTEXTS AND INTERVENTION FACTORS

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Diarrheal disease is a leading cause of morbidity and mortality in young children. Water, sanitation, and hygiene (WASH) improvements have historically been responsible for major public health gains by reducing exposure to pathogens, but many individual interventions have failed to consistently reduce diarrheal disease burden. Analytical tools that can estimate the potential impacts of individual WASH improvements in specific contexts would support program managers and policymakers to set targets that would yield health gains. To understand the impact of WASH improvements on diarrhea, we developed a disease transmission model to simulate an intervention trial with a single intervention. We accounted for contextual factors, including preexisting WASH conditions and baseline disease prevalence, as well as intervention WASH factors, including community coverage, compliance, efficacy, and the intervenable fraction of transmission. We illustrated the sensitivity of intervention effectiveness to the contextual and intervention factors in each of two scenarios in which a 50% reduction in disease was achieved through a different combination of factors (higher preexisting WASH conditions, compliance, and intervenable fraction vs higher intervention efficacy and community coverage). Achieving disease elimination depended on more than one factor, and factors that could be used to achieve disease elimination in one scenario could be ineffective in the other scenario. Community coverage interacted strongly with both the contextual and intervention factors. For example, the positive impact of increasing intervention community coverage increased non-linearly with increasing intervention compliance. Additionally, counterfactually improving the contextual preexisting WASH conditions could have a positive or negative effect on the intervention effectiveness, depending on the values of other factors. When developing interventions, it is important to account for both contextual conditions and the intervention parameters. Our modeling approach can provide guidance for developing locally specific policy recommendations.

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EXPLORING PERCEPTIONS AND UNDERSTANDING OF ORAL HEALTH: A STUDY ON ORAL GINGIVITIS AMONG UNDERGRADUATE STUDENTS IN IBADAN

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Abstract:Assessing oral health is crucial for organizing community-based programs aimed at promoting the health system. This includes evaluating the knowledge, attitude, and practices related to oral hygiene. Despite its importance, oral health often receives less attention in tertiary education settings. Gingivitis, characterized by gum inflammation, is an early stage of periodontal disease primarily caused by poor oral hygiene practices.A cross-sectional survey was conducted among undergraduate students in Ibadan, using a carefully structured questionnaire. The survey targeted undergraduate students, employing a descriptive survey design without manipulating variables. Closed-ended questions were utilized to assess students' knowledge, beliefs, and attitudes towards oral hygiene and gingivitis.The survey revealed that 67.1% of students strongly disagreed with having prior knowledge about oral gingivitis, while 1.3% disagreed

and 31.6% agreed. Additionally, 91.6% of students strongly disagreed with having been diagnosed with oral gingivitis, indicating a lack of engagement in preventive oral hygiene practices despite awareness of the condition. The majority of students believe they have adequate knowledge about oral hygiene and gingivitis. However, their lack of engagement in preventive practices suggests a gap between knowledge and behavior. Efforts are needed to bridge this gap and promote better oral health practices among tertiary students.

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USE OF THE HOUSEHOLD WATER INSECURITY ACCESS SCALE TO EVALUATE RURAL WATER DELIVERY IN SMALL COMMUNITIES

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Community-managed water systems play an important role in providing safely managed water to small and remote rural communities. New projects using this model continue to be implemented despite recent movement towards “professionalization” of water services. However, evaluating the efficacy of these projects at a community level may be challenging when the small number of households, or limited funds for long-term monitoring, limit statistical power to demonstrate health impacts. The household water insecurity access scale (HWISE), an experiential measure of water availability, accessibility, use, acceptability, and reliability, has been linked to health and social outcomes in research, and there is increasingly interest in its usefulness for project monitoring and evaluation. In 2023, the organization Green Empowerment and local partners integrated the HWISE into baseline evaluation surveys from 14 Ecuadorian communities across three regions of the country (coast, highland, and Amazon) where community-managed system are under development. Surveys were conducted in three languages (Spanish, Kichwa, and Cha’palaa). Communities either lacked piped water and were therefore reliant on rainwater, spring water, or surface water, or had highly unreliable, rudimentary piped water systems. The 4-question version of the HWISE (HWISE-4) retained the moderate internal consistency and limited floor and ceiling effects of the 12-question version (HWISE-12), making it a feasible and acceptable option for rapid community assessment, with similar performance for Spanish- and non-Spanish-speaking households. Community of residence explained 28.2% of variation in HWISE-4 scores, while region, survey language, and reported primary water source explained 20.2%, 18.9%, and 4.9% of variation respectively. Households with rudimentary piped water had mean HWISE-4 scores that were 0.9 points lower than communities that relied on surface water (the reference category) (95% CI: -2.2, 0.4). In the next phase of work, we will evaluate changes in HWISE scores as the same households gain access to safely managed water systems.

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MENSTRUAL MATERIAL DISPOSAL PRACTICES WITHIN THE GHANAIAN SOCIOCULTURAL CONTEXT: A QUALITATIVE STUDY

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Menstrual material disposal is a critical area of concern in management of menstruation. Disposal practices significantly vary across different nations and contexts with implications for environmental pollution and health hazards linked with improper disposal. While good menstrual hygiene practices culminate in having access to safe and convenient facilities to dispose off used menstrual management materials, disposal practices in the Ghanaian context are influenced by sociocultural beliefs which have not been explored empirically. This study explored the sociocultural beliefs underlying disposal of used menstrual materials among senior high school girls in the Volta region of Ghana. The study utilized descriptive qualitative research approach grounded in in-depth interviews to gather data from adolescent girls in senior high schools across five districts in the Volta region. In all, 25 in-depth interviews were conducted, transcribed verbatim and thematically analysed using MAXQDA version 2024. The findings project varied ways by which adolescent schoolgirls dispose off used menstrual materials. The main disposal practices include dumping into dustbins, latrines and pits, burying, and burning. The choice of menstrual material disposal methods was influenced by social or cultural beliefs. These beliefs included using menstrual materials for rituals and, in some cases, a fear of the unknown consequences of open-place disposal. Participants who disposed of materials in bins were generally unconcerned about what happened to them afterwards. Conversely, those who chose methods like pit latrines, burying, or burning were likely motivated by a desire to prevent their materials from being used in rituals. This study illuminates the varied disposal methods used by adolescent schoolgirls for menstrual materials. Their choices are influenced by a range of factors, primarily social and cultural beliefs, along with concerns about personal risks. However, environmental considerations appear to be a less significant factor for these participants.

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ISOTHERMAL AMPLIFICATION AND COLORIMETRIC DETECTION OFV*IBRIO CHOLERAE* IN ENVIRONMENTAL MATRICES

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Vibrio cholerae, cholera pathogen, which causes acute and fatal enteritis through consumption of contaminated food and water. Apart from aquatic habitats, *V. cholerae* can be found in other environmental media. In this study, we report an integrated detection protocol DNA extraction applicable in field with matrix alkaline lysis and loop-mediated isothermal amplification (LAMP) targeting the Rpob gene of *V. cholerae* with colorimetric reading in one hour. And Different environmental samples in France at Marseille: soil, plants, sea water, tap water and effluents were infected with suspensions bacterial (1 McFarland) of *V. cholerae* (Collection of Strains of the Rickettsia Unit ‘’CSUR” (IHU Méditerranée Infection, Marseille, France) and the same samples were infected with *V. alginolyticus*, and *E. coli* were used as negative controls to test the feasibility of our LAMP system. The LAMP assay reveals 100% specificity for *V. cholerae* by testing three non-*cholera Vibrio* species and four *Enterobacteriaceae* in culture as negative controls. Environmental samples containing *V. cholerae* showed positivity to the LAMP-*V. cholerae* protocol at a 1/50 dilution in one hour. This work contributes to the development of diagnostic tests for *Vibrio* Spp. pathogens mainly *V. cholerae*; and can be used in low-income countries for rapid screening purposes for other environmental disease. This study shows that the methods used are applicable in the field and contribute to the advancement of the diagnosis of environmental pathogens. And loop-mediated isothermal amplification (LAMP) method is effective for detecting very low numbers of bacteria in environmental samples, with the addition benefit of being inexpensive to realize in the field.

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INDICATORS OF DRINKING WATER ACCESS AND ESCHERICHIA COLI CONCENTRATION IN HOUSEHOLD DRINKING WATER IN MADAGASCAR

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Diarrheal diseases are a leading cause of morbidity and mortality in Madagascar, and *Escherichia coli* (*E. coli*) is one of the most common causes of diarrheal disease in children under five. Moreover, at least 80% of drinking water samples from Malagasy households have been found to be contaminated with *E. coli*, resulting in most households failing to meet the standard for safely managed drinking water as described in Sustainable Development Goal 6. Identifying relevant factors linked to contamination may inform initiatives to improve access to safer drinking water. This cross-sectional study aimed to determine whether different aspects of "access" to drinking water were associated with *E. coli* contamination in household drinking water in Madagascar, specifically (*i*) the use of an improved water source; (*ii*) time to get water; and (*iii*) perceived water sufficiency. The concentration of *E. coli* in household drinking water samples was available from 3,116 households from the sixth round of the nationally representative 2018 Madagascar Multiple Indicator Cluster Survey. Multinomial logistic regression modelling was used to investigate the association between water access variables and different concentrations of *E. coli* in water samples. The use of an unimproved water source significantly increased the odds of higher *E. coli* concentration in drinking water samples, whereas perceived insufficiency and increasing time to get water did not. Several additional contextual variables in the final model were found to increase the odds of *E. coli* concentration, including lower household wealth, rural residence, not treating drinking water at the household level, lacking improved sanitation facilities, and living in certain regions (East Coast, Tsaratanana Massif). A priority continues to be the reduction in reliance on unimproved sources for drinking water in Madagascar, as 54% of the population is dependent on surface water and unimproved wells and springs. Further inquiry is needed to understand the seeming lack of relationship between the risk of *E.coli* contamination and perceived water sufficiency and duration of time to obtain water.

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EVALUATION OF THE ANTIBACTERIAL SUSCEPTIBILITY PATTERN OF VIBRIO SPECIES ISOLATED FROM PERIWINKLES AND AQUATIC SNAILS SOLD AT UMUAGWO MARKET IN IMO STATE, NIGERIA

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Vibrio species occur in both marine and fresh water habitats and in association with aquatic animals. They are human pathogens and account for a significant proportion of human infections such as gastroenteritis. This study was carried out to evaluate the antibiogram of *Vibrio* species isolated from 60 samples of periwinkles and aquatic snails sold at Umuagwo market. The body surfaces of the samples were analyzed on thiosulphate citrate bile salt sucrose (TCBS) agar using standard microbiological method. Antibacterial susceptibility test was carried out using agar diffusion (Kirby Bauer) method. A total of 60 *Vibrio* belonging to six species was isolated. The frequency of occurrence showed that *V. cholerae* was the most predominant 20(33.3). It was followed by *V. vulnificus* 12(26.8%), *V. fluvalis* 8(16.6%), *V. mimicus* 7(16.6%), *V. alginolyticus* 7(13.3%) and *V. parahaemolyticus* 6(13.3%). There was no significant difference ($P<0.05$) in the frequency of occurrence of *Vibro* species on periwinkle and aquatic snail. Antibiogram testing showed that *V. cholerae* was sensitive to ciprofloxacin, pefloxacin and streptomycin. It was resistant to ampicillin, gentamycin, ceporex and ofloxacin. *V. fluvalis* was sensitive to ciprofloxacin, gentamycin and ofloxacin. It was resistant to ampicillin. *V. alginolyticus* was sensitive to ciprofloxacin, septrin and augumentin. It was resistant to ampicillin. *V. mimicus* was sensitive to ciprofloxacin, septrin, ceporex and ampicillin. *V. vulnificus* was sensitive to ciprofloxacin, ceporex and ampicillin. It was resistant to septrin. *V. parahaemolyticus* was sensitive to ciprofloxacin, ceporex and ampicillin. It was resistant to septrin. There was significant difference ($P>0.05$) in inhibition zone diameter between the test organisms. Sea foods like periwinkle and aquatic snail should be properly cooked and not eaten raw or undercooked to avoid *Vibrio* food borne disease.

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SOCIOECONOMIC AND COMMUNITY DRIVERS OF SAFE HOUSEHOLD WATER AND SANITATION: A MIXED METHODS ANALYSIS IN NORTHERN ECUADOR

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Large-scale household (HH) water, sanitation, and hygiene (WASH) interventions have had limited success. This finding may be partially explained by a lack of understanding of community priorities, limiting acceptability and uptake. Further, obtaining and maintaining HH WASH solutions (e.g., latrines, cisterns) places a financial and labor burden on individuals, and may be insufficient without community-level WASH infrastructure. We integrated quantitative data from household surveys (n=526) and qualitative data from thematically coded interviews (n=33) in 10 communities in northern Ecuador participating in the ECoMiD cohort study. Considering safe HH WASH as presence of improved water and sanitation in the home; safe community WASH as >85% safe HH WASH, and wealth based on asset data, we found that in communities without safe WASH, wealthy houses had 23% higher levels of safe HH WASH compared to poor houses in the same communities; this difference narrowed among houses in communities with safe WASH, where wealthy houses had just 10% higher levels, indicating that access to community infrastructure may mitigate inequalities in wealth in terms of safe HH WASH. We used multivariate logistic regression to estimate the effect of wealth on HH WASH, adjusting for location and maternal education, with a random effect on community. Wealthy houses had 3.7 (95%CI 1.8-8.8) times the odds of having safe HH WASH compared to non-wealthy houses. The burden of household WASH expenditures was considered high by all interviewees, particularly costs of drinking water and labor to obtain water in the absence of piped systems or rain. Piped systems were viewed as unreliable and contaminated; more wealthy households reported bottled water as the primary household drinking source compared to non-wealthy (51% vs 43%), despite higher access to piped systems among the wealthy (75% vs 49%). Interviewees expressed reluctance to invest in WASH in houses that were not owned or in informal settlements; and concern about installing cisterns in flood prone areas. Understanding these relationships is crucial to improve uptake and acceptance of future WASH interventions.

6752

MOXIDECTIN PLUS ALBENDAZOLE FOR LYMPHATIC FILARIASIS: EFFECTS THROUGH 36 MONTHS POST-TREATMENT

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The Moxidectin for LF study is a 3-year, randomized clinical trial comparing moxidectin + albendazole (MoxA) to ivermectin + albendazole (IA) and moxidectin + DEC + albendazole (MoxDA) to ivermectin + DEC + albendazole (IDA) for Bancroftian filariasis. The IA group was treated annually, while the MoxA, IDA, and MoxDA groups received a single dose at enrollment and were not retreated unless they were microfilaremic at 24 months post-treatment. We have previously reported that all three alternative treatments were superior to annual IA at 12 and 24 months. We now report efficacy data out to 36 months post-treatment. Thirty-six-month data are available for 73/96 (76%) participants with >40 microfilariae (Mf) per mL of blood at baseline. A modified intention to treat (mITT) analysis among these participants shows that 12/13 (92%) persons treated with MoxA were amicrofilaremic at 36 months, compared to 18/19 (95%) after IDA, 20/21 (95%) after MoxDA, and 12/17 (71%) after 3 annual doses of IA (Fisher's exact p=0.093). Two of sixteen (12%) MoxA participants required retreatment for microfilaremia at 24 months, as did 2/23 (9%) IDA and 2/25 (8%) MoxDA participants. Clearance of filarial antigen, measured by Filariasis Test Strip occurred in 1/18 (6%) IA, 3/14 (21%) MoxA, 2/19 (11%) IDA, and 9/22 (41%) MoxDA participants (Fisher's exact p=0.031). Among those with adult worm nests detected by scrotal ultrasound at baseline, 7/8 (88%) IA, 3/9 (33%) MoxA, 1/8 (13%) IDA, and 2/11 (18%) MoxDA participants had worm nests detected at 36 months (Fisher's exact p=0.005). Although preliminary, these data suggest that single-dose MoxA, like IDA and MoxDA, resulted in sustained amicrofilaremia out to 36 months in most participants. Complete results adjusted for baseline characteristics and infection intensity for all participants will be presented at the meeting. Results from this trial suggest that mass drug administration with MoxA could accelerate LF and onchocerciasis elimination in Africa.

6753

STRINGENT APPLICATION OF THE ESSENTIAL PACKAGE OF CARE WITH OR WITHOUT ADDITIONAL TREATMENT WITH DOXYCYCLINE IN PATIENTS WITH ADVANCED STAGES (4 - 6) OF FILARIAL LYMPHEDEMA

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Here, we report on a pilot trial with the aim to assess the efficacy of stringent hygiene measures using the Essential Package of Care with or without additional administration of doxycycline for the treatment of advanced stage (4 - 6) of filarial lymphedema (LE). The trial was carried out in Ghana (GH), India (IN), Mali (ML), Sri Lanka (LK) and Tanzania (TZ), as an add-on to 5 RCTs with the same aim, but with patients LE stage 1-3. Participants were randomized to receive either 200mg doxycycline (DOX) or matching placebo (P) for 6 weeks. Data were aggregated from the 5 country study sites. In total, 171 participants (GH: 58, IN: 20, ML: 19, LK: 19, TZ: 55) were included. Participants were followed up for two years after treatment onset with main follow-up assessments for stage and hygiene changes at 6, 12, 18 and 24 months and for acute adenolymphangitis (ADL) every 2 months. Quality of life (QoL) was assessed using the WHODAS 2.0 score every year. Multivariable analyses were performed to account for country and stage differences. Of the 171 participants, 89 were treated with DOX and 82 with placebo. In the DOX group, 13 (14.6%) participants had stage 4 or 5, whereas 76 had stage 6; in the placebo group, 22 (26.8%) presented with stage 4 or 5 and 60 with stage 6 (p = 0.058). After 24m, 16/82 (19.5%) of the DOX and 19/77 (24.7%) of the P group showed LE stage improvement, whereas only 1/82 (1.2%) and 8/77 (10.4%) showed progression, respectively. The significant influencing factors for progression were stage 4 or 5, ADL during the previous 6m, poor hygiene of the legs and less time lived in the endemic area. The median time to first attack was 12m for P and 14m for DOX (p = 0.42). In both DOX and P groups, there was a better QoL over time, indicated by a decrease of the QoL score from 20.7±1.4 at baseline to 9.1±1 at 24m (p <0.001). ADL during the previous 6m, body weight and poor hygiene of the legs were the most important factors affecting QoL. Overall, the results of this pilot trial suggest that there is good news also for patients with advanced LE stages that they benefit from stringent application of the Essential Package of Care for LE as recommended by WHO.

6754

EVIDENCE OF RENEWED ONCHOCERCIASIS TRANSMISSION AFTER TREATMENTS STOPPED IN 2017 IN THE METEMA SUB-FOCUS OF ETHIOPIA

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The Metema sub-focus is part of the Galabat-Metema international cross-border onchocerciasis (OV) transmission zone between Sudan and Ethiopia. The Metema sub-focus includes Metema, West Armachiho, Tegedie, Chilga, and Gendewuha and parts of Quara and Alefa districts of Amhara region, Ethiopia. Annual or semi-annual ivermectin mass drug administration (MDA) for OV occurred between 2003-2017. Ethiopia and Sudan made a coordinated decision to stop MDA from 2018 after both sub-foci met WHO Stop-MDA thresholds in 2017. The Wudi Gemzu hotspot in Metema was exempted and has since received MDA up to four times a year. During post-treatment surveillance (PTS), entomological evaluations of blackfly pools for parasite O-150 DNA by PCR were done to monitor for renewed signals of transmission. In 2021, 1068 *Simulium damnosum* flies were collected using human landing catch from 6 sentinel sites across the sub-focus. All flies were pooled for testing; 3 of 14 pools were positive, giving a prevalence estimate of 6 infective flies per 2000 (95% upper confidence limit [UCL] 17.7). We followed up with serological testing of 3,836 children less than 10 years old selected by multistage stratified sampling between April and March 2023 using ELISA for Ov16 antibodies, indicating exposure to the parasite. The seroprevalence was 2.3% (95% CI 0.3%-9.2%). Qualitative data identified intense internal conflict, displacement, and human immigration from known endemic areas as major issues during the PTS period. The results confirmed that transmission of onchocerciasis has re-occurred in the Metema sub-focus, representing one of the first global examples of OV PTS failure 5 years after stopping MDA. The program will reinitiate MDA in the sub-focus and investigate whether there was reintroduction of parasites through infected fly or human population movement, whether there was recrudescence from undetected parasites at the time of Stop-MDA assessments, and what factors contributed to renewed transmission. Elimination was declared in the cross-border Galabat sub-focus in early 2023 after successful PTS, but OV monitoring should continue given developments in Metema.

6755

ASSOCIATION BETWEEN ANATOMICAL HYPOSPLENISM AND *LOA LOA* MICROFILAREMIA IN A RURAL AREA OF THE REPUBLIC OF CONGO: A POPULATION-BASED CROSS-SECTIONAL STUDY (THE MORLO PROJECT)

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Loa loa filariasis (loiasis) is considered a benign disease. However, recent epidemiological data suggest an increased mortality rate in *L. loa* infected individuals, emphasizing the importance of studies on the morbidity associated with loiasis. As case-reports suggest anatomical lesions in the spleen among individuals infected with *L. loa*, we aimed at investigating the relationship between *L. loa* microfilarial density (MFD) and spleen volume. In 2022, we enrolled 990 subjects, with one-third being microfilaremic, in a prospective cohort in a general population in the Republic of Congo. At baseline, parasitological assessment, search for Howell-Jolly bodies (HJB), and spleen ultrasonography (US) were performed. Nested analyses of the baseline data from this cohort revealed that, after adjusting for age and sex, individuals with 1-8000 microfilariae (mf)/mL and >8000 mf/mL had a decreased spleen volume of 30.8 and 46.5 mL, respectively (P = 0.010 and 0.008, respectively). Additionally, a model run to explain the presence of a spleen volume <150 mL (the lower limit of normal volume range) demonstrated that individuals with *L. loa* MFD of 1-8000 mf/mL and >8000 mf/mL had adjusted Odds Ratios (aOR) of 1.9 (P = 0.042) and 4.2 (P = 0.016), respectively, when compared to amicrofilaremics. Given that a spleen volume <80 mL is associated with a significantly increased risk of death in patients with severe pneumonitis, further analysis was conducted using 80 mL as a cut-off. Compared to amicrofilaremic individuals, subjects with >35,000 mf/mL had an adjusted OR (aOR) of 14.9 (P = 0.032) to have a spleen volume <80 mL. Interestingly, HJB were also significantly associated with these small spleens (aOR = 3.7, P = 0.017), supporting the hypothesis of potential dysfunction of these spleens. In conclusion, our findings suggest a possible link between loiasis and the development of anatomical hyposplenism, potentially leading to spleen dysfunction. These results imply that loiasis may contribute to an increased risk of bacterial infections and associated mortality in Central Africa.

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IMPACT OF TRIPLE-DRUG MASS DRUG ADMINISTRATION ON THE SEROPREVALENCE OF ANTIBODIES TO LYMPHATIC FILARIASIS IN SAMOA

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In August 2018, Samoa was the first country to distribute triple-drug mass drug administration (MDA) to interrupt lymphatic filariasis (LF) transmission. Point-of-care tools to detect filarial antigen (Ag) are used by programmatic surveys but evidence suggests antifilarial antibody (Ab) markers may be more sensitive measures of transmission. We aimed to assess the utility of Abs as a surveillance tool by comparing LF Ag and Ab seroprevalence at baseline and 6-months post-MDA in Samoa and identify risk factors for seropositivity. A community-based serosurvey of participants ≥5 years old took place immediately post-MDA in 2018 and 6-months post-MDA in 2019 in 35 primary sampling units (30 randomly selected and five 'suspected hotspots'). Alere™ Filariasis Test Strips were used to detect Ag and multiplex bead assays to measure seropositivity to *Bm14* Ab, *Wb123* Ab and *Bm33* Ab. Seroprevalence was adjusted for study design and standardised for age and gender. Overall 3795 participants (mean 20.7 years; 49% male) were surveyed in 2018 and 4052 (mean 20.4 years; 48% male) in 2019. At follow-up, seroprevalence did not change significantly for Ag (3.7% vs 4.6%; *P*-value 0.66) or *Bm14* Ab (20.3% vs 18.5%; *P*-value 0.12) but increased for *Wb123* Ab (32.2% vs 43.6%; *P*-value 0.04) and *Bm33* Ab (51.5% vs 95.8%; *P*<0.001). Risk factors for seropositivity at follow-up were age ≥10 vs 5-9 years (aOR: Ag=3.73, *Bm14*=3.77, *Bm33*=4.28, *Wb123*=2.78), male gender (aOR: Ag=4.42, *Bm14* Ab=2.27, *Wb123* Ab=1.43), 'suspected hotspot' residents (aOR: Ag=3.44, *Bm14*=1.98, *Wb123*=2.38) and Savai'i residents (aOR: Ag=3.44, *Bm14*=2.10, *Bm33*=2.83). Contrasting seroprevalence trends were seen for Ag and each Ab from baseline to follow-up. The interpretation of increased *Wb123* Ab and *Bm33* Ab seroprevalence is unclear but may suggest these Ab are detecting increased transmission signals that are not picked up by Ag. Individual LF seromarkers may provide different information about an individual's infection status and population level transmission. Further research into Ab kinetics is needed to determine the utility of monitoring Ab and define target Ab thresholds for LF elimination.

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EVALUATION OF THE EFFECT OF ONE ROUND OF MASS DRUG ADMINISTRATION WITH IDA ON HUMAN *BRUGIA MALAYI* INFECTIONS IN BELITUNG DISTRICT, INDONESIA

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In Belitung District, that is located close to Sumatra Island, lymphatic filariasis (LF) is caused by zoonotic *Brugia malayi*. The district received mass drug administration (MDA) with DEC and albendazole (DA) from 2005-2010 and passed three transmission assessment surveys (TAS). After post TAS-3 surveillance indicated microfilaremia in adults, we conducted in June of 2022 a district-wide survey using the IDA (Ivermectin DA) impact survey design of WHO. More than 30 clusters of adults from 26 villages were examined for night blood microfilariae (Mf) by three-line blood smear. Mf-positive subjects were detected in 16 villages (62%) with the highest rate of Mf-positives in Lassar village (4.8%, 40/833). The overall Mf-rate was 2.7% (121/4417) and older males were more likely to be Mf-positive compared to other population groups. MDA with IDA was conducted by the local health authority in October 2022 with a reported coverage of 90.3%. We conducted a follow-up IDA impact survey in June of 2023. Survey clusters were selected based on geospatial modelling using Mf data from the previous year to focus on communities with high predicted transmission risk. During follow-up Mf-positive individuals were detected in 9 of 13 villages (69%). The overall Mf-rate was 0.84% (35/4174). Eleven villages were re-examined 2023 and the Mf-rate decreased in all of them except for one compared to 2022. These mid-term results indicate that IDA MDA can be highly efficient to clear zoonotic *B. malayi* despite more stringent IDA impact survey design and oversampling. At the same time *B. malayi* infection has been also found in animals in the area (cats, dogs, macaques) and genomic studies indicate exchange of parasites between human and animal populations. This is an additional risk for the elimination of LF in the area and high coverage MDA with intensified evaluation of MDA and post MDA surveillance is needed. Areas with zoonotic *B. malayi* infection may need to be declared by WHO to special intervention zones that need special attention.

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INVESTIGATION OF POTENTIAL ONCHOCERCIASIS HOTSPOTS IN PARTS OF ENUGU SOUTHEAST NIGERIA THAT ARE UNDER POST TREATMENT SURVEILLANCE

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In December 2022 the Nigeria Onchocerciasis Elimination Committee (NOEC) approved the cessation of mass drug administration (MDA) in Enugu state, Nigeria, after surveys indicated that it met WHO's serological and entomological criteria for interruption of onchocerciasis transmission. Shortly after, a publication by Ekpo and colleagues reported parasitological evidence (55% prevalence of nodules by physical examination and 41% microfilaria [mf] prevalence in skin snip microscopy) of persistent *Onchocerca volvulus* from concurrent studies in 225 adults in 6 villages in Enugu. NOEC thus advised a follow-up study be conducted in the same 6 villages and 12 neighboring villages in three local government areas (LGAs) of Enugu to confirm if there were onchocerciasis hotspots with ongoing transmission. We tested 1,434 children aged 5-9 years for Ov16 antibodies by ELISA and examined 1,539 adults (18+ years) for nodules and tested their skin snips for mf by microscopy. Skin snips from 12 Ov16 positive children were tested for mf by PCR; the resulting 5 positives gave a prevalence estimate in children of 0.35% (95% CI 0.11%-0.81%). In adults, prevalence of nodules was 11% and of skin mf was 1.36% (95% CI 0.78-1.94%). No adults had skin mf and no children were Ov16 positive in the villages of one LGA. These results indicated hypoendemic onchocerciasis in contrast to the high prevalences reported by Ekpo et al. (2022). These findings validate NOEC's recommendation that Enugu be classified as "transmission interrupted" and stop MDA, but the two LGAs with Ov16 or mf positives may be hotspots. Blackfly collections are ongoing, and they will be tested for parasite DNA to confirm transmission status. We recommend twice per year MDA in the potential hotspots to ensure transmission interruption.

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MITIGATING COLONIZATION WITH CARBAPENEM-RESISTANT ORGANISMS AMONG NEONATAL INTENSIVE CARE UNIT ADMISSIONS: EVALUATING THE EFFECTIVENESS OF INFECTION CONTROL INTERVENTIONS

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Antimicrobial resistance (AMR) is the global leading cause of death from infections, particularly affecting low- and middle-income countries. Colonization with carbapenem-resistant organisms (CRO) increases the risk of infections with CRO. In an interim analysis of a prospective cohort study, we found 77% (141/182) of neonates in a neonatal intensive care unit (NICU) of a tertiary-care hospital in Bangladesh were colonized with carbapenem-resistant *Klebsiella pneumoniae*, with 63% (89/141) acquiring colonization >48 hours after hospitalization. We aimed to assess the impact of infection control (IC) interventions on CRO colonization among neonates admitted to the NICU. From July 2023 to March 2024, we enrolled 529 neonates: 360 before the intervention and 169 after. Neonates were assessed for CRO colonization using rectal swabs collected on admission, days 3 and 7, and weekly thereafter. Swabs were plated on mSuperCARBA to assess colonization with carbapenem-resistant organisms (CRO, not differentiated to date). Positive blood cultures collected from patients with suspected sepsis underwent testing using VITEK® 2. Our IC interventions targeted hand hygiene (HH) and environmental cleaning (EC), including staff training on proper HH techniques and more frequent cleaning of high-touch surfaces, as well as regular audits to measure compliance with HH and EC. We conducted descriptive analyses using Pearson's Chi-square test. Compliance with HH improved from 13% to 28% following the interventions, while environmental cleaning improved from 9% to 43% based on fluorescent markers. Over the same time, CRO colonization decreased from 93% (333) to 80% (135) ($p<0.001$). Overall bacterial blood culture positivity remained stable at 54% (51/95) vs. 57% (30/53) ($p=0.87$). After implementing IC interventions, we observed a decrease in CRO colonization among NICU patients, though blood culture positivity was unchanged. Results suggest that even modest improvements in IC practices may have a role in curbing CRO transmission in high-risk settings.

6760

URBAN SANITATION UPGRADES IN MAPUTO, MOZAMBIQUE ASSOCIATED WITH REDUCED DETECTION OF ENTERIC PATHOGENS IN FECAL SLUDGES

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Environmental surveillance of pathogens has gained prominence in monitoring of SARS-CoV-2 infections, to assist in polio eradication, and increasingly in detection of a wide range of other targets to support public health programming. Because wastewater and fecal sludges represent excreta from many individuals, these matrices may also be useful in understanding the effects of interventions aimed to prevent infections. Here, we examine the utility of enteric pathogen detection in fecal sludges as an endpoint in a controlled health impact trial of urban sanitation upgrades in Maputo, Mozambique. We collected 50 fecal sludge samples from an intervention arm receiving upgraded shared latrines and 47 from a comparable control arm using existing poor-quality latrines between March 2022 and April 2023. We extracted total nucleic acid using the QIAamp 96 Virus kit and processed extracts using a customized TaqMan Array Card for RT-qPCR analysis. Overall, we observed a statistically meaningful impact of sanitation upgrades on the percent reduction of *Ascaris lumbricoides* (30%), *Trichuris trichiura* (17%), *Campylobacter jejuni/coli* (11%), enteroaggregative *E. coli* (30%), enteropathogenic *E. coli* (28%) and enterotoxigenic *E. coli* (16%) in the intervention arm ($p<0.05$) relative to control sites for fecal sludge samples. Results are consistent with similar reductions for bacterial and helminth targets observed in stool samples from children under 5 among those served by sanitation interventions compared with comparable controls lacking these upgrades. Detection of enteric pathogens in fecal sludges is a compelling option for further consideration as an outcome measure in water, sanitation, and hygiene (WASH) health impact trials.

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EFFECTS OF HOUSEHOLD CONCRETE FLOORS ON MATERNAL AND CHILD HEALTH (CRADLE TRIAL): A RANDOMIZED CONTROLLED TRIAL

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Early life soil-transmitted helminth infection (STH) and diarrhea are associated with growth faltering, anemia, impaired development, and mortality. Exposure to fecal contamination in soil inside the home may be a key contributor to enteric infections, and a large fraction of rural homes in low-income countries have soil floors. We present the protocol of The Cement flooRs AnD chiLd hEalth (CRADLE) trial, which will measure the effect of installing concrete floors in homes with soil floors on child STH infection and maternal and child health outcomes in rural Bangladesh. Our study site is Sirajganj district, a climate vulnerable region, where 66% of households have mud floors. We conducted a pilot study on the prevalence of STH among 6-24 months of children in Chauhali sub-district of Sirajganj (N= 50 households). The prevalence of any STH (*Ascaris lumbricoides*, *Necator americanus*, or *Trichuris trichiura*) was 27% using qPCR. Households with a pregnant woman, a soil floor, no plan to relocate for 3 years, and walls that are not made of mud will be eligible. We will individually randomize 800 households to intervention or control (1:1) within geographic blocks of 10 contiguous households with 100m buffers between households. We will install concrete floors when the birth cohort is in utero and measure outcomes at child ages 3, 6, 12, 18, and 24 months. The primary outcome is the prevalence of any STH infection detected by qPCR at ages 6, 12, 18, or 24 months in the birth cohort. Secondary outcomes include household floor and child hand contamination with *E. coli*, extended-spectrum beta-lactamase producing *E. coli*, child diarrhea, growth, and cognitive development; maternal stress, quality of life, discretionary time, executive function, and depression; and cost-effectiveness. Laboratory staff and data analysts will be blinded; participants will be unblinded. The trial's design and outcomes will be disseminated among local stakeholders from both the private and public sectors. The trial is expected to generate evidence about whether replacing soil floors with concrete is an effective health intervention in rural Bangladesh and similar settings.

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EFFECTS OF A WATER, SANITATION, AND HYGIENE PROGRAM ON DIARRHEA AND CHILD GROWTH IN THE DEMOCRATIC REPUBLIC OF THE CONGO: A CLUSTER-RANDOMIZED CONTROLLED TRIAL OF THE PREVENTATIVE-INTERVENTION-FOR-CHOLERA-FOR-7-DAYS (PICHA7) PROGRAM

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We aimed to assess whether the Preventative-Intervention-for-Cholera-for-7-Days (PICHA7) program reduced diarrhea and improved child growth in the Democratic Republic of the Congo (DRC). The PICHA7 cluster-randomized controlled trial enrolled diarrhea patient households in urban DRC. Diarrhea patient households were randomized to one of two arms: one in-person visit for the standard message given by the DRC government to diarrhea patients on oral rehydration solution use (standard arm); or this standard message and the PICHA7 program with quarterly in-person visits and weekly voice and text mobile health (mHealth) messages (PICHA7 arm). The primary outcome was self- or caregiver-reported diarrhea in the past two weeks assessed monthly for 12 months. The secondary outcomes were diarrhea with rice water stool (cholera symptom), health facility visits for diarrhea, stunting, underweight, and wasting over 12-months. Analysis was by intention to treat. This trial is registered at ClinicalTrials.gov, number NCT05166850. Between 22 December 2021 and 20 December 2022, 2334 participants were randomly allocated to two arms: 1138 to the standard arm and 1196 participants to the PICHA7 arm. For all age groups (children and adults), diarrhea prevalence during the 12 month surveillance period was significantly lower among participants in the PICHA7 arm (Prevalence Ratio (PR): 0.39 (95% Confidence Interval (CI): 0.31, 0.48) compared to the standard arm. Participants in the PICHA7 arm had a 52% lower odds of diarrhea with rice water stool (Odds Ratio (OR): 0.48 (95% CI: 0.27, 0.86)), and 56% lower odds of visiting a health facility for diarrhea during the 12 month surveillance period (OR: 0.44 (95% CI: 0.25, 0.77)). Children under five years were significantly less likely to be stunted in PICHA7 arm compared with the standard arm (52% vs. 63%) (OR: 0.65 (95% CI: 0.43, 0.99)) at the 12 month follow-up. All WASH components had high adherence. The PICHA7 program which combines mHealth with in-person visits lowered diarrhea prevalence and stunting in the DRC.

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REDUCED EXPOSURE TO ENTERIC PATHOGENS IN CHILDREN LIVING FROM BIRTH IN HOUSEHOLDS SERVED BY SANITATION UPGRADES IN URBAN MAPUTO, MOZAMBIQUE

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The Maputo Sanitation (MapSan) trial began in 2015 to evaluate the impacts of a shared (private) sanitation intervention in low-income, informal communities in Maputo, Mozambique. The design included four measurement points: immediately before sanitation improvements, and then at 12, 24, and 60 months post-intervention. Children under 5 were enrolled at each of these time points in household clusters served by better sanitation and in a comparable cohort lacking these improvements. At 60 months post-intervention, all enrolled children in the intervention arm have experienced better sanitation from birth through early childhood. From both intervention (n = 552) and control arms (n = 578), we collected stool samples for molecular analysis for 22 primary enteric pathogens of interest, including 13 bacteria, 5 soil-transmitted helminths (STHs), and 4 protozoa, using customized multi-parallel qPCR in Taqman Array Cards. The intervention effectively reduced the prevalence of combined bacterial pathogens detected (0.91 PR, 95% CI: 0.81-1.0) and combined STH infections (0.77 PR, 95% CI: 0.65-0.91), when adjusting pooled pathogen measurements for prespecified covariates and accounting for clustering. Specific targets reduced in the intervention arm compared with controls included *Trichuris trichiura* (0.65 aPR, 95% CI: 0.52-0.82), *Ascaris lumbricoides* (0.82 aPR, 95% CI: 0.68-1.0), *Shigella spp*/EIEC (0.72 aPR, 95% CI: 0.60-0.88), and *Enterotoxigenic E. coli* (0.76 aPR, 95% CI: 0.58-1.00). Results suggest that children living from birth in households served by upgraded sanitation experience reduced exposure to enteric pathogens.

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A CLUSTER RANDOMIZED CONTROLLED TRIAL FOR THE EFFECT OF A WATER, SANITATION AND HYGIENE KIT COMBINED WITH STANDARD OUTPATIENT TREATMENT ON DRINKING WATER QUALITY IN NORTHERN SENEGAL

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Globally, 17 million children are affected by severe acute malnutrition (SAM). Under the Community-based Management of Acute Malnutrition (CMAM), outpatient treatment is now recommended for uncomplicated cases. This moves treatment from generally more controlled hospital settings to the household, where the presence of environmental hazards is often higher. As part of the *Traitement Intégré de la Sous-Nutrition Aiguë* (TISA) trial in northern Senegal, we evaluate the effect of adding a water, sanitation, and hygiene (WASH) kit to standard outpatient treatment programmes (OTP) for uncomplicated SAM on household water quality. The control group received the standard CMAM protocol of care and the intervention group received this plus a "WASH kit", which included an eight-week supply of chlorination tablets, a 20-litre water storage container, soap, and hygiene promotion materials. Household water samples were collected among 445 households (203 control, 242 intervention) between 4-8 weeks after enrolment. Samples were analysed for turbidity, free chlorine residual, and indicators of faecal contamination. Child diarrhoea was reported by the caretaker with a 7-day recall at admission and week 4. The intervention was successfully delivered, with 94 % of intervention households having the WASH kit at week 4, *vs* <0.1% in the control. 72% of intervention households reported treating their water, *vs* 7% in the control, which was validated by the significantly higher median residual chlorine of 0.5 mg/l (IQR 0.1 - 1.61) compared to 0.1 mg/l (IQR 0.1 - 0.1) in the control. As a result, mean *E. coli* contamination was significantly reduced from 252 CFU/100ml in the control to 94 CFU/100 ml in the intervention. Child diarrhoea was reduced by 15.6% in the intervention arm, *vs* 4.3% in the control. Improved water quality in the intervention arm may reduce exposure to waterborne pathogens, thereby improving recovery rates for children undergoing outpatient treatment for SAM. Nonetheless, the water contamination remained at medium risk in the intervention arm.

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DRINKING WATER QUALITY AND ACCESS IMPACTS ON INFANT GUT MICROBIOME COMPOSITION IN MOZAMBICAN INFANTS

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The gut microbiome influences immune function, infection resistance, cognitive function, and growth. Gut microbiome composition is influenced by early environmental exposures such as delivery mode and diet, but gaps exist in our understanding of the impact of other environmental factors, notably drinking water, on the gut microbiome. To explore if drinking water quality and continuous access to a safe water supply impact gut microbiome composition during early life, we analyzed 16S rRNA gene amplicon sequences from 1200 child fecal samples from a birth-cohort study in Mozambique. We assessed microbiological water quality and access at each child's household at 3, 6, 9, and 12 months of age. We found that increased access to water was associated with an increase in alpha diversity, a measure of sample species richness and evenness, based on multiple metrics. For example, access to an improved water source on the premises was associated with an increase in Shannon's alpha diversity (RR=1.63, p <0.01). Among children living in households where E. coli was not detected in drinking water, differences in community composition between samples (beta diversity) were higher compared to children in households where E. coli was detected (p <0.01). Similarly, among children who did not have access to basic water, water on the premises, and sufficient quantities of water when needed, we found higher dissimilarity in beta diversity compared to children who did have such access (p <0.01 for all variables). Feature-wise association tests revealed differentially abundant taxa in each group across each water quality and access variable assessed, highlighting potential biomarkers associated with water quality and access. We found a null relationship between alpha diversity and microbiological water quality, as defined by the prevalence of E. coli in source (RR=0.93, p=0.68) or stored water (RR=1.05, p=0.71). This study is among the first to evaluate drinking water quality and access as an environmental exposure on the child gut microbiome and contributes valuable information on acute and chronic health outcomes associated with early perturbations to the gut.

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GENOME-WIDE ASSOCIATION STUDY OF AN AFRICAN SNAIL VECTOR OF SCHISTOSOMIASIS IDENTIFIES GENES ASSOCIATED WITH RESISTANCE TO INFECTION BY *SCHISTOSOMA MANSONI*

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Schistosomiasis, afflicting hundreds of millions of people worldwide, potentially could be controlled by blocking transmission to their freshwater snail vectors. Most infection of *Schistosoma mansoni* occur in sub-Saharan Africa, where they are vectored by *Biomphalaria sudanica* and related species. In contrast to the neotropical vector, *B. glabrata*, there has been little genomic work on African snails; therefore the genetic basis of African snail-parasite interaction is completely unknown. We performed a genome-wide association study (GWAS) of infected (N=493) and uninfected (N=295) *B. sudanica* originating from the shoreline of Lake Victoria. Pools were sequenced and variable regions SNPs assessed. Allele counts of infected vs. uninfected phenotypes at each SNP were compared to identify those with significant associations to the resistance phenotype. An amplicon panel was designed to validate SNPs in an independent group of infected (N=126) and uninfected (N=100) snails. Additive regression and a Fisher's exact test dominance model were used to identify significant hits. We observed population structure, namely two distinct clusters, within our *B. sudanica* data, which were accounted for in downstream analyses. Following validation, several genomic loci in two unlinked genomic regions of *B. sudanica* were associated with schistosome resistance. Both genomic regions occur on linkage groups previously tied to schistosome resistance in *B. glabrata*, but several megabases away from these known loci and thus representing different genes. Both regions are high in nucleotide diversity and contain several duplications, suggesting they are evolutionarily dynamic. Characterized genes associated with parasite resistance tended to contain transmembrane and other functional binding domains, suggesting a potential role in pathogen recognition. These results provide a first glimpse into the innate immune system of the major schistosome vector *B. sudanica*, informing future studies aimed at predicting/manipulating the vector competence of the snail host.

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GENERATING THE GENERATOR: A GIANT COMPLEX ESSENTIAL FOR MITOCHONDRIAL BIOGENESIS IN *PLASMODIUM FALCIPARUM*

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Although the *Plasmodium falciparum* mitochondrion is a validated antimalarial drug target, many *P. falciparum* mitochondrial proteins remain uncharacterized. We aimed to define the roles of a newly identified mitochondrial protein, PF3D7_0707400, in *P. falciparum* parasites, particularly in mitochondrial biogenesis. Bioinformatic analyses revealed PF3D7_0707400 to be an ortholog of ATAD3A (ATPase associated with diverse cellular activities), hence we refer to it as *Pf*ATAD3. To achieve our aim, we employed a CRISPR-Cas9 TetR-DOZI genetic approach to generate TOM22-mNG (Translocator of Outer Mitochondrial Membrane 22-mNeonGreen)/*Pf*ATAD3-3xHA-TetR transgenic parasites where expression of *Pf*ATAD3 can be regulated using anhydrotetracycline (aTc). We show that *Pf*ATAD3 is essential for asexual parasite development as parasites not expressing *Pf*ATAD3 are arrested at 72 hours and ultimately die by 96 hours. Northern blots of total RNA isolated from *Pf*ATAD3-knockdown parasites demonstrate a reduction in COX 1 and Cyt b mitochondrial mRNA transcripts as well as small mitochondrial ribosomal RNAs as early as 24 hours after *Pf*ATAD3 knockdown, with minimal to no COX 1, Cytb, and mitoribosomal RNA transcripts present at 72 hours after *Pf*ATAD3 knockdown. Through live cell scanning confocal imaging of parasites at 48 hours post-*Pf*ATAD3-knockdown, we observe a destabilization of the mitochondrial membrane potential in about 60% of *Pf*ATAD3-knockdown parasites as MitoTracker is unable to accumulate in the mitochondria of these parasites and consequently, diffuses across their cytosol. Furthermore, large-pore composite gel electrophoresis revealed *Pf*ATAD3 to be present in a ~ 4MDa complex indicating the presence of multiple interacting partners by which *Pf*ATAD3 is likely to be performing its essential functions in *P. falciparum* mitochondrial physiology. We are in the process of identifying these interacting partners through proteomic and structural analyses.

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A DRUGGABLE AGC KINASE CLRK MEDIATES TEMPORAL REGULATION OF CYCLIC NUCLEOTIDE SIGNALING AND CONTROLS PARASITE EGRESS AND INVASION

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Cyclic nucleotide signaling orchestrates crucial transitions in the *Plasmodium* life cycle. Therefore, its precise regulation is vital to prevent temporal dysregulation of subsequent pathways such as activation of kinases and proteases critical for parasite egress and invasion. Here, we identify an AGC family kinase and elucidate its function as a negative regulator of cyclic nucleotide signaling. Conditional deletion of CLRK (Cyclic Nucleotide Level Regulating Kinase) resulted in elevated levels of cGMP and cAMP, prematurely activating Sub1, a protease, and untimely processing of many downstream substrates. Loss of CLRK also disrupted MSP1 processing, essential for timely parasite egress. Notably, CLRK-null merozoites exhibited an inability to breach the RBC membrane during egress. Furthermore, through chemical genetic approaches, we identified small molecule inhibitors targeting CLRK, effectively blocking schizont development and merozoite invasion. Lastly, using conditional genetic and chemical genetic approaches we demonstrate an important role for CLRK during the sexual stages of the parasite life cycle. Overall, our findings implicate CLRK as a pivotal regulator of cyclic nucleotide signaling in *Plasmodium*, governing key transitions throughout the parasite life cycle and underscores its potential as a promising therapeutic target.

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INCREASED DUFFY BINDING PROTEIN 1 EXPRESSION CORRELATES WITH *PLASMODIUM CYNOMOLGI* GROWTH IN CONTINUOUS CULTURE

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A continuous culture system would revolutionize *Plasmodium vivax (Pv)* research but remains elusive. *P. cynomolgi (Pcy)* is a closely-related nonhuman primate malaria parasite that shares many biological traits with *Pv* except that *Pcy* preferentially, but not exclusively, invades and develops within reticulocytes. This difference has supported the adaptation of *Pcy* lines that grow in culture, but the mechanisms that enable continuous culture are undefined. Here, we generated a new line of the *Pcy* Berok strain, termed DC line, to grow continuously in culture and performed whole genome sequencing of parasites collected during adaptation to identify the genetic changes that promote growth in culture. Minimal single nucleotide variants emerged during adaptation. Structural variations comprised of insertions and deletions (INDELs) were more common and suggested that a subpopulation of parasites was selected for during adaptation versus de novo mutations that led to improved growth. INDELS were present in many genes associated with the parasite's metabolism, consistent with the nutrient-limited environment of culture. Interestingly, the DC line also had additional copies of the Duffy binding protein 1 gene that was associated with increased gene expression. Duffy antigen receptor for chemokines (DARC) is the ligand for DBP1, and the loss of this receptor has been shown to restrict *P. yoelii* to invading reticulocytes. Thus, we hypothesized that overexpression of DBP1 by the DC line may alter the invasion preference from reticulocytes to normocytes, enabling the parasite to grow effectively in culture. Indeed, invasion assays showed that the WT line preferentially invaded and developed within reticulocytes whereas there was no preference for the DC line. In summary, these data indicate that metabolic changes and alterations in invasion ligand expression through copy number variation support continuous growth of *P. cynomolgi* in culture. This information may help adapt additional *Pcy* strains to culture and inform efforts for culturing *Pv*.

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TISSUE COLONIZATION AND INFECTION ESTABLISHMENT OF *TRYPANOSOMA BRUCEI BRUCEI* AT THE BITE SITE

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Trypanosoma brucei parasite is known for causing diseases in humans and animals, leading to significant public health and economic burdens. Transmission of parasites occurs when epimastigote parasites colonize the Tsetse fly's salivary glands, transitioning into metacyclic parasites capable of infecting mammals. These metacyclic parasites transform into bloodstream form parasites upon entering the mammalian host, evading the immune system. Despite extensive research on systemic immune responses of the mammalian host to trypanosome infections, understanding the establishment of infection at the bite site remains largely unexplored. To understand early infection dynamics, our group focuses on targeting metacyclic parasites introduced into the host at the bite site. Single-cell RNA sequencing of parasites isolated at the bite site holds promise for unraveling infection establishment. However, the challenge lies in separating parasites from host cells or tissues without altering their transcriptomes. To address this challenge, we developed a transgenic parasite expressing a fusion protein containing tdTomato, red-shifted firefly luciferase, and the TY1 tag. These parasites, sorted based on tdTomato expression, were evaluated for infectivity in tsetse flies and their ability to transmit to mice. Following infection initiation, Fluorescence-Activated Cell Sorting (FACS)

was used to isolate tdTomato-expressing parasites from mouse skin tissue at various time points for single-cell RNA sequencing.The transgenic strain demonstrated stability under culture conditions, high infectivity towards tsetse flies, and efficient transmissibility to mice via natural fly bites or needle injection of isolated parasites. Sorting parasites based on fluorescent signals enabled the collection of samples at multiple post-infection time points. Single-cell RNA sequencing of these sorted parasites provided insight into the transcriptomic profiles during differentiation from metacyclic to bloodstream form trypanosomes, facilitating the study of trypanosome infection establishment at the bite site.

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BROKERED DESIGN: COMMUNITY-DRIVEN LEARNING FOR MALARIA ELIMINATION IN THE DOMINICAN REPUBLIC

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Effective community engagement is crucial for achieving the ambitious goal of malaria elimination. *Brokered Design* (BD) is a novel strategy for program co-design and organizational learning, initially developed by the Human Engagement Learning Platform at Emory University in collaboration with The Carter Center, to address declining participation in Mass Drug Administration (MDA) for lymphatic filariasis elimination in Haiti. In January 2024 BD was adapted to malaria elimination efforts in the Dominican Republic (DR). The first co-design round of BD occurred in the San Juan and Azua regions, employing a rapid assessment through community conversations to inform a communications strategy for a Reactive Drug Administration (RDA) implementation in response to a malaria outbreak in these regions in early 2024. The conversations engaged 36 people including community health workers, non-Spanish-speaking agricultural workers, and other community members. Key insights included the importance of recognizing and safeguarding close relationships within the community, incorporating community partners into engagement strategies, respecting all community members, favoring in-person communication channels, providing comfortable settings for conversations with community members, ensuring inclusivity and fairness of communications, and explaining and justifying the health interventions. These insights support the Ministry of Health (MOH) in their developing communications strategy. Consequently, initiatives were undertaken to hire ethnically diverse health workers, involve community groups in strategy implementation, and shape key intervention messages with the national communications team. The rapid assessment served as an initial step in a broader application of BD to support organizational learning for CECOVEZ (DR MOH's tropical diseases center) and its partners to align health intervention designs and implementations with the interests of community stakeholders. We describe subsequent applications of the BD method in the MOH's implementation of RDA in the DR and highlight other potential applications of the method in global health programs.

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ACCELERATING PROGRESS TOWARDS THE ELIMINATION OF MALARIA AND OTHER VECTOR-BORNE DISEASES: ENGAGING WOMEN IN VECTOR CONTROL, THE PAN-AFRICAN MOSQUITO CONTROL ASSOCIATION (PAMCA) EXPERIENCE

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Despite the progress made in the control of vector-borne diseases (VBDs), the burden of VBDs remains significantly high in tropical and subtropical regions. The ccomplexity of global health problems demands involvement and leadership that represents pluralism in society. The Pan-African Mosquito Control Association (PAMCA), through its Women in Vector Control (WiVC) program seeks to strengthen women's participation and leadership in VBDs control and elimination initiatives in Africa as per the SDG goal 3. In 2021 - 2023, PAMCA WiVC successfully hosted and co-organized trainings including effective communication and leadership skills, proposal, and manuscript writing, safeguarding, among others. A total of 95 women from 29 countries in Africa were trained. Further, the program rolled out a structured mentorship program "LiftHer2", where 42 mentees and 30 mentors in cohorts 1 and 2, of a 12 month period each, were enrolled. To increase visibility and networking, 17 women in early, mid and senior career level from 11 countries in Africa were recognized and awarded for their excellent work and contribution to VBDs. Ten early-career women received travel sponsorship to attend and present their research work during the 8th and 9th PAMCA annual conference in 2022 and 2023, respectively. Enrollment or recruitment to program activities was done through a competitive process, external evaluation and regional balance consideration. Monitoring and evaluation of the program indicate that several women who participated in the activities advanced in their careers, with 6 successfully completing their PhDs, several enrolled for post graduate studies, while others secured new jobs or received promotions at their workplace. The WiVC program has showcased that training, mentorship and recognition of excellence are important in empowering, enhancing leadership roles and addressing VBDs in Africa. The program has immensely contributed to the pool of skilled and knowledgeable African women with capability and confidence to address VBDs, thus contributing to the sustainability of vector control initiatives and elimination programs in the continent.

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ADDRESSING HEALTH DISPARITIES AMONG TRANSGENDER WOMEN IN THE MIDDLE EAST: APPLYING THE ADAPT-ITT MODEL TO REFINE AND ENHANCE A COMMUNITY-BASED HIV INTERVENTION

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The Middle East is one of two world regions with increasing HIV incidence. HIV risk and mental health morbidity are high among transgender women in Lebanon, a complex humanitarian setting. Our previous single-group feasibility study of the culturally specific, transgender women-led intervention, 'Baynetna,' demonstrated improved access to HIV testing and mental health outcomes compared to standard of care, but gaps were still observed in HIV prevention and among refugees suffering from traumatic war events and violence. We therefore sought to refine and enhance this intervention by incorporating data on transgender women's lived experiences of health and social disparities in preparation for a full randomized-controlled trial. Applying the ADAPT-ITT model, we conducted focus group discussions (FGDs) with transgender women to gather information on HIV prevention disparities as well as unmet mental health needs related to war trauma and transphobic violence. Based on

these data, we produced a draft of the adapted intervention, consulted with topical experts who provide care to this community, and integrated their feedback into a refined draft intervention. We then theater-tested the enhanced intervention content in FGDs with transgender women and incorporated their opinions into the final intervention. A total of 27 transgender women from Palestine (4%), Syria (30%), and Lebanon (66%) participated in the FGDs. The overwhelming majority experienced extreme poverty and shelter insecurity and did not have health insurance. FGDs demonstrated: poor knowledge of and access to HIV prevention; internalized and experienced HIV and gender identity stigma; traumatic experiences of transphobic and political violence; and refugee-host tensions within the transgender community. Interactive content on HIV and gender identity stigma, HIV prevention, human rights, and community solidarity were adapted and added to the intervention following consultation with topical experts. All theater-testing participants (n=14) regarded the new content as beneficial, appropriate, and feasible for incorporation into the broader intervention.

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TOWARDS INCLUSIVE HEALTHCARE: UNDERSTANDING CAREGIVER PERCEPTION ON THE USE OF A DIGITAL TOOL BY CLINICIANS TO MANAGE SICK CHILDREN IN PRIMARY HEALTHCARE SETTINGS OF TANZANIA: A MIXED METHOD STUDY

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With ongoing global digitalization, more and more digital tools are being used to provide health services. So far, most research on perception of digital healthcare tools has been done in settings with high levels of digital literacy or from a healthcare provider's perspective. Little is known about how digital tools are perceived by caregivers with low levels of digital literacy who seek care for their sick children. We investigated caregivers' perception of the use of a tablet-based clinical decision support algorithm to manage sick children in rural and peri-urban primary healthcare settings in Tanzania using a mixed-method approach. 222 surveys and 18 focus group discussions with caregivers of children, who were managed using the digital tool, were conducted in the vicinity of nine primary healthcare facilities in Morogoro and Mbeya region, Tanzania. 67% of caregivers interviewed did not use smartphones regularly and 82% had never received any services with smartphones or tablets before, confirming low levels of digital literacy and penetration of such tools. Survey results showed that perceived quality of care increased (81.5%), interaction between caregiver and provider improved (79.7%), caregivers trusted the digital tool (81.1%), and usage of the tool would not negatively influence future healthcare seeking (98.2%). Focus group discussions confirmed the caregivers' overall positive perception of the digital tool. The positive perception of caregivers on using a digital tool to manage sick children in primary healthcare settings suggests that such tools may be used even in settings with low levels of digital literacy.

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DECOMPOSITION ANALYSIS OF CHANGE IN THE BURDEN OF NEGLECTED TROPICAL DISEASES, 1990-2021

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The global burden of neglected tropical diseases (NTDs) has decreased significantly due to factors such as improved sanitation, vector control, and treatment availability. Demographic trends also play an important role in understanding and estimating this burden. We aim to describe the change in the burden of NTDs attributable to demographic changes and disease rates from 1990 to 2021. This analysis includes results of 22 NTDs from the Global Burden of Disease (GBD) Study 2021. We describe the disability adjusted life years (DALYs), defined as the sum of years lived with disability and years of life lost. We present global results within super-region, age and cause levels. To estimate the change in the number of NTDs DALYs due to population growth, change in population age-structure, and change in disease rate, we used the Das Gupta three-factor method. Globally, the number of DALYs due to NTDs decreased by 44.3% (95% UI 48.1 to 45.1) from 1990 to 2021, from 29.5 to 16.5 million (95% UIs 22.5 to 41.4, 12.3 to 21.4). Changes in diseases rates contributed to a decline of 73% in the number of DALYs from 1990 to 2021. On the other hand, population growth contributed to an increase of 33% in the number of DALYs. Changes in population age structure had a small effect, contributing to a decrease of 4% in the number of DALYs. Rates of DALYs decreased across all age groups, with similar decreases spanning age groups from 2 to 70, whereas counts of DALYs increased for ages 70 and up. South Asia had the highest decrease in the number of DALYs, moving from 8.88 million in 1990 to 4.08 million in 2021. Changes in disease rates contributed to a decrease of 96% in the number of DALYs, and population growth contributed to an increase of 43%. The age-standardized rate of DALYs decreased from 791 (503 to 1379) to 230 (156 to 318) per 100,000. Our estimates demonstrate that changes in population and rates of NTDs have significantly varied since 1990, by age, geography and cause. These estimates can be utilized as a resource in consideration of policy and intervention strategies to reach control, elimination, and eradication goals of NTDs.

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SPATIAL ACCESS TO HEALTH SERVICES IN THE TRI-BORDER REGION OF ARGENTINA, BOLIVIA, AND PARAGUAY

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Increasing access to healthcare services is one of the key objectives of health systems worldwide, as inadequate access contributes significantly to social health inequities. This challenge is particularly pronounced in regions like the Tri-Border area of Argentina, Bolivia, and Paraguay, which face geographical isolation and marginalized healthcare services. Indigenous communities in this region encounter significant obstacles in accessing healthcare, exacerbated by insufficient infrastructure, primary healthcare coverage, and essential resources such as ambulances. The government of Salta province declared this area a "socio-sanitary emergency" in 2020 due to these challenges, highlighting the urgent need for improved healthcare accessibility. In this context, the main objective of this study was to assess the accessibility to health services for indigenous communities in the Tri-Border region using artificial intelligence tools, spatial analysis, and remote sensing. We used a high-resolution SPOT satellite image provided by the Argentine Space Agency (CONAE) and cartographic data obtained from open data sources. For the analysis, the AccessMod5 tool developed by the World Health Organization was used. First, an accessibility analysis was conducted to calculate the spatial distribution of travel time to/from

medical care centers, followed by a geographic coverage analysis to define the influence zone associated with each healthcare center. The resulting maps revealed isolated regions located more than an hour away from the nearest hospitals as well as disparities in healthcare coverage distribution, underscoring areas with fewer healthcare centers and a pressing need for improved infrastructure. These findings emphasize the critical necessity of enhancing the healthcare system in the region and implementing targeted interventions to ensure equitable access to medical services for indigenous communities. Our findings will be disseminated to regional authorities to inform decision-making and promote enhanced access to healthcare services.

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ASSOCIATION OF BLOOD PRESSURE AND ANTHROPOMETRIC INDICATORS WITH GENE VARIANTS IN ADULTS IN THE KASSENA NANKANA MUNICIPAL AND KASSENA NANKANA WEST DISTRICT OF GHANA

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Cardiovascular diseases are a global health issue with an increasing burden and are exacerbated by hypertension and obesity. High blood pressure and obesity are partly attributed to genetic variants that are generally not known in sub-Saharan African populations. Genome-wide association studies (GWAS), mainly performed in European, African American, and Asian cohorts, have identified variants associated with blood pressure and anthropometric indices. However, few studies have been performed in sub-Saharan Africans.This study evaluated the effect of single nucleotide polymorphisms (SNPs) in eight candidate genes (*ABCA1*, *LCAT*, *LPL*, *PON1*, *CETP*, *PCSK9*, *MVK*, and *MMAB*) on blood pressure and anthropometric indicators among 1,839 Ghanaian adults. DNA was extracted and genotyped using the H3Africa SNP array. Linear regression models were used to test the association between SNPs and log-transformed blood pressure levels and anthropometric indices, adjusting for sex, age, and body mass index (BMI). In addition, Bonferroni correction was performed to account for multiple testing. One variant of the *PCSK9* gene (rs17111557) was significantly associated with diastolic blood pressure (DBP) at $p = 0.003$ with or without Bonferroni correction and $p = 0.006$ after covariate adjustments. This variant was located in the intronic region of the *PCSK9* gene. The functional prediction of this gene variant suggests an impact on the binding site of transcription factors, thereby altering the rate of transcription. The novelty of this study lies in its ability to identify the rs17111557 variant in the *PCSK9* gene to be associated with DBP.

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USE OF A ONE HEALTH APPROACH TO DETECT EIGHT NOVEL HIGH RISK PATHOGENS IN ACUTE FEBRILE PATIENTS IN NIGERIA

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The Surveillance of AFI Aetiologies in Nigeria (SAFIAN) study aims to investigate infectious etiologies of acute febrile illnesses (AFIs) which are commonly misdiagnosed and treated as malaria. SAFIAN uses the TaqMan-Array Card (TAC), a customizable tool allowing simultaneous screening of up to 380 targets. Pathogens commonly surveilled in Nigeria include Lassa and dengue virus, and Plasmodium spp. However, climate change, urbanization and transportation networks have increased risk of pathogen spread into new geographic locations. We developed a One Health methodology to assess Nigeria's susceptibility to a list of pathogens by evaluating their transmission potential (TP). The evaluation included transmission route, previous detection, and vector presence and habitat suitability in Nigeria. We applied this methodology to select pathogens for the TAC used in SAFIAN. We identified 8 previously undetected or scarcely detected pathogens, including two Category A pathogens. Rickettsia spp. was detected in 55 participants, despite no previous human molecular detection in Nigeria. Its inclusion in SAFIAN was based on prior molecular detection in its tick vector in Nigeria, whose geographic range was documented to have extended to Nigeria in 2013. Crimean-Congo Hemorrhagic Fever Virus and Brucellosis spp., each detected in 4 participants, were included based on existing seroprevalence among humans and/or cattle. Four arboviruses were detected, O'nyong-nyong(5), Chikungunya(4), Zika(3) and West Nile(1); inclusion was based on human seroprevalence and presence of their vectors. Hepatitis E virus(1) was documented in humans and animals and its transmission to humans, fecal-oral route/contaminated water, is vector-independent, such that transmission could occur anywhere. In Nigeria, these 8 pathogens are not surveilled/routinely tested for and are rarely included in research. The number of unexpected findings with public health significance in a modest sample size of 465 demonstrates the utility of our One Health-based methodology. We recommend a broader consideration of pathogens in research beyond established approaches.

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PATHOGEN ANALYSIS NETWORK FOR DETECTING MICROBES IN REAL-TIME (PANDEMIC)

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Preparing for emerging biological threats has become increasingly challenging. One of the key components of the first line of defense against a biological threat is our biosurveillance systems. Most surveillance strategies rely on PCR assays, which are inexpensive, fast, and target specific. The disadvantage of using PCR-based methods is that they cannot be highly multiplexed (due to loss of sensitivity), so only a limited number of targets may be detected and monitored within a single reaction. While the BioFire® filmarray® provides panels with up to 14 to 43 targets, it still is sensitive to another disadvantage of PCR-based assays, target erosion. Next-generation sequencing has become a viable complement to PCR-based biosurveillance systems. In metagenomics, unbiased sequencing methods can be applied to known or unknown samples to identify and characterize potential pathogens. Although this unbiased approach offers the advantage of detecting anything, it comes at the cost of sensitivity, generally 100-1000 times lower than PCR. With precision metagenomics, hybrid-capture technology is used to detect a wide range of targets with comparable sensitivity to PCR. A major advantage of this technology is its flexibility (targets can be added to the panel as needed), scalability (the same assay can be used in any health care setting and for any number of patient samples), and ability to detect near-neighbors (probes can capture targets up-to 20% divergent at the nucleotide sequence level). The disadvantages of hybrid-capture are the technical expertise needed to run the assay, longer time-to-answer compared to PCR, and cost of running the assay. We have worked towards simplifying hybrid-capture sequencing and making it more deployable in any laboratory setting. We have developed a platform that includes software for designing probes, protocol for running hybrid-capture on multiple sequencing platforms, and software for the analysis of the data. Precision metagenomics adds another tool to help supplement current biosurveillance systems that rely on PCR and metagenomic sequencing.

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SPATIAL VARIATION IN ENVIRONMENTAL AND SOCIODEMOGRAPHIC DRIVERS OF LEPTOSPIROSIS IN THE DOMINICAN REPUBLIC USING A GEOGRAPHICALLY WEIGHTED REGRESSION

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Between 1970 and 2012, South America (SA) and the Caribbean region accounted for approximately one-third of all leptospirosis outbreaks reported globally. Annual morbidity per 100,000 residents varied significantly from 3.9 in SA to 50.7 in the Caribbean. Drivers of infection, such as exposure to carrier mammals, contaminated water or soil, differ across geographical areas. This geographical variation is not accounted for in non-spatial models, leading to potential inaccuracies. This study aimed to explore spatial variation at the household level of drivers of leptospirosis seroprevalence in the DR using a geographically weighted regression (GWR) and provide evidence to inform public health interventions. Human infection and socio-demographic data were collected from 2,078 participants in 23 communities in two distinct provinces (Espaillat and San Pedro de Macoris (SPM)), in a 3-stage random cross-sectional serosurvey conducted from Jun-Oct/2012. Based on conceptual risk frameworks for leptospirosis, publicly available remote sensing and census data supplemented the survey. Bivariate mixed-effect models identified variables (p <0.2) for the GWR. In the non-spatial model, significantly higher odds ratio (OR) of leptospirosis seropositivity were observed in older age groups, males, households in a flooding risk area, and increased density of rivers and bare ground within 250 meters of households. Conversely, higher mean value of gross domestic product (GDP) at the community level was associated with lower OR of leptospirosis seropositivity. The GWR identified spatial variation in the effect of each covariate included in the model within and across the two provinces. OR of contact with freshwater varied the most across space (7.8, range 0.8-8.2) with limited variation observed in the OR of GDP while still significantly protective across both regions. Older age groups, males, farmers, and contact with rats were associated with higher ORs of leptospirosis seropositivity in SPM compared with Espaillat. These results and framework can be used to inform more targeted and cost-effective public health actions in the DR and regionally.

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UTILIZATION OF NEAR REAL-TIME ENVIRONMENTAL DATA FOR AN 'EARLY WARNING SYSTEM' TO INCREASE PUBLIC PREPAREDNESS OF THE SEASONALITY AND SPREAD OF LYME DISEASE IN THE UNITED STATES

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Quantifying the spatiotemporal spread and risk of Lyme disease (LD) in humans remains a major global challenge. Predictive models can identify environmental associations with LD incidence to better inform risk trends. We demonstrate how environmental data can provide near real-time information on the seasonal onset of LD (seasonal model) and which factors most describe the spread of LD in the United States (US) since 2003 and projected into 2030 (spatial model). Centers for Disease Control and Prevention LD incidence data (2001-2021) in 16 high incidence (>10 cases/100,000 persons) and 18 low-incidence LD jurisdictions were used for the spatial model. Administrative claims data were used to estimate LD incidence (2001-2019) in two high incidence states for the seasonal model. Explanatory variables of climate, normalized difference vegetation index (NDVI), land cover, *Ixodes scapularis* presence, and distribution of tick hosts and reservoirs for *Borrelia burgdorferi* were used to train generalized linear and machine-learning algorithms. The seasonal model found a strong association (R^2=0.90) between daily temperatures (p<0.001) and weekly accumulation of NDVI (p<0.001) with the weekly percentile of reported LD cases. NDVI accumulation (>5) and percentile (25th) of annual reported LD cases accelerated by 3 and 5 weeks, respectively, between 2001-2018 suggestive of increasing LD incidence is in part due to earlier or longer LD seasons (p<0.0001). Spatial models (AUC: 0.98) found the variables that best explained LD spread were mostly (71%) non-climate, including county adjacency of LD cases (22%), *I. scapularis* presence (8.4%), variable forest growth (6.3%), and shrew and skink abundances (5.1% each). By 2030, the model predicted 600 counties (20.5% increase from 2019) categorized as high-incidence LD counties with northward expansion into Canada and westward from US Midwest and Northeast regions. We show how our models utilized as 'early warning systems' could be valuable public health tools to increase public preparedness and uptake of protective measures including vaccination to mitigate increasing global health threats like LD.

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COUNTRIES' PROGRESS TOWARDS GLOBAL HEALTH SECURITY WITH INCREASED HEALTH SYSTEMS RESILIENCE DURING THE CORONAVIRUS DISEASE-19 (COVID-19) PANDEMIC: A DIFFERENCE-IN-DIFFERENCE STUDY OF 191 COUNTRIES

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Research on health systems resilience during the COVID-19 pandemic frequently used the Global Health Security Index (GHSI), a composite index of six categories spanning 37 indicators which score countries' health security and related capabilities. Conflicting results, however, raised questions about the index's validity. This study attempted to clarify these varying results and better characterize the effect of countries' progress towards Global Health Security (GHS) on health systems resilience during the pandemic. We used longitudinal data from 191 countries and a difference-in-difference causal inference strategy to quantify the effect of GHSI scores on countries' essential childhood immunization coverage rates. We divided countries into treatment and control groups for all tested indices by testing cutoff values on a sliding scale to determine the minimum value at which a safeguarding effect was observed. All analyses were adjusted for potential confounders and World Bank governance indicators were employed for robustness tests. While overall GHSI scores prevented declines in childhood immunization coverage rates from 2020 - 2022 (coef: 0.91; 95% CI: 0.41 - 1.41), this safeguarding effect was strongest in 2021 (coef: 1.23; 95% CI: 0.05 - 2.41) as compared with 2020 (coef: 0.74; 95% CI: 0.28 - 1.20) and 2022 (coef: 0.76; 95% CI: 0.06 - 1.46). The coefficient sizes for overall GHSI scores were smaller than the coefficients of many of the GHSI's sub-components, including countries' environmental risks (coef: 4.28; 95% CI: 2.56 - 5.99), biosecurity (coef: 1.87; 95% CI: 0.83 - 2.91), and emergency preparedness and response planning (coef: 1.82; 95% CI: 0.54 - 3.11). Our findings indicate that GHS was positively associated with health systems resilience during the pandemic, that GHS may have had the most significant protective effects in 2021 as compared with 2020 and 2022, and that countries' underlying characteristics, including governance quality, also played a key role in health systems resilience during the pandemic.

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DISTRICT READINESS TO RESPOND TO INFECTIOUS DISEASE PUBLIC HEALTH EMERGENCIES ACCORDING TO THE 7-1-7 TIMELINESS METRICS IN EASTERN UGANDA

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Among districts in Uganda, there is varying capacity to respond to Public Health Emergencies (PHEs). The WHO categorizes PHEs into 4 levels. Grades 1-3 necessitate a WHO response; ungraded PHEs are monitored. The 7-1-7 timeliness metrics include detecting an infectious disease outbreak in 7 days, notifying authorities in 1 day, and response completion in 7 days. These metrics allow for the assessment of the performance of surveillance, reporting, investigation, and response systems. Required capacities and response components include response initiation, epidemiological investigation, laboratory confirmation, medical treatment, countermeasures, communications and community engagement, and response coordination. We determined; 1) the number of WHO-ungraded PHEs in the Mbale and Teso regions of Eastern Uganda from January-March 2024, and 2) the ability of districts to respond according to 7-1-7 metrics. We identified 5 WHO-ungraded infectious disease outbreaks including anthrax (x2), cholera, measles, and rabies in 5 (19%) of 27 districts in Eastern Uganda. The median (IQR) number of days for detection, notification, and response was 8 (4-24.5), 3 (1.5-11), and 15 (8-19.5), respectively. None of the districts met all 7-1-7 targets due to deficiencies in vaccine access, drug availability, clinician training, and notification, which resulted from poor reporting structures for animal and human teams for zoonoses. Delays in response initiation included laboratory confirmation and putting countermeasures in place. Enhancing public health responses at the district level requires multi-hazard risk assessments, contingency plans, and capacity-building for rapid response teams. Using the 7-1-7 metrics could help districts conduct early action reviews to identify performance setbacks and guide resource allocation. Guiding documents can help districts effectively respond to ungraded PHEs.

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A SUBSET OF CAMBODIAN *PLASMODIUM VIVAX* PARASITES TREATED WITH ARTESUNATE DISPLAY SLOW CLEARANCE AND A DELAYED AND UNIQUE GENE EXPRESSION RESPONSE

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Artemisinin-based combination therapies (ACTs) are the frontline antimalarial drugs for the treatment of malaria infections but the efficacy of artemisinin has been threatened by the rise and spread of resistance in *Plasmodium falciparum* since its emergence in Cambodia in the 2000s. Here, we analyze 158 *P. vivax* infections from Cambodian patients treated with 2 mg/kg/day of artesunate for 7 days. All infections were successfully cleared by day 4. However, 9 of the infections (5.7%) showed parasite clearance time (defined as the slope half-life after regression of log-transformed parasite counts) greater than 5 hours, meeting the WHO definition of artemisinin resistance. We observed no significant association between slow clearance and either patient- (e.g., age, weight) or infection characteristics (e.g., parasitemia, stage composition). We characterized by RNA-seq the parasite gene expression of 15 fast- and 16 slow-clearing infections at baseline and 1, 2 and 4 hours after treatment. While the fast-clearing parasites showed significant changes in gene expression immediately upon treatment (with 408 and 1,463 genes differentially expressed 1 and 2 hours after treatment, respectively), slow-clearing parasites displayed a significantly delayed gene expression response (with no genes differentially expressed one hour after treatment and 1,384 and 2,443 differentially expressed genes 2 and 4 hours after treatment). Many of the genes that changed their expression after treatment in both fast- and slow-clearing parasites were indicative of a global shutdown of transcription and translation, as well as of an overall decrease of proteosome activity (similar to the effects of artesunate on *P. falciparum*). By contrast, many genes only differentially expressed in the slow-clearing parasites were associated with hemoglobin endocytosis (e.g., VSP45, PIP3) and hemoglobin digestion (e.g., falcilysin, vivapain). Overall, our results indicate that some Cambodian *P. vivax* parasites are cleared slowly after artesunate treatment, possibly due to their lower hemoglobin metabolism that would reduce the efficiency of the drug.

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EVALUATION OF AN IMPROVED SYBR GREEN I ASSAY FOR SURVEILLANCE OF ANTIMALARIAL RESISTANCE IN *EX VIVO* AND CULTURED ISOLATES

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Malaria morbidity and mortality continues to be a public health concern in endemic regions and has been aggravated by emergence of artemisinin resistance. A SYBR Green I fluorescent based assay has been widely used in drug testing of fresh isolates. However limited studies have reported on parallel evaluation of SYBR green I assay using *ex vivo* and culture adapted isolates. We retrospectively analyzed susceptibility data for six drugs to evaluate SYBR Green I assay ability to produce comparable data in *ex vivo* and cultured isolates. Samples were collected under an approved surveillance protocol between 2018 to 2023 collected from hospital sites in all the six malaria epidemiological zones in the country. Total of 530 isolates were tested, *ex vivo* (330) and 200 tested through adaptation against chloroquine (CQ), quinine (QN), artemether (AT), lumefantrine (LU), artemisinin (AR) and amodiaquine (AMQ). Response curves were obtained from relative florescence units (RFU) using Graph Pad Prism. *Ex vivo* versus cultured isolates data for each drug was compared using Wilcoxon matched paired test. Chloroquine had a median concentration of 9.447ng/ml (4.732-15.79) in isolates tested for *ex vivo* and 15.82ng/ml (9.783-25.41) in cultured isolates, p=0.0001. QN median, 21.41ng/ml (11.93-35.17) in *ex vivo* and 22.45 ng/ml (14.10-40.09) in cultured isolates, p=0.17. AR median, 2.762 ng/ml (1.425-4.302) in *ex vivo* and 3.071 ng/ml (2.029-4.352) in cultured. AT 1.884 ng/ml (1.010-3.241) in *ex vivo* and 1.848 ng/ml (1.164-3.116) in cultured, p=0.91. LU, 9.791 ng/ml (2.196-29.55) in *ex vivo* and 10.57 ng/ml (2.924-25.20) in cultured, p=0.19. AQ, 1.897 ng/ml (0.8870-4.142) in *ex vivo* and 1.199 ng/ml (0.7374-2.870) in cultured isolates p=0.10. Median IC_{50}s in five drugs compared in *ex vivo* versus cultured adapted had no significant variation except chloroquine which had a variation but still within the resistance threshold. Therefore in remote laboratory settings where samples cannot be received and tested within 6 hours of collection, they can be cultured and thereafter drug screening done at a convenient time without compromising on data integrity.

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EMERGING BIOLOGICAL THREATS TO MALARIA CONTROL IN UGANDA: EVIDENCE OF VALIDATED MARKERS OF PARTIAL ARTEMISININ RESISTANCE AND *PFHRP2/3* DELETIONS IN A HIGH TRANSMISSION SETTING

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Artemisinin-based combination therapy is the recommended treatment option for uncomplicated malaria, however emergency of partial artemisinin resistance threatens their effectiveness. Similarly, P. falciparum histidine-rich protein-2 (HRP2) based Rapid diagnostic tests (RDTs) are extensively deployed, however deletion of the *pfhrp2/3* gene threatens their usefulness. Genomic surveillance was conducted in Karamoja, Lango, Acholi and West Nile regions between 2021 and 2023. Symptomatic patients were screened for presence of parasites with HRP2 and pLDH detecting RDTs. Dried blood spots (DBS) were used to confirm parasite species with a conventional multiplex PCR, *pfhrp2* and *pfhrp3* gene with a real-time multiplex qPCR and *pfk13* mutations by Sanger sequencing with Big Dye Terminator. Regional variations in proportions of *PfK13* mutations were assessed using the chi square or Fisher's exact tests while Kruskal-Wallis test was used to compare absolute parasite DNA levels between wild type and mutants parasites. Overall, 238/240 samples (99.2%) were successfully sequenced. Three mutations were identified; *PfK13* C469Y in 32/238 (13.5%) samples, *PfK13*A675V in 14/238 (5.9%) and *PfK13* S522C in (1/238 (0.42%). The prevalence of *PfK13* C469Y mutation was significantly higher in Karamoja region (23.3%), P=0.007. Majority of parasites in West Nile are of wild type (100%), P=0.002. Relative parasite DNA quantity did not differ between the wild type C469Y and A675V alleles (Kruskal-Wallis test, p=0.6373). Overall, qPCR confirmed single *pfhrp2* gene deletion in 1 out of 416 (0.2%) samples that were confirmed of *P. falciparum* mono-infections. Prevalence of validated markers *PfK13* A675V and *PfK13*C469Y in multiple geographical locations provides additional evidence of emerging threat of artemisinin resistance in Uganda. Findings showed limited threat of *pfhrp2/3* gene deletions suggesting HRP2 RDTs are still useful diagnostic tools. Periodic genomic surveillance is recommended to monitor the proportions of gene deletions and its effect on RDTs as well monitor levels of *PfK13* mutations in parallel with in-vivo therapeutic efficacy studies.

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ARTESUNATE-PYRONARIDINE IS EFFICACIOUS FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM VIVAX* INFECTIONS AND BLOCKS TRANSMISSION MORE THAN CHLOROQUINE IN ETHIOPIA.

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In Ethiopia, *Plasmodium vivax* accounts for approximately 40% of malaria cases. The rapid generation of gametocytes contributes to high infectivity of clinical *P. vivax* patients, even before symptoms arise. The impact of antimalarial treatment on this infectivity and the importance of primaquine to prevent onward transmission remains uncertain. We assessed the efficacy, safety, and transmission-blocking effects of artesunate-pyronaridine (PA) and chloroquine (CQ) in combination with 14 days of primaquine (PQ). *P. vivax* infected patients (n=206) were randomly enrolled in the CQ (n=99) and PA (n=107) arms plus PQ administered starting on day 0 to evaluate efficacy on day 28 or 42. To assess transmission potential in the absence of PQ, additional patients were enrolled to receive delayed PQ starting on day 3 following schizonticidal treatment with CQ (n=15) or PA (n=15). Transmission to mosquitoes was thus evaluated by direct membrane feeding on days 0, 1, 2 and 3 after CQ (n=15), CQ + PQ (n=15), PA (n=15), and PA + PQ (n=15). Treatment success on day 42 was high in both the CQ + PQ (95.3%, 82/86) and PA + PQ (98.0%, 97/99) arms. One early treatment failure was observed in the CQ arm whilst 5 late failures were observed in both arms (CQ, 3/86, PA, 2/99). Asexual parasite clearance was higher in the PA (87.7%, 93/106) than CQ (46.5%, 46/99, *P*=0.001) arm on day 1. Similarly, shorter gametocyte clearance time was observed in PA than the CQ arm (*P*<0.001). Before treatment, 91.7% (55/60) of patients infected mosquitoes. On day 1, 46.7% (7/15) and 13.3% (2/15) of patients still infected mosquitoes in the CQ and PA arm, respectively. In the arms that included PQ, only 26.7% (4/15) patients in the CQ + PQ arm was infectious whilst no infection was observed in the PA + PQ arm. None of the patients infected mosquitoes on days 2 and 3. While both the first line, CQ, and alternative drug, PA, were efficacious for the treatment of uncomplicated *P. vivax* malaria in Ethiopia, PA cleared *P. vivax* asexual parasites as well as gametocytes faster than CQ with indications for a greater transmission blocking effect compared to CQ.

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INTERACTIVE GENETIC EPIDEMIOLOGY TOOLS FOR SURVEILLANCE OF DRUG-RESISTANT MALARIA PARASITE STRAINS

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The rapid emergence and spread of drug-resistant malaria threaten elimination efforts in the Greater Mekong Subregion (GMS). The GenRe-Mekong project, in collaboration with National Malaria Control Programs (NMCPs), conducts genetic surveillance of *Plasmodium falciparum* to monitor drug resistance in the GMS. Translating the generated genetic data into graphic outputs easily interpreted by NMCPs requires extensive analyses, posing a major challenge that demands powerful and intuitive tools. We developed the grcMalaria package for genetic analyses and drug resistance mapping using the R language. The package processes standardized genetic surveillance data, as defined by the SpotMalaria Data Dictionary, using public-domain libraries and data sources. Its companion Web-based interface is based on the R Shiny platform, allowing interactive usage of the R package without requiring programming knowledge. The grcMalaria package turns genotyping data into intuitive geographical maps of drug resistance, allele prevalence, diversity, and relatedness with minimal coding. It also provides clustering analyses that identifies and maps genetically similar strains. Furthermore, the grcMalaria Web application provides easy-to-use access to key features of grcMalaria, bypassing the need for R installation and scripting. The grcMalaria R package and web application offer easy access to crucial information on the spread of drug-resistant parasite strains, and help predict changes in drug efficacy at regional, national, provincial and district levels. These tools render genetic epidemiological analysis accessible, and allow NMCPs to integrate and contextualize their findings within broader regional analyses, strengthening future elimination strategies.

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PARTNERSHIP FOR ANTIMALARIAL RESISTANCE MONITORING IN AFRICA (PARMA) HUBS: LOCALIZATION AND CAPACITY STRENGTHENING FOR AFRICAN RESEARCHERS BY AFRICAN RESEARCHERS

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Therapeutic efficacy studies (TESs) are recommended by WHO to be performed every two years in malaria-endemic countries to evaluate antimalarial therapies. Testing samples collected in a TES helps explain treatment failure at the molecular level and allows for timely revisions to national and global policies. The Partnership for Antimalarial Resistance Monitoring in Africa (PARMA) project trains local scientists in malaria-endemic countries to perform these tests independently.
The first PARMA hub was launched in 2022 at the Centre International de recherche, de formation en Génomique Appliquée et de Surveillance Sanitaire (CIGASS) in Dakar, Senegal to address the growing number of TESs and to center analysis and training on the African continent. During training, researchers learn to perform molecular correction to distinguish recurrent from new infections, sequence samples to characterize molecular markers of drug resistance, and analyze bioinformatic data to identify key mutations. The Senegal PARMA hub has proved to be a meaningful opportunity to build expertise, partnership, and collaboration among TES researchers across Africa. Between 2022 and 2024, the hub generated molecular data for 5 countries, hosted 7 African researchers from 4 countries, and produced standardized high-quality reports for stakeholders. One important challenge is bridging the gap between a country sending researchers for PARMA training and the ability of that country to perform the next TES analysis domestically. Because training is intended to encompass a broad overview of topics, developing expertise requires additional practice at the bench. This also depends on key external infrastructural factors such as availability of equipment and reliable electricity. To bridge the gap, in the next 2-3 years the project aims to leverage existing sequencing instruments and highly multiplexed next-generation sequencing panels to lower costs, improve efficiency, and more easily deploy TES assays in countries without highly equipped labs. At least two additional hubs in sub-Saharan Africa will be set up within five years for greater reach and throughput.

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NEW INSIGHTS ON SELECTION OF MALARIA PARASITES REVEALED BY GENOMES OF OLDEST ARCHIVED *PLASMODIUM FALCIPARUM* POPULATION SAMPLES

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Studies of selection on malaria parasites have been driven by the goal of understanding the emergence of resistance to different classes of antimalarial drugs. Investigations on other selective processes and their targets has been overshadowed by that on the evolution of drug resistance. To investigate such processes, *Plasmodium falciparum* genomes were sequenced from malaria-infected blood samples collected in The Gambia between 1966 and 1971, before any drug resistance was detected in West Africa. Genomic complexity within infections was higher than in recently collected samples, consistent with a higher intensity of transmission during this period. Although the overall genomic diversity is similar over time, there were fewer clusters of related parasites among the older samples, suggesting that parasite inbreeding was less frequent. There was no signature of selection on drug resistance loci, but strong signatures of directional selection were seen at several chromosomal locations coding mostly for immune and invasion-related genes. A few of these have also been seen in more recent samples, but some are unique and indicate older selective processes. A genomic scan over time confirms major drug resistance loci have undergone marked changes, but changes are also seen at other loci. The most significant of these are at the *gdv1* locus on chromosome 9 that regulates conversion to sexual transmission stages, and at the *Pfsa1* locus on chromosome 2 and *Pfsa3* locus on chromosome 11, both associated with parasite infections of individuals carrying the HbS haemoglobin variant. These results highlight the significant role of human immune and genetic factors in shaping the evolution of malaria parasites

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A COMPLEX *PLASMODIUM FALCIPARUM* CRYPTOTYPE CIRCULATING AT LOW FREQUENCY ACROSS THE AFRICAN CONTINENT

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The population structure of the malaria parasite *Plasmodium falciparum* can reveal underlying demographic and adaptive evolutionary processes. Here, we analyze population structure in 4,376 *P. falciparum* genomes from 21 countries across Africa. We identified a strongly differentiated cluster of parasites, named AF1, comprising ~1.2% of samples analyzed, geographically distributed over 13 countries across the continent. Members of AF1 carry a genetic background consisting of a large number of highly differentiated variants, rarely observed outside this cluster, at a multitude of genomic loci distributed across most chromosomes. At these loci, AF1 haplotypes appear to have common ancestry, irrespective of the sampling location; outside the shared loci, however, AF1 members are genetically similar to other parasites from the same region. AF1 parasites sharing up to 23 genomic co-inherited regions were found in all major regions of Africa, at locations over 7,000 km apart. Many of the differentiated variants are functionally related, comprising structural variations and single-nucleotide polymorphisms in components of the merozoite surface protein 1 complex, and several other genes involved in interactions with host red blood cell membranes, including invasion, egress and erythrocyte antigen export. This is the first report of a genetic background of such complexity and geographical spread. We coined the term *cryptotype* to denote that AF1 is difficult to detect due to its low frequency, and its recombination with local strains. As AF1 spread across the continent, it appears that the

constellation of mutations remained mostly intact in spite of recombination events, suggesting a selective advantage. We propose that AF1 parasites have adapted to an as yet unidentified evolutionary niche, by acquiring a complex compendium of interacting variants that are otherwise absent from Africa. *In vitro* studies may identify AF1's evolutionary niche, providing new perspectives on host-parasite interactions. It is also possible that other cryptotypes circulate in Africa, and new analysis methods may be needed to identify them.

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UNDERSTANDING GENETIC AND TRANSCRIPTIONAL COMPLEXITY IN MALARIA: INSIGHTS FROM SINGLE-CELL RNA-SEQUENCING IN MALI

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Malaria, caused by *Plasmodium* parasites transmitted through mosquito bites, poses a significant threat to human life. Regions with a high prevalence of malaria often exhibit complex infections, where individuals harbour multiple genetically distinct strains of *P. falciparum*, some showing symptoms while others remaining asymptomatic. Our study, employing Chromium 10x single-cell RNA sequencing (scRNA-seq), delved into the circulating sexual and asexual populations of *Plasmodium* parasites among approximately 60 volunteers in Faladie, Mali, sampled during the transmission seasons of 2021 and 2022. Using both short and long-read RNA single cell sequencing techniques, we scrutinised the transcriptional and genotypic diversity of parasites within and between hosts, offering unprecedented insights for the first time into strain-specific patterns within malaria carriers. Leveraging full-length single-cell RNA sequencing (MAS-seq/Kinnex), we explored isoform differences between strains and cell types, revealing an additional layer of transcriptional complexity. Expanding our analysis to include *P. ovale* and *P. malariae*, which are prevalent in Mali, we examined their intraerythrocytic life stages at single-cell resolution for the first time. Our investigation across these species seeks to understand the behaviour of individual strains within complex infections and their potential role in determining the symptomatic status of the hosts and propensity for sexual conversion. Moreover, we made these detailed cell atlases accessible as a valuable resource for the malaria research community via the Malaria Cell Atlas website www.malariacellatlas.org.

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GENETIC VARIATIONS IN *PLASMODIUM FALCIPARUM* INVASION LIGANDS AND THEIR COGNATE HUMAN RECEPTOR VARIANTS IN MALARIA CASES FROM THE GAMBIA

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The malaria parasite *Plasmodium falciparum* invades the human erythrocytes through ligand-receptor interactions which initiate the clinical signs of malaria. The genes encoding the parasite ligands and human receptors might have experienced some evolutionary changes as a result of these interactions, and this could impact malaria incidence and outcomes. However, variations in parasite ligands and their corresponding receptors in the same individuals have received far less attention even though such studies may be useful in vaccines and drug design, refinement of control strategies as well as provide better understanding of disease development, and progression. To investigate this, a paired study of *P. falciparum* merozoite invasion ligands and their corresponding erythrocyte receptor genes from the same infected individual was carried out using the Nanopore amplicon sequencing approach. Blood samples were collected from 288 malaria-positive individuals from four health facilities in The Gambia. Genomic DNA was extracted from the samples and 12 *P. falciparum* genes: EBA175, EBA181, EBA140, Clag2, Clag8, Rh4, Rh5, merozoite surface protein (MSP)1, MSP6, Duffy binding-like MSP (DBLMSP), erythrocyte binding-ligand 1 (EBL-1), and surface-associated interspersed protein 4.2 (SURFIN4.2), and four human receptors: glycophorin (GP) A, GPB, GPC, and complement receptor 1 (CR1) were sequenced. Moderate to high levels of within-host complexity of infection across sites and high inter-SNP linkage disequilibrium were observed in the DBLMSP and SURFIN4.2 genes of *P. falciparum*, and the human glycophorin B, C, and CR1 gene. There was also a lack of spatial structure between *P. falciparum* from different sites while for the human population, individuals from Basse (Upper River Region) were more distinct from the rest of the population. Analysis of the distribution of variants in receptors identified several SNPs in CR1 and a single variant in GPC associated with severe malaria. These findings suggest that specific host-parasite allelic combinations may determine the infection and severity of malaria.

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DEFINING IMMUNE ESCAPE POLYMORPHISMS IN *PLASMODIUM VIVAX*: INSIGHTS FROM THE ANALYSIS OF ALLELIC TURNOVER OF 16 ANTIGENS IN A LONGITUDINAL COHORT OF PAPUA NEW GUINEAN CHILDREN

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Plasmodium vivax, a malaria species causing relapse infection, generates a number of "antigenically distinct strains" that trigger sequential waves of immune escape within hosts. Understanding parasite genetic diversity aids in identifying circulating strains in the population, providing important information in designing broadly efficacious vaccines. However, the exact genetic determinants underlying antigenic diversity remain unknown. This study is one of the first investigations to identify immunologically relevant diversity and polymorphisms in the leading *P. vivax* antigen vaccine candidates. We employed multiplexed long-read amplicon sequencing on 603 samples (paired infection among 126 children) obtained from a longitudinal paediatric cohort in Papua New Guinea. Sequence comparison between paired infections in the same individual was conducted to identify the association between the polymorphic sites and the patient's clinical outcome (symptomatic or asymptomatic infection). Immune escape polymorphisms were defined when the proportion of the polymorphic site associated with a transition to symptomatic infection was significantly varied ($p \leq 0.5$) from those associated with asymptomatic transition. The within-host analysis revealed polymorphisms in blood-stage antigens, including AMA-1, DBP, MSP-1, and CyRPA, significantly linked to symptomatic malaria, suggesting involvement in strain-specific immunity. These polymorphisms also surround residues crucial for merozoite binding and invasion, indicating that they could be maintained by immune selection pressure. Categorising these immune escape polymorphisms into immunologically distinct groups showed widespread distribution of non-vaccine strains, while the Sal-1 vaccine strain had relatively low global frequency, potentially compromising the efficacy of the current vaccine formulations. Overall, this study narrowed down the diversity into immunologically relevant strains, which could guide researchers in their rational selection of antigens or constructs to be considered in designing a highly and broadly effective *P. vivax* vaccine

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SOFTWARE TO ESTIMATE THE PROBABILITY THAT A RECURRENT MALARIA INFECTION IS A REINFECTION, RECRUDESCENCE OR RELAPSE.

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A recurrent *Plasmodium falciparum* infection can be caused by a failure to treat a preceding infection (recrudescence) or by a new mosquito inoculation (reinfection). In addition, a recurrent *P. vivax* blood-stage infection can be caused by the activation of latent liver-stage parasites called hypnozoites (relapse). Estimating the cause of recurrence is important; for example, when monitoring antimalarial resistance, in therapeutic efficacy studies of treatments for *P. falciparum*, recrudescence needs to be separated from reinfection; to improve treatment for *P. vivax*, in trials of radical cure treatment regimens, relapses need to be separated from reinfection and recrudescence. We developed an R package that practitioners can use to visually interrogate parasite genetic data used for recurrent state inference, and to estimate the probability that a recurrence is a relapse, recrudescence or reinfection (both Pv3Rs and Pf2Rs inference). The inferential framework is built around the modification of a model used previously to estimate relapse probabilities from genetic data on *P. vivax* infections in clinical trial participants. The original model demonstrated the feasibility of *P. vivax* recurrent state genetic inference, but was limited to data on only a few microsatellite markers and at most two recurrences per participant. The updated model is faster and more powerful. It scales linearly with the number of markers, generating probability estimates from genetic data on the many markers typical of amplicon sequencing data. It is able to directly estimate recurrent state probabilities for participants who experience more than two recurrences. Besides a few edge-cases, which we will describe, the estimates generated by the new model are comparable to those generated previously. In summary, we have built a user-friendly tool for malaria recurrent state inference. To facilitate uptake by practitioners and to promote enhancement by methodologists, we will describe the updates to the underlying model, demonstrate how to use the software, outline current limitations and describe future developments.

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GENETIC REGULATION OF *PLASMODIUM FALCIPARUM* OXIDATIVE STRESS RESPONSES

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Malaria caused by Plasmodium falciparum ranks among the deadliest infectious diseases worldwide, responsible for over 600,000 deaths in 2020. Continuing spread of drug-resistant parasites prioritize the search for new drug targets and understanding resistance mechanisms. Drug treatment, fever conditions, and infected sickle cells induce oxidative stress during the asexual stages. Recently, we demonstrated that oxidative stress compromises the effectiveness of antimalarial drugs, suggesting that prolonged exposure to intraerythrocytic microenvironmental oxidative stress, as would occur in endemic regions with high prevalence for sickle trait and other hemoglobinopathies, may predispose malaria parasites to develop tolerance to the oxidative damage caused by antimalarial drugs like artemisinin. To understand the underlying mechanisms linked to this phenomenon, we used large-scale forward genetic screens of P. falciparum piggyBac-transposon mutants to identify genetic mutants with altered sensitivity to oxidative stress. Comparing results from previous piggyBac genetic screens for dihydroartemisinin, heat-shock, and sickle-trait cell, revealed that the underlying mechanisms important in the oxidative stress inducible tolerance to artemisinin in malaria parasite is central to the other blood stage stress survival responses. The most significant altered parasite metabolic activities linked to increased sensitivity to stress conditions are linked to lipid metabolism, exported proteins, and RNA metabolism similar to changes associated with emerging artemisinin resistance in different field isolates. Further investigations are needed to elucidate how the genetic regulation of oxidative stress responses can lead to artemisinin resistance.

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ASSESSMENT OF STRATEGIES USED IN THE MALARIA ELIMINATION DEMONSTRATION PROJECT FOR THE REDUCTION OF MALARIA IN A TRIBAL DISTRICT OF MADHYA PRADESH, INDIA

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The Malaria Elimination Demonstration Project (MEDP) in the tribal-dominated, malaria-endemic Mandla district of Madhya Pradesh, India, represents a pioneering public-private partnership aimed at addressing the persistent public health challenge of malaria, which constitutes a significant burden in India, particularly within tribal regions. India, noteworthy for being the only High-Burden High-Impact country in the WHO SEAR to report a decline in malaria cases amid the COVID-19 pandemic, sees approximately 70% of its malaria cases originating from tribal areas. MEDP, a collaborative effort involving the Indian Council of Medical Research, Government of Madhya Pradesh, and the Foundation for Disease Elimination and Control of India, was designed to leverage field-tested malaria elimination strategies, with adaptations to local contexts. The project's multifaceted approach encompassed the T4 strategy (tracking, testing, treating, and tracking treatment efficacy), optimisation of vector control measures such Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS), alongside the deployment of a mobile surveillance tool and community-centric Information, Education, and Communication (IEC) initiatives. The project has published over 24 peer-reviewed manuscripts describing various learnings and findings. This study, employing a mixed-methods cross-sectional design, evaluated the project's impact on malaria case reduction, vector control practices, frontline worker knowledge and practices and identified implementation gaps by the state. Conducted across 71 malaria-reporting villages in Mandla, the study involved a diverse cohort of participants, including healthcare workers, malaria patients, supervisory staff, and technical experts. The findings highlighted notable achievements in case reduction and diagnostic and treatment efficiency among frontline staff and illuminated various challenges. The study uncovers valuable insights into effective malaria elimination strategies, which can be adapted to similar local and global contexts.

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ADVANCING MALARIA ELIMINATION ASSESSMENT IN LORETO, PERU THROUGH THE FREEDOM FROM INFECTION MODEL

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Perú has experienced a substantial decrease in malaria incidence over the past two decades, after intense control programs successfully interrupted transmission in historically endemic regions. In 2023, 90% of malaria cases occurred within Loreto, prompting the National Malaria Elimination Plan to target this region for elimination by 2030. Currently, claims of elimination rely on the absence of reported malaria cases for 36 consecutive months,

following the World Health Organization's (WHO) standard approach, but this method fails to consider limitations and potential underperformance of the surveillance system (SS). This study aims to probabilistically identify areas in Loreto, Perú that are likely to have achieved malaria elimination. We employed a Bayesian modelling approach within the Freedom from Infection (FFI) framework to estimate the probability that malaria transmission is below a critical threshold, defined here as less than 1 case per 10,000 people (PFree). We used passive case detection data (PCD) from 474 health facilities across 53 districts from 2010 to 2022. The primary outcome was PFree measured for both *Plasmodium vivax* (*Pv*) and *P. falciparum* (*Pf*). We defined the threshold for elimination as having a PFree>0.95 for 36 consecutive months in the most recent 3 years (2020-2022) as per the WHO criteria, and compared concordance in classifying facilities as eliminated using the two methods. Overall, PFree values for *Pf* were higher than PFree values for *Pv*. Preliminary results had 24 HFs for *Pf* and 3 HFs for *Pv* with a PFree>0.95 for 36 consecutive months. In contrast, 181 and 126 HFs had zero cases reported for *Pf* and *Pv* respectively. Our results provide a data driven assessment of the progress made towards malaria elimination in the Peruvian Amazon jungle with potential application to others subnational areas in track for malaria elimination in the Region.

6799

COMMUNITY EXPERIENCES AND PERCEPTIONS OF THE BOHEMIA TRIAL OF IVERMECTIN MASS DRUG ADMINISTRATION: A LONGITUDINAL QUALITATIVE STUDY IN KWALE COUNTY, KENYA

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The efficacy of ivermectin MDA for malaria control has been tested in clinical trials in sub-Saharan Africa. Multiple individual, social, and operational factors influence uptake and adherence to MDA. For sustained involvement of participants in MDA trials it is essential to understand the local context, including health concerns, previous experiences of MDA, and trial expectations. This knowledge helps develop appropriate community engagement strategies and interpret responses of participants to the trial and the MDA. This paper describes a longitudinal qualitative study undertaken to explore experiences of trial participation and perceptions of effects of ivermectin MDA among participants in the BOHEMIA cluster randomised trial of ivermectin MDA in Kwale, Kenya. Purposive maximum variation sampling was used to select five villages (2intervention and 3 control) involved in the trial. Before the start of the trial social science researchers lived in each village for a period of one month conducting participant and non-participant observations, in-depth interviews and focus group discussions. Just prior to the first round of MDA, the social scientists returned to the villages and stayed there throughout each of the 3 rounds of MDA, conducting participant and non-participant observations of the implementation process; and in-depth interviews on experiences and perceptions of the trial and the effects of the MDA. Observation reports for each village before and during the MDA were developed. 25 IDIs and 18 FGDs were conducted prior to the MDA and 22 IDIs during the MDA. The conduct of the trial (MDA distribution strategy, use of informed consent, detailed checking of eligibility) as well as confidence in the implementing institution, enhanced trust in the trial and the efficacy of the MDA. Poor past experiences with MDA and perceptions of exclusion from community engagement process contributed to unwillingness to participate. In intervention and control arms, the MDA was widely perceived to be effective at reducing mosquitoes and malaria. In the intervention arm the MDA was also perceived to be very effective at killing bedbugs.

6800

REACTIVE CASE DETECTION IN ZANZIBAR, A MALARIA ELIMINATION-TARGETED SETTING EXPERIENCING MALARIA UPSURGES IN 2023

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Reactive case detection (RACD) is a malaria elimination intervention that aims to assess malaria transmission among individuals exposed to the same malaria risks as an index case. In Unguja, Zanzibar, in 2023, RACD was conducted by District Medical Surveillance Officers (DMSO) using malaria rapid diagnostic tests (mRDTs) on household members of parasitologically-confirmed malaria cases reported to the national malaria case notification (MCN) system. Positive cases were treated with artemether-lumefantrine. Data were collected using Android tablets and analyzed descriptively. In 2023, 18,283 malaria cases from Unjuja, Zanzibar, were reported to MCN (reference: 4,544 cases in 2022). Household (HH)-level case investigations were conducted for 9,203 (50%) of index cases, and 30,160 household members (including index case) were present during DMSO visits. Of these, 20,957 (70%) were HH members who consented to testing, and 2.5% (530/20,957) tested positive for malaria. HH denominator data were not collected; however, DMSOs reported that HH members, including those at highest risk for malaria infection (adult males), were frequently absent at the time of case investigation. The positivity rate varied across districts: rural Kaskazini A (5.6% [43/766]) and Kati (5.4% [126/2345]) had the highest, while urban Magharibi B (1.3% [68/5195]) and Magharibi A (1.2% [44/3731]) had the lowest. Individuals aged 15-<25 years had the highest positivity rate (3.4% [160/4532]), followed by 5-<15 (3.1% [152/4842]), under 5 (2.3% [56/2458]), and 25+ (1.8% [162/8966]) years. Males had a higher positivity rate (2.8% [272/9892]) than females (2.3% [258/11065]), p=0.055. RACD data demonstrated low coverage of index case HHs and family members, together with low test positivity rates. HH-focused RACD might not be targeting individuals sharing risk factors with the index case. For many, the likely source of infection is outside of the HH, such as the workplace or location of evening activities. As RACD is not a burden reduction tool, higher coverage, better targeted RACD would likely be of more benefit to areas where transmission is closer to zero.

6801

RE-EMERGENCE OF *PLASMODIUM VIVAX* MALARIA CASES IN BORDER AREAS OF MYANMAR AND STRATEGIC EFFORTS TO INTEGRATE NEW TOOLS AT NATIONAL LEVEL FOR ELIMINATION OF *P. VIVAX* MALARIA FROM 2021 TO 2023

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Despite advances in malaria control, *Plasmodium vivax* malaria remains a problem in border areas of Myanmar. Cases have increased from 43,578 in 2020 to 103,216 in 2022, posing a threat to the country's 2030 elimination goal. The main barriers to addressing *P. vivax* malaria include lack of glucose-6-phosphate dehydrogenase (G6PD) testing before antimalarial treatment, patient adherence to antimalarial treatment, and political instability. This abstract highlights PATH Myanmar's strategic efforts to revise the National Treatment Guideline (NTG) in partnership with the National Malaria Control Program (NMCP), to ultimately reduce the *P.*

vivax malaria case burden in Myanmar. PATH Myanmar has collaborated with the Partnership for Vivax Malaria Elimination (PAVE) to introduce four new tools in Myanmar: primaquine (PQ) treatment counselling, feasibility studies for G6PD testing, PQ shorter regimen, and the establishment of a pharmacovigilance (PhV) working group to raise awareness and knowledge of utilization of tools. PAVE developed an optimized radical cure road map in 2020, followed by the development of PQ adherence counselling tools in 2021. In 2022, PAVE organized the first technical advocacy meeting for use of optimized radical cure tools at the national level and for the introduction of a PhV system for antimalarial medication in Myanmar. In 2023, PAVE advocated to the NMCP for the implementation of operational research for G6PD testing and organized a central-level workshop focusing on PQ adherence counseling and integration of the PQ 7-days regimen into the NTG. Through these strategic efforts, the tools for PQ treatment adherence and counselling are used nationwide, and the PQ 7-days regimen will be integrated into the NTG. Moreover, a PhV system is being developed at the national level. Although operational research for G6PD testing has been delayed due to the political instability in Myanmar, PAVE efforts have successfully encouraged the NMCP to integrate new tools into the NTG to guide reduction of *P. vivax* malaria in Myanmar.

6802

OPTIMIZING LAST-MILE DELIVERY THROUGH THE INTEGRATION OF MALARIA COMMODITIES DISTRIBUTION IN MALAWI

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Efficient supply chain management is crucial for malaria management in Malawi, where 6.4 million cases were reported in 2023, necessitating timely and effective distribution of life-saving commodities. The country's supply of malaria commodities is predominantly funded by the U.S. President's Malaria Initiative (PMI) and the Global Fund (GF), and the historical use of separate storage and distribution systems had become a logistical burden to its National Malaria Control Program (NMCP). Monthly coordination of two plans resulted in duplication, complexity, inefficiency, delays, and higher costs, and recording transactions for two distribution streams at service delivery points meant an increased workload for health facility staff. To address this, the NMCP, supported by the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project, in coordination with GF and PMI, facilitated the signing of a Memorandum of Understanding (MOU) in 2022 between the GF project implementation unit (PIU) and GHSC-PSM. The MOU formalized the launch of an integrated distribution mechanism that facilitated visibility of central warehouse inventory data and distribution schedules, and alternated distribution every other month between the two service providers. This initiative resulted in a substantial (30%) reduction in overall distribution costs between October 2022-September 2023, notably in operational, transportation, and personnel expenses. Annual cost savings for the period totaled $133,000 for PMI alone. The reduced frequency in delivery, from 12 to 6 deliveries per year, significantly reduced the workload for health facility staff, while maintaining low stockout rates (<1% for first-line Artemisinin-based combination therapy treatments). These results of substantial cost savings, operational transparency, and improved efficiency in managing malaria commodities validate the integrated system's ability to enhance distribution and provide a basis for potential implementation in similar contexts, especially to optimize limited resources and improve last-mile delivery of health commodities.

6803

EXAMINATION OF PATHOGENS AND FECAL MARKERS IN THE ENVIRONMENT DUE TO INADEQUATE SANITATION SERVICES IN THE ALABAMA BLACK BELT.

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It is estimated that 2.2 million Americans live in homes that lack access to running water or basic plumbing. These shortcomings in access are even more likely to be experienced in Black, Indigenous, and Latino communities when compared to their white counterparts. One region where these inequalities in access to safe and reliable water and sanitation services persist is Alabama's Black Belt. This research aims to get an idea of the microbes present in the environment due to inadequate sanitation infrastructure in a small rural Black Belt community. We collected surface water and soil samples at properties owned by the Auburn Rural Studio and public spaces in the community over January, February, and May of 2023. We collected 125 samples (92 water samples and 33 soil samples) over the course of three months. Of the 125 samples collected 43 were cultured for total coliform, *E. coli*, and Enterococci by IDEXX, and 88 were examined for 48 molecular targets through real-time quantitative PCR using a custom TaqMan Array Card. Of the environmental samples collected and cultured by IDEXX, 43/43 (100%) contained total coliforms, 35/43 (81.4%) contained *E. coli*, and 31/31 (100%) contained enterococci. Of the 88 environmental samples analyzed by TaqMan Array Card, 39 (44.3%) contained gene targets specific to *E. coli* and 67 (76.1%) contained gene targets specific to enterococci. We found *Blastocystis spp.* in 5 of 63 soil samples (7.9%) and 16 of 25 water samples (64%) and *Cryptosporidium spp.* in 20/25 (80%) of surface water samples examined. There was no significant difference in concentration of *E. coli* or enterococci between sites that were impacted and unimpacted by inadequate sanitation in January ($p = 0.561$ for *E. coli* and $p = 0.941$ for enterococcus *Wilcoxon Rank Sum Test*) and February ($p = 0.102$ for *E. coli* and $p = 0.346$ for enterococcus *Wilcoxon Rank Sum Test*). However, the concentration of *E. coli* or enterococci was significantly higher from those samples collected in sites impacted by inadequate sanitation when compared to unimpacted sites in May ($p = 0.0284$ for *E. coli* and $p = 0.0158$ for enterococcus *Wilcoxon Rank Sum Test*).

6804

FECAL EXPOSURE PATHWAYS FOR CHILDREN IN LOW-INCOME, UNPLANNED COMMUNITIES OF URBAN MAPUTO, MOZAMBIQUE USING A QUANTITATIVE MICROBIAL RISK ASSESSMENT FRAMEWORK

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Enteric pathogen exposures are critical drivers of child mortality in Mozambique with 6.6% of total deaths among children <5 attributed to enteric infections. Despite high prevalence of enteric infections in children, the household transmission pathway(s) driving these exposures are still being explored. To identify the critical exposures for children <24 months in low-income, unplanned communities in Maputo, Mozambique, we collected and analyzed environmental samples (n=574) for culturable *E. coli*: drinking water (source [n=48], stored [74]), food (solid [61], liquid [28]), hands (mother [78], child [76]), surface swabs (floor [75], food preparation area [71]), and soil [63] in the household setting. We estimated daily quantitative *E. coli* exposure doses for a child using a stochastic quantitative microbial assessment (QMRA) model (10,000 iterations, mc2d package) and caregiver-reported food consumption rates. Relative reductions in *E. coli* dose were calculated for water treatment (boiling once daily) and handwashing (uniform distribution: 1-4 times daily, 30-90% efficacy). Among all samples, 251 (44%) were positive for culturable *E. coli*, with the highest concentrations in soil (mean $\log_{10}$: 4.77 per 1g) and child's hands

(mean $\log_{10}$: 3.55 per two hands). The lowest *E. coli* concentration was for source drinking water (mean $\log_{10}$: 1.07 per 100 mL). Using the QMRA model, solid food consumption was the dominant *E. coli* exposure pathway: median 710.5 CFU/day (95th percentile range: 2.3, 2.0 x 10^{5}). The lowest *E. coli* dose was associated with child's hands: median 0.4 CFU/day (95th percentile range: 4.7 x 10^{-4}, 381.6). Simulating single interventions, boiling of stored water reduced the *E. coli* dose by > 99.999% to a median 1.4 x 10^{-4} CFU/day, whereas handwashing resulted in an attenuated dose reduction (22%) to a median 3.1 x 10^{-1} CFU/day. This study underscores the importance of food-mediated fecal exposures among children. Forthcoming enteric pathogen data aims to corroborate the relevant exposure pathways and impact on child health. Evaluation of targeted food interventions to interrupt food-mediated exposures are warranted.

6805

UNDERSTANDING ANTIBIOTIC RESISTANCE, VIRULENCE, AND BIOFILM FORMATION IN *ACINETOBACTER BAUMANNII*: INSIGHTS FROM GORANCHATBARI SUB-CATCHMENT, DHAKA CITY

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Increased incidence of hospital acquired infections may be attributed due to the existence of ESBL producing *Acinetobacter baumannii,* a serious health concern for both hospitals as well as community healthcare environment. The biofilm forming capacity makes them a persistent pathogen in these environments. This study aimed to isolate *A. baumannii* positive for ESBL production from environmental samples, characterization of key virulence and ESBL genes, assessment of antibiotic resistance profile and biofilm forming capacity. A total of 21 environmental samples were collected between April-December, 2022. In this study, 56 isolates of ESBL producing *A. baumannii* were investigated. The ESBL producing *A. baumannii* were subjected to PCR to detect resistance and virulence genes. Among those isolates, 71.4% and 5.4% contained bla_{TEM} and bla_{SHV} genes respectively. In the case of virulence factors, 76.8%, 69.6%, 64.3%, 62.5%, 28.6%, 10.7% and 5.4% of the isolates harbored *pgaB*, *bfmS*, *csuE*, *ompA*, *kpsMII*, *fimH* and *bap* genes respectively. Whereas, 26.8% of the isolates were positive for each of *ptk* and *epsA* genes. During the biofilm formation assay, it was observed that 1.8% of the isolates formed strong and 66.1% formed weak biofilm respectively at 25ºC. In addition, at 37ºC, 1.8% of isolates were moderate and 76.8% were weak biofilm formers respectively. Antibiotic susceptibility testing revealed that 8.9% of the studied isolates were found resistant to cefotaxime and 5.4% were to cotrimoxazole. In addition, 87.5% and 91.1% of studied isolates were found intermediately resistant to ceftriaxone and cefotaxime respectively. As indicated by this study, *A. baumannii*, which produces ESBLs, is rapidly migrating from clinical settings into the environment and could serve as a reservoir for antimicrobial resistance. The data could significantly impact how well public healthcare initiatives are implemented. Exposure to them may create a severe threat to public health.

6806

ENVIRONMENTAL EXPOSURES ASSOCIATED WITH ENTERIC PATHOGEN CARRIAGE IN CHILDREN AGED SIX MONTHS IN NORTHERN ECUADOR

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Enteric pathogens are a major cause of mortality and morbidity globally, disproportionately impacting populations in low- and middle-income countries with limited access to water, sanitation, and hygiene (WaSH) resources. We identified environmental risk factors associated with enteric infection in 6-month-old infants along an urban-rural gradient in northern Ecuador; communities were grouped as urban, semi-urban, and rural with road or river access. We collected exposure data on household WaSH, animal exposure, floor material, crowding, and fecal contamination of drinking water and hand rinses, as well as covariates including mother and child demographics, child vaccination status, food insecurity, and socioeconomic status. Child stool samples were analyzed for bacterial (n=10), viral (n=6), and parasitic (n=6) pathogens using multiplex TaqMan Array Cards. We utilized multivariate models, elastic net regression, and distance-based statistical methods to explore factors associated with: i) any infection, ii) coinfection, iii) total number of pathogens, and infection with any iv) bacteria, v) virus, or vi) parasite. Among 276 children, most (87%) were positive for at least one pathogen and 71% were positive for multiple pathogens. Bacterial pathogens were most common (81%), followed by viruses (57%) and parasites (8.3%). Factors associated with reduced risk of infection (p<0.05) included: ceramic tile floors, improved hygiene, and unshared household toilet attached to a sewer system. Risk factors included living in a semi-urban or rural community; having unimproved sanitation; and having a drinking water source from a well or surface water. Seasonality was associated with the likelihood of infection, with fewer viral infections and more bacterial infections in the rainy season. We will also report on specific pathogens, for example *E. coli* detection in child hand rinse was associated with *Giardia* infection. Environmental conditions are associated with enteric infection risk, varying by pathogen type. This data suggests areas of focus for future WaSH interventions with the goal of reducing enteric disease burdens.

6807

SOIL-BORNE EXPOSURE TO ANTIMICROBIAL RESISTANT *E. COLI* AND SOIL-TRANSMITTED HELMINTHS THROUGH SOIL FLOORS IN RURAL BANGLADESH

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Floors made of soil are common in low-income countries and are increasingly recognized as an exposure route for childhood infectious diseases, including soil-transmitted helminth (STH) infections. Soil is also a critical reservoir for antimicrobial resistant organisms. We aimed to investigate associations between flooring material and detection of antimicrobial resistant *E. coli* and STH on floors among rural Bangladeshi households. We enrolled 49 households with a child <2 years (28 with soil floors, 21 with concrete floors) in villages of Sirajganj district in northwestern Bangladesh. Field staff identified the room where the child slept to swab a 50 x 50 cm area using a sterile pre-hydrated sponge and sweep floor dust from up to ten 50 x 50 cm areas with a clean brush. Swab samples were eluted from the sponge with sterile water and analyzed using IDEXX QuantiTray/2000 with Colilert-18 and cefotaxime supplementation to enumerate the most probable number (MPN) of cefotaxime-resistant *E. coli*. We detected *Ascaris lumbricoides* and *Trichuris trichiura* with qPCR in floor dust samples and with microscopy in floor swab samples. There was a mean of 8.0 g of dust on soil floors vs. 0.2 g on concrete floors (t-test p-value=0.005) per m^2. We detected cefotaxime-resistant *E. coli* on 86% of soil floors vs. 38% of concrete floors (chi2 p-value=0.001), with a mean $\log_{10}$-transformed MPN of 3.1 on soil floors vs. 1.6 on concrete floors (t-test p-value<0.0005). Using qPCR, we detected *Ascaris* on 18% of soil floors

and none of concrete floors, and *Trichuris* on 29% of soil floors and 31% of concrete floors. Using microscopy, we detected STH on 33% of soil floors and none of concrete floors (chi^2 p-value=0.01). Our findings indicate that soil floors are a source of child exposure to antimicrobial resistant organisms and STH in low-income countries; children can ingest soil from floors via dust or geophagia and indirectly through contaminated hands and objects. Efforts to mitigate infectious diseases and antimicrobial resistance in low-income countries should test flooring improvements to reduce soil-borne exposure to fecal organisms.

6808

ASSOCIATION OF WATER, SANITATION AND HYGIENE (WASH) AND ANIMAL OWNERSHIP TO RELAPSE TO ACUTE MALNUTRITION (AM) FOLLOWING RECOVERY FROM SEVERE ACUTE MALNUTRITION (SAM) AMONG CHILDREN 6-59 MONTHS IN MALI, SOUTH SUDAN AND SOMALIA: A PROSPECTIVE COHORT STUDY

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In the context of high burdens of acute malnutrition (AM), children recovered from severe acute malnutrition (SAM) may frequently relapse upon returning to households with inadequate water, sanitation and hygiene (WASH) conditions which may increase the risk of infection with enteric pathogens and disease. This study aimed to identify the association of WASH, and animal ownership, to relapse to AM. This prospective cohort study examined the association of WASH-related risk factors, and animal ownership, to relapse to AM over six months among children treated and recovered from SAM in Mali, Somalia, and South Sudan. A total of 1008 children recovered from uncomplicated SAM were recruited and followed for this study. Within six months after initial recovery, 32%, 64% and 21% of children relapsed to AM in Mali, South Sudan and Somalia, respectively. In Mali, the use of multiple drinking water sources led to a 71% increased risk of relapse to AM (aRR1.71, 95% CI:1.21-2.43, p=0.003) and a lack of soap led to a 71% increased risk (aRR1.71, 95% CI:1.03-2.82, p=0.037). In South Sudan, using an unimproved or surface drinking water source was associated with 20% increased risk of relapse to AM (aRR1.20, 95% CI:1.05-1.36, p=0.006), practising open defecation was associated to 14% increased risk (aRR1.14, 95% CI:1.00-1.29, p=0.043) and compounds with observable animal faeces had 13% increased risk (aRR1.13, 95% CI:1.04-1.24, p=0.006). Ownership of sheep (aRR0.57, 95% CI:0.40-0.81, p=0.002) and cattle (aRR0.79, 95% CI:0.72-0.86, p=0.000), was a protective in Mali and South Sudan, respectively. In Somalia, no risk factors for relapse were identified. Our study identified several WASH-related risk factors for relapse to AM including inadequate drinking water sources, practising open defecation, a lack of soap and exposure to animal faeces. Identifying the relative importance of factors for adverse outcomes following initial SAM recovery could help improve the identification of children and communities at greater risk of relapse and inform interventional efforts for post-discharge support to sustain recovery.

6809

COMMUNITY PERCEPTIONS OF OPEN DEFECATION AND SCHISTOSOMIASIS CONTROL: LESSONS LEARNED FROM A RAPID ETHNOGRAPHIC ASSESSMENT STUDY IN THREE ENDEMIC LAKESHORE COMMUNITIES IN MAYUGE, UGANDA

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Schistosomiasis is a neglected tropical disease, infecting over 240 million people globally, with over 4 million people infected in Uganda. Open defecation in high endemicity areas is a significant driver of transmission. Improved understanding of practices and perceptions of open defecation will help inform how best to reduce it. Data were collected over six weeks in each of three high endemicity communities using rapid ethnographic assessment, comprising 60 individual in-depth interviews, 19 focus group discussions, Village Health Team (VHT)-guided walks, transect walks, and structured observations. Guided walks focused on latrines and open defecation sites. Data were analyzed thematically using iterative categorization. Observations and walks revealed open defecation to be a commonly occurring practice in all communities, coupled with low private and public latrine coverage, and public latrines often described by VHT guides as unusable due to lack of cleanliness or being full. Interviews and focus group discussions supported these findings and further highlighted perceptions of public latrines as costly and dangerous to health when dirty, unequal access to private latrines, and perceptions of *who* engaged in open defecation: accusations ran along existing lines of status and inequality, emphasising children, certain tribes, people who use alcohol and in particular (low status, often itinerant) fishermen. This practice thus sits at the intersection of infrastructure, poverty, logistical and bodily limitations, and accusation as an amplifier of inequality. Reducing schistosomiasis transmission by reducing open defecation therefore requires a multi-scalar response: more public latrines coupled with effective cleaning and emptying, situated sensitively to where people live and work; affordable cost, and; working with communities on the risks of open defecation, why some (are perceived to) choose it, and identifying 'best fit' solutions that people will be willing to take up in order to reduce, even if not eliminate, onward *Schistosoma* transmission risk.

6810

HOST GASTRIC CORPUS MICROENVIRONMENT FACILITATES *ASCARIS SUUM* LARVAL HATCHING AND INFECTION IN A MURINE MODEL

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Ascariasis (roundworm) is the most common parasitic helminth infection globally and can lead to significant morbidity . Children become infected with *Ascaris* spp. via oral ingestion of eggs. It has long been assumed that *Ascaris* egg hatching and larval translocation across the gastrointestinal mucosa to initiate infection occurs in the small intestine. Here, we show that *A. suum* larvae hatched in the host stomach in a murine model. Larvae utilize acidic mammalian chitinase (AMCase; acid chitinase; Chia) from chief cells and acid pumped by parietal cells to emerge from eggs on the surface of gastric epithelium. Furthermore, antagonizing AMCase and gastric acid in the stomach decreases parasitic burden in the liver and lungs and attenuates lung disease. Given Ascaris eggs are chitin-coated, the gastric corpus would logically be the most likely organ for egg hatching, though this is the first study directly evincing the essential role of the host gastric corpus microenvironment. In addition, we show that the gastric corpus

downregulates AMCase and acid in response to repeated *A. suum* infection to reduce larval migration. These findings point towards potential novel mechanisms for therapeutic targets to prevent ascariasis and identify a new biomedical significance of AMCase in mammals.

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COMPREHENSIVE SINGLE CELL RNA SEQUENCING UNVEILS THE TRANSCRIPTIONAL DYNAMICS OF *PLASMODIUM VIVAX* HYPNOZOITE FORMATION

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On one of the primary objectives of *Plasmodium vivax* malaria parasite liver stage research is to understand the formation, persistence, and activation of hypnozoites, the dormant liver stage parasites that are responsible for recurrent relapses. However, this research faces severe challenges, due to the limited access to *P. vivax* sporozoites. To unravel the molecular pathways governing hypnozoite formation, we adopted a comprehensive strategy. We revisited the utilization of Chesson strain *P. vivax* sporozoites, as well as P. vivax field strains from Thailand, for hypnozoite biology analysis in conjunction with the highly infectable human hepatocyte cell line HCO4. Furthermore, we employed single-cell RNA sequencing to analyze the transcriptional profiles of both oocyst and salivary gland sporozoites as well as a time course of developing liver stage parasites - both schizonts and hypnozoites. Our efforts resulted in the transcriptional profiling of over 50,000 individual sporozoites and 500 liver stage parasites. We have delineated multiple gene expression clusters and, as to be expected, observe stark differences in expression profiles between sporozoites and liver stage parasites. Preliminary analysis indicates an upregulation of genes related to RNA-binding in the hypnozoite population, suggesting a potential regulatory role in hypnozoite formation. Additionally, we have devised a reliable RNA-FISH/IFA protocol capable of specifically identifying transcripts expressed solely in hypnozoites. This multifaceted approach promises a deeper understanding of hypnozoite biology and holds promise for uncovering novel interventions to mitigate relapses.

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PLASMODIUM VIVAX-INDUCED BONE MARROW ALTERATIONS PERSIST LONG AFTER ACUTE PHASE OF INFECTION

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Plasmodium vivax (*Pv*) infection can lead to poor clinical outcomes, despite low peripheral parasitaemia. Estimation of total *P. vivax* biomass based on markers in peripheral blood (PB) indicates a "hidden" population outside of circulation. Indeed, recent studies revealed a major *Pv* reservoir in bone marrow (BM) and spleen. The development of *Pv* parasites in the BM raises questions about the locally established host-parasite interactions and their clinical relevance in malaria pathogenesis. Here, we aimed to define *Pv*-induced immune responses in the BM and their effect on BM function and disease development. Matched BM aspirates and PB samples have been collected from a prospective longitudinal cohort of uncomplicated *Pv* patients from Brazil, to investigate parasite and host signatures in the hematopoietic niches of BM compared to blood. So far, we analysed host signatures by combining clinical data and multiplexed profiling of 64 protein markers in matched BM and PB material sampled at hospital admission (day 0), as well as 45 and 60 days after, in comparison to healthy donor BM samples. Luminex results demonstrate that *Pv* infection induces a wide range of host responses in the BM during acute phase, most of which persist long after infection is resolved. Persisting upregulated responses were related to megakaryopoiesis, lymphopoiesis, granulopoiesis, myeloid chemoattraction, neutrophil and endothelial cell activation, inflammasome activation, type II IFN response, Th1 response and T-cell exhaustion/inhibition. Persisting downregulated protein markers were related to BM function, such as hematopoietic quiescence, dendritic cell differentiation. In contrast, persisting responses are largely absent in the PB. Ongoing single cell and bulk transcriptomics of host response and parasite signatures in both compartments will be presented. This study emphasises the relevance to investigate the impact of *Pv* infection in the hematopoietic niches. As such, our work will contribute to a better understanding of *Pv* biology and pathogenesis, and hence to our efforts to reduce the burden of this important human disease.

6813

A HUMAN PLURIPOTENT STEM CELL DERIVED MODEL OF THE NEUROVASCULAR UNIT COMPRISED OF BRAIN MICROVASCULAR ENDOTHELIAL CELLS, ASTROCYTES, AND NEURONS IN CEREBRAL MALARIA

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Damage to the blood-brain barrier (BBB) and neurovascular unit (NVU) leading to long-term neurologic impairment in cerebral malaria (CM) remains a poorly understood complication of *Plasmodium falciparum (Pf)* infections. How *Pf*-infected RBCs (*Pf*-iRBCs) sequestered to brain endothelial cells cause damage to neuronal cells without crossing the BBB is unclear. *In vitro* models have advanced our knowledge of CM-mediated BBB disruption, but few have investigated NVU damage. Previously, using induced pluripotent stem cell-derived brain microvascular endothelial cells (iPSC-BMECs) co-cultured with *Pf*-iRBCs, we've demonstrated *Pf*-mediated damage to the BBB. In this study, we have expanded our *in vitro* model of the BBB in CM to include iPSC-derived neurons and astrocytes along with BMECs in co-culture with *Pf*-iRBCs to represent the NVU in CM. Our novel, multicellular model of the NVU represents near *in vivo* like barrier resistance (3800 Ωxcm^2) by transendothelial electrical resistance (TEER) that is 10 times that observed in human primary BMEC based models ($\leq$400 Ωxcm^2). iPSC neurons and astrocytes were characterized using β-tubulin III and GFAP staining. Using HB3var03 parasite strain that binds endothelial surface proteins ICAM-1 and EPCR—key mediators of CM neuropathology, we conducted co-culture experiments up to 9 hours (h). At 6 h post co-culture with *Pf*-iRBCs, there was a significant reduction in barrier resistance of the iPSC-BMEC (1827 Ωxcm^2) compared to uninfected RBC co-culture (2937 Ωxcm^2); which remained low at 9 h (all $P<0.005$). We observed increased sodium fluorescein permeability indicative of a leaky barrier in *Pf*-iRBC co-cultures compared to uninfected RBC co-cultures at 6 h. Breaks in tight junction protein localization further confirmed BBB disruption in *Pf*-iRBC co-cultures at 6 h. Ongoing experiments will identify altered expression of endothelial surface markers and efflux proteins. Our multicellular iPSC-derived model of the NVU with enhanced barrier integrity replicates key features involved in the pathogenesis of CM and can serve as a surrogate to investigate pathogenic stimuli underlying NVU damage in CM.

6814

DIETARY EFFECTS ON THE COURSE OF VISCERAL LEISHMANIASIS IN A MOUSE MODEL

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The demographics of leishmaniasis has changed dramatically in endemic regions of Brazil, concurrent with changes in socioeconomic status and consequent shift towards a high-fat high-cholesterol diet (HFHC). With this shift, a novel presentation of cutaneous leishmaniasis due to *L. braziliensis* has emerged in obese patients, characterized by poorer treatment response with higher recurrence rates in obese individuals, s reported previously. A direct link between diet-induced changes in metabolic and immune status and the manifestations of visceral leishmaniasis (VL) has not been established. We hypothesize that diet-induced changes in immunometabolism may also affect the progression and outcome of VL. To address this, we examined the effects of a HFHC and protein-deficient (LP) diet in a murine model of VL. BALB/c mice were maintained on HFHC, LP, or control diets for 4 weeks, then either infected or not with L. *infantum*. The course of infection was monitored by histology and by qPCR to document inflammation and parasite loads. The HFHC diet abrogated the expansion of parasite loads in the liver and caused exacerbated parasite growth in spleens ($P<0.0001$). Mice on a LP diet, in contrast, developed higher parasite loads in livers than control mice ($P<0.0001$). Control mice developed granulomas in the livers as the disease progressed. In contrast, mice on a HFHC diet developed a basal inflammatory response in the liver and failed to develop organized, mature granulomas ($P<0.0001$). Mice on a LP diet had increased numbers of granulomas in the liver ($P<0.0001$). These findings suggested that the basal inflammation of the HFHC diet led to failure to contain the parasite and early dissemination of infection to the spleen. Dietary factors may influence the changing spectrum of VL.

6815

PERSPECTIVES ON EQUITABLE PARTNERSHIPS IN GLOBAL HEALTH

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Equitable global health partnerships (EGHPs) are gaining traction amid decolonization global health movements, spotlighting power imbalances rooted in colonial legacies. There is an increased call among global health institutions for a meaningful change that fosters equity, inclusivity, and fairness, and values local knowledge in research partnerships. The Emory Global Health Institute (EGHI) took a methodical approach, with a literature review and an explanatory sequential QUAN-QUAL mixed methods strategy to assess perspectives on EGHPs. A quantitative survey and key informant interviews were conducted among Emory faculty in the US and their partners in low- and middle-income countries (LMICs) engaged in global health research collaborations. Additionally, a decolonizing global health working group was convened to deliberate on the findings and establish priority areas. The literature identified key principles for advancing equitable partnerships: authentic collaboration, inclusion, shared benefits, commitment to the future, responsiveness to inequities, and humility. Survey analysis revealed agreement between US and LMIC partners across 16 out of the 22 indicators with marginal differences in responses with regards to infrastructure, communication, bidirectional training, fair compensation, financial transparency, and sustainability. LMIC partners prioritized capacity strengthening, equity principles, communication, and relationship building, while US participants focused on operational efficiency and equity. The findings are consistent with previous studies in the literature. Based on all the results and discussions the main priorities to advance EGHPs are; establishing tools and frameworks to integrate equity, measure progress, bidirectional capacity building, knowledge sharing, and creating a platform for constructive dialogue to influence policies for fair access to financial and technical resources. The building momentum to advance EGHPs can be furthered and expanded on with collective efforts to implement key principles and actionable steps that center equity in global health practice.

6816

INNOVATION FOR NEGLECTED DISEASES: TWO DECADES OF PROGRESS AND GAPS IN NEW DRUG APPROVALS

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Therapeutic innovations have an essential role to play in addressing the burden of neglected diseases. This study analyzes the approval landscape of novel medicines for diseases that disproportionately affect populations in low- and middle-income countries (LMICs) to inform drug research, development, and access strategies. We examined the online databases of 26 medicines regulatory authorities (from the record of World Health Organization-Listed Authorities), the WHO Prequalification Program, and other online platforms for medicines approved between 2003 and 2023. The focus was on 47 diseases identified by WHO, the Access to Medicines Foundation, or Policy Cures Research to be priority health conditions in LMICs. Inclusion criteria were new chemical entities (NCEs), new therapeutic biologics (NBs), new fixed-dose combinations (FDCs), new dosage forms of existing medicines, or "repurposed" medicines for new indications. We estimated the ratio of the number of approvals to the burden of each disease in Disability Adjusted Life Years (DALYs). Of 55 medicines approved over the study period, 11 were NCEs (eight medicines) or NBs (three medicines): three for tuberculosis; two each for Ebola, malaria, and sickle cell disease; and one each for human African trypanosomiasis and onchocerciasis. Eight of the 11 NCEs and NBs were approved after 2015. Forty-four of the approved medicines were repurposed drugs (12), FDCs (11), and new dosage forms (21). Of these, 23 were for tuberculosis, 11 for malaria, two each for sickle cell disease and leishmaniasis, and one each for six other diseases. No novel medicines were approved for 35 diseases. The number of approvals to DALY ratios in all disease areas studied was substantially lower than those that are typical for leading diseases in high-income countries. Therapeutic innovation for neglected diseases is severely limited, especially for new chemical or biologic entities, and unbalanced across disease areas. Given severe unmet needs including, in some cases, the threat of resistance to existing therapies, there is urgency to scale up R&D for novel medicines that address global health diseases.

6817

BUILDING CAPACITY FOR MATERNAL, NEWBORN AND CHILD HEALTH RESEARCH IN LOW-INCOME COUNTRY SETTINGS: A RESEARCH FELLOWSHIP EXPERIENCE IN ETHIOPIA

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In low- and middle-income countries, there is a need to build capacity for research to improve maternal, newborn and child health (MNCH). Collaborating with the Ministry of Health (MoH) and academic institutions, we co-designed the HaSET MNCH research fellowship program for academics and policymakers in Ethiopia. Based on interviews and focus group discussions on a landscape analysis of the MNCH research environment, we developed an innovative "learning by doing" model where fellows identified research questions, developed proposals, obtained IRB approvals, conducted research, analyzed data, disseminated their findings, and developed policy briefs. Post-doctoral fellows were paired with policymakers and health professionals at the MoH to foster translation of research findings to policy and programs. The HeSET fellowship curriculum was designed to include 10 modules covering topics from biostatistics to study operations and professional development. From March 2021 to July 2023, HaSET trained five post-doctoral fellows from local universities and four policymakers from the MoH and government research institutes to generate high-quality evidence to answer priority research questions and guide the implementation of national policies and programs. Leveraging existing data, the fellows completed 15 manuscripts and 11 policy briefs. Fellows presented their work at international and national conferences. The program established a functional research link between the Ministry of Health, regional health bureaus, local universities, and leveraged the expertise of a scientific advisory group for mentorship. This robust and comprehensive HaSET MNCH Research Fellowship cultivated a cohort of dedicated and effective public health professionals. Fellows conducted high-quality studies for informed policy decisions regarding MNCH interventions in Ethiopia. There is potential to scale the program to sustain successful capacity-building programs to build the next generation of leaders in research in low- and middle-income countries.

6818

EAST AND SOUTHERN AFRICAN CONSORTIUM FOR OUTBREAK EPIDEMIOLOGY TRAINING (ENTRANT)

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East and Southern African countries are susceptible to disease outbreaks, and vulnerable to public health emergencies due to constrained health system resources. The East and Southern Africa Consortium for Outbreak Epidemiology Training (ENTRANT) programme was established with funding from EDCTP in collaboration with Africa CDC. The objective of ENTRANT is to provide epidemiological training and mentorship to early- to mid-career public health professionals working in the region. Through this we aim to promote the development of a critical mass of epidemiologists to work with National Public Health Institutes and Ministries of Health and thus strengthen public health and outbreak response capacity. ENTRANT is coordinated by a consortium of institutional partners relevant to outbreak response in the region, and supported by an independent Advisory Committee comprising experts in capacity strengthening for epidemiology in sub-Saharan Africa. A competitive application process was implemented to identify high-calibre public health professionals for entry into the programme. Fellows undertake MSc Epidemiology at London School of Hygiene and Tropical Medicine (LSHTM) followed by further focussed short course multidisciplinary training on the emergence, spread and response to pandemics. Fellows receive mentorship from LSHTM tutors and experienced epidemiologists in their home country, take part in regular transferable skills training and networking activities, and are supported to attend conferences. From a total of 324 applications, 15 public health professionals (eight female, seven male) from Botswana, Ethiopia, Kenya, Tanzania, Uganda and Zambia have been awarded Fellowships. To date, 13 have completed their MSc Epidemiology training, with the remaining Fellows due to complete in October 2024. Fellows who have completed formal training have gone on to work for Ministries of Health and public health research institutions. Fellows at all stages of the programme have formed a strong, mutually-supportive cohort through regular meetings and networking events.

6819

WHO ANC POLICY AND SKILLED BIRTH ATTENDANCE IN SUB-SAHARAN AFRICA

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Over half a million mothers are lost each year due to pregnancy-related complications. The World Health Organization (WHO) recommends that all pregnant women have a minimum of eight ANC contacts (WHO 2016 ANC policy) and delivery by an accredited health professional - such as a midwife, doctor or nurse. This study explores the association between skilled birth attendance at a prior pregnancy and the number of ANC contacts in the index pregnancy. A secondary analysis of data from 19 sub-Saharan African countries with available Demographic Health surveys from 2018 to date was performed. Key variables were skilled birth attendance (by a doctor, nurse, midwife and auxiliary nurse or midwife) during a participant's second most recent pregnancy and the number of ANC contacts in the most recently completed pregnancy in the past two years. Propensity score matching was used to explore the treatment effects of having a skilled birth attendance on the number of ANC contacts during pregnancy. 40,077 women had had at least two pregnancies in the five years preceding the survey. 60% of women had had a skilled delivery in their second most recent pregnancy which varied by county, with Ethiopia (37%) to Gabon (95%).The majority of these skilled providers (44%) were nurses. The mean number of ANC contacts in a woman's most recent pregnancy ranged from Mauritania (2.8) to Ghana (6.2) (mean 3.6). Having a skilled provider in their second most recent pregnancy had an average treatment effect of 1.20 (95% CI: 1.12-1.28), indicating a modest increase in number of ANC visits of their subsequent pregnancy compared to not having a skilled delivery, accounting for country, age, wealth, urbanization, and religion. This study highlights the influence of skilled delivery in current and subsequent pregnancies. Improving ANC contacts allows for an improved life course, providing more opportunities for health promotion, early detection of health complications, and many more benefits to the pregnant woman and unborn child. In countries with low percentages of skilled deliveries, improving access could increase ANC contacts and support more linkages to further health and wellbeing.

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ENHANCING THE QUALITY OF COMMUNITY HEALTH SERVICES IN MADAGASCAR: A MIXED METHODS EVALUATION OF A COMMUNITY HEALTH VOLUNTEERS (CHVS) PEER SUPERVISION MODEL IN FOUR REGIONS

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In 2019, Madagascar's Ministry of Public Health (MoPH) launched a national community health strategic plan, aiming to strengthen community health services through improved supervision of community health volunteers (CHVs). CHVs are traditionally supervised by health facility (HF) heads; however, insufficient facility staffing and high workloads have resulted in inadequate supervision. The MoPH is collaborating with the USAID ACCESS program to implement a new CHV supervision model that engages high-performing CHVs as peer supervisors in 13 regions; an evaluation of the model is expected to guide national scale-up and planning in other countries. We completed a mixed-methods study in 2023, conducting secondary data analysis to characterize the program and collecting primary data in four regions. In 16 health facility catchment areas, we conducted in-depth interviews (IDIs) with peer supervisors (n=16), CHVs (n=32), HF heads (n=16), and other stakeholders engaged in the peer supervision model rollout (n=41). IDI themes included how the model worked, the functionality of model components, and feasibility and acceptability. Qualitative data were coded using NVivo; a deductive approach was used for the thematic analysis. The new model was perceived to result in greater information sharing between CHVs and peer supervisors, better management of health providers' schedules, and improved quality of CHV services, including reporting. Aspects of the model not found to work well included the process of selecting peer supervisors, inadequate clinical supervision, high ratio of CHVs to peer supervisors, less time for peer supervisors to engage in income-generating activities, and lack of supervision tools and training for the HF heads. The new model shows promise; however, several aspects require reconsideration to improve the model's acceptability and feasibility, including reducing the number of CHVs per peer supervisor, bolstering clinical supervision, and providing adequate remuneration, training, and tools for CHVs, peer supervisors, and HF heads. Findings were shared with MoPH and ACCESS to inform national scale-up of the model.

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AI IN GLOBAL HEALTH: CHALLENGES AND OPPORTUNITIES

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AI has enormous potential in healthcare, from aiding diagnosis to personalising medical care and predicting disease outbreaks. However, the accuracy of AI algorithms depends on the quality and diversity of the data used to train them. Concerns exist regarding the reliability and sufficiency of data from low-and-middle-income countries (LMICs) for training AI algorithms. There is a risk that a lack of contextually relevant data may result in incorrect algorithms or limited application of AI in LMICs. How, then, can we ensure that the benefits of technology are accessible to all? We present the results of a mixed-methods study exploring challenges and opportunities in using existing health data from LMICs. We conducted a cross-sectional study with 643 clinical researchers and 24 in-depth interviews with computational health scientists. The study reveals low data usage, especially for AI, mainly due to challenges with data findability. The study also highlights inequity in gains realised from data reuse. Career progression from data reuse was associated with affiliation with high-income and upper-middle-income countries (p=0.046, chi=8.0), while scientific progress through publications and collaborations was associated with gender (p=0.012, chi=10.9), with males more likely to benefit. Publicly publishing metadata of health datasets in machine and human-readable formats will enhance data discoverability without compromising data privacy. Intentional efforts to encourage and enable more analysts in LMICs, especially females, may reduce the equity gap. Capacity building in data management may improve the overall quality of prospectively collected data, while targeted efforts to curate existing data will increase the pool of data available for secondary use, including AI applications.

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CLINICODEMOGRAPHIC PROFILE AND SURVIVAL PROSPECTS OF WOMEN WITH PERIPARTUM CARDIOMYOPATHY IN TANZANIA: A PROSPECTIVE COHORT STUDY.

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Background: Irrespective of a higher rate of complete recovery relative to other forms of systolic heart failure, peripartum cardiomyopathy (PPCM) remains the leading cause of non-obstetric feto-maternal morbidity and mortality worldwide. In view of the paucity of data, this present study aimed to shed light on the clinicodemographic characteristics and prognosis of PPCM in Tanzania. Methods: This prospective, multicenter PPCM study in Tanzania commenced in April 2016. Data was systematically collected at the very first contact and then upon three-, six-, and twelve-months visits. Clinical outcomes including complete recovery (LVEF>55%), persistent dysfunction, and death were recorded. Bivariate comparison and subsequent Cox proportional-hazards regression model were used to compare the women with respect to the primary end point. Results: We screened 1639 women and consecutively recruited 1210 who met the inclusion criteria. The mean age at diagnosis was 29.4 ± 6.7 years and in 31.2% women it was their first pregnancy. During a mean follow-up of 889 days, 23.6% of women had complete recovery, 48.2% had persistent LV systolic dysfunction, and 28.1% died. We observed thromboembolic events in 10.2% of women and infant mortality rate was 23.4%. Amongst 870 survivors (286 resolved, 584 persistent heart failure), 121 women (78 in the resolved group and 43 in the persistent heart failure) had subsequent deliveries. Recurrence was observed in 51.3%, resolution in 31.4%, and death in 8.3%. Following multivariate analysis in a cox regression model of 16 variables; Atrial fibrillation (HR 5.0, 95%CI 2.6-9.8, p<0.001), LVIDd ≥60 (HR 2.8, 95%CI 1.9-4.3, p<0.001), EF<30% (HR 1.7, 95%CI 1.1-2.5, p<0.001), TAPSE<14 (HR 7.4, 95%CI 5.1-11.1, p<0.001), and LV thrombus (HR 2.3, 95%CI 1.3-3.9, p<0.01) proved to be the predictors of mortality. Conclusions: In this largest cohort of African women with well-phenotyped PPCM, we observed myocardial recovery in just under a quarter of patients and maternal death in over a quarter of the enrolled women. Despite its relative rarity yet poor prognosis, PPCM remains a challenge to diagnose, prognosticate, and treat.

6823

BURDEN, DISTRIBUTION, TIMING AND CAUSES OF STILLBIRTH AND NEONATAL MORTALITIES IN A HEALTH AND DEMOGRAPHIC SURVEILLANCE SYSTEM (HDSS) IN KAREMO AND MANYATTA IN WESTERN KENYA, 2018-2023

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Sub-Saharan Africa has the highest stillbirth and neonatal mortality rates worldwide. We sought to estimate the burden, distribution, timing and causes of stillbirth and neonatal mortality using data from a Health and Demographic Surveillance System (HDSS) site operated by the Kenya Medical Research Institute and CHAMPS in western Kenya. Approximately 179,317 residents, in Karemo - Siaya County and Manyatta - Kisumu County are monitored every six months using a standardized questionnaire about events that happened since prior visit. All women of reproductive

age (12-49 years) are asked about their pregnancy status and outcome. Community health volunteers report deaths, births and pregnancies. Minimally invasive tissue sampling was conducted on stillbirth and neonatal deaths. Aseries of biopsies, blood and body fluids samples were analyzed and cause of death determined by medical experts. A total of 454 stillbirth and 606 neonatal deaths were reported of which 277 stillbirths and 268 neonates had cause of deaths determined. Between 2018 and 2023, stillbirth mortality rate (SMR) in Karemo was 18.0 and 23.6 and in Manyatta 12.4 and 28.1 deaths per 1000 births; Neonatal mortality rates (NMR) in Karemo was 23.1 and 23.2 and in Manyatta 13.9 and 22.6 deaths per 1000 livebirths. SMR among women aged 15-19 was 15.6, 20-24 (17.0), 30-34(20.0) 35-39 (24.8) and 45-49 (48.8) deaths per 1000 births. NMR among women aged 12-14, 15-19, 25-29, 30-34, 40-44 and 45-49 years was 32.8, 30.4. 20.2, 20.8, 31.0 and 54.1 deaths per 1000 livebirths respectively. Overall, 57% of the stillbirth deaths happened among fetuses over 38 weeks old; 63% of neonatal deaths happened on the delivery day. Leading cause of neonatal deaths were intrauterine hypoxia (33%), sepsis (20%) and respiratory distress syndrome (18%) while intrauterine hypoxia (88%) was leading cause of stillbirths. We observed an increase in neonatal and stillbirth mortality rates overtime. The highest mortality rates were observed among young women and those with advanced ages. Most deaths happened around time of delivery due to intrauterine hypoxia. There is need for improved obstetrical care for pregnant women in the study.

6824

VACCINATION COVERAGE AND TIMELINESS AMONG INFANTS IN ETHIOPIA

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Vaccinations are key for preventing and controlling infectious diseases. However, in Ethiopia, a significant proportion of children remain unimmunized. This study aimed to describe the vaccination coverage among children in a rural site in Ethiopia, and to quantify the proportion of infants who were vaccinated on time according to the National vaccination schedule. We analyzed data of a longitudinal study conducted in Ethiopia, which includes a health and demographic surveillance system (HDSS) with house-to-house surveillance every 3 months. The study population were children born between 2018 and 2021, and enrolled in the HDSS. Vaccination data were collected through questionnaires administered as part of the routine surveillance. Data were abstracted from vaccination cards and caregivers reports. We used two analytical approaches to calculate the vaccination coverage of the full set of vaccines recommended in Ethiopia, the coverage of each specific recommended vaccine, and timeliness of vaccine administration. Data of 7,417 children were included in the analysis. The proportion of fully vaccinated children was between 25.8% (2018) and 30.6% (2021) using a longitudinal approach, and between 32.0% (2018) and 41.8% (2021) using a method that mimics a cross-sectional survey. Coverage of specific vaccines followed a similar pattern. Three quarters and 2 thirds of children who were measles vaccinated before 1 year of age received the vaccine within 4 weeks of vaccine eligibility using the longitudinal and the cross-sectional strategies, respectively. Four out of 10 received the third doses of oral poliovirus, pentavalent and pneumococcal vaccines, and the second dose of rotavirus vaccine within 4 weeks of vaccine eligibility. Vaccination rates in the study area were low. Less than half of infants received their vaccinations within 4 weeks of the recommended administration time. To ensure an accurate assessment of vaccine coverage and timeliness, it is recommended to implement strategies that leverage longitudinal data, reducing reliance on cross-sectional studies, and allowing for more precise monitoring of immunization efforts.

6825

UNDERSTANDING IMPACT OF DOMESTIC VIOLENCE ON PERINATAL DEATH IN RURAL BANGLADESH; FINDINGS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE, BANGLADESH

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Domestic violence is a public health issue, different studies suggested that globally 15% to 71% of women experienced some form at some point in their lives. An estimated 40% to 70% of Bangladeshi married women experience domestic violence from their husbands, in-laws, and/or close relatives at least once during their lifetime. A countrywide sample-based study found that 3 out of 4 Bangladeshi women experienced domestic violence from their husbands especially who were less educated and poor. Various studies suggested that domestic violence during pregnancy can cause adverse pregnancy outcomes. The Child Health and Mortality Prevention Surveillance (CHAMPS) in Bangladesh is identifying the causes of stillbirths and death among children under five by employing minimally invasive tissue sampling (MITS) with clinical documents and verbal autopsies (VAs). We have reviewed VAs of 800 MITS cases, including narratives where mothers described the death events of their babies. A total of 12 mothers participating in the study (12/800; 1.5%) mentioned experiencing domestic violence during their pregnancies. Out of these 12 cases, 7 (58%) were stillbirths and 5 (42%) were early neonatal deaths. All MITS reports, clinical documents, and VAs were reviewed by an expert panel composed of epidemiologists, neonatologists, pediatricians, obstetricians, and pathologists to determine the cause of death. The panel considered domestic violence as a contributing maternal factor for perinatal death in 5 out of the 12 cases (5/12, 42%), all of which involved domestic violence close to the delivery date. Reporting of the violence was based on interviews with the mother at home, which could lead to underestimation of the problem due to fears of disclosing. Additional strategies could be used to identify women experiencing domestic violence during pregnancy. Engagement of field-level government health workers, and the introduction of social prescriptions by engaging support groups and community people can help these women in the future and connect them with appropriate authorities to prevent domestic violence and save lives.

6826

MASS AZITHROMYCIN DISTRIBUTION AND CAUSE-SPECIFIC MORTALITY AMONG CHILDREN AGED 1-59 MONTHS IN BURKINA FASO

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Mass azithromycin distribution has been shown to reduce all-cause child mortality in several settings in the Sahel, with an approximately 14-18% relative reduction in the risk of mortality in children living in communities receiving twice-annual mass azithromycin distribution compared to placebo. A previous trial in Niger found that mass azithromycin distribution to children aged 1-59 months reduced cause-specific mortality due to malaria, dysentery, meningitis, and pneumonia. However, this study was done in the absence of seasonal malaria chemoprevention (SMC), a mass drug administration strategy that involves distribution of sulfadoxine-pyramethamine and amodiaquine monthly to children aged 3-59 months during the high malaria transmission season. Here, we evaluated cause-specific mortality in a trial of mass azithromycin distribution compared to placebo in Burkina Faso, in a setting that was receiving SMC. The Child Health with Azithromycin Treatment (CHAT) trial randomized 341

communities in Nouna District, Burkina Faso to twice-yearly mass distribution of a single oral 20 mg/kg dose of azithromycin or matching placebo to children aged 1-59 months of age. Six rounds of distribution occurred over a 36-month period. An enumerative census was conducted during each twice-yearly distribution, during which vital status for all children in the community was collected. Verbal autopsy was performed to assess cause of death. Of 1,086 deaths recorded in the trial, verbal autopsy results were available for 919 (85%). The most common causes of death were infectious, including malaria (34%), diarrhea (24%), and pneumonia (9%). Children living in communities receiving azithromycin had significant reduction in malaria mortality (incidence rate ratio, IRR, 0.67, 95% confidence interval, CI, 0.50 to 0.90, P=0.008). Other infectious causes of mortality, including diarrhea and pneumonia, were lower in communities receiving azithromycin but were not statistically significantly different. Mass azithromycin distribution for child mortality has benefits in the context of SMC for reducing mortality, including for malaria mortality.

6827

CLUSTER VARIATION IN UNDER-FIVE MORTALITY IN A PROACTIVE CASE DETECTION INTERVENTION BY COMMUNITY HEALTH WORKERS IN MALI: ANALYSIS OF THE PROCCM TRIAL

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Community-based services delivered by community health workers (CHWs) have been shown to improve access to care for diarrhea, malaria, pneumonia, and malnutrition among children under five. Yet, evidence from national CHW programs has been mixed, in part from a lack of evidence on optimal delivery design, including how best to specify CHW workflows. In a three-year cluster-randomized trial, we tested the effectiveness of proactive case detection versus passive workflow by CHWs in rural Mali. Village clusters (N=137) were 1:1 randomized to receive daily case-finding home visits by CHWs or passive workflow (control), in which CHWs worked from a fixed post in the community. Using lifetime birth history data among women ages 15 to 49 at enrollment from annual surveys of all households in the study area at 12, 24, and 36 months, we analyzed cluster-level variance and predictors of U5M controlling for intervention arm, age, and child sex in mixed-effects regression models. We enrolled 31,587 children under five years of age over the trial (16,248 intervention, 15,339 control; 52,970 person-years of observation); 1,736 died during the trial period with no significant difference in under-five mortality (U5M) by study arm. We found substantial variation in crude death rates by cluster, ranging from 0.0 (8 clusters) to 142.3 deaths per 1,000 person-years (mean 32.5, SD 19.0). However, we observed greater within-cluster than between-cluster variance (ICC 0.039, SE 0.009). Distance to the nearest primary health center was not meaningfully associated with U5M in the intervention context, while CHW coverage indicators were associated with U5M. Children who lived in a cluster where < 50% of symptomatic children received care from a trained provider within 24 hours were twice as likely to die as children in clusters where > 75% of symptomatic children received timely care with a trained provider (OR 2.05, 95% CI 1.28, 3.29). Placing a trained, supervised, paid, and supplied CHW in each cluster can address distance-related barriers to care; empowering CHWs to identify and correctly treat symptomatic children in a timely manner can promote further reductions in U5M.

6828

COMBINATION OF A REDUCTASE INHIBITOR WITH PRIMAQUINE PREVENTS HEMOLYSIS OF G6PD DEFICIENT RBCS

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The only two approved drugs that clear the hepatic hypnozoite phase of *P. vivax* (the 8-aminoquinolines (8-AQ) - primaquine and tafenoquine) can cause potentially lethal hemolysis in glucose-6-phosphate dehydrogenase deficient (G6PDd) patients due to drug metabolites that generate reactive oxygen species (ROS) in RBCs through redox cycling. Primaquine-5,6-orthoquinone (5,6-POQ) is a major hemolytic primaquine metabolite (PM). An enzymatic reductase in RBCs is required to drive redox cycling of PMs, but the specific enzyme(s) have never been identified. Using electron paramagnetic resonance (EPR) to measure superoxide, we report that treatment of intact murine RBCs with 5,6-POQ induced a robust increase in steady state superoxide levels (44 nM) compared to vehicle treated RBCs (5 nM), p =0.001. The addition of ES936, a selective inhibitor of the NAD(P)H:quinone oxidoreductase (NQO1), reduced levels of 5,6-POQ induced superoxide to 28 nM. Because most hemolysis is extravascular (consumption by macrophages), murine RBCs humanized to express the A- variant of human G6PD (hG6PD(A-)) were infused into mice and in vivo circulation was used as a metric of hemolysis. 5,6-POQ treatment of hG6PD(A-) RBCs resulted in a rapid clearance of 33% of RBCs with no clearance of control non-deficient RBCs. ES936 reversed 44% of 5,6-POQ induced hemolysis (p = 0.002). In addition to elucidating basic primaquine toxicology, these findings constitute a novel therapeutic approach with the potential to allow combination of an ES936-like inhibitor with primaquine or tafenoquine to achieve radical cure of *P. vivax* regardless of G6PD status. ES936 is predicted to not decrease the anti-relapse activity of 8-AQs for two reasons. First, ES936 does not inhibit cytochrome P450s, which drive redox cycling in hepatocytes but are not expressed in RBCs. Second, as an irreversible inhibitor, a short course of ES936 has been shown to only transiently inhibit reductases in hepatocytes (that can resynthesize the enzyme) but is predicted to provide permanent inhibition in RBCs, which cannot synthesize new proteins.

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RUXOLITINIB AS AN ADJUNCTIVE TREATMENT TO REDUCE INFLAMMATORY RESPONSES IN MALARIA: A RANDOMIZED PLACEBO CONTROLLED TRIAL IN VOLUNTEERS EXPERIMENTALLY INFECTED WITH *PLASMODIUM FALCIPARUM*

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Case-fatality from severe malaria remains high despite the use of highly effective antiparasitic agents, due in part to the marked host inflammatory response to infection. Identification of agents that interrupt inflammatory pathways, without compromising anti-parasitic immune responses, may lead to novel adjunctive treatments for severe malaria. The JAK 1/2 inhibitor ruxolitinib exerts potent anti-inflammatory effects in *in vitro* models, and reduces inflammatory biomarkers when used

in the treatment of myeloproliferative disorders. Ruxolitinib also targets type-1 interferon mediated immunoregulatory pathways that impede development of antiparasitic immunity. We conducted a randomised placebo-controlled trial to evaluate the ability of ruxolitinib to reduce inflammatory responses and boost antimalarial immunity when administered alongside antimalarial treatment to volunteers experimentally infected with *Plasmodium falciparum*. Twenty participants were inoculated with blood-stage *P. falciparum*, and randomised on day 8 or 9 to receive artemether/lumefantrine in combination with either ruxolitinib (n=11) or placebo (n=9). All study drugs were given twice daily for 3 days. The primary endpoint was safety and tolerability. Ruxolitinib was safe and well tolerated, with a median of 4 (range 0 - 16) adverse events per participant in the ruxolitinib group compared to 7 (range 0 - 24) in the placebo group (p=0.25). Most adverse events were mild to moderate, and consistent with clinical symptoms of malaria. In the placebo group, the inflammatory marker CRP increased significantly following treatment. This increase was not seen in participants treated with ruxolitinib, with CRP levels on day 3 post-treatment significantly higher in the placebo vs ruxolitinib groups (p<0.01). Participants treated with ruxolitinib also had reduced post-treatment increases in ICAM-1 (p<0.001) and the liver enzyme alanine transaminase (p<0.001), and a reduced post-treatment fall in lymphocytes (p<0.001). Further studies evaluating the ability of ruxolitinib to reduce inflammatory responses and improve outcomes in clinical malaria are warranted.

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IMPROVING ANTIMALARIAL DRUG EFFICACY ASSESSMENT: COMPARATIVE ANALYSIS OF LENGTH POLYMORPHIC MARKERS AND CLASSIFICATION ALGORITHMS IN TWO PHASE II CLINICAL TRIALS

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Development of new antimalarial drugs with new modes of action is crucial due to the emergence and spread of artemisinin partial resistance in Southeast Asia and Africa, and treatment failures after treatment with ACTs. Sensitive and robust methods for PCR-correction to distinguish recrudescences (treatment failures) from reinfections following new mosquito bites are essential to determine the accurate efficacy of a treatment in clinical trials. Since 2021, the WHO recommends genotyping the length polymorphic markers *msp1* and *msp2*, and replacing the marker *glurp* for one selected microsatellite due to biases that hinder the correct classification of recrudescences and reinfections. We reassessed the efficacy of two phase II clinical trials, including approximately 750 patients in total, by genotyping four combinations of length polymorphic markers, including *msp1* and *msp2*, and different microsatellites as the third marker (*PfPK2*, *Poly-α* and *TA40*), and compared them to *glurp*. We used three algorithms to classify recurrences into recrudescences or reinfections: the currently recommended WHO/MMV, the two out of three and the Bayesian algorithms. We compared twelve marker-algorithm combinations in total. We found that the use of *glurp* coupled with the WHO/MMV algorithm, used in the trials, indicated the least number of recrudescences across all methods tested, potentially underestimating treatment failure. We also found that the bin size used to classify two alleles as equal or different can influence the efficacy results and should be standardized in genotyping guidelines. The results observed in this study confirm, on the largest scale to our knowledge, results observed with *in silico* simulations, mixed laboratory strains or smaller-scale trials. The amount of samples included significantly increments the information available to determine a better recommendation for a sensitive and robust method, coupled to an appropriate algorithm of classification to determine treatment efficacy, which would translate in providing patients with a new effective treatment and bringing us closer to malaria elimination.

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FUNGAL DERIVED DEOXAPHOMINES TARGET *PLASMODIUM FALCIPARUM* SEGREGATION THROUGH INHIBITION OF PFACTIN1

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Malaria remains a deadly disease that impacts millions every year. Resistance to all current frontline drugs has been observed, underscoring the urgent need for new therapeutic agents. Herein, we report the discovery of a natural product scaffold isolated from the fungi *Trichocladium asperum* with potent antiplasmodial activity. In total, six analogs were identified and have been dubbed methyldeoxaphomin NPDG A-F. The most potent compound, methyldeoxaphomin NPDG F displayed an EC_{50} of 550 nM in Dd2 and 290 nM in 3D7, with a selectivity index >60 over human HepG2 cells. This compound exhibited a gradual rate of killing, similar to atovaquone, with a lag phase of 24 h and a log (PRR) of 0.64. Morphologically, methyldoxaphomin NPDG F induced numerous abnormalities in merozoite segmentation during schizogony in both the blood and liver stages of *P. falciparum* and *P. berghei*, respectively. The *in vitro* evolution with NPDG F and whole genome sequencing revealed the probable drug target to be Pfactin1 (PF3D7_1246200). Of the 29 missense mutations found in the core genome of Dd2-Pol δ, 4 were observed in Pfactin1. A single nucleotide mutation, A136S, independently confers resistance in two of the three biological replicates. In the third biological replicate, SNPs A171V and I290L were found in 76% of the parasites with the remaining 24% bearing the mutations A171S and I290L. A molecular docking study with Pfactin1 found that methyldeoxaphomin NPDG F occupies the same binding pocket as cytochalasin D. The amino acids A171 and A136 line the binding cavity, while I290L was localized to the periphery. Resistance line parasites were found to be cross resistant to cytochalasin D (but not actin stabilizer Jasplakinolide), suggesting NPDG F displays a similar mode of action and interaction with PfActin1. Isobologram data also demonstrated that this compound exhibits an antagonistic effect with known inhibitors of actin polymerization, Latrunculin B and SMIFH2. Taken together, these findings support the inhibition of Pfactin1 polymerization as the likely mechanism of action of NPDG F, augmenting drug discovery efforts to target *Plasmodium* motor proteins.

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PLASMODIUM FALCIPARUM FIELD ISOLATES TO GUIDE CLINICALLY RELEVANT DOSE RATIOS FOR CABAMIQUINE: PYRONARIDINE COMBINATION USING TRANSLATIONAL MODELING

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The emergence of drug resistance calls for the development of effective antimalarial combinations. However, the selection and combination of drug dose regimens involve complex considerations based on a totality of evidence approach, including pharmacokinetic (PK) and pharmacodynamic (PD) data, including potential interactions. We evaluated PD interactions between cabamiquine and pyronaridine, a combination currently in Phase 2 clinical trial. To do so, we used a real-world setting using immediate *ex vivo*

Plasmodium falciparum field isolates combined with translational modelling. The apparent parasite killing rate was simulated for cabamiquine and pyronaridine, alone and in combination to generate an interaction heat map. Concentration and time-dependent *in vitro* cidal activity of cabamiquine and pyronaridine alone as well as in combination were determined using *P. falciparum* field isolates and standard 48 hours SYBR Green assay-Mitotracker readout at different concentrations and time points. Potential PD interactions were quantified using non-linear mixed effects modelling describing the parasite growth and drug mediated-killing. These data are then fed into model to generate an interaction map that later is used to simulate meaningful clinical dose ratios.The parasite kinetics of field isolates was well described by the model. Whereas for cabamiquine, the regrowth observed in monotherapy arm suggesting adaptive resistance, was suppressed in combination when pyronaridine concentrations exceeded its EC50, highlighting the importance of the combination in controlling possible adaptive resistance to one of the two drugs. A stable killing rate was observed in cases where concentrations of pyronaridine or cabamiquine exceeded either EC50 after full adaptation. Finally, we were able to generate a range of EC50s for the two drugs, both as monotherapy and combination, that could then be translated into human doses.
This study innovatively used *P. falciparum* field isolates data, modeling and simulation techniques to assess cabamiquine and pyronaridine combination selection and reducing animal testing in pre-clinical studies.

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DIHYDROARTEMISININ-PIPERAQUINE PLUS SULFADOXINE-PYRIMETHAMINE FOR INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANT WOMEN: A DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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The spread of antifolate resistance threatens the effectiveness of sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment of malaria in pregnant women (IPTp) in Africa. Dihydroartemisinin-piperaquine (DP), an alternative to SP for IPTp, has shown superior antimalarial effects, but it does not reduce the risk of adverse birth outcomes compared to SP, suggesting that SP may have non-malaria benefits that impact on birth outcomes. Combining DP and SP could optimize the benefits of IPTp. We are conducting a double blinded randomized controlled trial comparing monthly IPTp with SP vs. DP vs. DP+SP (1:1:1) in HIV-uninfected pregnant women living in Busia district, Uganda, a high malaria transmission setting. From December 2020 to December 2023, we completed enrollment of 2757 women who were between 12-20 weeks of gestation. At enrollment, the prevalence of parasitemia was 38% by microscopy and 70% by PCR. Women are started on study drugs at 16 or 20 weeks of gestation and followed in a study clinic for all medical care. The primary outcome is the risk of a composite adverse birth outcome (spontaneous abortion, preterm delivery, low birth weight, small for gestational age, stillbirth, or neonatal death). Secondary outcomes included measures of malaria during pregnancy and at delivery and presence of reproductive tract infections (RTIs) at delivery. As of December 31, 2023, 199 women were prematurely withdrawn before delivery and 2101 had delivered. Malaria incidence during pregnancy was 1.19 and 0.18 episodes per person year before and after starting study drugs, respectively. Of the 2101 deliveries, 605 (28.8%) had a composite adverse birth outcome. The risk of placental malaria was 733/1723 (42.5%) by histopathology (presence of parasites or malaria pigment) and parasite DNA was detected in placental blood by PCR from 239/1918 (12.5%). At delivery, the risk of *Chlamydia trachomatis* was 107/1797 (6.0%), 47/1797 (2.6%) for *Neisseria gonorrhea*, 132/1989 (7.3%) for *Trichomonas vaginalis*, and 131/1343 (9.8%) for group B *Streptococcus*. We expect all women to deliver by August 2024. Unblinded results of the trial will be presented.

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EFFECT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY ON VAGINAL MICROBIOTA, HOST IMMUNE RESPONSE AND PREGNANCY OUTCOMES: A CASE-CONTROL STUDY FROM THE ASPIRE TRIAL IN ZAMBIA

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High prevalence of malaria and curable sexually transmitted and reproductive tract infections (STI/RTI) represent significant burden among pregnant women in East and Southern Africa. These are associated with adverse outcomes including preterm birth and low birthweight (LBW). The ASPIRE trial compared intermittent preventive treatment of malaria in pregnancy (IPTp) using sulfadoxine-pyrimethamine (SP) vs SP with metronidazole (MTZ) vs dihydroartemisinin-piperaquine (DP) with MTZ to reduce adverse pregnancy outcomes attributable to malaria and curable STIs/RTIs. Mechanisms by which these treatments may improve outcomes remain unclear. We aimed to investigate the effects of IPTp regimens on the vaginal microbiota, STI profiles and host immune response in term deliveries vs preterm and/or LBW. DNA was extracted from vaginal swabs collected from randomly selected sub-groups (SP n=99; SP+MTZ n=98; DP+MTZ n=94) at i) enrolment, prior to IPTp, ii) not less than one month after enrolment, before second IPTp dose, iii) prior to last IPTp dose before delivery. Microbiota were characterised using metataxonomic profiling. STIs were detected using quantitative PCR. Immune mediators were investigated using multiplexed Luminex assays. At enrolment, five vaginal microbiota community state types (CSTs) were identified i) *Lactobacillus iners* dominated (47.1%), ii) high-diversity compositions (36.4%), iii) *L. crispatus* (14.4%), *L. gasseri* (1.7%) and *L. jensenii* (0.3%). No change in vaginal microbiota composition was observed in women receiving three or more doses of SP or SP+MTZ. However, DP+MTZ was associated with reduced prevalence of high-diversity vaginal microbiota compositions and increased *L. iners* dominance (P<0.002). Integration of vaginal microbiota profiles with immune mediators, STI profiles, and clinical data is ongoing. Our data indicates that DP+MTZ is associated with reduced vaginal microbiota diversity, and may provide insight into how antenatal interventions alter microbe-host interactions associated with pregnancy outcome.

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SEROPREVALENCE OF *TAENIA SOLIUM* ANTIBODIES AND ASSOCIATED RISK FACTORS AMONG CHILDREN 0-14 YEARS IN NIGERIA

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Children are vulnerable to *Taenia solium*, a parasitic tapeworm causing cysticercosis and taeniasis. Brain cysts may cause seizures. We sought to better understand risk factors for and prevalence of *T. solium* in Nigeria. We used data from a nationally representative, cross-sectional household survey estimating HIV incidence (2018) in which questionnaires and dried blood spots were collected from >31,000 children <15 years old. We determined the seroprevalence of *T. solium* IgG antibodies to rES33 (taeniasis) and T24H (cysticercosis) detected in a multiplex bead assay. We performed separate bivariate and multivariate logistic regression of weighted survey data for taeniasis and cysticercosis using household questionnaire and laboratory data. Positive antibodies against each antigen were detected in children from all states, with an overall antibody seroprevalence of 6.0% for T24H (range, 1.4%-19.3%) and 2.8% for rES33 (range, 0.5%-5.3%). Bivariate analyses found risk for each disease varied by state of residence and was significantly (P<0.05) associated with increasing age, rural (vs. urban) residence, association with pigs (vs. no free-roaming pigs), progressively lower socioeconomic status (vs. highest status), unimproved drinking water source, and lack of toilet facilities. In multivariate analyses, increasing age, rural residence, association with pigs, and lower socioeconomic status remained significant risks for cysticercosis. For taeniasis, the highest socioeconomic status had lower odds of infection compared to the lowest (aOR=0.40, 95% CI 0.22-0.75). Adjusting for all the other variables noted above, the individual impacts of safe water and improved toilets were not associated with decreased risk for each disease; but, regression results suggested a lower risk for cysticercosis when both safe factors were present. To our knowledge, this is the first nationally representative survey providing data on *T. solium* prevalence in Nigeria. The results support prioritizing control and public health strategies such as simultaneous access to improved water and safe toilet facilities to prevent brain cysts and epilepsy.

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PULMONARY CYSTIC ECHINOCOCCOSIS TREATMENT OUTCOMES AMONG 280 PATIENTS AT TWO TERTIARY CARE CENTERS IN CUSCO, PERU

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The management of pulmonary cystic echinococcosis (pCE) is influenced by local practice and center volume. Treatment recommendations are largely based on expert opinion and small single-center case series. We reviewed medical records of patients discharged with a diagnosis of pCE from two referral centers in the Cusco Region of Peru between January 2009 and December 2019. Adverse hospitalizations outcomes were defined as discharge condition recorded as 'unchanged', 'worse', or 'dead'. Two hundred eighty cases with pCE were identified, 45% were younger than 18 years and 43% were female. A single lung cyst was diagnosed in 56% while 16% had 2 cysts, and 16% had ≥ 3 cysts. In 41% of cases the diameter of the largest cyst was ≥10 cm. Ten patients (4%) received pre-surgical albendazole (ABZ), 57 (20%) post-surgical ABZ, and 4 (1%) pre- and post-surgical ABZ. In 163 (58%) surgery was performed without documentation of ABZ prescription. Eight patients (3%) received ABZ with no surgery. The type of treatment prescribed was not documented in 29 patients (10%) and 9 (3%) received surgery and ABZ but the exact order of the interventions was unknown. Multivariate backwards logistic regression found pre-surgical respiratory insufficiency (OR=3.12, 95%CI 1.03-9.47) as predictor for adverse hospitalization outcomes. Subjects referred from a healthcare center (OR=0.21, 95%CI 0.1-0.5) and those hospitalized ≥1 month (OR=0.07, 95%CI 0.01-0.4) were less likely to have adverse hospitalization outcomes. Subjects with documentation of "infected cyst" (OR=11.39, 95%CI 1.2-108.2) and those having a concomitant liver cyst (OR=6.34, 95%CI 3.01-13.35) were more likely to have at least one readmission. No statistically significant differences were found for pre- or post-surgical ABZ and hospitalization outcome or readmission. Further studies analyzing the appropriate timing of antiparasitic therapy in patients with pCE are needed.

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TAENIA SOLIUM FATTY ACID BINDING PROTEIN 1 INDUCES SUPPRESSES TLR4 SIGNALING AND DOWNREGULATE IRE-1α IN A PPAR-G DEPENDENT MANNER

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Neurocysticercosis is a major neurological threat, accounting for over 30% of cases in endemic areas. *Taenia solium*, the causative agent, and its other helminthic counterparts lack key components of the cellular machinery required for endogenous lipid biosynthesis. This deficiency enables the parasite to obtain all required lipids from its host organism. To facilitate effective lipid transport, the cestode parasite employs Fatty Acid Binding Proteins (FABPs), which bind to lipid ligands and allow lipid transport across membranes and into the cytosol. *T. solium* expresses an abundance of FABPs. Apart from transporting ligands, FABPs interacts with the host immune system, however the functional aspect of *T. solium* FABP is still unknown. Elucidating the functional outcome of FABP on host immune system will contribute to understand the detailed immunopathology of cysticercosis infection. TsFABP1 is one of the members of *T. solium* FABP family, which is secretory in nature, interacts with neighbouring cells, potentially modulating their functions. We expressed TsFABP1 in the pET23a vector, purified it with Ni-NTA affinity chromatography, and measured the molecular weight at 15 kDA. TsFABP1 purified form induced anti-inflammatory gene expression in THP-1-derived macrophages in a dose-dependent manner. TsFABP1 inhibits the CD14-TLR4 pathway by binding to CD14 at the LPS binding site, reducing ROS and cleaved IL-1β production. Interestingly macrophages readily internalize the cyanine5-labelled TsFABP1 and in the cytosol the protein may play significant role in immunomodulation. Here for the first time, we report that the TsFABP1 play role in PPAR-γ pathway, which was previously unknown. TsFABP1 suppresses IRE-1α in a PPAR-γ-dependent manner. In conclusion, TsFABP1 is an anti-inflammatory molecule that also downregulate the endoplasmic stress response associated molecule and apart from that TsFABP1 can be explored for therapeutic potential.

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HIGH PREVALENCE AND HOUSEHOLD CLUSTERING OF LIVER CYSTIC ECHINOCOCCOSIS IN A RURAL COMMUNITY IN THE CENTRAL ANDES OF PERU: A POPULATION - BASED SURVEY

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Human cystic echinococcosis (CE), a zoonotic disease caused by the larval stage of the *Echinococcus granulosus* tapeworm, presents a significant public health challenge in the Peruvian central highlands. In this region, the disease's impact is profound, with some families reporting multiple infected individuals. The current study aimed to estimate the prevalence of CE in Corpacancha, a rural community in the Peruvian central highlands, utilizing abdominal ultrasound (US), electroimmuno transfer blot (EITB), and computed tomography (CT) scans for individuals with positive US or EITB results. Additionally, we explored household clustering of CE cases using the intraclass correlation coefficient (ICC) with 95% credibility intervals (CrI) estimated through Bayesian multilevel model, updating prevalence

data, and identifying risk determinants, particularly focusing on household clustering. The findings revealed a liver CE prevalence of 16.1% (95% CI: 11.1% - 22.7%) as detected by ultrasound and a seroprevalence of 24.1% (95% CI: 15.4% - 35.6%) using the EITB assay. Active liver CE was present in 11.9% (95% CI: 7.8% - 17.9%) of participants, predominantly in the CE1 stage, while inactive liver CE had a prevalence of 4.1% (95% CI: 2.3% - 7.4%). Lung involvement was identified in 30.6% (95% CI: 16.9% - 48.8%) of individuals undergoing CT evaluation. Our survey also indicated that approximately one quarter of households had at least one case of CE, with a third of these households reporting multiple cases. After adjusting by relevant predictors of liver CE and accounting by household as a random intercept, we found an ICC of 0.3334 (95% CrI 0.0025 to 0.7379). Overall, this study not only demonstrates hyperendemic levels of CE but also highlights significant household-level influences on disease prevalence, suggesting that intervention efforts may be more effective when targeted at the household level.

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DIAGNOSTIC PERFORMANCE OF A MULTIANTIGEN PRINT IMMUNOASSAY FOR ANTIBODY DETECTION IN HUMAN NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) stands as the most prevalent helminthic infection affecting the human central nervous system. Although neuroimaging is required for definitive diagnosis, the gold standard for serology is the antibody detection using the enzyme-linked immunoelectrotransfer blot assay (EITB, Western blot), which uses seven highly antigenic lentil-lectin purified parasite glycoproteins. EITB is poorly accessible due to is technical complexity and the requirement of sophisticated equipment and parasitic material. We recently developed a 3-antigen-multiantigen print immunoassay (MAPIA) based on recombinant/synthetic antigens (rGP50, rT24H and sTs14), corresponding to the three principal EITB diagnostic families, that effectively address many of the aforementioned barriers. We expanded the initial evaluation of performance of this MAPIA assay using a well-defined set of serum samples from NCC patients confirmed by imaging, including 73 individuals with subarachnoid NCC, 73 with more than 5 parenchymal cysts, 62 with 3-5 parenchymal cysts, 98 with 1-2 parenchymal cysts and 80 healthy controls devoid of neurological disease. The assay overall sensitivity was 97.71% and specificity 97.5%. Subgroup analyses by type of NCC demonstrated a sensitivity of 100% for subarachnoid and parenchymal NCC with more than 5 cysts, slightly decreasing for the groups with 3-5 cysts (96.77%) and 1-2 cysts (94.9%). Equivalent results were obtained when comparing its performance with that of the reference EITB, reaching a sensitivity of 100% for subarachnoid and parenchymal NCC for more than 3 cysts and 95.92% for 1-2 cysts. Our 3-antigen MAPIA is comparable to EITB and emerges as a simpler, reproducible, and available alternative for antibody diagnosis in NCC.

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COMPARISON OF THE ANTIBODY DYNAMICS IN TWO MODELS OF EXPERIMENTAL PIG CYSTICERCOSIS USING A MULTIPLEX BEAD ASSAY

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Cysticercosis is a parasitic infection caused by *Taenia solium* that can invade the brain causing Neurocysticercosis (NCC). Controlled experimental infections of pigs allow to accurately determine timepoints during cysticercosis infection. Antibody responses have been characterized using the traditional lentil-lectin enzyme-linked immunoelectrotransfer blot (LLGP-EITB) assay; however, this qualitative technique presents technical challenges and depend on parasite material. We have developed a Multiplex Bead Assay (MBA) coupled to six recombinant/synthetic antigens used for diagnosis (rGP50,rT24H,sTs14,sTs18,sTsRS1,sTsRS2). To simultaneously quantify the dynamics of the antibody responses against mentioned antigens during infection, and to explore differences in antibody responses in two different experimental porcine cysticercosis models, one using oral infection with eggs and the other using intracarotid injection of activated oncospheres, we analyzed 60 archived serum samples from pigs orally (n=6) and intracarotid (n=6) infected, who developed viable cysticercosis and that were sampled at five time points post-infection (PI). Cyst establishment in brain tissue was predominant in the carotid model. Our 6-antigens MBA determine significantly higher antibody responses against sTs14 and sTs18 for both models ($p<0.01$) and differences against rGP50 and rT24H antibody levels, which were higher only in pig orally-infected. Antibody dynamics in both models described a similar pattern in which rT24H and rGP50 responses were detected from day 28 onwards with a gradual increase throughout the infection course, while smaller antigenic peptides showed a stronger response from day 35PI. Pigs orally infected exhibited a significant decrease in antibody response from day 57PI until necropsy, while this decrease occurred by day 70PI in pigs carotid infected. Although, antibody dynamic is consistent in both models, differences in antibody levels could be explained by the route of infection; natural route that parasite must go through to stablish as a cyst in oral infection could stimulate more antibodies against anchoring antigens (rGP50).

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CHARACTERIZATION OF THE ACUTE NEUROINFLAMMATORY RESPONSE INDUCED BY ANTIPARASITIC TREATMENT IN THE CAROTID PORCINE MODEL OF NEUROCYSTICERCOSIS

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Antiparasitic treatment (APT) in NCC causes cyst damage and activates the host's immune system, triggering early neuroinflammation. We evaluated the development of treatment-induced neuroinflammation in the experimental NCC pig model by intracarotid-oncosphere injection using histopathological, immunohistochemical, and molecular markers to provide evidence for the suitability of this model for studying neuroinflammation. Twelve NCC pigs by intracarotid-oncosphere injection were distributed as untreated (T1), treated with ABZ plus PZQ and sacrificed 48h (T2) and 120h (T3) after APT (n=4 pigs each). Before euthanasia, all pigs received intravenous Evans-Blue (EB) infusion to assess BBB disruption. EB-stained (blue) and non-stained (clear) cysts with adjacent tissue were stored in 10% formalin and paraffin-embedded; pericystic inflammation was assessed using histopathological scores (ISC, range: 0-400). Astrocytosis and microglia were assessed by IHQ using primary antibodies anti-GFAP and anti-IBA 1 and expressed as immunoreactive areas (percentages). Cysts with capsules were also assessed for gene-expression levels of cytokines (IFN-γ, TNF-α, IL6, IL10, and VGEF) by real time PCR. Almost all cysts from treated NCC pigs showed EB-disruption (94.3% [48h] and 100% [120h]) versus untreated pigs (50%, $P< 0.001$). EB-stained cysts showed increased ISCs 120h after APT (median: 400) versus 48h after APT and no-treatment (median: 283, and median: 275, $P<0.001$). Astrocyte and microglia immunoreactivity was higher in NCC pigs 120h after treatment versus 48h after treatment or untreated pigs ($P<0.05$). Increased expression levels of TNF-alpha, INF-gamma, IL-6, and VGEF were found in EB-stained cysts from NCC pigs 120h after APT compared to NCC pigs 48h after APT and untreated pigs ($P<0.005$); IL-10 levels increased 48h after treatment but decayed 120h after treatment ($P<0.005$). Acute pericystic neuroinflammation can be properly induced by 120h after treatment in the carotid model, thus providing a valuable tool to study neuroinflammation and evaluate pharmacological interventions to reduce pericystic neuroinflammation.

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A CRISPR-CAS13A ASSAY FOR DETECTION OF CIRCULATING CELL FREE RNA (CCFRNA) IN ACTIVE *WUCHERERIA BANCROFTI* INFECTION

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Detecting parasitic circulating cell free nucleic acids (ccfDNA/ccfRNA) in plasma is a promising approach for sensitive and specific detection of active helminth infection including *Wuchereria bancrofti* (Wb). To identify potential Wb RNA targets, we performed Plasma-RNAseq using plasma from 10 Wb microfilaria-positive (mf-positive) individuals and 10 healthy blood bank individuals and used bioinformatic tools to ensure specificity. Six targets were identified that were specific to Wb and/or *Brugia malayi* (Bm), the causative agents of lymphatic filariasis, and not found in *Loa loa* (Ll) or *Onchocerca volvulus* (Ov), two closely related filarial parasites. Reverse transcriptase-PCR (RT-PCR) assays for each of these six targets were developed and tested on RNA from extracted daytime plasma from mf-positive patients with Wb and shown to be variably positive. To improve the sensitivity of the detection of ccfRNA in Wb infection and to develop a possible point-of-care (POC) assay concurrently, guide RNAs for the set of six ccfRNA targets were designed and used in a CRISPR-Cas13a (RNA-directed RNA nuclease) assay. We first tested these guide RNAs against synthetic target RNAs in the presence of reporter molecules that fluoresce after cleavage by activated Cas13a. By combining the most active guide RNAs into a pooled assay, results showed a limit of detection of approximately 1000 copies/µL using synthetic targets. The Cas13a assay requires no RNA purification, reverse transcription, or amplification and can be detected by a simple fluorescent reader. To demonstrate this, we added fluorescence illumination to a compact mobile phone-based digital microscope known as the NTDscope (aka LoaScope) and were able to detect an increasing fluorescence signal in the presence of RNA biomarkers compared to a control reaction without them. These data suggest that molecular testing for ccfRNA for Wb at the POC with an amplification-free Cas13a assay is feasible. The assay will be optimized prior to assessing the sensitivity and specificity using cryopreserved plasma samples from mf-positive Wb patients and Wb-uninfected controls.

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A BIOMARKER ASSAY TO DETECT PEOPLE WITH HIGH *LOA LOA* MICROFILARIA COUNTS

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Loiasis is a disease caused by infection with the nematode *Loa loa*. Some people with high *L. loa* microfilaria counts develop serious adverse drug reactions after treatment with ivermectin. This poses a significant challenge for lymphatic filariasis and onchocerciasis elimination programs in Central Africa where loiasis is endemic, as these programs rely on mass distribution of ivermectin. To address this problem, improved methods are needed to efficiently identify individuals with loiasis who are at increased risk of ivermectin-related adverse events. We have previously reported detection of the *L. loa* protein Ll-Bhp-1 in the sera of people with loiasis. Here, we describe use of this antigen as an infection biomarker that may be especially useful for identifying people with high *L. loa* infection burdens. We developed a prototype antigen capture ELISA that detected Ll-Bhp-1 in 74 of 116 (63.8%) loiasis patient sera. Antigen levels were significantly correlated with *L. loa* microfilarial counts. Assay sensitivity was excellent in samples from people with microfilarial counts that would put them at risk for serious adverse events (sensitivities of 94% and 100% in samples from people with ≥20,000 and ≥50,000 *L. loa* microfilaria per milliliter of blood, respectively). The assay is highly specific and did not detect Ll-Bhp-1 in any of 112 sera from people with other filarial infections or in 34 sera from non-endemic controls. Thus, this antigen assay appears to be highly sensitive for identifying people with high *L. loa* microfilarial counts who are at increased risk of serious adverse events after ivermectin. Optimization of this prototype assay and use of a rapid diagnostic platform could facilitate loiasis mapping and efforts to eliminate lymphatic filariasis and onchocerciasis in Central Africa.

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A RANDOMIZED DOUBLE-BLIND STUDY COMPARING THE EFFECT OF 3 ANNUAL OR FIVE 6-MONTHLY SINGLE DOSES OF MOXIDECTIN OR IVERMECTIN IN INDIVIDUALS ≥12 YEARS OLD WITH *ONCHOCERCA VOLVULUS* INFECTION IN ITURI PROVINCE, DEMOCRATIC REPUBLIC OF CONGO: EFFICACY AND SAFETY DATA 12 MONTHS AFTER THE FIRST TREATMENT

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Long-term community-directed treatment with ivermectin (IVM) has reduced onchocerciasis prevalence and may have eliminated onchocerciasis in some foci in Africa, but alternative strategies are needed for accelerating elimination across Africa. The US Food and Drug Administration approved moxidectin (MOX) 8 mg for treatment of individuals ≥12 years old with onchocerciasis based on Phase 2 and 3 study data showing that a single MOX dose reduced skin microfilariae levels (SmfL) better and for longer than a single 150 µg/kg IVM dose. MDGH is seeking regulatory approval for children 4 to 11 years old. A double-blind trial, initiated in the Ituri province of the Democratic Republic of Congo in May 2021, is comparing the safety and effect on SmfL in individuals ≥12 years old randomized in a ratio of 3:1:3:1 to three annual MOX doses, three annual IVM doses, five 6-monthly MOX doses or five 6-monthly IVM doses. The primary efficacy endpoint is the percentage of participants who received a single or two 6-monthly MOX doses and had undetectable (0) SmfL both 6 and 12 months after the first treatment. Safety endpoints are vital signs and the incidence and severity of adverse events (AEs) to 36 months and liver function to 12 months after the first treatment. Secondary efficacy analyses include SmfL 6, 12, 18, 24, 30 and 36 months after the first treatment. A total of 8925 people from 45 villages in the Logo and Nyarambe Health Zones were screened. Enrolment was completed in July 2023 with 323 participants with ≥10 mf/mg skin (based on 4 skin snips, mean 23.1 ± 20.8 mf/mg, range 10.0 to 175.4 mf/mg skin) randomized and treated. To-date, treatments have been well-tolerated. The majority of participants reported no AEs. The types of AEs were similar to those in the Phase 2 and 3 studies. AEs occurred primarily within the first 5 days after treatment. The severity of 96% of AEs was mild or moderate. Details of the study design, including the cost- and time-effective nested recruitment and screening strategy with a concurrent single dose safety study, participant population and results of the 12-month efficacy and safety analyses will be presented.

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MULTIPLEXING NOVEL BIOMARKERS TO AID POST-ELIMINATION SURVEILLANCE IN LYMPHATIC FILARIASIS

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The success of mass drug administration (MDA) at reducing the prevalence of lymphatic filariasis (LF) in endemic areas has led to an increased need for diagnostic assays with high sensitivity and specificity. To be useful in post-elimination surveillance (PES) areas with low to zero prevalence, high test performance characteristics are required to enable the early detection of infection recrudescence without eliciting high numbers of false positive results. Antibodies to several *Wuchereria bancrofti* [*Wb*]- and *Brugia malayi* [*Bm*]-encoded antigens (e.g. Wb123, Bm33, BmR1) have been utilized to this end, but suffer either from sensitivity or specificity levels that fail to meet recently adopted target product profiles. Additional targets that could be used as confirmatory tests or in multiplexed assays could overcome these issues. From a screen of 12 targets (reported previously) we identified that immunoassays detecting IgG antibodies against Wb5 and Wb4 antigens were highly sensitive and specific for Wb and/or Bm infection and were associated with pre-patent (Wb5) or patent (Wb4) infection. Recombinant Wb4 and Wb5 proteins were generated for use in a variety of IgG4-based immunoassays. Screening of serum from *Brugia*-infected humans (n=19) revealed high prevalence of anti-Wb4 antibodies (14/19 positive) and minimal cross reactivity with other filarial infections. Using IgG4 based immunoassays at 100% specificity, Wb5 and Wb123 had individual sensitivities of 53.7% and 75.3%, respectively, while a combination resulted in 81.0% sensitivity in 381 samples (231 Wb-infected; 150 Wb-uninfected controls). Testing of prototype Wb5 IgG4-based lateral flow assays supports the finding that the addition of Wb5 to Wb123 increases sensitivity of LF detection. Moreover, kinetic studies of patients that were treated and followed longitudinally demonstrated a sharper decline in Wb5 titers compared to Wb123, suggesting the use of Wb5 as a marker of active infection. Ongoing studies to improve the detection of Wb4 and Wb5 paves the way for their use in combination with Wb123 (or other antigens) to increase the sensitivity of Ab-based assays for PES.

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FIELD EVALUATION IN GHANA OF A NEW OVND5 REAL-TIME PCR METHOD FOR DETECTION OF *ONCHOCERCA VOLVULUS* DNA IN POOLED *SIMULIUM DAMNOSUM S.L.* BLACKFLIES

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Onchocerciasis is a parasitic disease transmitted by blackflies and targeted by the World Health Organization (WHO) for elimination. WHO guidelines for stopping treatment (MDA) require screening pools of *Simulium* blackflies for the presence of *O. volvulus* using the O150 PCR-ELISA. A new qPCR assay using the ND5 region (OvND5) was found to be more sensitive and species-specific than O150 molecular methods. It is also faster, easier to perform, lower cost, and uses room-temperature stable reagents. However, the OvND5 qPCR method has not been evaluated in *Simulium* blackflies collected in endemic regions. As part of a larger study evaluating serological thresholds to stop MDA in Northern Ghana, DNA extracted from pools of heads from 22,772 *Simulium damnosum s.l.* blackflies, collected from 10 capture sites in 4 districts, were tested by OvND5 and O150 qPCR assays. A sample was considered positive if both OvND5 and O150 qPCRs were positive. Samples with discordant qPCR results were repeated at a higher (1/20) dilution of DNA. Of 233 pools analyzed, 3 were positive, each from a different site. Cycle threshold (Ct) values ranged from 29-34 (OvND5) and 24-27 (O150). The prevalence calculated using the Poolscreen software was 0.013% (95% CI 0.003-0.038%), which met WHO criteria for stopping MDA. There were 9 pools of blackflies with discordant qPCR results (O150+/OvND5-), 7 of which were from sites with a positive pool. All discordant samples had O150 Ct values > 36. Repeat testing of these samples with diluted DNA did not reveal inhibition; no OvND5 result became positive. It is possible that the high O150 qPCR Ct value represents a small amount of *O. volvulus* DNA that does not indicate an L3 larvae in the head or cross-reaction with another *Onchocerca* species. Further evaluation of the samples is ongoing including genetic sequence analysis to verify species identity, which would help better understand how to use this new method to inform stopping decisions. This evaluation of the OvND5 qPCR provided information on how this test will perform programmatically. Additional evaluations, including those ongoing in Tanzania, Benin, and Malawi, will be important.

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SAFETY AND EFFICACY OF A SINGLE DOSE OF 2 MG MOXIDECTIN IN *LOA LOA* INFECTED INDIVIDUALS: A DOUBLE-BLIND, RANDOMIZED IVERMECTIN-CONTROLLED TRIAL WITH ASCENDING MICROFILARIAL DENSITIES

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In 2018, the US FDA approved the macrocyclic lactone moxidectin (MOX) at 8 mg dosage for onchocerciasis treatment in individuals aged ≥12-year-old. Severe adverse reactions have occurred after ivermectin (IVM), also a macrocyclic lactone, in individuals with high *Loa loa* microfilaria density (MFD). This study compared the safety and efficacy of a 2 mg MOX dose and the standard 150 µg/kg IVM dose in individuals with low *L loa* MFD. A double-blind randomized, ivermectin-controlled, trial of a 2 mg moxidectin dose was conducted in Cameroon between May 2022 and May 2023. It enrolled 72 adult men with *L. loa* MFD between 5-1000 microfilaria/mL. Outcomes were occurrence of adverse events (AE) and *L. loa* MFD reduction rate during the first month off treatment. No serious or severe AEs occurred among the 36 MOX or the 36 IVM treated individuals. Forty-nine AEs occurred in the MOX arm vs 59 AEs in the IVM arm. Grade 2 AE incidence was higher among IVM than MOX treated participants (38.5% and 14.3%, respectively, p=0.043). Median MFD reduction rates were significantly higher after IVM than MOX at day 3 (D3) (70.2% vs 48.5%), D7 (76.4% vs 50.0%) and D30 (79.8% vs 48.1%). Efficacy results at D180 and D365 will be available in June 2024. A single 2 mg MOX dose is as safe as 150 µg/kg IVM in patients with low *L loa* MFD. Further studies with higher moxidectin doses and in patients with higher MFD are warranted.

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NEXT GENERATION OV16-BASED RAPID TESTS: FIELD DATA

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Improved diagnostics are required to map onchocerciasis in low endemicity areas. In 2021 WHO issued a Target Product Profile (TPP) that calls for a sensitivity ≥ 60% and specificity ≥ 99.8%. To reach this stringent specificity requirement, we developed a prototype rapid diagnostic test that detects IgG4 antibodies to different recombinant *O. volvulus* proteins arranged as two different test lines. Both test lines must be visible to count the test positive. In the latest iteration, called “Biplex D”, the first test line (TL1) is made of Ov16 and the second test line (TL2) contains a mixture of OvOC3261 and Ov33.3. When evaluated in the laboratory against a panel of cryopreserved sera containing 86 microfilariae (Mf) positives and 234 other infections, the sensitivity of Biplex D was 79% (95%CI 69-86%) and its specificity 100% (99.95-100). An earlier test version, called “Biplex C” contains only OvOC3261 and no Ov33.3 at TL2. These two versions are being validated in the field using fingerstick blood. In Bong, Liberia, a preliminary dataset on 19 patients with onchocerciasis (all Mf and nodule positive before ivermectin 18 month ago) gave a sensitivity for Biplex D of 17/19 = 89% (69-97). Combining this with the specificity data obtained in the lab, we conclude that Biplex D meets the TPP sensitivity and specificity specifications, even at the lower bound of the 95% CI. The sensitivity of Biplex C was in Liberia 16/19 = 84% (62-94%), and in Nkwanta, Ghana 11/13 = 85% (57-97%). Combining the two data sets gives a mean sensitivity of 27/32 = 84 % (68-93%), above the 60% sensitivity threshold at the lower bound of the 95% CI. Antibody prevalence data were collected in Ghana with Biplex C. In Adaklu, which is not endemic for onchocerciasis and where no skin snip were Mf positive by microscopy, the seroprevalence in adult males was 3% (1.1-7.4), suggesting that at that level no MDA should be initiated. In adult males in Nkwanta, the Mf prevalence was 4% (1.9-7.9) and the seroprevalence 44% (37-51). Despite proven transmission, both the Mf prevalence and seroprevalence was 0% in children under the age of 10, suggesting that children would be an inadequate sentinel group post-MDA.

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IXOKALLIPIN, A NEW PLASMA KALLIKREIN INHIBITOR FROM *IXODES SCAPULARIS* BINDS TO THE CELL MEMBRANE AND IMPAIRS HEMOSTASIS AND THE SKIN WOUND HEALING

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Besides its role in blood coagulation, plasma kallikrein (KLK) also induces keratinocyte migration accelerating wound healing process. Since ticks are blood pool feeders, we rise the hypothesis that KLK-kinin system components would have contact with keratinocytes from the skin and tick salivary proteins at the bite site. In this work we described for the first time an interesting molecule from *I. scapularis* saliva that binds to keratinocyte and endothelial cell membrane, blocking hemostasis and KLK-induced wound healing. We found a strong KLK inhibitory activity in *I. scapularis* saliva. This activity was purified, characterized and a new molecule from the serpin family, that was named ixokallipin, was identified. Ixokallipin inhibits the intrinsic pathway of blood coagulation targeting specifically KLK and factor XIIa. Ixokallipin inhibits the KLK generation on endothelial cell surface *in vitro* and the venous thrombosis *in vivo* without causing a significant bleeding effect. Ixokallipin binds to endothelial cell and keratinocyte surface mainly through phosphatidic acid. Keratinocyte surface supports high molecular weight kininogen-dependent plasma preKLK activation and production of active kallikrein. This event is modulated and completely blocked by ixokallipin. Ixokallipin inhibits keratinocyte migration by reducing cellular focal adhesions and membrane protrusions. The keratinocyte migration is dependent on PAR-1 but not PAR-2 activation. KLK cleaves PAR-1 at a non-canonical site generating a protective response associated with PKC-dependent calcium signaling which was down-regulated by ixokallipin. Looking in more details, ixokallipin inhibits kallikrein/PAR-1-dependent EGF/EGFR transactivation, down-regulating ERK1/2, AKT and paxillin activation, decreasing actin polymerization and consequently the cell migratory responses. Finally, using an *in vivo* model, we confirmed that ixokallipin causes a delay in the wound healing. Our results highlighted interesting new strategies used by the ticks to avoid host hemostasis and skin barriers at the same time.

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TSETSE-ENDOSYMBIONT METABOLIC COMPETITION FOR ACYL-CARNITINES REGULATES FLY FECUNDITY BY SUPPRESSING THE VIABILITY OF STORED SPERM

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Competition between insects and their endosymbiotic bacteria for environmentally limited nutrients can compromise the fitness of both organisms. Tsetse flies, the vectors of pathogenic African trypanosomes, harbor a host species and population-specific consortium of vertically transmitted endosymbiotic bacteria that range on the functional spectrum from mutualistic to parasitic. Tsetse’s indigenous microbiota can include a member of the genus *Spiroplasma*, and infection with this bacterium causes fecundity-reducing phenotypes in the fly that include a prolonged gonotrophic cycle and a reduction in the motility of stored spermatozoa post-copulation. Herein we demonstrate that *Spiroplasma* and tsetse spermatozoa utilize fly-derived acyl-carnitines, which in animals are a component of the carnitine shuttle that transports fatty acids across the mitochondrial matrix for use in energy production. The fat body of mated female flies increases acyl-carnitine production in response to infection with *Spiroplasma*. Additionally, their spermathecae (sperm storage organs), and likely the sperm within, up-regulate expression of *carnitine O-palmitoyltransferase-1*, which is indicative of increased carnitine shuttle activity and thus increased energy demand and energy production in this organ. These compensatory measures are insufficient to rescue the motility defect of spermatozoa stored in the spermathecae of *Spiroplasma* infected females and thus results in reduced fly fecundity. Our results provide insight into the mechanisms that facilitate the maintenance of bacterial endosymbioses, and how these relationships impact sperm motility and host fecundity. In the case of pest insects, a better understanding of the metabolic mechanisms that underlie these associations can lead to the development of novel control strategies.

6851

ANALYSIS OF THE SCABIES ASSOCIATED MICROBIOTA DEMONSTRATES A SHIFT TO OPPORTUNISTICALLY PATHOGENIC BACTERIA.

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Scabies is a neglected tropical disease with a prevalence of 400 million cases annually. The disease is prevalent in tropical regions where there is an established link with secondary bacterial infections. The causative agent *Sarcoptes scabiei* is an obligate ectoparasitic mite that burrows into the superficial layers of the host skin. This action combined with a complex interaction between scabies mite excretory proteins and the host's immune system leave patients susceptible to secondary bacterial infections. It is these secondary complications that account for the disease burden that is estimated to be 0.21% disability-adjusted life years. Clinical research has shown a correlation between scabies infections and opportunistic pathogens. Despite this accepted correlation there is little molecular data to underpin this complex relationship. Our aim is to provide the fundamental molecular evidence of how scabies infections interfere with the host microbiome. We undertook a collaborative multi-national study that collected skin scrapings from scabies infected patients in India, France and Australia representing a diverse climate and socio-economic range. Microbial DNA was extracted and 16s full length rRNA and ITS[1-4] sequencing were performed using the PacBio sequel,utilising single molecule real-time technology to generate long read lengths. Using an established bioinformatics pipeline, a total of 22,678 amplicon sequence variant (ASVs) were identified from 751 samples. Community composition and microbial abundance was then analysed using the programing language R. Our data demonstrates that there is a significant increase in *Staphylococcus aureus* ($P<0.05$) in scabies infected lesions across all countries and in India and Australia there was a significant increase in *Streptococcus pyogenes* ($P<0.05$) in scabies infected lesions. We found no significant changes in the fungal microbiome and we found several commensal skin bacteria were significantly decreased. This study is the first to quantify the scabies associated microbiome at the molecular level, and address how it might differ globally.

6852

LEISHMANIA TRANSMISSION IS DISRUPTED IN SANDFLIES COLONIZED BY *DELFTIA TSURUHATENSIS* TC1 BACTERIA

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Most human pathogenic *Leishmania* species are zoonotic agents; therefore, sandfly-based control strategies are essential to prevent parasite circulation. Here, we used a *Delftia tsuruhatensis* strain that inhibits the development of *Plasmodium* in mosquitoes, but in the context of *Leishmania*-infected sandflies. Using GFP-expressing *D. tsuruhatensis* TC1, we show that this bacterium colonizes the midgut of *Phlebotomus duboscqi* sandflies. Such colonization impacts the development of *L. major* parasites in the vector, as per the significantly lower number of both total and infectious metacyclic parasites detected in the midguts of bacteria-fed *versus* control sandflies (90% reduction). This phenotype was consistently observed, regardless of the timing of bacterial feeding (from 1 week prior to infection to 8 days after infection), and was even stronger in sandflies given a second, uninfected, bloodmeal. Curiously, our data suggests this phenotype is likely an indirect effect of TC1 colonization, related with the induction of sandfly gut dysbiosis. These results have biological significance, since we observed that *Leishmania*-infected, bacteria-fed sandflies are less able to transmit *Leishmania major* parasites and cause disease in a mouse model of cutaneous leishmaniasis (parasites detected in 27% of animals bitten by bacteria-fed flies *versus* 100% of animals in the control group). Relevantly, modelling studies based on our results support the disruption of disease endemicity in the field. Altogether, these results highlight TC1 as a promising vector-based approach for the control of leishmaniasis in the field.

6853

BLOOD FEEDING ACTIVATES THE TERMINAL DIFFERENTIATION OF PRECURSOR CELLS IN TICK SALIVARY GLANDS

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Tick salivary glands secrete a complex saliva into their hosts to facilitate blood feeding and pathogen transmission. Thousands of transcripts coding for structural and secreted protein have been identified in tick salivary glands. The transcriptomic profile changes over time during feeding, indicating a switch in the sialome. Bulk RNA-seq of *Ixodes scapularis* salivary glands revealed temporal differences in the transcriptomic profile as blood feeding progresses, confirming the "sialome switching" takes place. To uncover the cellular mechanisms behind this phenomenon, we performed single cell RNA sequencing (scRNA-seq) of salivary glands. Salivary gland cells exhibited hypertrophy throughout the feeding process. Clustering analysis identified a total of ten different cellular clusters. Four clusters were observed in unfed ticks; and one of them expresses genes related to cell signaling, signal transduction, and transcription factors, including genes related to the non-canonical Wnt signaling pathway. This suggests that it may represent salivary gland cells in an undifferentiated stage. The abundance of these putative cells presents in unfed ticks decreased as blood feeding progresses, while new clusters appear which express canonical salivary genes. The identity and distribution of the cell clusters and their apparent differentiation were validated by RNA *in-situ* hybridization. Sialome switching appears as a result from cell differentiation rather than cell proliferation. Furthermore, the pJNK is activated during the transition from unfed to fed stage. Based on these findings, we propose that blood feeding activates terminal differentiation of tick salivary gland precursor cells into cells that express subsets of salivary genes in a dynamic process involving the non-canonical Wnt signaling pathway. These findings provide new insights on the dynamic transcriptional response of salivary glands required for successful blood feeding. Disrupting this process may offer potential strategies for controlling tick feeding and, consequently, tick-borne diseases.

6854

SEASONAL VARIATION IN TSETSE FLY APPARENT DENSITY AND TRYPANOSOMA SPP. INFECTION RATE AND OCCURRENCE OF DRUGRESISTANT TRYPANOSOMES IN LAMBWE, KENYA

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Tsetse flies are major vectors of trypanosomes causing debilitating African animal trypanosomiasis. Emergence of drug resistant trypanosomes is a common problem in sub-Saharan Africa. This study aimed to identify tsetse flies' seasonal variation in apparent densities and their infection rates and occurrence of drug resistant trypanosomes. Tsetse flies were collected from Lambwe, Kenya in May and September 2021. Genomic DNA was extracted from them and *ITS1* gene amplified to detect *Trypanosoma* infection with subsequent species detection. Transporter genes *DMT*, *E6M6*, *TbAT/P2* and *TcoAde2* were targeted to detect polymorphisms associated with drug resistance using sequencing and comparison to drug sensitive species referenced in Genbank. A total of 498 tsetse flies and 29 non-tsetse flies were collected. Apparent density of flies was higher in wet season 6.2 fly per trap per density (FTD) than in dry season 2.3 FTD ($P = 0.001$). Male tsetse flies ($n = 311$) were numerous than females ($n = 187$) ($P = 0.001$). Non-tsetse flies included Tabanids and *Stomoxys* spp. *Trypanosoma* infection in tsetse was 5% (25/498) whereby *T. vivax* was 4% (11/25), *T. congolense* 36% (9/25) and *T. brucei* 20% (5/25) ($P = 0.186$ for species distribution) with infections being higher in females ($P = 0.019$) and during wet season ($P < 0.001$). Numerous polymorphisms and insertions associated with drug resistance were detected in *DMT* and *E6M6* genes in two *T. congolense* isolates while some isolates lacked these genes. *T. brucei* lacked *TbAT/P2* genes. *TcoAde2* in three *T. congolense* isolates were related to those in trypanosomes from cattle blood in our previous study, supporting tsetse fly involvement in transmission in the region. We report *Trypanosoma* associated with drug resistance in tsetse flies from Lambwe, Kenya. Female tsetse flies harbored more *Trypanosoma* infections than males. Tsetse transmission of trypanosomes is common in Lambwe. Risk of trypanosome infection seem higher in wet season when tsetse flies and *Trypanosoma* infections are more prevalent than in dry season. More efforts to control animal trypanosome vectors in the region are needed with particular focus on wet seasons.

6855

CHANGES IN CYTOFORM (CYTOSPECIES AND CYTOTYPE) COMPOSITION OF VECTORS OF ONCHOCERCIASIS IN NORTHERN CAMEROON AND ITS POSSIBLE IMPLICATIONS FOR DISEASE ELIMINATION

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Onchocerciasis, caused by *Onchocerca volvulus*, is the second leading cause of infectious blindness worldwide. Members of the *Simulium damnosum* species complex are the major vectors in Africa, host to over 99% of the global disease burden. Attaining the WHO goal of transmission elimination (TE) requires regular surveys of vector cytoform composition (as part of monitoring and evaluation), since cytoform composition may change over time. This is especially important because cytoforms of the vectors differ in their vectorial efficiency, ecological distribution and biting pattern, and therefore influence disease epidemiology. Northern Cameroon (NC) is a savanna area with varying success towards TE. Cytoforms previously reported in NC are *S. damnosum* sensu stricto, *S. squamosum* cytotype A, *S. sirbanum* and *S. mengense*. There is paucity of recent information on the cytospecies/cytoform composition in NC, with data available only for few selected sites, and most available data date decades ago. We sampled larvae from rivers in three administrative regions that constitute NC. Larvae were identified by cytotaxonomy of polytene chromosomes. Five cytoforms were identified: *S. damnosum* s.s., *S. sirbanum*, *S. squamosum* cytotype C, *S. yahense* and a cytotype that we call *S. damnosum/sirbanum* because it could not be placed under either cytospecies. This is the first report of *S. yahense* in NC, a restricted species known only in forest areas. *S. yahense* is a very competent vector, more than all previously known vectors in NC. Also, this is the first report of *S. squamosum* C from NC. The *S. squamosum* cytotypes have been associated with differences in biting pattern. In addition, *S. damnosum* s.s. was observed to possess high frequency of inversion 2L-st/2b; this inversion was only previously reported in Ethiopia. Hence, there have been significant changes in cytoforms composition in NC. This change may be due to adaptation of species like *S. yahense* to dryer environments, and possibly due to climate change whose impact is tangible in NC with recorded increase in mean annual temperature. The observed changes in cytoform composition may impact the drive toward TE in NC.

6856

MATERNAL MICROCHIMERISM IS ASSOCIATED WITH AN ALTERED TRANSCRIPTIONAL PROFILE OF *PLASMODIUM FALCIPARUM*-SPECIFIC T CELLS IN MALIAN CORD BLOOD

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Plasmodium falciparum (Pf)-responsive T cells have previously been identified in cord blood from malaria-endemic settings, a phenomenon known as prenatal immune priming (PIP). We have found that maternal microchimerism (MMc) at delivery was associated with increased susceptibility to Pf infection in childhood, and we hypothesized that MMc modulates the quality of PIP. To investigate this hypothesis, we developed an approach to identify and characterize Pf-responsive T cells using single cell RNA sequencing (scRNAseq). Whole cord blood from Malian primigravidae living in a malaria endemic setting was first screened for MMc using qPCR assays targeting a maternal specific allele. Cord blood mononuclear cells (CBMC) from n=8 MMc+ and n=3 MMc- offspring were stimulated with purified Pf merozoite extract for 18 hours and CD3+ CD69+ cells were sorted by flow cytometry for scRNAseq using the 10X Genomics platform. Data from 31,792 T cells across 11 samples were normalized and aggregated for further analysis, including 19,882 CD4 T cells, 6,082 CD8 T cells, and 2,308 γδ T cells. To identify true antigen-specific vs. bystander activated T cells, we developed a T cell activation gene signature that included genes upregulated in the setting of T cell receptor (TCR) engagement (NR4A, IRF4, IL2RA, MIR155HG, CD40LG, TNFRSF4, and TNFRSF9). The gene signature identified 1,178 CD4 T cells, 184 CD8 T cells, and 375 γδ T cells with evidence of TCR engagement, suggesting antigen specificity. Within CD4 T cells, Pf-responsive vs. bystander cells had significantly increased expression of HLA-DR and HLA-DP genes, as well as IL1B, GZMB, IFI30, and CXCL8 (IL-8). Pf-responsive cells from MMc+ vs. MMc- cord bloods had significantly decreased expression of IL1B, GZMB, CXCL1, and CXCL2; and significantly increased expression of the immunoregulatory molecule CD52. Together, these data demonstrate the ability to identify Pf-responsive T cells in CBMC using modern, robust, single cell approaches and suggest the potential for differential function of these cells by MMc status.

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TRANSPLACENTAL TRANSFER OF FUNCTIONAL ANTIBODIES DIRECTED AGAINST *PLASMODIUM FALCIPARUM* BLOOD STAGE ANTIGENS

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The transplacental transfer of maternal antibodies to the fetus is crucial in protecting neonates in early life. However, several studies have shown that infants born from mothers with *Plasmodium falciparum* Malaria infection at Delivery (MiD) present a high risk of infection and constitute a particularly vulnerable population. Many studies have investigated the efficacy of maternal antibodies transfer in MiD whereas the functionality of those antibodies remains to be assessed. The study was carried out in a rural region of southern Benin and neonates were followed-up from birth to 18 months of age. The functionality of immunoglobulin G (IgG) against 5 *Plasmodium falciparum* antigens was determined using a bead-based opsonic phagocytosis assay (BPA) and THP1 monocyte line with available maternal and cord serum (n=355). IgG, IgG1 and IgG3 specific to *Pf*-antigens were quantified from the same samples using ELISA. We observed that phagocytosis in the maternal compartment is strongly dependent on the concentration of antibodies specific to each antigen (AMA1 p=0.002; MSP1 p=0.014; MSP3 p=0.017; GLURP-R0 p<0.001 and GLURP-R2 p<0.001) whereas maternal hypergammaglobulinemia (total IgG greater than 16g.L^{-1}) was negatively associated with phagocytosis (AMA1 p=0.014, MSP3 p=0.013). Functional antibody transfer was positively associated with maternal antibody concentration (AMA1 p<0.001, MSP1 p=0.025, MSP3 p=0.043, GLURP-R0 p=0.013, GLURP-R2 p<0.001) and negatively associated with maternal exposure to malaria vector (AMA1 p= 0.07, MSP3 p= 0.008). Taken together, our data suggest that maternal specific antibodies are strongly secreted during MiD. They are functional until total IgG reaches a high concentration which will reduce the capability of specific IgG to induce phagocytosis. The transplacental transfer of functional antibodies is impaired when mothers are exposed to malaria vectors.

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ANTIBODY FC GLYCOSYLATION MODULATES NATURAL KILLER CELL-MEDIATED ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC) IN MALARIA-EXPOSED PREGNANT WOMEN

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Antibody-dependent cellular cytotoxicity (ADCC) mediated by natural killer "NK" cells has been associated with clinical immunity to malaria in both children and adults in several endemic settings. However, it remains unclear whether NK cell-mediated ADCC is also protective against malaria in pregnancy. To study the NK cell response in malaria-exposed pregnant women, we leveraged peripheral blood mononuclear cell (PBMC) samples from the DPSP Clinical Trial (ID: NCT04336189), in which participants living in Busia District, Uganda were randomized to receive sulfadoxine-pyrimethamine, dihydroartemisinin piperaquine, or a combination of these drugs for intermittent preventive treatment of malaria in pregnancy. We first observed that primigravid donors had a higher risk of malaria-related complications than multigravid donors, suggesting that adaptive immune mechanisms may confer protection in this context. When we profiled the ability of NK cells to perform ADCC against erythrocytes infected with VAR2CSA-expressing *Plasmodium falciparum* (CS2), we observed that the magnitude of ADCC was significantly enhanced when infected erythrocytes were opsonized with pooled plasma from multigravid compared to primigravid donors. VAR2CSA-specific IgG titers were similar in both plasma pools. NK cell degranulation and cytokine production was similar between primigravida and multigravida PBMC donors, leading us to hypothesize that NK cell-extrinsic factors present in plasma underlie this observation. Previous serology work has shown that afucosylation of VAR2CSA-specific antibodies increases with gravidity, which enhances Fc-dependent effector responses. When we opsonized CS2-infected erythrocytes with pooled plasma with high and low Fc fucosylation of VAR2CSA-specific IgG, we found that lowly fucosylated plasma induced significantly more NK cell degranulation than highly fucosylated plasma in DPSP donors. We are currently working to identify phenotypic features of NK cells that respond to afucosylated VAR2CSA-specific IgG and to search for correlations between these phenotypes and birth outcomes within the DPSP study cohort.

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CHRONIC *PLASMODIUM* INFECTIONS CAUSE PERSISTENT CHANGES IN THE HOST IMMUNOLOGICAL LANDSCAPE

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Chronic *Plasmodium falciparum* infections are the norm in endemic areas. While minimally symptomatic, these infections predispose individuals to secondary bacterial infections and reduce malaria vaccine efficacy. Thus, understanding how chronic infections alter the immunological landscape of infected individuals is needed. Here, we used samples collected from macaques infected with *P. coatneyi*, a model of *P. falciparum* malaria, to define host transcriptional changes and immunological responses that lead to the establishment of a chronic infection. Using whole blood RNA sequencing, we show that infections reach chronicity 50 to 80 days after inoculation with sporozoites. Based on transcriptional analysis of the host response, progression to chronicity is generally independent of parasitemia and, instead, related to time an infection has persisted. The transition from acute to chronic infections was defined by upregulation in gene signatures related to B cells and cytokine signaling and downregulation of interferon gamma signaling. Interestingly, Type I interferon signaling remained elevated from the acute to chronic phases. Inflammatory cytokine gene expression was upregulated during acute infection and decreased as the infection progressed to the chronic phase. However, some pro-inflammatory cytokines like TNFα remained elevated. Anti-inflammatory cytokines (e.g., IL-10) increased in the acute and returned to baseline when chronicity was reached. Flow cytometry analysis showed an increase in multiple B cell subsets, including CD21^{neg-} CD27^{neg-} B cells, and effector memory CD8^{+} T cells. Control of parasitemia was significantly correlated with the changes in B and T cell populations in addition to IgG and IgM against *P. coatneyi*, suggesting these responses are key for maintaining parasite control during chronic infections. In sum, this study defines the progression of a Plasmodium infection from acute to chronic and shows persistent derangements in the host immunological landscape that may influence malaria vaccine efficacy.

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BASELINE INNATE IMMUNE ACTIVATION AND INFLAMMATION IS CORRELATED WITH CONTROL OF SUBSEQUENT PARASITEMIA IN VERY YOUNG MALIAN CHILDREN

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Reliable immune correlates of protection against *Plasmodium falciparum* (*Pf*) malaria remain elusive, in part because sustained protection from parasitemia through natural exposure is rarely observed. In a prospective cohort study of Malians living in an area of intense malaria transmission, we identified a subset of young children who remained aparasitemic during 7 months of biweekly active and passive surveillance. These children showed boosting of malaria-specific IgG during the season, suggesting evidence of malaria exposure despite remaining aparasitemic. To identify immune responses associated with apparent elite control of infection, we carried out CITE-seq of PBMCs from 7 pairs of age- and sex- matched aparasitemic and parasitemic children. We included *Pf* antigens MSP1- and AMA1- specific B cell tetramers in the CITE-seq cocktail and sequenced B cell receptors (BCRs) from these cells. To identify epigenetic changes that confer the aparasitemic phenotype, we performed scATAC-seq on cells from additional samples. Immune cell types from aparasitemic and parasitemic children exhibited markedly different transcriptional states and epigenetic landscapes. Notably, $CD14^+$ monocytes in aparasitemic children showed enrichment of inflammatory signatures including TNFα signaling via NF-κB along with differently accessible chromatin in the target genes of these pathways. We also identified 44 antigen-specific B cells, primarily from aparasitemic children, and cloned their BCRs into expression plasmids with the goal of producing *Pf*-specific monoclonal antibodies *in vitro* to assess their ability to control parasite growth and enhance the opsonophagocytosis capacity of monocytes.

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PVDBP GENE AMPLIFICATION PROTECTS *PLASMODIUM VIVAX* IN VIVO AGAINST HOST NATURALLY ACQUIRED ANTI-PVDBP IMMUNITY

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The key ligand involved in *Plasmodium vivax* (Pv) invasion is the Pv Duffy Binding Protein (PvDBP) binding to the Duffy. Anti-PvDBP human monoclonal antibodies (Abs) can inhibit the PvDBP-Duffy binding and neutralize invasion of reticulocytes by parasites. However, parasites with multiple copies of the PvDBP gene are protected *in vitro* against neutralization. Here, we aim to determine if this gene amplification also protects parasites *in vivo.* We hypothesize that: (i) multi-*pvdbp* copy parasites are more frequent in areas with a high Pv prevalence compared to low prevalence areas and (ii) individuals with naturally-acquired binding inhibitory anti-PvDBP Abs (Blabs) are predominantly infected over time by multi-copy parasites. To test these hypotheses, we analyzed samples from a longitudinal cohort of individuals living in nine villages in Eastern Cambodia with low (~5%) to high (~30%) prevalence. Using a PCR assay targeting the boundaries of the *pvdbp* duplication, we show a significant association between Pv prevalence and proportion of multicopy parasites (35% in low prevalence villages to 47% in high prevalence ones, p=0.0246). Then, using a flow cytometry assay, we determined the presence of naturally-acquired Blabs in the plasma of 657 participants of the cohort. The more inhibitory the Abs in the hosts' plasma, the higher the proportion of multicopy parasites: 87% (40/46) from individuals with highly inhibitory Abs (>90% inhibition) while 38% (167/436) from individuals without any Blabs ($p<0.0001$). Finally, we compared the gene copy number of parasites over the 21-month follow-up in the cohort participants according to the presence of Blabs at month 0. We show that the frequency of multicopy parasites was consistently higher in participants with highly inhibitory Abs compared to those without any Blabs for the entire follow-up. Overall, these results demonstrate that *pvdbp* duplication protects parasites *in vivo* against hosts' anti-PvDBP immunity. These results warrant further investigations to determine if immunization of individuals with a PvDBP vaccine could overcome this new immune evasion mechanism.

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IMMUNO-INFORMATIC APPROACH TO IDENTIFYING VARIANT-TRANSCENDENT NATURALLY-ACQUIRED PROTECTION AGAINST *PLASMODIUM FALCIPARUM*

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Plasmodium falciparum antigenic diversity compromises the development of lasting immunity. Current available vaccines for malaria contain a single sequence of P. falciparum circumsporozoite protein (CSP), and protection following vaccination is variant-specific. Multi-variant vaccines may help to overcome antigenic diversity, but identifying a minimum set of variants that provide cross-protection against a broad range of CSP variants remains a challenge. We recently reported an epidemiologic signature of natural immunity to *P. falciparum* in which time to reinfection with parasites bearing homologous CSP T cell epitopes was delayed following symptomatic vs asymptomatic infections. We hypothesized that this delayed reinfection would extend to cross-protective 'epitope types' which are likely to be physiochemically similar. Thus, we applied 10 quantitative metrics of amino acid physiochemical properties (PCPs) to group CSP Th2R and Th3R epitope types via hierarchical clustering. Using *pfcsp* sequences (344 infections, 155 unique haplotypes) from a 14-month longitudinal cohort in Western Kenya, we evaluated PCP-based epitope clusters by assessing the phenotype of increased time to reinfection with parasites bearing physiochemically-similar epitopes after symptomatic vs asymptomatic infections. At Th2R, clustering epitope types by any of the PCP metrics reproduced the phenotype with >20 groups, but the Yampolsky and Stolzfus measure shows the phenotype in as few as 10 groups; no PCP metric displayed the phenotype with <10 groups. The Th3r epitope displayed the phenotype with 8 groups, but the PCP measures that meaningfully clustered epitypes were distinct from those identified for the Th2R locus. Overall, our study demonstrates that amino acid properties can identify immunologically-similar CSP epitopes that share recognition by naturally-acquired immune responses. This offers a path forward to exploiting parasite diversity and reducing the search space for variant-transcendent responses.

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OLYSET®PLUS CEILING NETS PROTECT AGAINST MALARIA: FINDINGS FROM A CLUSTER RANDOMIZED CONTROLLED TRIAL OF THE EFFECTIVENESS OF OLYSET®PLUS CEILING NET ON REDUCING MALARIA PREVALENCE AND INCIDENCE ON MFANGANO ISLAND, LAKE VICTORIA BASIN, KENYA

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Novel vector control tools, such as Olyset®Plus ceiling net (2% permethrin+1% piperonyl butoxide), are needed to fight the malaria resurgence reported since 2016, especially in sub-Saharan Africa. We evaluated the protective effectiveness of adding Olyset®Plus ceiling net to existing control interventions on *Plasmodium falciparum* malaria prevalence and incidence. We conducted a two-arm, parallel group, superiority cluster randomized controlled trial with 10 clusters per arm during November 2021-May 2023 on Mfangano Island in western Kenya. Olyset®Plus ceiling nets were installed in eligible households in the intervention arm. The primary outcome, malaria prevalence in children (3-15 years old) at 12 months post-intervention, was measured during cross-sectional school surveys. The secondary outcome, cumulative malaria incidence in all age groups during a 12-month follow-up post-intervention, was tracked monthly for 12 months in a community cohort. Malaria infection was determined using malaria rapid diagnostic test (Paracheck-Pf® Orchid Biomedical Systems, India). Olyset®Plus ceiling nets were installed in 1006 houses (mean coverage: 93.4%). Eight hundred six eligible children were recruited in the control- and 831 in the intervention- arms to determine malaria prevalence. At 12 months post-intervention, malaria prevalence was 30.1% (95%CI: 27.1-33.3) in the control- and 16.4% (14.0-19.2) in the intervention- arms (prevalence ratio 0.55; 95% CI: 0.33-0.91, p = 0.056). Two hundred six eligible persons were recruited in the control- and 266 in the intervention-arms to determine malaria incidence. During the 12-month follow-up, malaria incidence was 0.11 per person-year (ppy) (0.07-0.15) in the control- and 0.05 (0.02-0.09) ppy (1.21-1.65) in the intervention- arms (incidence rate ratio 0.47; 95% CI: 0.24-0.95, p = 0.030). Olyset®Plus ceiling nets protected against malaria in addition to the effects of existing control interventions. Multi-county studies across different malaria transmission intensities are needed for wider adoption to complement existing vector control interventions.

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EFFECTIVENESS OF CHLORFENAPYR-PYRETHROID INSECTICIDE-TREATED NETS ON DECREASING MALARIA IN LIBERIA: AN OBSERVATIONAL ANALYSIS USING ROUTINE HEALTH FACILITY DATA, 2019-2023

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Dual-active ingredient (AI) chlorfenapyr-pyrethroid insecticide-treated nets (ITNs) were distributed nationwide in Liberia in June 2021 to address growing pyrethroid resistance in malaria vector populations. This retrospective observational study evaluated the post-intervention impact of the new ITNs on epidemiological and entomological indicators of malaria compared to the pre-intervention baseline period when pyrethroid-only ITNs had been distributed. A negative binomial Bayesian mixed effects interrupted time series model was used to estimate the effect of dual AI ITN distribution on reported confirmed malaria cases from July 2019 to June 2023 in all 15 counties of Liberia and the number of cases averted by dual AI ITNs, controlling for month, community health worker reporting, non-malaria outpatient attendance, precipitation, and vegetation. Trends in vector human biting rate (HBR) and indoor resting density (IRD) measured during the high transmission season (March to June) one year before and after dual AI ITN distribution were descriptively analyzed. During the two years post-dual AI ITN distribution, an estimated 87.6 malaria cases per 1,000 population (95%CI=65.0 - 112.9) were averted with an estimated case incidence decrease of 41.0% (95%CI=43.9% - 38.4%) overall (from an estimated 239.9 [95%CI=236.6 - 243.4] cases per 1,000 during the baseline to an estimated 170.1 [95%CI=167.6 - 172.6] cases per 1,000). Case incidence reductions compared to baseline were greater in the first year post-distribution (mean=49.0%; 95%CI=52.4% - 45.6%) than in the second year (mean=33.9%; 95%CI=37.4 % - 30.7%). Indoor HBR of *An. funestus* s.l. and *An. gambiae* s.l. decreased in the year following dual AI distribution, although only *An. funestus* s.l. experienced a decrease in IRD during the same period. Dual AI chlorfenapyr-pyrethroid ITNs appeared to substantially reduce malaria case rates following nationwide mass distribution in 2021 and were associated with declining trends in malaria vector HBR.

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REDUCTION IN MALARIA CASES AFTER DEPLOYMENT OF IG2 NETS IN AN AREA WITH KNOWN PYRETHROID RESISTANCE AND MARKED OUTDOOR BITING - AN INTERRUPTED TIME SERIES ANALYSIS.

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In 2019, the first-ever stratification for subnational tailoring was conducted using data routine health facility data from 2015-2018. Results showed that the Western North region had one of the highest malaria burden in the country. Notwithstanding the high rate of outdoor biting, reported pyrethroid resistance in the region warranted the distribution of new generation ITNs in all the 9 districts in July 2021 to help reduce the cases. In this study we assessed the effect of IG2 nets on malaria cases between 2019 and 2023. Monthly health facility data on reported suspected, tested, confirmed, and presumed malaria cases were aggregated for each district from 2019 to 2023. We conducted a trend analysis and an interrupted time series analysis of the confirmed malaria cases for the period January 2019 to December 2023. The auto ARIMA function in R was used to choose the best model and adjust for seasonality and other dependency. A total of 1,235,126 confirmed malaria cases were reported between 2019 and 2023. Confirmed malaria cases decreased from 317,495 in 2019 to 182,856 in 2023. The baseline confirmed cases (intercept) from the regression model was 25,025 (95% CI = 22, 672, 27,737). The time coefficient showed a declining trend but was not statistically significant (-21.7; 95% CI = -150.1, 106.6). We observed an immediate, statistically significant decrease of 6,130 malaria cases (95% CI = -9,441, -2,820) after the intervention compared to the period before the intervention. Assessing the trend that would have been expected in absence of the intervention, the results

showed a non-significant sustained decrease of 107 (95% CI = -298, 84) in the monthly number of confirmed malaria cases during the intervention period. The ACF plot of the residuals showed the autocorrelations were not significant. This study shows that deployment of next generation ITN may have contributed significantly to the reduction in malaria incidence in Western North. The findings will support IG2 deployment decision making in the country to complement other malaria control interventions ultimately to reduce malaria burden in the country.

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EFFECT OF ATTRACTIVE TARGETED SUGAR BAITS (ATSBS) ON MALARIA INCIDENCE IN CHILDREN IN WESTERN KENYA: A CLUSTER-RANDOMIZED CONTROLLED TRIAL

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Attractive Targeted Sugar Baits (ATSBs) are a novel malaria vector control tool designed to attract and kill mosquitoes outdoors. We conducted an open-label, cluster-randomised trial to evaluate the impact of ATSBs on clinical malaria incidence in Siaya County, western Kenya. Overall, 70 clusters (1-3 villages) were randomised 1:1 (35 per arm) to intervention (ATSBs) vs control (no ATSBs) using restricted randomisation. A 'fried egg' design was used for deployment of ATSBs (whole cluster) and evaluation of outcomes (core only), with a buffer zone of 600-1200m to limit contamination in the control arm. Two ATSB stations were hung on the outside walls all eligible structures and replaced every 6 months over 2 years. In total, 267,987 ATSBs were hung. All clusters received long-lasting insecticidal nets (LLINs) delivered by the Ministry of Health and supplemented by the study team, targeting a desired ratio of 1 net per every two people. From March 2022 to March 2024, three consecutive cohorts of children aged 1 to <15 years were enrolled and followed up sequentially over 2 years to assess the primary outcome of malaria incidence, aiming to accrue 1,260 person-years of follow-up time. Here, we present blinded results. Of 3,704 children screened, 217 declined, 525 were excluded, and 2,962 were enrolled into the cohorts, including 784 (26%) aged 1-4 years, and 2,178 (74%) aged 5 to <15 years. Cohort children completed 21,800 routine visits and 2,365 sick visits over the follow-up period. At 2,568 visits, children were tested for malaria by RDT; 1,766 (69%) were positive. Overall, 2,862 children were included in the endpoint analysis; 104 were excluded due to loss to follow-up (n=56), lack of at-risk person-time (n=31), and other (n=17). In total, 1,939 malaria cases over 1,435 person-years were captured, (1.35 malaria episodes per person-year). Complete unblinded results will be presented.

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SAFETY < EFFICACY OF INTERMITTENT PRESUMPTIVE TREATMENT IN PREGNANCY WITH SULFADOXINE-PYRIMETHAMINE USING RAPID DIAGNOSTIC TEST SCREENING < TREATMENT WITH DIHYDROARTEMSININ-PIPERAQUINE AT FIRST ANTENATAL CARE VISIT PRELIMINARY RESULTS

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Intermittent presumptive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is a life-saving intervention for African pregnant women and their offspring, but increasing parasite resistance to SP has challenged its effectiveness. Alternative strategies are therefore being tested in clinical trials throughout Africa that include the incorporation of artemisinin-based combination therapy as an alternative to SP. We conducted a randomized controlled trial to assess the safety and efficacy of an IPTp approach that incorporates screening with RDT and treatment with dihydroartemisinin-piperaquine (DP) at the first antenatal care (ANC) visit. Asymptomatic pregnant women were randomized to IPTp-SP or hybrid IPTp-SP plus screening and treatment (IPTp-SP+). In the IPTp-SP+ arm, mothers testing positive by RDT were treated with DP at the first ANC visit, while those who screened negative received SP. In the control arm, IPTp-SP was administered per current guidelines. All received SP on days 35 and 63 and were followed biweekly up to day 63 then monthly until delivery. 393 pregnant women were recruited. Our results showed that the intervention was associated with 41% reduced odds of clinical malaria during pregnancy (OR = 0.59, 95% CI 0.38-0.92, P=0.019), adjusted for age, net use, indoor residual spraying, and gravidity. We found no significant difference in hemoglobin on day 63 (Hb 10.9±1.6 vs 11.1±1.4 g/dL, P=0.22), hemoglobin at delivery (Hb 10.9±1.6 vs 10.9±1.6 g/dL, P=0.77), congenital malaria (6% vs 3%, P=0.24), birth weight (3.0 ±0.4 vs 2.9±4.9 kg, P=0.092) or the prevalence of stillbirth (1% vs 3%, P=0.16) in the control compared to the intervention arm, respectively. The odds of low birth weight (LBW; OR 2.56, 95%CI 1.17 - 5.61, P=0.019) were higher in the IPTp-SP+ arm. However, no significant difference in LBW was detected between first-visit SP and DP in an IPTp-SP+ within-group analysis (61% vs 39%, P=0.94). IPTp-SP+ reduced the odds of malaria in pregnancy compared to the current standard of care and was shown to be safe and well-tolerated.

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THE IMPACT OF SEASONAL MALARIA CHEMOPREVENTION ON THE EDUCATIONAL OUTCOMES OF SCHOOL-AGED CHILDREN IN SUB-SAHARAN AFRICA

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Early childhood is a time of substantial growth and cognitive development—it is also the time when children are most at risk of malaria-related morbidity. Severe malaria, especially cerebral malaria, is associated with increased individual-level risk of adverse neurocognitive and behavioral outcomes. However, the population-level impact of repeated events of uncomplicated malaria on cognitive development and early learning is not known. Seasonal malaria chemoprevention (SMC) has led to substantial reductions in the burden of malaria in young children. To address this knowledge gap, we conducted a literature review to establish a foundational understanding of the nexus between health and educational outcomes, as well as define a set of harmonized malariometric, educational and other indicator data studies investigating the link between malaria and education should collect. This groundwork facilitated the use of ecological analyses to measure the impact of SMC on cognitive function and early learning. We identified countries (Gambia, Guinea, Senegal) in which cognitive and/or educational

assessments took place before/after SMC introduction and/or in areas with and without SMC. We used generalized additive mixed models (GAMMs) to investigate the relationship between SMC implementation and education indicators, and show that educational indicators have significantly improved in regions where SMC has been implemented over several years. Findings broaden our understanding of the potential educational and economic impacts of malaria prevention and may support further multi-sectoral investments in malaria control.

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URGENCY OF PHARMACEUTICAL SECTOR REFORM TO ACHIEVE UNIVERSAL HEALTH COVERAGE IN NEPAL

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The Constitution of Nepal 2015 has established health as a fundamental right of the citizens. Both the National Health Sector Strategy and the National Health Policy were developed to realize the constitutional aspirations and are anchored to Nepal's commitment to Universal Health Coverage. The government cannot provide financial risk protection without equitable access to pharmaceuticals. Quality assured medicine are needed to expand health coverage and services. To fulfill the government's promise to improve public health, key policy reforms are required to unleash this potential. To discuss critical issues of Nepal's pharmaceutical sector, including the regulatory environment and domestic manufacturing, a high-level multispectral policy dialogue was organized in November 2021, and a series of intensive focus group discussions were carried out to encapsulate a vision for Nepal's pharmaceutical sector, outline the building blocks for pharmaceutical sector reform, and propose key reform priorities. The paper aims to provide a holistic view of the reform agenda and is mainly intended for the consumption of policymakers, development partners, and stakeholders directly or indirectly associated with Nepal's pharmaceutical sector. To unleash the full potential of Nepal's pharmaceutical sector, several critical challenges need to be addressed. The main buckets of issues and challenges are self-reliance, regulation, quality assurance, institutional restructuring, innovation, and strategic positioning of the pharmaceutical sector. The building blocks of the pharmaceutical sector fall under seven domains: policy coherence and harmonization, regulatory stewardship, local manufacturing promotion, institutional governance, pharmaceutical services, and technology and innovation. As Nepal transitions to federalism, the government shoulders the mandate of safeguarding the health of the citizens by espousing the principles of equality, prosperity, and social justice, the question "What should be the new vision for the pharmaceutical sector?" needs to be answered from the perspective of both consumers and providers.

6870

UNDERSTANDING COVID-19 VACCINE HESITANCY AMONG KEY STAKEHOLDERS IN A CONFLICT AFFECTED AREA OF CAMEROON, A FOCUS GROUP DISCUSSION APPROACH

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The COVID-19 vaccine hesitancy issue is a significant challenge in Africa, influenced by historical, cultural, and socio-political factors. Health workers play a crucial role in shaping public perceptions of vaccines, and understanding their perspectives is essential for informed decision-making. Focus group discussions (FGDs) can help uncover these factors and provide insights into regional variations, enabling targeted interventions in urban and rural areas. This qualitative survey explored perceptions and attitudes towards COVID-19 vaccination in the Kumba community, South West Cameroon. Ten focus groups representing diverse demographics were involved. Recorded Discussions lasted less than 60mins on 24 themes. The recordings were uploaded into Nvivo version 12, coded and transcribed during narration. Results revealed a lack of understanding about vaccines' preventive nature, with 68% initially welcoming the vaccine with fear due to social media misinformation. Seventy-three percent of participants, including health workers, had not been vaccinated, citing fear and misinformation. Despite acknowledging their ethical responsibility, 42.1% negatively influenced others' vaccination decisions. Only 37.5% believed measures against COVID-19 in Cameroon were effective. Unvaccinated participants stressed the need for clarification and rural outreach. Recommendations include culturally tailored communication, community engagement, health education, equitable vaccine distribution, and continuous research to address vaccine hesitancy. Addressing vaccine hesitancy in Cameroon demands a multifaceted approach. The findings underscore the urgency of combating misinformation on social media and involve health workers actively in vaccination campaigns. Continuous research and evaluation will guide adaptive strategies, ensuring a comprehensive and inclusive response to COVID-19 vaccination challenges in Cameroon

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THE INFLUENCING FACTORS OF QUALITY OF LIFE AMONG INDIVIDUALS RESIDING IN RURAL AND URBAN AREAS OF THAILAND DURING THE COVID-19 PANDEMIC

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The COVID-19 pandemic has profoundly impacted individuals' quality of life worldwide. This cross-sectional study was designed to explore the factors influencing the quality of life among residents in rural (Ban Luang district, Nan province) and urban (Lak Si, Bangkok) areas of Thailand during the pandemic. Participants were selected using a stratified sampling method. Quality of life was assessed using the WHOQOL-BREF-THAI questionnaire. Descriptive statistical methods and logistic regression analysis were applied to analyze the collected data. Of the 867 survey participants, 420 individuals were from rural areas and 447 were from urban areas. The mean age of participants was 35.6 ± 10.2 years in rural areas and 38.2 ± 9.8 years in urban areas. In urban areas, a majority of participants were women, married, and had lower education levels (71.1%, 50.3%, 58.8%, respectively). The overall quality of life (QOL) score was 98.2 (SD = 10.8) in rural areas and 98.5 (SD = 14.5) in urban areas. In urban areas, living in a nuclear family was associated with approximately 3.3 times higher QOL compared to living in an extended family (AOR = 3.31, 95% CI [1.75-6.27]). Additionally, using social media was associated with approximately 3.3 times higher QOL compared to not using social media (AOR = 2.06, 95% CI [1.03-4.10]). In rural areas, having an average household monthly income over 10,000 THB was associated with approximately 3.7 times higher QOL compared to lower income levels (AOR = 3.68, 95% CI [1.39-9.72]). Similarly, drinking alcohol in rural areas was associated with approximately 2.1 times higher QOL compared to not drinking (AOR = 2.12, 95% CI [1.36-3.31]).This study emphasizes the differences in QOL and related factors between rural and urban areas of Thailand during the COVID-19 pandemic. To enhance QOL, it is important to address specific challenges unique to each setting, such as those living in extended families and the use of social media in urban areas, as well as among individuals in rural areas with lower income levels. Our findings can inform the development of public health policies aimed at improving QOL in these specific settings.

6872

MEASURING CLIENT EXPERIENCE OF CARE FOR PERENNIAL MALARIA CHEMOPREVENTION IN BENIN

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The right to dignified, respectful health care is enshrined by WHO. Client experience in the health system is an important driver of health service attendance and treatment adherence. There is a lack of measurement of client experience of care in malaria chemoprevention and malaria service provision more broadly. The Plus Project (funded by Unitaid, implemented by ABMS/PSI) provides Perennial Malaria Chemoprevention (PMC) to children under 2 years in selected districts of Benin. This study aims to develop and test measures for client experience of care with respect to PMC in children in Benin and goes beyond measures of client satisfaction to centre clients' voices in defining the metrics. We conducted in-depth interviews (IDI) (N=30) to establish key domains of client experience and priorities among caregivers of children under 2 in the three project zones in Benin who have received PMC. We used these data to develop survey questions which were then piloted and improved through cognitive interviews (N=30) with the target population. Once finalised. the questions were fielded in a quantitative client exit survey (N=308). Data collection was between December 2023 and March 2024. IDIs revealed the importance of caregivers' interactions with health providers, including greetings, health center cleanliness and security, perceptions of fairness in service provision, quality of explanations from providers, and quality of products. Of the 22 questionnaire items developed from IDIs, six were significantly reformulated through cognitive interviewing. Quantitative data reveal mothers attending PMC with their child had a mean age of 27.5 years and over 55% had no formal education. We found overall good client experience across all domains, with variability by geographic zone and respondent demographics. The person-centered, iterative approach to questionnaire development enabled us to readjust the collection tools so that they are adapted to socio-cultural realities and participants' lived experiences and priorities. We demonstrate how client experience may be captured for PMC and can lead to actionable recommendations to improve service provision.

6873

THE WHO VACCINE INNOVATION FRAMEWORK: COUNTRY STAKEHOLDER DELIBERATIONS TO ASSESS THE PROGRAMMATIC NEED AND USE CASE FOR INNOVATIVE VACCINE PRODUCTS

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Insufficient understanding of country needs and preferences cam lead to development of vaccines and vaccine technologies that do not meet country requirements. This results in uncertainty in market demand and poor country uptake. To strengthen country-level engagement in product development for immunization, the World Health Organization (WHO) has developed the Vaccine Innovation Framework, with an objective to assess country needs and preferences. The Framework is conceived as a four-step inclusive process which fosters deliberation and communication between stakeholders from diverse levels and disciplines across national immunization systems. It aims to evaluate vaccine product innovations that facilitate vaccine storage, delivery or handling, or improve acceptability. Multi-stakeholder discussions occur in a workshop setting, enabling participants to compare current practices with novel innovations and express their opinion on perceived value and acceptability in the context of country-level immunization challenges and priorities. This allows for the identification of criteria and evidence needed for decision-making processes. To date, the Vaccine Innovation Framework has been used by the WHO as a platform for engagement with relevant country stakeholders from 14 countries in the African, Southeast Asian and American Regions. It has been adapted for three innovations: Microarray Patches (MAPs), thermostable vaccines and oral cholera vaccine capsules. In this presentation, we provide an overview of how this Framework generates evidence, promotes equity, informs research agendas, optimizes product development and implementation, and has the potential for still broader applicability.

6874

EQUALITY IN AJTMH PUBLICATIONS FROM 1952 TO 2024: WHAT CAN WE LEARN TO MAKE GLOBAL HEALTH RESEARCH PUBLISHING MORE EQUITABLE? PROTOCOL FOR A BIBLIOMETRIC ANALYSIS

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The long overdue focus on decolonising global health has prompted various institutions to assess existing inequities in global health research partnership and resulting publications. Recent reviews have demonstrated inequities in published global health research between researchers from high-income countries and low- and middle-income countries in terms of authorship, gender and academic affiliations, among others. Reflecting the American Society of Tropical Medicine and Hygiene's aim to advance health equity globally, we propose to conduct a bibliometric analysis of the American Journal of Tropical Medicine and Hygiene (AJTMH) publications between 1952 and 2024. Specifically, we propose to assess the following: -Author order-Author affiliation(s), classified using World Bank country income classifications-Author gender, when available-Funding source-Study type-Study topic-Region of publication-Year of publication.Funding sources will be recorded primarily to identify main stakeholders for further dissemination of our findings. Data will be analysed using Student's t-tests and Chi-square, followed by logistic regression. Results from this review will 1) inform a widening participation strategy launched by the ASTMH in 2022, to reflect the current make-up of global health researchers worldwide and 2) strengthen the record of AJTMH as an innovative publication with not only its finger on the pulse of change, but also actively seeking to equalise the field of global health reporting. Finally, the authors will propose further direct collaboration with the AJTMH and its affiliates to update guidelines and prepare authorship guidelines describing the Journal's commitment to inclusivity, equality and fairness.

6875

FINANCING LANDSCAPE FOR KEY POPULATIONS HIV/AIDS IN UGANDA: MARCH 2022

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Uganda, a low-income country with a growing population of 45.74 million, faces challenges in healthcare financing. Amidst economic fluctuations and the COVID-19 pandemic, Uganda's health sector struggles with inadequate funding, especially for key populations affected by HIV/AIDS. HIV prevalence remains high at 6.2%, necessitating targeted interventions. This study examines Uganda's health financing and its implications for key populations affected by HIV/AIDS. It reviews government expenditure, donor contributions, and out-of-pocket spending. The study also assesses funding trends for HIV/AIDS response, particularly for key populations. Uganda's health expenditure constitutes 9.5% of the GDP, with public, private, and donor contributions. Notably, donor funding comprises 42% of total health financing. HIV/AIDS intervention expenditures peaked in 2016/17 and then declined. While the government's domestic public expenditure on the HIV/AIDS response increased significantly, it remains below recommended levels. Key populations, disproportionately affected by HIV/AIDS, receive less than 1% of HIV prevention funding, with sex workers receiving the majority. Uganda's health sector faces financial challenges, with HIV/AIDS interventions for key populations requiring urgent attention. Donor reliance raises sustainability concerns, and declining

funding threatens progress. Sustainable financing strategies, innovative resource allocation, and increased government commitment are crucial for addressing HIV/AIDS in key populations. Without addressing these financial gaps, achieving the 90-90-90 goals and mitigating the HIV epidemic's impact will remain challenging.

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EXPLORING ROLES, POWER DYNAMICS, AND CULTURAL SIGNIFICANCE OF ELDERS' AUTHORITY DURING DEATH IN RURAL SOUTH AFRICA

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In rural South African villages, the authority of elders during the process of death holds profound significance. An elder typically refers to an older person who holds a position of respect and authority within their community or family. They are valued for their wisdom, experience, and role in preserving cultural traditions and values. Elders may certify deaths, guide mourning, organize funerals, and transmit cultural knowledge surrounding death. We thematically analysed 20 in-depth interviews of community members who experienced a death in the past 2 years within the Agincourt Health and socio-Demographic Surveillance System site and 6 focus group discussions from different stakeholders to investigate the role of elders in managing the challenges of death rituals in distinct cultural contexts. Determinants sustaining the elder's authority included age, gender, and familial hierarchy. In some families, elders believe in miraculous resurrections and wait 2-6 hours to confirm the death before notification. Additionally, reflecting cultural values, infants are typically buried by elderly women at sunset. These practices underscore the deep-rooted cultural significance and reverence for rituals surrounding death within these communities. Elders' knowledge of traditional customs is often unfamiliar to younger generations and their absence results in incomplete traditional customs, with subsequent misfortunes that befall families often attributed to not following burial rituals. Elders hold considerable authority within the family structure, giving them influence over decision-making processes, including whether to participate in Minimally Invasive Tissue Sampling in research studies. Our work underscores the role of elders in rural communities as primary decision-makers in death rituals. We emphasize their authority and contributions in shaping communal responses to death, offering valuable cultural insights and wisdom. Recognizing elders' significance in future studies is crucial for understanding traditional customs and coping mechanisms related to death.

6877

CENTRING LIVED EXPERIENCE WITHIN HEALTH SYSTEMS REFORM CO-PRODUCED APPROACHES AMONG PEOPLE AFFECTED BY SKIN NEGLECTED TROPICAL DISEASES IN LIBERIA

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Persons affected by skin Neglected Tropical Diseases (NTDs), are one example of a vulnerable population who often experience stigma and discrimination due to supernatural beliefs aboutcausation. Discrimination often leads to barriers accessing timely, quality health services,limiting participation and within their community contributing to worsening physical andmental morbidities. Involving persons affected by skin NTDs in health systems and policyreform is essential, yet there is limited evidence surrounding best practices for equitable co-production. Persons affected by skin NTDs, together with academic researchers, presentlearnings from co-produced research study (REDRESS) in Liberia guided by Gaventa's powercube analysis, which aimed to focus on our lived experience and perspectives to support thedevelopment of more person-centred care. We carried out in-depth interviews with Ministry of Health at county and national levels (17),persons affected (12), paired in-depth interviews (3) and ripple effect mapping with co-researchers (2) to reflect on the value of their participation and the impact of co-production onhealth systems reform for persons affected.When underlying power dynamics are considered, with co-produced activities shaped toencourage engagement e.g. using world café small group discussions to prompt contributionsfrom all, these approaches bring value for both the individuals and the wider community andhealth system. Involving persons affected to shape the proposal, and as co-researchers broughtstronger advocacy and awareness raising within community, national and global levelsgenerating awareness of the needs and priorities of persons affected, with stronger relationshipsand ability to engage with policy actors. Persons affected placed greater trust in those withshared lived experience strengthening referral pathways.Using co-produced research approaches promotes inclusion and belonging for persons affectedwithin decision-spaces, contributing to greater capacity and advocacy roles by those directlyinvolved as co-researchers, as well as more inclusive health services.

6878

EMPOWERING EARLY-CAREER WOMEN IN BIOSCIENCES: A PILOT MENTORSHIP INITIATIVE AT NNAMDI AZIKIWE UNIVERSITY, NIGERIA

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Female early-career academics often face gender biases and stereotypes that hinder their professional growth. This pilot mentorship program aims to equip women with the skills for effective leadership, drawing inspiration from the WHO TDR Health Research Mentorship in low- and middle-income countries (HERMES) Practical Guide for institutionalizing health research mentorship. The absence of a formal mentorship program at the University since its inception in 1991 underscores the significance of this initiative, which seeks to institutionalize mentorship, and enhance diversity, inclusivity, and excellence within the biosciences faculty. To address this gap, a needs assessment survey was conducted in March 2024 to identify the challenges and needs of early-career women in biosciences, recruiting participants through the university networks using an online platform. All 19 participants were women aged 25-44 years, with 85% having 1-10 years of academic experience. Most (90%) were married, with 65% having children aged 3 months to 10 years. Challenges included balancing family and career, lack of mentorship, and financial support. All participants expressed the need for mentorship programs, implicit bias training, and family-friendly policies for academic career support. Of the participants, 36.8% (7/19) had prior mentorship experience, while 63.2% (12/19) had not. Among those with prior experience, 42.9% (3/7) reported mixed experiences or challenges, and 28.6% cited a lack of follow-up or short program duration. Respondents suggested promoting gender equity initiatives, providing mentorship and sponsorship programs, creating inclusive and supportive environments, offering professional and leadership development opportunities, encouraging work-life balance, effective time management skills, celebrating achievements and visibility, addressing implicit bias and stereotypes, and supporting networking and collaboration. The findings underscore the critical role of tailored support in advancing early-career women's careers in biosciences, emphasizing the importance of mentorship and inclusive policies.

6879

NAVIGATING HEALTHCARE HURDLES IN LORETO: EVALUATING BARRIERS TO ACCESS

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Covering nearly one-third of Peru's territory, Loreto faces a complex healthcare landscape with significant challenges that hinder healthcare-seeking behavior. Barriers to healthcare seeking are generally attributed to the lack of healthcare facilities and, consequently, long travel time to the facility, as well as limited economic resources. However, it is yet to be determined if discrimination in healthcare settings is perceived as a barrier in Loreto. This study was implemented as a sub-study of The Enterics for Global Health study and utilized an already validated survey to measure discrimination in health establishments. Its aim was to determine if discrimination was a barrier to seeking care among children with acute diarrheal illness and to determine if structural deficiencies were prevalent among health posts, including the presence of health care providers, treatment options, and basic services, such as potable water and electricity. The survey was deployed in the area of influence of 5 health care centers in Iquitos, Loreto, and the availability of services was evaluated using spot checks by health care workers once a week. Between June and December 2023, 2183 participants completed the questionnaire. Of these, 67.9% (1483/2183) attended a health post in the last year, of which 8.3% (82/977) had a child under 5 with diarrhea. 38.3% (836/2183) of participants indicated they felt mistreated or discriminated against in a health center. Additionally, each healthcare center was surveyed on 190 days on average. It was identified that services, including electricity and water, were generally available in all 5 health centers, yet piped water was only available in one. Healthcare personnel worked on over 90% of the days in which spot checks were performed. Diarrhea treatment options, including antibiotics, were available in over 90% of days surveyed. However, zinc was not available on 37% of days and ORS in 18% of days surveyed.

6880

ADDRESSING STRUCTURAL BARRIERS AND HUMAN RIGHTS IN MALARIA SERVICES IN UGANDA AND KENYA

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The Global Fund's Breaking Down Barriers (BDB) initiative provides support in Uganda and Kenya for the scale-up of evidence-based programs to remove equity-, rights-, and gender-related barriers to malaria services, with the aim to increase the effectiveness of Global Fund grants and ensure that health services reach those most affected. An evaluation of these efforts was conducted in both countries in 2023, and findings were compared with an earlier 2017 baseline assessment which found in both countries few or no formalized programs to address these barriers. By 2023, both countries had created programs seeking to better understand and strengthen availability and accessibility of services. For example, Malaria Matchbox assessments identified populations most at risk, as well as those underserved by existing interventions. Both countries integrated human rights and gender into their national strategies, and in policy and program implementation. Community leadership - through, for example, community dialogues - led to increased resources closer to communities, allowing for timely identification of challenges and locally driven solutions to drive a more effective malaria response. The evaluation also found that there has been a renewed focus within both countries on understanding gender norms and their influence on the effectiveness of malaria programming, and increased collaboration across health sectors, for example in mapping vulnerable populations and implementing some malaria activities. Nonetheless, significant challenges remain. Many malaria stakeholders lack the training, staff and technology for integrating human rights principles and approaches into service delivery. A dearth of disaggregated data by age, gender and other factors related to risk and vulnerability impedes the ability to effectively tailor approaches to subnational levels, and remove structural barriers that exist. Advocacy to reduce law and policy-related barriers to malaria services remained in early stages. Local capacity for effective monitoring and evaluation related to malaria and human rights programs needs to be strengthened.

6881

ADVANCING GENDER EQUALITY WILL STRENGTHEN INTERVENTIONS FOCUSED ON ENDING THE MALARIA EPIDEMIC

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Gender equality is increasingly recognized as a crucial element in the fight against malaria. Drawing from evidence-based approaches and experiences gleaned from Malaria Matchbox assessments conducted in over 20 countries receiving Global Fund funding, and other interventions, three programmatic entry points for advancing gender equality have demonstrated to be contributory to the malaria response. Firstly, women's economic empowerment ensures women's participation in markets, control over resources, access to decent work, and agency in decision-making processes. Evidence suggests that integrating activities to enhance women's economic agency accelerates the malaria response, resulting in greater net use within households and improved health seeking behaviors. Second, ANC promotes healthy behaviors such as the use of insecticide-treated bed nets and intermittent preventive treatment of malaria during pregnancy. However, barriers such as poverty, mobility constraints, and power dynamics within households impede women's access to and utilization of ANC services. Strengthening access to and utilization of ANC services not only improves maternal and child health, but also provides opportunities to reach more people with malaria prevention commodities and services. Furthermore, addressing gender disparities within the malaria health workforce is imperative. Women are disproportionately represented in lower-paid roles and face discrimination and exploitation. Women are often inadequately compensated and lack opportunities for professional advancement. Achieving gender equality within the health workforce is essential for ensuring equitable access to malaria care and improving program effectiveness. Strategies aimed at challenging gender inequalities and norms enhance the effectiveness of investments and contribute to long-term program outcomes. In 2024, the Global Fund has newly committed at least US $2 million to specifically advance gender equality and thereby accelerate progress towards ending the malaria epidemic.

6882

LEVERAGING GLOBAL FUND INVESTMENTS: PROTECTING THE RIGHT TO HEALTH AND LIMITING FINANCIAL HARDSHIP

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Financial barriers to healthcare, rooted in economic disparities, structural inequalities and health system financing models, can significantly impede accessibility to essential health services. These barriers manifest in many forms including out-of-pocket expenditure, lack of adequate health insurance coverage, costs of additional medicines, transportation costs to reach a clinic or care provider, lost income, informal payments, and intra-household decision making on family finances. For many individuals and families, particularly those living in low-income communities or rural areas, these financial barriers can be prohibitive, keeping people away

from essential health services, causing financial hardship, and deepening poverty. Addressing financial barriers to healthcare is more than an issue of affordability, it is a fundamental imperative for ensuring equitable access and for protecting the right to health for all. Global Fund resources have been instrumental in driving change in this area. It has supported health financing and insurance schemes to prevent catastrophic financial impact as a result of severe malaria; strengthened community-based service delivery models to reduce transport costs incurred by patients; subsidized malaria commodities to ensure they are provided at no cost to users; enabled the use of non-malaria medications for integrated community case management of childhood illness, reducing indirect costs to families that may have prevented them seeking care; and supported ongoing monitoring of financial barriers through community-led monitoring (CLM). By working to reduce financial barriers to health services, and prioritizing high risk and underserved populations, the Global Fund partnership has accelerated progress towards malaria elimination and realizing a world free of the burden of malaria with better, equitable health for all.

6883

CITIZENS AS INFLUENCERS OF HEALTH SERVICE AVAILABILITY AND NOT AS CONSUMERS ONLY

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Advocacy for health services is critical for availability of health services in resource limited settings. Availability of health services influences utilization and ultimately the health status of the community. While advocacy for health service has been recognized as a major tool to influence service, often advocates focuses on service providers or duty bearers with limited engagement of service citizens in influencing availability of health services. It is oftentimes led by external, leaving the citizens as consumers of services and not influencers. World Vision adopted Citizen Voice and Action advocacy approach which is a social accountability methodology that empowers communities to monitor the performance of local governments in providing essential services like health care at the local level. It empowers citizen to monitor actual availability, quality and quantity of health services in their community against the government standards and use the identified gaps to engage and influence through dialogues. Communities were first sensitized on the health facilities (HFs) monitoring standards and relevant health policies, like patient charters. This was followed by gatherings at HFs, involving about 50 community members, grouped according to sex and age. During the gathering, communities scored availability, quantity and quality of services against government standards. Based on identified gaps, dialogues were created between the citizens, health workers and duty bearers to close the identified gaps. This resulted in actions to closing the identified gaps. Implementation of actions was monitored by the CVA for 18 months. Improvement in staffing in HFs, from 54% to 72%, and recruitment of more critical staffs. The district allocated 500 million in additional funding for infrastructure development. Absenteeism among health workers reduced, while blood transfusion services were operationalized at Nankoma H/CIV. Citizens are critical influencers of service availability, when considered as being more than consumers.

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LESSONS LEARNED FROM GEOGRAPHIC INFORMATION SYSTEMS FOR INFECTIOUS DISEASES RESEARCH AND SURVEILLANCE

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WRAIR-Armed Forces Research Institute of Medical Sciences (WRAIR-AFRIMS) collaborates closely with public health partners in Nepal, the Philippines, Thailand and other areas in Southeast Asia, forming an infectious disease research and surveillance network. Medical research and surveillance often entail the collection of vast amounts of data, which are then analyzed for clinical and statistical significance, as well as for generating hypotheses. Geographic Information Systems (GIS) technology emerges as a valuable tool for researchers and epidemiologists, facilitating the graphical representation of infectious disease outbreak results in a universally understandable manner, displaying both temporal and spatial aspects. WRAIR-AFRIMS utilizes GIS-based procedural visualization for conducting infectious disease research and surveillance, generating crucial insights necessary for decision-making at local, national, and international levels. WRAIR-AFRIMS' Virology department integrates clinical and laboratory data related to respiratory illnesses, SAR-CoV2, febrile and vector-borne infections (FVBI) including geolocation data on thousands of samples collected annually. Employing GIS software such as ArcGIS and QGIS, they create visual maps illustrating the spread of infectious diseases over time and surveillance areas such as FVBI and respiratory surveillance. These maps facilitate the analysis of spatial patterns encompassing disease incidence, prevalence, and distribution. The resulting data enables authorities to monitor disease trends, detect anomalies, and allocate resources effectively for targeted interventions. Through collaborations facilitated by WRAIR-AFRIMS, GIS technology has advanced in monitoring infectious diseases in real-time, enhancing the accuracy of disease risk assessments, and supporting decision-making processes. These efforts contribute to improved communication of surveillance findings to stakeholders and the public, ultimately bolstering public health responses and outcomes.

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SYNDEMIC MODELLING: A NOVEL MATHEMATICAL MODELLING FRAMEWORK FOR SIMULATING MULTIPLE PATHOGENS DYNAMICS IN CONTEXT

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Mathematical models have historically been used to understand and predict disease transmission dynamics, slowly evolving along with our understanding of the underlying biology of disease spread. Knowledge of disease dynamics and interactions can be combined with socio-economic considerations to produce models robust enough to simulate and compare control strategies, thus becoming useful tools to inform health policy making. It is still a challenge, however, to produce robust mathematical models that can concomitantly address the dynamics and interactions among multiple etiological agents. Models for multiple strains or species of pathogens are challenging due to the number of equations required to accurately account for the inter-species interactions, which increases exponentially with the number of species, making numerical and structural identifiability increasingly improbable.We have developed a mathematical approximation which allows the dimension of the resulting model to increase linearly with the number of species (instead of exponentially). For a two-species SIRS model, we have shown through mathematical analysis that this approximation is appropriate for species with low levels of interaction. We have recently been working on generalising this framework through further analysis and numerical simulations, and exploring less analytically tractable examples of multi-species malaria and multi-pathogen epidemics (e.g. COVID-19 and flu syndemics). Our overarching aim is to use the proposed framework to develop better context-informed models with policy-making impact at local, national and international levels.

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MALARIA IN THE REPUBLIC OF GUINEA: COSTS ASSOCIATED WITH THE CARE PATHWAY FROM THE PATIENT'S PERSPECTIVE, 2022 - 2023

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Access to safe, affordable healthcare is crucial for reducing health disparities. In Guinea, malaria is a major public health issue with significant economic consequences. In 2010, the country introduced free healthcare services for malaria to control the endemic disease. This paper analyzes the costs (out-of-pocket expenses) associated with the care of malaria patients in the Republic of Guinea. An economic analysis of the costs of managing malaria in Guinea was conducted using data from a cross-sectional survey on the determinants of malaria prevention. Data were collected between December 2022 and March 2023 in health facilities and at the community level. The Time-Driven Activity Based Costing approach and micro-costing were used to evaluate the costs associated with care-seeking, management, and related costs. The study enrolled a total of 3,300 patients from 60 healthcare facilities, predominantly in urban areas (65%), with one-third being children under 5 years of age (mean age 27 months). Most patients were accompanied by their mothers, had no formal education, came from households led by husbands, and had a median monthly income of $115.95. Around 41% were seeking care for the first time. The costs of seeking care varied based on the type of malaria, with $3.48 for uncomplicated cases and $13.45 for severe cases. The median direct care costs in healthcare facilities for uncomplicated malaria were $7.30, and $30.84 for severe cases. Overall costs associated with malaria varied by type and age group, with median costs borne by patients estimated at $17.57 for uncomplicated malaria and $44.87 for severe cases. Delay in seeking care accounted for 19% of the costs incurred by malaria patients in Guinea ($p < 0.001$). Despite the implementation of free malaria prevention services, patients continue to experience costs and income loss. An approach based on selective free access and affordable flat-rate costs could ensure the financial sustainability of healthcare facilities and reduce out-of-pocket expenses for patients.

6887

EXPLORING THE MIGRATION PATTERNS AND POPULATION HEALTH OUTCOMES IN URBAN AFRICA: A CASE OF NAIROBI CITY

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Understanding the dynamics of transitions between different residency states is essential for informing effective population management strategies. Our aim is to characterize the trajectories of residency events within the Nairobi Urban Health and Demographic Surveillance System (NUHDSS), encompassing key residency events. Thus, we intend to unravel patterns and trends that can guide the development of targeted policies and interventions to address the evolving needs of the population. We proposed a continuous time homogeneous multi-state Markov model for the NUHDSS longitudinal residency data collected from 223,350 individuals in Korogocho and Viwandani slums in Nairobi. The model is used to effectively capture and model residency events; births, deaths, in-migrations, and out-migrations that directly impact the population dynamics including population growth, and population decline. However, exit and entry are included in the descriptive analysis to offer some insights into the magnitude and patterns of internal population movements over time. From the findings the hazard ratio (HR) of 0.7684 suggests that adjusting for the effects of gender, ethnicity, area of birth and age, the transition of individuals in Viwandani from birth to death is associated with a 23.16% lower than those in Korogocho. Same results are seen for the individuals in Viwandani for the transitions from enumeration to death, and in-migration to death. Our findings provide unique insights into the frequency of events, their transition rates, and the impact of gender, slum area, age, ethnicity, and area of birth. These results have implications for preventive health interventions and planning for appropriate levels of residential care. Moreover, modelling the residency events helps in understanding the expected burden of the migration and population growth.

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WHATSAPP MESSAGING AND USE OF MALARIA SERVICE GUIDES AND FEVER MANAGEMENT TOOLS IN CROSS RIVER STATE, NIGERIA

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Appropriate and timely fever management are crucial to prevent severe malaria (Agunbiade et al, 2022). The U.S. President's Malaria Initiative for States project (PMI-S) aimed to improve fever case management in 165 health facilities (HFs) in Cross River State using Behavioral Economics Prototypes (BEPs), a set of tools and processes designed to guides appropriate fever management. In March 2023, BEP monitoring teams observed that the tools were not adequately used or accessible on request. PMI-S addressed this poor BEPs use by sharing them across four relevant WhatsApp groups with 32, 66, 43 and 36 participants. The BEPs were disseminated twice a week from July to September 2023: (1) "Is it malaria?" An interactive group discussion guide, (2) Whole Site Counseling Tool, (3) Performance-Tracking Poster, (4) Malaria Testing and Treatment Tally Form, (5) Fever Evaluation Tool, and (6) Pediatric Evaluation Form. Netnographic and conversation analyses were conducted on the WhatsApp platforms where the BEPs were shared. This revealed that more than 50% of participants downloaded the tools over a three-month period (July to September 2023). Conversational analysis of the WhatsApp response thread showed that sharing BEPs enabled discussion on their application, including challenges. District Health Information System data analyzed found that malaria test positivity rate (TPR) reduced across 165 HFs from an average of 64% from July to September 2022 to 58% with BEP implementation in the same period in 2023. TPR reductions rely on improved testing, which may have been aided by the shared BEPs being made immediately available on WhatsApp. Additional studies could further explore the utility of sharing BEPs through mobile messaging platforms, the uptake of tools, and the resulting changes in key malaria case management indicators.

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COMPARATIVE ANALYSIS: USING A HYBRID ICF VERIFICATION TOOL IN A 28,000-PARTICIPANT CLINICAL TRIAL AT COMMUNITY LEVEL IN MOZAMBIQUE AND KENYA

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Clinical trials in low- and middle-income countries (LMICs) face unique challenges when adapting traditional methodologies to comply with Good Clinical Practice (GCP) standards and ensuring participant safety. The BOHEMIA trial in Mozambique and Kenya assessed the impact of mass ivermectin distribution on malaria transmission, enrolling over 58,000 participants. Handling 50,000+ paper-based informed consent forms (ICFs) per country was risky and inefficient. In Mozambique, paper reliance and manual tracking led to potential compliance issues with ICH E6 (R2) standards due to cumbersome systems and disconnection from the main database. Conversely, the Kenyan team implemented a hybrid approach, integrating paper ICFs with an electronic registry, enhancing real-time management, data security, and stakeholder collaboration. This system streamlined verification, query resolution, and archiving, also enabling prompt identification and correction of missing ICFs, ensuring data integrity. The digital tool developed in Kenya outperformed traditional methods, improving transparency, efficiency, and safety in participant management. Its potential integration with machine learning and AI, and compatibility with existing electronic data capture systems (EDC), exemplifies innovative approaches in clinical trial methodologies, particularly suitable for LMIC settings where resources are limited. The BOHEMIA study's success demonstrates the effectiveness of this approach in overcoming traditional research barriers.

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NETWORKING OF MEDICAL LABORATORY DATA IN MADAGASCAR

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The Ministry of Health (MOH) in Madagascar, through the Directorate of Pharmacies, Laboratories and Traditional Medicine (DPLMT), the Malagasy Medical Analysis Laboratory (LA2M) and the Directorate of Studies, Planning and Information System in Health (DEPSI) is strengthening its data reporting system of medical analysis laboratories, through the digitalization of an electronic laboratory register. To date, each health program has its own laboratory reporting system, making compilation and monitoring difficult for an integrated approach to communicable disease control. This strengthening of the electronic reporting system meets the MOH's digitalization objective for the surveillance of malaria, tuberculosis, HIV and COVID. 19.73 (37%) of the 198 analysis laboratories in Madagascar with internet connection have benefited from training and provision of electronic tablets for this electronic register. Laboratories were selected to represent the 12 TB and HIV priority districts, those with the highest malaria risk level and those in pre-elimination, alongside public and private facilities. Among the 73 laboratories supported for this intervention between October 2023 and January 2024, 77% (56/73) reported data electronically, including 47% (34/73) on diagnosed malaria cases diagnosed, 52% (38/73) on detected tuberculosis cases, 47 % (34/73) for HIV testing and 3% (2/73) for COVID19 cases. The 23% of laboratories not reporting was due to the poor-quality connectivity, non-daily data entry, the absence of post-training monitoring for the period, and a reported lack of willingness for some. Future supportive supervision by regional laboratory managers will aim to resolve these obstacles. Laboratory data, training curricula and modules are currently available in the Ministry of Health's DHIS2 server, under the responsibility of DEPSI.

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PHYSICIANS' PERSPECTIVES OF INFORMAL HEALTH PRACTITIONERS IN BANGLADESH AND POTENTIAL FOR ENGAGEMENT

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The healthcare landscape of rural Bangladesh faces various complex challenges, including limited resources and a shortage of qualified healthcare professionals. Informal healthcare providers, locally termed village doctors, fill this void and provide the majority of primary care, especially in remote villages and hard-to-reach areas. In many parts of Bangladesh, patients who present to formal healthcare facilities have first been to see a village doctor for assessment and treatment. This study aimed to qualitatively explore the perspectives of formally trained physicians on the role of village doctors in Bangladesh's healthcare system. This study was conducted in the Sitakunda Upazila subdistrict of Southeast Bangladesh. We recruited twelve formally trained physicians through a purposive sampling technique. Individual in-depth interviews were conducted by an ethnographic research team in Bangladesh. Interviews were transcribed and thematically coded to examine both positive and negative opinions of village doctors. The interviews unveiled three prominent themes highlighting the perceived positive contributions of village doctors: 1) provision of essential services and resources in isolated areas, 2) enhanced accessibility and familiarity with the community, and 3) active involvement in public health education. Additionally, the interviews revealed five themes related to physician's perspectives of the negative impacts of village doctors in the healthcare system: 1) insufficient education and training, 2) use of inappropriate treatments, 3) inappropriate referral practices, 4) the misuse and overuse of antibiotics, and 5) prioritization of financial gain. This study sheds light on the complex relationship between formal and informal healthcare providers in the larger healthcare system and emphasizes both the contributions and impedance of village doctors to rural healthcare settings. Coordination between formal and informal healthcare providers is necessary to meet the needs of rural patients in Bangladesh.

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MODELING THE IMPACT OF CORE AND SUPPLEMENTARY TOOLS ON PYRETHROID RESISTANCE AND MALARIA TRANSMISSION DYNAMICS

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Significant investments in malaria vector control during the previous 20 years have led to a 40% decrease in the number of clinical cases of malaria and the anticipated prevention of 663 million cases in sub-Saharan Africa. Vector control methods such as indoor residual spraying (IRS), larval source management (LSM), insecticide-treated nets (ITNs) have been credited with these results. The unexpected increase in malaria incidence and prevalence in Africa is concerning, even if there has been a decrease in malaria cases and fatalities as a result of ITNs and IRS deployments. A number of factors have led to the decline in these achievements, including changes in the behavior of the malaria vector species and, most importantly, insecticide resistance in the malaria vectors. The most dependable instruments in Tanzania for controlling malaria vectors, IRS and ITNs, are seriously threatened by the outbreak of insecticide resistance. For example, by 2020,

more than 80% of sentinel sites had pyrethroid resistance, up from 0% in 2004. Therefore, a new mathematical model for the dynamics of malaria transmission has been developed and thoroughly examined in this study in order to assess the effects of ITNs, IRS, and Attractive Sugar Baits (ATSB) on pyrethroid resistance in the context of Tanzania. This model takes into account the susceptible and resistant *Anopheles gambiae s.l.* and *An. funestus* species and the fact that the effectiveness of vector control measures deteriorates with time. Once more, the model takes into account the varying resistance levels of the resistant *An. funestus* and *An. gambiae s.l.* species. Using secondary data from previously published studies and datasets, a number of simulations using the Python programming language are being run to assess the effects of combining various forms of ITNs with IRS and ATSB. The preliminary findings demonstrate the substantial impact of supplementing ITNs with IRS and ATSB. Additionally, the study plans to evaluate the impact of these vector control methods on the allele frequencies of the mosquito species using the Epidemiological Modeling Software (EMOD).

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THE EFFICACY OF MOBILE SERIOUS GAMES (SWAZIYOLO) IN INCREASING HIV RISK PERCEPTION IN ESWATINI: A RANDOMIZED CONTROL TRIAL.

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Eswatini has one of the highest HIV prevalence rates globally (24.8% among people ≥15 years of age). Unprotected heterosexual transmission accounts for more than 90% of new HIV infections in the country. Mobile phone technology is growing rapidly, offering opportunities for technology-driven interventions for HIV prevention. Our team developed SwaziYolo, a smartphone, interactive, educational story game that places the player in the role of a young adult looking for love in Eswatini's capital city. We conducted the Serious Games HIV Prevention Trial (SGPrev-Trial), a 4-week, 2-arm, 1:1 randomized controlled trial of SwaziYolo among people 18-25 years of age in Eswatini. The main outcome was HIV risk perception scores (10-item index and a subscale 8-item index), assessed using intention-to-treat and per-protocol difference-in-difference (DID) analysis. Secondary analyses examined differences in reported sexual behavior and serious game acceptability. Of 380 people who agreed to participate in this study, 130 in the control arm and 127 in the intervention arm completed follow-up. Among the 79.5% (101/127) of intervention arm participants who completed at least one game (per-protocol analysis) we observed an increase in the 10-item HIV risk perception index compared to control arm participants (DID mean score of 1.63, p-value 0.048) and a borderline increase for the 8-item HIV risk perception index (DID mean of 1.37, p-value 0.060). In intention to treat analysis, there were no significant differences between arms in both the 10-item and 8-item indices. Nearly all (96.1%) participants strongly agreed or agreed that they would recommend SwaziYolo to their peers. The high retention rate observed in this study demonstrates the feasibility of online technology-based interventions for HIV prevention in Eswatini. Our preliminary results suggest that serious game interventions can be effective at increasing HIV risk perception. Future research will explore how to optimize SwaziYolo to promote and sustain HIV prevention among young people in Eswatini and adapt the intervention to other settings.

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DIGITIZATION OF COMMUNITY HEALTH IN BURKINA FASO: CONSIDERING THE PERSPECTIVES OF COMMUNITY WORKERS THROUGH USER ACCEPTABILITY TESTING

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Malaria remains a major public health burden in Burkina Faso. With an incidence of 525.4 per 1000 inhabitants (2022), it is the leading cause of morbidity and mortality. The government of Burkina Faso implemented a 2019-2023 community health strategy, with digitization of service delivery as a priority intervention. The aim was to set up a digital solution to provide decision support to community health workers to improve the quality of services, the quality of data and the performance of these players. One of the fundamental principles of digitization is the end-user-centered approach. To comply with this principle, Digital Square at PATH with funding from the US Presidential Malaria Initiative, provided technical support to the Ministry of Health to conduct a training of 58 community health workers and 15 supervisors, followed by user acceptance tests in the Boromo health district. The training consisted in showing the participants how to use the Android mobile phone and the decision-support application developed on Commcare platform. An evaluation using interview and observation gathered feedback and suggestions from the participants. Although a good satisfaction (70%) about application accessibility, user-friendliness and stability, concerns about the applications were raised by 35% of participants, including data not being transmitted via SMS, certain modules not being displayed, discrepancies between the content of the modules and actual actions in the field, and the need for the supervisor to have controlled access to the CHW's telephone. In addition, concerns were raised about the system in general, particularly the security of the devices in the hands of CHWs, maintenance/updating, renewal, and the availability of an energy source for recharging at the community level. Overall, the UATs make it possible to check that applications and devices are working in real time on the ground, to assess the ability of stakeholders to use them, and to gather concerns and worries, with a view to improving the system so that it meets the expectations of the first users as well as the goals of community health digital transformation.

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EXPLORING PERSPECTIVES ON THE SCANNABLE MATERNAL & CHILD HEALTH HANDBOOK IN SIAYA, KENYA: A QUALITATIVE ASSESSMENT OF HEALTHCARE PROVIDERS & ANC CLIENTS

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A scannable version of the Kenyan Ministry of Health (MOH) Maternal and Child Health (MCH) handbook was piloted to assess impact on data quality and utility in Siaya, western Kenya. Acceptance by healthcare providers and antenatal care (ANC) attendees is crucial for successful implementation and adoption of such a tool. We conducted a qualitative assessment to explore the perspectives of healthcare providers and ANC clients on implementation and associated challenges. From the pilot, 36 ANC clients were purposively identified and split into 3 focus groups by number of contact visits: a) 2-3, b) 4-5, and c) 6-8. Additionally, 10 key informant interviews (KIIs) were conducted individually with 8 service providers and 2 county health officials. Interviews were transcribed, coded, and thematically analyzed in NVivo v.12. The results showed that the scannable handbook's resemblance to

the standard handbook made it familiar and user friendly, with its revised structure and flow simplifying data entry. Digitization of individual data from the handbook facilitates tracking ANC services individual women received across multiple facilities. Results also suggested that the books' design, size, material quality, spiral binding and hard cover provided extra protection, making it durable, aesthetically pleasing, easier to handle and minimized chances of misplacement or loss. Possible barriers identified included scanning (photographing) difficulties to abstract data with some providers finding it time-consuming. ANC clients faced difficulties at non-pilot facilities with providers unfamiliar with the handbook emphasizing the need for sufficient sensitization and training before implementation. The scannable MCH handbook is widely accepted in Siaya county due to several advantages including its user-friendliness, durability, and the ability to digitally abstract data and track ANC clients across multiple health facilities. Addressing the challenges such as scanning, training, and orientation are crucial to improving negative experiences before potentially scaling up.

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EXPLORING EXPERTS' PERSPECTIVES ON THE ADOPTION AND USE OF MULTIPLEX BEAD ASSAYS FOR INTEGRATED SEROSURVEILLANCE IN LOW- AND MIDDLE-INCOME COUNTRIES

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Serological surveillance ('serosurveillance') enables health systems and researchers to estimate a community's level of exposure or immunity to various pathogens and guide the implementation and monitoring of public health interventions. The use of multiplex bead immunoassays (MBAs) can streamline this approach by allowing for the simultaneous detection of several antibodies to different antigens and pathogens in a single reaction. However, this technology has not been universally adopted, particularly in low- and middle-income countries (LMICs). To understand experts' perceptions on the value of MBAs for integrated serosurveillance, and challenges to adoption and scale-up in LMICs, we conducted 20 semi-structured interviews with key informants working in LMICs and high-income countries (HICs) who were familiar with MBAs. These experts came from academia, funding agencies, implementing organizations, and the private sector. We recorded and transcribed the interviews and used inductive and deductive coding to support thematic analysis of the data. Although MBAs can serve as powerful tools for integrated serosurveillance and have demonstrated value in several settings, not all countries are well-positioned to adopt this technology. Some prioritize other investments, including those which could support the use of these assays in the future, like improvements to maintain stable electricity supplies and controlled laboratory environments. The immense amount of data that MBAs produce can be a double-edged sword as analytical bottlenecks can impede the use of data to guide public health responses. Amid these challenges, the LMICs which have been best prepared to adopt and scale the use of this technology are often those which possess comparably strong laboratory networks. Many of these countries have longstanding relationships with laboratories in HICs. Commercialization and standardization of some assays could support the adoption and expansion of this technology to other LMICs, but maintaining a country's ability to decide what they monitor is critical for establishing buy-in.

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DETECTION OF RECURRENT MALARIA BY IMPROVING THE ACCURACY OF UNIQUE PATIENT IDENTIFICATION WITH BIOMETRICS IN PAPUA, INDONESIA

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Detection of malaria recurrence requires unique identification of patients through multiple presentations to a health facility. This can be challenging in resource-limited settings. The impact of adding fingerprint identification to an existing physical "malaria card" identification system was assessed at two remote clinics in Papua, Indonesia. A three-stage approach was taken with one clinic serving as a control. In Stage 1 (3 months), standard patient identification practices using the malaria card system for malaria patients were observed at both clinics. In Stage 2 (6 months), fingerprint scanning using the Flexcode 4500™ system was added to standard patient identification procedures for suspected malaria patients at the intervention clinic. In Stage 3 (6 months) fingerprint scanning continued at the intervention clinic but with the addition of linkage to prior fingerprint registrations. At the intervention clinic, the proportion of malaria patients carrying a malaria card rose from 24.3% (467/1,925) in Stage 1 to 44.0% (3,566/8,103) in Stage 3 ($p<0.001$), compared to a more modest increase from 18.2% (397/2,187) to 25.1% (1,019/4,067, $p<0.001$) at the control clinic. Detection of duplicate (1 number assigned to multiple patients) or multiple (1 patient assigned multiple numbers) malaria card numbers increased from 0.3% (6/1,925) in Stage 1 to 4.1% (246/5,939) in Stage 2 with no corresponding increase at the control clinic. The proportion of repeat visit increased from 42.4% (816/1,925) in Stage 1 using standard patient identification practices, to 44.0% (2,612/5,939) in Stage 2 and 56.0% (4,556/8,103) in Stage 3 after adding fingerprinting to the patient verification process. In Stage 3, 99.8% of patients attending the intervention clinic could be definitively linked to a unique malaria card identification number versus 88.9% at the control clinic. Very few patients refused fingerprinting. The use of biometric fingerprinting was well-accepted and was associated with improved patient identification through multiple presentations to a healthcare facility.

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THE ROLE OF DIGITIZATION IN IMPROVING DATA QUALITY FOR ITN DISTRIBUTION CAMPAIGNS IN MALI

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From 2011 to 2020, Mali made efforts to provide universal coverage of Insecticide-Treated Nets (ITN) through campaigns. The campaigns covered all regions an average of three times, except for the northern regions, which were not covered as much. However, these campaigns faced challenges such as poor data quality, complex stock management, uncovered areas, and long wait times for beneficiaries. NMCP is partnering with other organizations to digitize data for ITN distribution campaigns. The aim is to improve data quality and support evidence-based decisions. This study aims to compare the benefits of digitization using two different approaches. The ITN campaign was conducted in 29 health districts using digital means, while 17 health districts used non-digitized methods. All villages in the health areas were mapped and integrated into DHIS2 to allow for comprehensive analysis of ITN campaign data at all levels of the health system, including the distribution sites. ITN enumerators and distributors collected data at the community level using smartphones and unique QR code coupons in digitized areas. Non-digitized areas used paper collection and an Excel file as the database. However, data collection in non-digital

zones was slow and often riddled with errors. Digitization has highlighted the many challenges posed by traditional distribution methods. It also enabled us to identify non-covered areas and ensure household traceability for better decision-making. According to the report, out of the planned 10,878,186 ITNs, 10,673,108 ITNs have been distributed at an impressive rate of 99.26% for the 46 districts. This distribution rate represents 98.8% for the 29 digitized districts and 99.2% for the 17 non-digitized districts. Regarding household and population coverage rates, 2,067,913 households were served out of 2,106,140, meaning a household coverage rate of 98.17%. Additionally, 21,285,182 people were covered out of 22,048,413, resulting in a coverage rate of 97%. 638. In short, digitization optimizes net distribution and combined with recommended practices, effectively reinforces malaria prevention.

6899

SUCCESSFUL TASK SHIFTING: CROSS-SECTIONAL STUDY OF AN EMERGENCY OBSTETRIC CARE PROGRAM IN AN LMIC SETTING

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Direct obstetric causes of maternal mortality still account for approximately 86% of all global maternal deaths, the majority of which are preventable. In Nepal, 12% of all deaths for women of reproductive age are due to preventable obstetric complications. However, the distribution of human resources (HR) and availability of healthcare workers capable of providing CSs in LMICs is a significant limiting factor to reducing MMR. To address this disparity the Advanced Skilled Birth Attendant (ASBA) task-shifting initiative was developed to train medical officers to perform Cesarean sections (CSs) to manage obstetric emergencies. Until now, there has been limited study of the program's efficacy. A survey targeting all 234 ASBA graduates resulted in 93 usable surveys. Additionally, 7 rural CEONC government hospitals with posted ASBAs were selected for 13 in-depth interviews and 6 focus group discussions with Operation Theater (OT) staff. Results were then triangulated. Immediately after the training, 92.7% of ASBA graduates reported performing CSs at their hospital with the majority (65.6%) continuing to perform CSs today. Of the ASBAs not performing CSs, 51.7% could be explained by the lack of a functional operating theater, underscoring the need for a holistic approach to clinical service provision. ASBAs were significantly more likely to be performing CSs if a family physician or another ASBA was present at their current hospital ($p < 0.001$; $p < 0.001$). Their work was perceived to increase the use of services by the community, facilitate a positive working environment, improve healthcare access, reduce referrals, and reduce the burden of CSs on any one staff member. Staff were motivated to provide CSs when they otherwise might not have been able to and perceived the hospital to be in better standing with the community. The ASBA program is a successful task-shifting initiative that reduces human resource shortages, expands the provision of CSs, and improves the working conditions in rural hospitals within the LMIC setting. The program should be continued to further increase access to CSs in rural hospitals with a functioning operating theater.

6900

COMMUNITY-BASED PARTICIPATORY INTERVENTION TO FIGHT DENGUE FEVER IN CÔTE D'IVOIRE

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Dengue fever is the most widespread mosquito-borne viral infection. Abidjan has a population of nearly 6 million, and Aedes breeding sites are ubiquitous. Given that people's knowledge, attitudes, practices and beliefs play an important role in the resurgence of mosquitoes, it is therefore important to carry out a community-based participatory intervention to sustain mosquito control actions, as mosquito control is essential for effective dengue prevention. Measure the population's knowledge, attitudes, practices and beliefs (KAPB) related to dengue fever in the Cocody-Bingerville health district. Probability sampling was used and a questionnaire survey was carried out among heads of households or their representatives in 40 clusters, with 11 households visited per cluster. Individual interviews were also conducted with community leaders. A participatory photovoice approach, as already implemented in the context of malaria vector control (Makungu et al., 2017) was used. The results showed that communities are not aware of dengue fever. Only 40% know about it. Those who have heard of it have little information about the disease. Admittedly, the populations do not strictly refute the thesis of the existence of a link between dengue fever and dengue fever. For an effective fight against dengue, we need to improve the population's knowledge of this emerging disease in our country.

6901

METHODOLOGICAL INSIGHTS FROM REFLEXIVE VIDEO ETHNOGRAPHY: A CASE STUDY OF LEPROSY PATIENTS IN MALAYSIA

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This methodological review presents reflexive video ethnography (RVE) as a novel approach to exploring health-related social phenomena, illustrated through a case study of six leprosy patients in Malaysia. The study's core methodology integrates video ethnography with reflexive practices to capture and analyse the complex experiences of individuals affected by leprosy, living both within a leprosarium and in community settings. Our approach is distinguished by its emphasis on the participatory analysis of video data, facilitating deep engagement with the lived realities of participants. The research process was structured around three principal phases: extensive video documentation of participants' daily interactions and environments, reflexive review sessions involving researchers and participants, and a thematic analysis rooted in reflexive discussions. Ethical considerations were paramount, guiding the informed consent process and ensuring the confidentiality and dignity of all participants. This reflexive process enabled a contextual understanding of leprosy's social, emotional, and physical impacts, revealing insights into patient resilience, community integration, and the stigma associated with the disease. Our findings demonstrate the efficacy of RVE in uncovering the depth and breadth of patient experiences, emphasizing the methodology's capacity to elicit rich, participatory insights beyond traditional qualitative research methods. The case study of leprosy patients in Malaysia is a compelling example of RVE's potential to contribute to health sciences research, offering a comprehensive framework for researchers seeking to adopt a similar approach. This review argues for adopting RVE in the health sciences to enhance our understanding of patient experiences and inform the development of more empathetic and effective health interventions. By detailing the methodological execution and outcomes of our study, we aim to contribute to the broader discourse on qualitative research methodologies, advocating for reflexivity as a catalyst for methodological innovation and deeper social understanding.

6902

REASONS FOR NON-PARTICIPATION IN AZITHROMYCIN MASS DRUG ADMINISTRATION TO REDUCE MORTALITY AMONG CHILDREN 1-11 MONTHS OLD IN NIGER: A CROSS-SECTIONAL COVERAGE EVALUATION SURVEY

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The World Health Organization recommends biannual azithromycin mass drug administration (MDA) among infants aged 1-11 months to reduce mortality, following promising results of trials in Africa. However, with less resources than trials, coverage may decline during programmatic delivery, with the children missed likely at a higher risk of mortality. We aimed to understand reasons for participation and non-participation, how the intervention was received, and adverse events following azithromycin MDA in Niger by utilizing a coverage evaluation survey. In August 2023, trained community health workers delivered oral azithromycin MDA to children 1-11 months of age across 2,028 communities (42 integrated health centers [CSI]) in Tahoua, as a part of the AVENIR trial. Within 4 weeks of receiving the MDA, a separate data collection team conducted the survey. Separate mixed effects logistic regression models were used to analyze community-, household-, and child-level predictors associated with non-participation in azithromycin MDA, with random effects for community to account for clustering. A total of 3,848 households across 57 communities (7 randomly selected CSIs) were surveyed. Among children who were eligible for the distribution, 69% (n=721) received treatment based on caregiver self-report, compared to 92% community-health worker reported coverage. When asked why the treatment was not taken, the most frequently stated reasons were; not being in the age range (26.4%), someone not coming to the house (26.1%), absence (23.9%), and not receiving enough information (14.3%). In unadjusted models, factors that increased the odds of a child receiving treatment included being older (OR: 1.41, 95% CI: 1.33-1.49, p<0.0001) and receiving information about the program before (OR: 33.06, 95% CI: 21.82-50.07, p<0.0001, REF=did not receive information or do not know). Adverse events were reported among 6.5% of children who received treatment, and fever was the most reported symptom. Strengthening community preparation activities and understanding why younger children were less likely to be included may help to increase treatment coverage.

6903

TRENDS IN ANTENATAL CARE (ANC) CONTACTS AND EXCLUSIVE BREASTFEEDING IN SUB-SAHARAN AFRICA

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Exclusive breastfeeding is the safest and healthiest option for the first six months of life recommended by the World Health Organization (WHO), particularly in low resource settings. It is associated with reduced risk of malaria, diarrhea and other tropical health outcomes. The WHO 2016 ANC policy recommends at least eight (8+) ANC contacts during pregnancy and frequent antenatal care (ANC) contacts is correlated with exclusive breastfeeding. This study explores trends in breastfeeding practices in sub-Saharan Africa since the roll-out of the WHO 2016 ANC policy. A secondary analysis of data from 19 countries with available Demographic Health surveys from 2018 to date was performed. Key variables include exclusive breastfeeding, early initiation (within one hour of birth) of breastfeeding and number of ANC contacts (0-3, 4-7, 8+) in the most recent pregnancy in the two years prior to the survey. Exclusive breastfeeding ranged from 19% in Gabon to 81% in Rwanda (median=53%) while early initiation of breastfeeding ranged from 32% in Senegal to 85% in Rwanda (median=60%). Minimal women had 8+ ANC contacts, ranging from 0.3% in Rwanda to 39% in Ghana (median= 4%). The overall number of ANC contacts was positively associated with exclusive (AOR: 1.06, 95% CI: 1.05-1.08) and early initiation (AOR: 1.02, 95% CI: 1.01-1.03) of breastfeeding. However, women with 8+ ANC contacts were not more likely to exclusively or quickly initiate breastfeeding compared to women with 4-7 contacts. Study findings highlight the abysmally low rates of eight or more ANC contacts amidst a backdrop of suboptimal breastfeeding rates across sub-Saharan Africa. Findings also suggest a limited utility of eight compared to four ANC contacts and the WHO 2016 ANC policy in the context of exclusive and early breastfeeding. Behavior change efforts to improve the quantity of ANC contacts and complementary health service delivery interventions to improve the quality of ANC contacts are sorely needed and should remain a priority for sub-national and global stakeholders.

6904

ASSOCIATIONS BETWEEN IMMUNE STATUS AND CHILD DEVELOPMENT IN RURAL BANGLADESH

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A healthy immune system will mount controlled inflammatory responses to physiological stressors. High levels of inflammation are known to disrupt memory and learning, which has detrimental implications for child development. Here, we conducted observational analyses on the association between immune status, including markers of protective, regulatory, and pathological responses, and development in the first two years of life among participants in the WASH Benefits trial. We used Cox proportional hazard models to assess differences in the rate of attainment of motor milestones at the 75th and 25th percentiles of exposure. We used generalized additive models to assess the relationships between immune markers and scaled development measures and reported the mean difference in predicted outcomes. We found that children with a larger concentration of Th1 cytokines relative to Th2 cytokines at 14 months were more likely to be crawling [Hazard ratio (HR) 1.15 95% CI (1.02, 1.29)] and standing alone [HR 1.19 (1.03, 1.39)] by 14 months. An increased ratio of Th1/Th2 was also predictive of improved development at 28 months, though these results were marginally significant. Previously, we reported on a high prevalence of intracellular pathogens at 14 months and evidence of chronic gut inflammation in the study population; elevated levels of Th1 cytokines, which respond to intracellular pathogens, may therefore reflect a robust protective immune response to the environment. In contrast, C-reactive protein (CRP) and alpha-1-acid glycoprotein (AGP), markers of systemic inflammation, were negatively associated with early development. CRP at 14 months was negatively associated with the number of motor milestones achieved by 14 months [-0.26 (-0.5, -0.02)]. AGP at 28 months was negatively associated with EASQ communication scores [-0.24 (-0.44, -0.04)] and the CDI expressive language score [-0.34 (-0.57, -0.11)] at 28 months. Our results suggest that in early life, regulated protective immune

responses may be key for healthy development, but development may be impaired by systemic inflammation and unregulated pathological immune response.

6905

CONTRIBUTION OF VACCINE PREVENTABLE DISEASES TO CHILD MORTALITY IN AFRICA AND ASIA - CHILD HEALTH AND MORTALITY PREVENTIONS SURVEILLANCE (CHAMPS)

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Despite significant reductions in child mortality, children under five years of age remain disproportionately at-risk in Africa and Southern Asia. This is mainly attributed to uneven immunization, with over 30 million infections and 500,000 deaths annually estimated as due to vaccine-preventable diseases (VPD). We aimed to describe deaths attributed to VPDs using data from the Child Health And Mortality Prevention Surveillance network (CHAMPS). Cause of death determination was carried out through minimally invasive tissue sampling for microbiological and histopathological assessments, and determination of the chain of events leading to death using an expert panel at each CHAMPS site. During the study period, 6119 deaths had a COD determined through a DeCoDe panel on time for the analysis. Not considering stillbirths and neonates, 1459 deaths were counted: VPD deaths were responsible for 617 (42.28%) of deaths, of which 267 (18.3%) were included in the EPI schedules (*VPD-EPI* deaths: diphtheria, hepatitis B, Haemophilus influenzae type B infection (Hib), measles, whooping cough or pertussis, pneumococcal disease (PND), poliomyelitis, rotavirus diarrhea (Rota), rubella, tetanus or tuberculosis); and 350 (23.9%) were not (*VPD-non-EPI* deaths). Considering VPD-EPI deaths, the main etiology in was PND, being present in around 4 out 5 of deaths; followed by Rota (10%) and Tuberculosis (6.7%). Malaria accounted for vast majority of *VPD-non-EPI* deaths (90.6%). The second leading cause was Influenza and there were also cases reported of cholera, meningococcal meningitis, COVID-19, and rabies. A number of deaths presented with more than one VPD, and both, *VPD-EPI* and *VPD-non-EPI*, also presented with other pathologies in the casual chain. Malnutrition was especially important but also infectious diseases like HIV, LRTIs, malaria and sepsis. Updating the documented role of VPD's through postmortem sampling information on the subject is a strong and reliable tool to monitor vaccine delivery and uptake and surveillance of VPD remains crucial to improve vaccination programs and reduce child mortality due to VPDs.

6906

ENHANCING DATA AVAILABILITY AND QUALITY WITH AN EASY-TO-USE TOOL DURING THE LOGISTICS MANAGEMENT INFORMATION SYSTEM REFORM IN MADAGASCAR, 2022-2023

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The logistics management information system (LMIS) in Madagascar faced significant challenges for years, including low reporting rates, poor data quality, and lack of data visualization. To address these issues, the Ministry of Public Health (MOPH) decided to replace the offline national LMIS software (CHANNEL) with the online and open-source system, OpenLMIS, but this has been extensively delayed. During the wait, a reliable data tool was needed to maintain data quality and reporting. In October 2022, the PMI-funded Improving Market Partnerships and Access to Commodities Together (IMPACT) program supported the MoPH to develop e-LMIS (an Excel-based web, easy-to-use tool) and deploy it in all 115 districts beginning in January 2023. IMPACT conducted quarterly supportive supervision visits and routine data quality assessments (RDQA) at district pharmacies with reports from January to December 2022 for CHANNEL and January to December 2023 for e-LMIS. RDQA data were used to evaluate changes in quality of data on malaria commodities during the transition from CHANNEL to e-LMIS, comparing results from the 78 supported pharmacies in 2022 and 2023; we focused on completeness, timeliness, and accuracy. For malaria commodities, of 936 reports expected each year, 847 (90%) were submitted in 2022 and 907 (97%) in 2023 ($p<0.001$). In the same period, the on-time reporting rate increased from 579 (68%) of the 847 reports received in 2022 to 807 (89%) of 907 reports received in 2023 ($p<0.001$). Accuracy scores for three malaria products (rapid diagnostic tests and artemisinin-based combination therapy [1- to 5-year-old formulation and adult formulation] were 80% in 2022 and 96% in 2023.The use of e-LMIS tool was helpful and will continue to be used while awaiting deployment of Open-LMIS to generate quality data for commodity quantification, supply planning, and optimize availability of malaria commodities where and when needed.

6907

INTEGRATED DISEASE SURVEILLANCE AND RESPONSE SYSTEM: NEED FOR LABORATORY CONFIRMATION OF CASES IN BONO REGION, GHANA

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The Bono Regional Health Directorate with focus on one health, uses the various programs in the surveillance systems adopted by Ghana to identify and contain disease outbreaks and pandemics. Laboratory confirmation of identified cases is key in control and preventive measures in IDSR. We undertook a review of the IDSR records in the Bono Region to assess laboratory infrastructure necessary for commonly identified pathogens. This review of IDSR data from 2015-2024 in the Bono Region of Ghana considers weekly IDSR summaries from the District Health Information Management System (DHIMS2). The summaries include cases of diseases, recorded deaths from the diseases and the number of the cases that are confirmed by the laboratory, collated from the respective health system units and uploaded by public health officers. The data was organized and analyzed basically with Microsoft Excel version 2020. Permission for use of the data was sought from the Regional Director of Health Service. The diseases that were highlighted in the surveillance with laboratory confirmation were acute watery diarrhoea, cholera, COVID-19, diarrhoea by shigella, Measles, Meningococcal meningitis, Rabies, and Yellow Fever. With the exception of Rabies that had 100% of identified cases being confirmed by the laboratory in 2018, and Cholera with 90% in 2015, none of the cases identified for all the diseases had more than 25% laboratory confirmation. Even though Meningococcal meningitis consistently had some of the identified cases confirmed by the laboratory from 2015 to 2024, it was only in 2024 that a highest of 21% of the cases recorded was confirmed in the Bono Region. Considering COVID-19, less than 20% of the cases were confirmed by the laboratory.Laboratory confirmation of diseases earmarked for surveillance is low in the Bono Region of Ghana. Availability and access to laboratory facilities play critical role in laboratory confirmation. Adequate logistics and laboratory consumables hinder the ability of the health systems to confirm identified cases. Laboratory facilities are required foundations for effective IDSR implementation.

6908

RECURRENT ADMISSIONS AND MORTALITY RATE IN CHILDREN LESS THAN TWO YEARS OLD IN RURAL GAMBIAN SETTING

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Diseases resulting from hospital admission contribute to a significant clinical and economic burden globally. Some of these are reported to be recurring. Recurrent hospital admissions may have negative developmental effects, particularly in chronically ill children. The cost of hospitalization for serious medical problems can be up to 60 times higher than that of a mild or moderate condition managed by primary care services. In the Gambia, the direct cost of inpatient admission is $9.19, and indirect costs are $4.07 per visit. There have been no studies that looked at longitudinal data to provide more insight into readmission and death in a rural sub-Saharan environment. This calls for action to better understand and, therefore, contribute to the design of interventions to reduce recurrent admissions in young infants. We assessed the proportion of children less than 2 years of age readmitted, predictors associated with readmission, and the incidence of mortality in health facilities within the Basse Health and Demographic Surveillance System (BHDSS). A retrospective analysis of admitted patients that are less than 2 years of age with medical problems as the principal diagnosis at health facilities in BHDSS between January 2011 and December 2017 was performed. We calculated risk-standardized mortality rates at the first admission, risk-standardized readmission rates, and in-hospital mortality at 30 days, 90 days, and 2 years of readmission by using a multivariate mixed model. We included 4773 patients admitted with medical problems. The mean age was 7.6±5.5 months, and 56.9% were male. A total of 588 (12.3%) experienced at least a single episode of readmission. The number of readmissions for 30 days, 90 days, and 2 years is 103 (17.5%), 170 (28.9%), and 15 (53.6%). In-hospital mortality during the readmission episode was 128 (2.7%) throughout the years of follow-up. Readmissions are a significant contributor to the burden on the healthcare system, and early detection of patients who are at risk can help launch efficient interventions that lower costs and boost the standard of care.

6909

UTILIZING GEOSPATIAL DATA FOR TARGETED ADVOCACY TO ENHANCE MINIMALLY INVASIVE TISSUE SAMPLING (MITS) COLLECTION FOR CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) IN PAKISTAN

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The Child Health and Mortality Prevention Surveillance (CHAMPS) project is focused on understanding and preventing child mortality through comprehensive data collection, including post-mortem minimally invasive tissue sampling (MITS). However, MITS can be challenging to perform in resource-constrained settings with limited community engagement. Geographic Information Systems (GIS) offers the opportunity to improve MITS collection by informing targeted CHAMPS advocacy, which can increase the number of death alerts received from the community and improve awareness and acceptability of MITS within the catchment area. In Pakistan CHAMPS, we started by collecting and cleaning data on child mortality rates, healthcare facilities, and MITS collection sites. We then analyzed this data using GIS techniques to identify hotspots of child mortality: these areas were then targeted for increased MITS collection and optimized resource allocation. The integration of geospatial data is crucial to creating an accurate picture of community needs: we combined population demographics, healthcare accessibility, and environmental factors onto one database. Preliminary findings from GIS data revealed a direct correlation between increased advocacy efforts and an increased number of death alerts, thereby improving potential effectiveness of MITS. Furthermore, targeting areas of high mortality with decreased MITS consent allowed us to make our advocacy and MITS efforts more effective overall. By mapping areas with lower advocacy coverage, we identified gaps in community engagement and targeted these areas with intensified advocacy campaigns to improve child mortality surveillance. GIS-driven targeted advocacy has revolutionized MITS collection in Pakistan, bridging gaps in community engagement and maximizing study impact. This innovative approach highlights the power of data-driven strategies to enhance public health interventions.

6910

PERCEPTIONS TO AND DECISION-MAKING DYNAMICS OF ANTENATAL CARE DURING PREGNANCY: A QUALITATIVE EXPLORATION IN RURAL BANGLADESH

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Antenatal care (ANC) visits can identify pregnancy complications and promote optimal birth outcomes. The Child Health and Mortality Prevention Surveillance project in Bangladesh, uses minimally invasive tissue sampling (MITS) to determine the cause of death for stillbirths and deaths of children aged <5 years. Among the deaths enrolled in MITS, 94% were perinatal deaths and perinatal asphyxia was the leading cause of these deaths. In the catchment area rural Baliakandi, 90% of women received at least one ANC, but care was often sought late and from non-qualified providers. We explored the pregnant women's ANC perceptions and practices, aiming to design a culturally credible intervention to increase the uptake of timely and quality ANC. We interviewed 41 women between May and October 2022, who experienced a child loss and a subsequent pregnancy with a birth outcome to understand if any changes in ANC practices between their first and second pregnancy. Women perceived pregnancy is a normal physiological phenomenon in a woman's life and 46% believed that ANC is only required if they experienced a complication. Thirty-seven percent said that they should visit a qualified physician for an ultrasonogram between 5-7 months of the pregnancy to identify the sex, health condition and position of the fetus, so their family could plan for a home delivery if no complications were found. Fifty-three percent of women did not receive any ANC during the pregnancy where the child died, but did receive one to three ANC during the subsequent pregnancy; they stated that the child loss increased their interest in ANC. However, only 7% of these women met the guideline for at least 4 ANC visits in their subsequent pregnancy and were unaware about possible danger signs. Unfortunately, 23% of the women experienced a miscarriage or early neonatal death during their subsequently pregnancy. The existing practices of not seeking timely and quality ANC suggested the gap between perceived risks during pregnancy and required action points. Counseling women and families for quality ANC, outcome of the danger signs and ensuring quality care could promote care seeking during pregnancy.

6911

HOW SUPPLY CHAIN SHAPES LABORATORY PERFORMANCE IN SEROSURVEILLANCE BEFORE, DURING, AFTER COVID-19

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The importance of the supply chain (SC) in effectively supporting laboratory-based serosurveillance is often overlooked. We identified the

SC pain points before, during, and after the COVID-19 pandemic to extract lessons learned for Sierra Leone, Kenya, Malawi, South Africa and beyond. SC bottlenecks contributed to months- and even year-long delays in receiving deliveries resulting in low efficiency/higher costs and impacted evidence-based decisions. We used a mixed-methods approach, reviewed 52 papers (published 2006-2023), conducted 12 interviews and surveyed 8 key SC principals: researchers/staff, manufacturers, and SC professionals. Transcribed data were coded using inductive and emergent coding methods then analyzed by narrative synthesis and thematic analytic processes. Sites (75%), before COVID-19, dealt with delayed and incomplete shipments and deliveries, did not have procurement planning/ forecasting capabilities, lacked SC resource allocation, lacked inventory management systems and transportation logistics. During COVID-19, all SCs were severely disrupted: non-alignment of customs procedures and regulations between countries, disrupted shipping and inconsistent cold-chain handling instructions added to the challenges suppliers and users had to navigate. After COVID-19 customs-related issues improved for half of the sites with differing issues that will require both general and context-specific solutions. Many researchers tell us that they find "off-book" SC alternatives to ease their pain points. We will discuss the potential solutions tailored to fix infrastructural and systematic needs: adopting model regulations, personnel SC training, inventory management, one-stop serosurveillance bundles and fostering collaboration among stakeholders. During and post-COVID-19, the SC for genomics has paved a way for solutions by bundling purchases and improved logistics processes that have not been reflected for serosurveillance activities. These efforts should be better coordinated and funded. Innovations in product design and one-stop bundle packaging could ameliorate key barriers.

6912

ASSESSING THE QUALITY OF CARE PROVIDED TO WOMEN ATTENDING ANTENATAL CLINIC IN SIAYA COUNTY WESTERN KENYA

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In Kenya, up to 52% of women do not reach the minimum 8 antenatal care (ANC) visits recommended by the Ministry of Health (MOH). While ANC plays a crucial role in the well-being of both mother and child from pregnancy through postpartum, the quality of care (QoC) can vary significantly across healthcare settings, impacting maternal and neonatal outcomes. To evaluate this, we assessed the QoC of ANC in Siaya County, western Kenya. Women aged 13-49 attending any ANC visit from Aug-Oct 2023 in 7 health facilities (HF); level 2 (n=4), 3 (n=2), and 5 (n=1) participating in a scannable maternal and child health (MCH) handbook feasibility pilot were included. Each woman was issued a scannable handbook and followed for six months. If women were enrolled after the first ANC visit, data from previous visits were copied into the scannable book. Data on services, including physical examination, ANC profile, ultrasound, and intermittent preventive treatment (IPTp) of malaria, were electronically abstracted. QoC was evaluated using 19 MOH recommended services, 11 of which were scored per pregnancy (once), while 8 were scored at every routine ANC visit; scores >75% were considered high quality, 50-74% moderate, <50% low. 567 women participated in the pilot. Most underwent both physical exam and ANC profile tests 97%(n=549), but fewer received deworming (36%) or ultrasound (12%) at any visit. The average QoC score per the national guideline was 71.9% (SD=7.6). Most women received moderate (64%) or high (34%) quality care. Primigravida women (aOR=0.6, 95%CI=-0.9-0,01, p=0.03) and those attending HF level 3 or higher (vs level 2) (aOR=0.5, 95%CI=-1.1-0.3, p=0.002) were less likely to receive higher QoC. While the average QoC score was moderate, indicating a reasonable adherence to MOH guidelines, there is need to ensure the highest standard of care for all women. The relationship between gravidity and HF level and QoC suggests the need for targeted efforts to improve ANC service quality. Using a scannable handbook to track women longitudinally across facilities provides a robust framework for assessing and potentially improving ANC quality over time.

6913

COMMUNITY-BASED ASSESSMENT OF SOCIAL BEHAVIOR AND INTERACTION PATTERNS USING WEARABLE PROXIMITY SENSORS AND CONTACT DIARIES IN PAKISTAN: A QUALITATIVE STUDY

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In Pakistan, cultural norms, and community dynamics - including complex social hierarchies, traditional practices, and close-knit family structures - play a crucial role in shaping contact behaviors. Moreover, there are significant differences in contact behaviors between urban and rural areas due to varying lifestyles, population densities, and access to resources. Exploring a community's structure through innovative and direct methods can provide valuable insights. We completed a qualitative study in Karachi, Pakistan, to understand the social dynamics in urban vs. rural areas and assess the feasibility and acceptability of tracking community social interactions through contact diaries and proximity sensors. We conducted 24 focus group discussions (12 rural/ 12 urban) and 36 cognitive interviews (17 rural/ 19 urban) and analyzed data using thematic analysis. In analysis, key themes emerged, including gender preference, pre-appointment permission, and privacy concerns related to the documentation of daily interactions. Both urban and rural participants considered contact diaries to be important tools for interaction documentation, while rural participants emphasized the need to record interactions within extended families due to shared living spaces, the urban participants highlighted the need to document diverse interactions with individuals both within and outside of the household. The community overall identified the proximity sensors as new and unfamiliar. The urban participants were particularly concerned about privacy when wearing the sensors, while rural participants were concerned about wearability. Potential solutions brainstormed with the community included using Ajrak (Sindhi block-print fabric) pouches for rural wearers, blue pouches for urban adults, and T-shirts with concealed pockets for urban children. These results gave valuable insight into how cultural factors impact the acceptability of contact tracking tools. These findings laid the groundwork for successful implementation of a social behavior study in both rural and urban settings of low- and middle-income countries.

6914

ENGAGING PRIVATE PROVIDERS FOR ROUTINE IMMUNIZATION (RI) -INTEGRATED HEALTH SERVICES IN URBAN SLUMS OF HIGH-RISK UNION COUNCILS IN KARACHI, PAKISTAN

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Fully Immunized Children coverage is low (39%-48%) in Karachi's high risk urban areas due to sparse government health infrastructure and lack of engagement of private sector in providing preventive health services. An implementation research project to integrate RI and nutrition counseling, screening, and management through private sector health care providers

in collaboration with the Expanded Program of Immunization, Department of Health, Sindh, and the Aga Khan University is underway in 8 high risk urban areas of Karachi. Through private provider engagement model, RI-integrated health service corners have been established at 18 private clinics enrolled on criteria including registration with the health care commission, lack of public health facility in the geographical proximity, adequate maternal deliveries or child OPD volumes and agreement for no charging policy for immunization. The child friendly corners have been supplemented with two vaccinators and one female counselor to provide vaccination, nutrition screening, and counseling (nutrition, breastfeeding, balanced diet, and WASH) services at no service charge. The project uses an innovative social mobilization and digital communication approach for community awareness and engagement, ensuring active participation through social gatherings planned in collaboration with local community influencers. We present retrospective data collected from the Sindh Electronic Immunization Registry for percentage coverage against quarterly 0-11 month vaccination target for 2023 at the 18 private immunization centers. Continuous improvement in vaccination coverage was seen, exceeding targets in Q4 of 2023. The coverage of Penta-1 improved from 74% in Q1 to 108% in Q4 of 2023. Similarly, Penta-2 increased from 64% to 98% , Penta-3 went from 70% to 105%, while IPV-1 rose from 74% to 104%. The MR-1 increased from 47% to 83% in the Q4 of 2023. BCG's trend was similar, increasing from 56% to 86% in Q4 of 2023. Private sector involvement is crucial for addressing immunization gaps and the inequities developed due to inaccessibility to government health infrastructure and services.

6915

UNDERSTANDING COMMUNITY PERSPECTIVES AND DECISION MAKING TO INFORM CHILD MORTALITY SURVEILLANCE AND MINIMALLY INVASIVE TISSUE SAMPLING (MITS) STRATEGIES IN KARACHI PAKISTAN: ESTABLISHING A NEW SITE

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Under-five child mortality is of major concern in Pakistan.[1] The CHAMPS Network collects data globally to understand these deaths using minimally invasive tissue sampling (MITS). A CHAMPS site in Karachi, Pakistan, presents the opportunity to understand regional causes of child mortality, but MITS in this setting can be challenging without a culturally nuanced approach. To assess CHAMPS implementation feasibility, we conducted a five-month-long qualitative investigation with community leaders and members. This included eight focus group discussions, 43 in-depth interviews in three low-income peri-urban communities with diverse categories of stakeholders. Major themes were derived from coded data to identify patterns and were analyzed using thematic analysis framework. We examined study acceptability, practicality, and ease of implementation. Most perspectives aligned with study goals: primary motivators of acceptance included understanding cause of death and a desire to prevent future deaths. Grief counseling was supported as an additional incentive for participation. Challenges to acceptability included worry about MITS invasiveness and discomfort a child's spirit might feel during MITS; belief that death is predetermined, and therefore cause of death is irrelevant; and social pressure during consent. Logistical challenges included the narrow window between death and ritual bathing/shrouding during which samples can be collected. Considering this, we implemented key strategies to improve study feasibility. These include strong community and religious advocacy to increase awareness and reduce stigma of participation; a robust network of key informants to encourage early death alerts for timely MITS sample collection; using a MITS van to assist families with rituals after conducting post-mortem sampling; and strengthening relationships between staff and community through transparency, targeted advocacy, and communication in local languages. These strategies have helped improve community acceptance, enhance community-based mortality surveillance, and successfully implement MITS in Pakistan.

6916

HEALTHCARE SEEKING BEHAVIOR AND DISEASE PERCEPTION ASSOCIATED WITH CHOLERA AND DIARRHEAL ILLNESSES AMONG POPULATIONS IN CHOLERA ENDEMIC REGIONS IN NAMPULA PROVINCE, MOZAMBIQUE

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Healthcare seeking behavior and knowledge on cholera and diarrheal diseases in local populations influence disease control and prevention strategies. During November 10-19, 2023, we conducted a cross-sectional household survey in Nampula province, one of the most cholera affected regions in Mozambique. Households were selected using a two-stage cluster random sampling in cholera endemic and high priority hotspots in Nampula city and Meconta and Monapo districts of the province. A total of 838 households participated in the survey using tablet-based data collection and Electronic Data Capturing (EDC) system (REDCap). Age-group stratified healthcare seeking behavior associated with cholera and diarrheal diseases are being analyzed, which will support tailored community engagement for cholera control and serve as an adjustment factor in cholera incidence estimation. Accessibility to healthcare facilities by local populations is investigated by looking into various types of healthcare options near household, mode of transportation, travel distance, travel time, and travel cost to visit healthcare facilities. Socio-economic and demographic factors such as wealth and education level of household heads and history of symptoms related to acute watery diarrhea are analyzed to explore the potential association with healthcare seeking behavior for cholera and diarrheal diseases. Vaccination history of household members in each surveyed household and the community perception towards the oral cholera vaccine are being analyzed. These analyses will be ready for presentation at the upcoming ASTMH conference. Our study findings will fill the basic knowledge gap on the population-level risk factors associated with cholera, contributing to formulating more practical and appropriate community interventions to better control and prevention the disease in areas affected by periodic and persistent cholera epidemics.

6917

PROGNOSTIC PREDICTION MODELS FOR ADVERSE BIRTH OUTCOMES: A SYSTEMATIC REVIEW

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Despite progress in reducing maternal and child mortality globally, adverse birth outcomes have been observed to be disproportionately high in low- and middle-income countries (LMICs). Developing and validating a prediction model for adverse birth outcomes allows for early risk detection and prevention strategies. This systematic review aimed to assess the performance of existing prediction models for adverse birth outcomes and provide a comprehensive summary report of their findings. We used the Population, Index prediction model, Comparator, Outcome, Timing, and Setting (PICOTS) approach to retrieve studies PubMed/MEDLINE, Scopus, CINAHL, Web of Science, AJOL, EMBASE, and the Cochrane library.

We searched for grey literature using WorldCat, Google, and/or Google Scholar. Data were extracted using the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS), and analyzed for risk using the Prediction model Risk of Bias Assessment Tool (PROBAST). We descriptively reported results in tables and graphs**.** We included 115 prediction models: composite adverse birth outcomes (6), low birth weight (17), small for gestational age (23), preterm birth (71), and stillbirth (9). Maternal clinical and medical characteristics were the most widely used prognostic factors for preterm and low birth weight prediction, while uterine artery pulsatility index was used for stillbirth and small for gestational age prediction. The discrimination performance of preterm birth prediction ranged from an area under the curve of 0.51 to 0.83. Only 6% of the models reported model calibration. Current adverse birth outcome prediction models have poor to very good discrimination performance, but most did not report calibration performance. Inconsistent prognostic factors were included for each adverse birth outcome prediction. Prediction models with consistent prognostic factors that warrant external validation should be accessible to practitioners.

6918

UNDERLYING CONDITIONS AND CONTRIBUTORS OF PERINATAL ASPHYXIA AMONG STILLBIRTHS AND EARLY NEONATAL DEATHS ENROLLED IN THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS), WESTERN KENYA, 2017 TO 2022

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Perinatal asphyxia (PA) describes neonatal encephalopathy resulting from severe oxygen deprivation during childbirth, largely due to pre-existing maternal or fetal conditions and events around labor and delivery. We describe conditions and contributors of PA among stillbirths and early neonatal deaths enrolled in the Kenya Child Health and Mortality Prevention Surveillance (CHAMPS). CHAMPS investigates causes of death (CoD) in children under-five years (U5) in defined catchment areas in 9 countries in Sub-Saharan Africa and South Asia. CoDs are determined by an expert panel using data from post-mortem minimally invasive tissue specimen testing, child and maternal clinical records, and verbal autopsy. Designated immediate, intervening, and underlying conditions are considered to be in the causal chain (CA) leading to death. Between 2017 and 2022, CHAMPS-Kenya enrolled 911 U5 deaths, of which 27.9%(254) were stillbirths and 25.0%(228) early neonates. Two thirds (64.1%) of the stillbirth and <7-day decedents had PA in the CA; 304 (63.1%) as underlying CoD and 5(1.0%) as immediate CoD. Nearly all deaths (296,95.8%) occurred in a health facility. The 5 cases with PA as immediate CoD all had other underlying conditions that likely increased the risk of asphyxia. Underlying maternal conditions were identified in most asphyxia deaths (264,85.4%), including hypertension (61,23.1%), HIV (57,21.6%), antepartum hemorrhage (39,14.8%), multiple pregnancy (27,10.2%), chorioamnionitis (27,9.5%), anemia (21,8.0%) and malaria (14,5.3%). Nearly all deaths (302,97.7%) were determined to be preventable and recommended public health actions to the deaths included improvement in obstetric care and management (34.6%), infection prevention and control (31.3%), maternal health education (21.1%) and emergency transportation (17.8%). HIV disease, hypertensive disorders and antepartum hemorrhage accounted for >65% of all maternal conditions underlying PA. A high index of clinical suspicion with appropriate antenatal and labor management should be encouraged to aid in diagnosis and management of high-risk pregnancies likely to result in PA

6919

SOCIO-DEMOGRAPHIC AND OBSTETRIC RISK FACTORS ASSOCIATED WITH LATE INITIATION OF ANTENATAL CARE (ANC) IN RURAL BANGLADESH: FINDINGS FROM THE CHAMPS PROJECT

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Antenatal care (ANC) is important for ensuring optimal pregnancy outcomes by detecting and managing pregnancy complications. Late initiation of ANC, defined as receiving the first ANC visit after 12 weeks of gestation, can have major adverse impacts on maternal and child health. To improve timely ANC utilization in rural Bangladesh, we aimed to identify the socio-demographic and obstetric risk factors associated with delayed ANC initiation. Child Health and Mortality Prevention Surveillance (CHAMPS) has been conducting pregnancy surveillance in Baliakandi, a rural sub-district of Bangladesh, monitoring each pregnancy, including antenatal care utilization. A cross-sectional study was conducted among women from Baliakandi who were pregnant in 2022 and received at least one ANC visit. The association between socio-demographic and obstetric characteristics and late ANC initiation was analyzed using multivariate logistic regression. Out of 7085 pregnancy events, in 2317 pregnancies, mothers did not take any ANC. A total of 4768 pregnancies with ≥1 ANC were recorded; ANC was delayed in 44% (n=2081) of these cases. Women who received delayed ANC were younger in age compared to women who sought ANC on time (37% were aged ≤20 years, compared to 34.5%). In our study population, 81% of the mothers had educational attainment only up to 10 years. Women who sought care on time were more educated than those who initiated ANC late (24% vs 13% with more than 10 years of education). In multivariate logistic regression, age ≤20 years (adjusted odd ratio [aOR]: 1.79, 95% CI: 1.36-2.36), maternal education ≤10 years (aOR: 1.40, 95% CI: 1.13-1.73), and spousal education ≤10 years (aOR: 1.41, 95% CI: 1.17-1.71) were significantly associated with delayed ANC initiation. With each living child, the risk of late initiation of ANC was increased (aOR: 1.40, 95% CI: 1.26-1.55). Whereas a history of miscarriage (aOR: 0.75, 95% CI: 0.63-0.90) showed higher chances of timely ANC. Our study suggests that younger women with lower levels of education tend to receive their first ANC later. Interventions designed to target this group may help minimize the gap.

6920

IMPACT OF TWO-DOSE ORAL CHOLERA VACCINE IN CHOLERA ENDEMIC AND HIGH PRIORITY HOTSPOT IN CUAMBA DISTRICT IN CONTEXT OF THE 2023 CHOLERA OUTBREAK IN MOZAMBIQUE: FIVE YEARS AFTER A PREEMPTIVE MASS VACCINATION CAMPAIGN

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Cholera remains a major public health concern in Mozambique with outbreaks occurring almost every year since 1989 with a marked seasonal pattern. Mozambique has experienced several large cholera outbreaks over the past four decades with more than 35,000 cases reported between 2022 and 2023 alone, the largest in last 20 years. The Northern and Central regions, particularly Nampula, Niassa, and Zambezia Provinces have been disproportionately affected, compared to the South region. Cholera outbreaks occurred across multiple districts in Niassa province in 2023 with 3,500 cholera cases (clinically suspected with a sub-set of patients positive

with rapid diagnostics test and culture confirmed with *V. cholerae)* and case fatality rate (CFR) of 0.71% (25/3500). Here we describe the impact of a two-dose OCV mass vaccination campaign we had conducted in Cuamba district located in Niassa province in 2018 (two-dose coverage of 60.4% (±3.4%)); in context of the recent cholera outbreaks in Niassa province. Routine epidemiological data from the local government were analyzed. During the cholera outbreaks in 2022-2023, 69% (11/16) of all districts in Niassa province were affected. Cuamba district was unaffected (no cases reported) and the remaining four districts minimally affected. The most affected districts were Lichinga (1,719 cases, 8 deaths, 4.4 attack rate (AR), 0.47% CFR), followed by Lago (652 cases, 7 deaths, 9.5% AR, 1.07% CFR) and lake region of Mecanhelas bordering Cuamba District (392 cases, 3.95 AR, 0.26% CFR, mainly fishermen aged 20-29 years) districts. These areas and Cuamba district are considered traditional cholera hot zones in Niassa province but had no history of OCV vaccination in the past five years, except for Cuamba. Two of the five unaffected or minimally affected districts also border Cuamba district, which were Mandimba (11 cases, 0.1% AR, no deaths) and Metarica (no cases) districts. Our findings suggest a preventive OCV use in cholera endemic and high priority hotspots with at least 60.4% coverage rate demonstrated the direct and indirect protection against cholera outbreaks at five years post-vaccination timepoint.

6921

ASSESSMENT OF HEALTHCARE WORKERS AND COMMUNITIES BEHAVIORS TOWARDS ANTIBIOTICS IN YIRIMADIO, MALI

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Antibiotic resistance is becoming a public health problem worldwide. A systematic analysis estimated 4.95 million deaths associated with bacterial AMR in 2019. A study in Mali has observed 93.8% and 92.6% of *E. coli* resistance to some of the antibiotics widely used in Mali, amoxicillin and cotrimoxazole, respectively. To better understand this problem there is a need for scientific information at the community and healthcare personnel levels regarding antibiotics. This study aims to assess the knowledge, attitude, and practices of antibiotics use and prescriptions in the Yirimadio health district in Mali. The population aged more than 18 years and health workers of Yirimadio health district was surveyed between 07 to 13 September 2023 and the survey was carried out in 11 sectors of the Yirimadio health area. Community permission was obtained from sector heads and interviewers were trained to collect data from the population, health workers, and focus groups. A total of 300 people were quantitatively surveyed, 100 health workers were interviewed and 6 in-depth interviews were carried out. Of those surveyed, 61% were women and 82% were aged between 24 and 65 years. In the general population, 57% declared that they had heard about antibiotics, 84% said they obtained antibiotics without a prescription, and 75% confirmed that they self-medicated with antibiotics. In our study, 61% of health workers surveyed were women, 81% prescribed antibiotics without requesting a bacteriological test, 83% prescribed without antibiogram testing. Moreover, 47% of health workers advised antibiotics without a prescription, 31% advised by phone, and 22% advised using social media. This study revealed that, in addition to the general population, some health workers need more training, awareness-raising, advice, and education on the optimal use of antibiotics.

6922

HAPPY FEET: UNDERSTANDING THE PREVALENCE OF PODOCONIOSIS AND ASSOCIATED RISK FACTORS IN SODO ZURIA AND OFFA DISTRICTS, SOUTHERN ETHIOPIA.

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Podoconiosis is non-infectious lymphedema caused by barefoot exposure to irritant volcanic red clay soil. An estimated one-third of the 4 million global cases are reported in Ethiopia. However, reliable data on prevalence and risk factors associated with the disease are scarce. We investigated the prevalence and risk factors of podoconiosis in two districts of southern Ethiopia to provide evidence for policy and control programme planning. A mixed methods study was conducted in Sodo Zuria and Offa districts. Cross-sectional surveys were conducted with household heads in 968 households, including 116 household members with podoconiosis. In addition, four focus group discussions (FGDs) were carried out, two with community members with the disease and two without. Each FGD included eight female or male participants, totalling 32 community members (16 female and 16 male). Our results show the prevalence of podoconiosis among in the study districts was 3.95% with prevalence twice as high in women (5%) than men (2.5%). Although knowledge of podoconiosis and the prevention methods was high among community members, 29.7% were observed without shoes and 50% reported regularly walking to work barefoot. In addition, the mean age for first shoe-wearing among participants was 13.44 (± 9.4) years. Furthermore, among participants with podoconiosis, only 32% had clean and intact feet, and 71% reported seeking treatment for swelling from health facilities. FGD participants reported financial limitations and cultural barriers as reasons for not wearing shoes. FGD participants also reported men have greater access to shoes, are more likely to be able to afford shoes and spend more time outside which may be reasons for higher rates of shoe wearing among men. This study found a high prevalence of podoconiosis in Sodo Zuria and Offa districts in Ethiopia. Women were most affected by the disease and were reported to have lower access to shoes. To improve access to shoes and other preventative measures and encourage treatment-seeking behaviour we are implementing contextualized social behaviour change and healthcare interventions in these communities.

6923

ALL-CAUSE MORTALITY ATTRIBUTABLE TO THE COVID-19 PANDEMIC IN THE CONTEXT OF URBAN POVERTY: INSIGHTS FROM A COHORT IN PAU DA LIMA IN BRAZIL

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There is limited evidence on the direct and indirect health burdens of the COVID-19 pandemic on the vulnerable populations. The aim of this study was to identify the causes of mortality in a cohort of residents of an urban informal settlement in the city of Salvador, Brazil and estimate excess mortality attributable to COVID-19 in comparison to trends before (2017-2019) and after (2020-2023) the pandemic. We extracted information on the primary causes of death (ICD-10 codes) from the Brazilian Mortality Information System (SIM) to identify for individuals ≥5 years old who participated in the cohort from 2016 to 2023. We computed the P-score (percentage difference between reported and expected number of deaths)

to estimate pandemic-related excess mortality. Among 4538 cohort participants, we identified 124 deaths from 2016 to 2023. We estimated the expected number of deaths to be 13 based on mortality date from 2017-2019. The reported number of deaths was 17 (P-score 31%) in the first two years of the pandemic period, rose to 27 (P-score 108%) in 2022, and was 20 (P-score 54%) in 2023. Men who died during the pandemic were younger than women (40 vs. 55 years; p<0.001). Among men, the most frequent cause of deaths were external causes (EC, 44%), such as accidents and assault, and non-communicable diseases (NCD, 40%). In contrast, the most frequent case of death among women were NCDs (68%). Overall, infectious diseases, including COVID-19, accounted for 10% of deaths throughout the study period. Compared to the pre-pandemic period, the proportion of deaths attributable to infectious diseases and EC increased by 1.6- and 1.9-fold, respectively, during the pandemic. In this vulnerable and marginalized urban population, the COVD-19 pandemic was associated with increased mortality due to NCD and EC in addition to infectious causes, suggesting that the pandemic was associated with a significant indirect burden with respect to mortality. This finding highlights the critical importance of structural interventions to address the social determinants of health during periods of major social and economic disruption that occurred during the pandemic.

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IMPACT OF LADY HEALTH WORKER VISITS IN THE PRENATAL AND POSTNATAL PERIOD ON THE UPTAKE OF CONTINUUM OF CARE INTERVENTIONS AND MORTALITY IN PAKISTAN

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In Pakistan, Lady Health Workers (LHWs) play a crucial role in bridging the gap between communities and healthcare facilities since the inception of the LHW initiative in 1994. However, the quality of care offered, and their impact on population level coverage of key maternal, newborn, and child health (MNCH) interventions, as well as mortality are not yet fully understood. We used household survey data from eight districts across Pakistan with each household having at least one woman of reproductive age (WRA) with a child under the age of five. The study aimed to quantify the uptake of MNCH interventions by examining the association between a woman's interactions with LHWs, measured by coverage of antenatal and postnatal visits, and MNCH intervention coverage and mortality. We classified interaction with LHWs into three groups: no contact, contact during the antenatal period or the postnatal period, and contact during both the antenatal and postnatal periods. Logistic regression, accounting for survey design, determined the odd ratios of receiving each intervention at each LHW contact level. After adjusting for apriori confounders, it was found that compared to households who had received no LHW visits, there was a statistically significant difference in key interventions across the continuum of care including antenatal care visits, skilled birth attendance, postnatal checkups for mother and newborn. Similarly, among households that had reported receiving antenatal or postnatal visits by LHW, or both, there was significant improvement seen in childhood health interventions such as BCG vaccinations, care-seeking for diarrhea and full immunization (p-value<0.001). No statistically significant differences were observed in neonatal, post neonatal, or under-5 mortality in LHW-covered areas. This study provides evidence for the impact of LHW contact towards improving maternal and child health. Thus, the work of LHWs remains critical to empowering communities, specifically within the rural context of Pakistan.

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ETIOLOGY OF POSTPARTUM SEPSIS AMONG RECENTLY DELIVERED WOMEN IN PAKISTAN

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ETIOLOGY OF POSTPARTUM SEPSIS AMONG RECENTLY DELIVERED WOMEN IN PAKISTAN Type: Abstract SubmissionShabina Ariff1, Uswa Jiwani2, Tooba Jawed Khan2, Muhammad Jawwad1, Sajid Soofi1*1The Aga Khan University Hospital, Pediatrics & Child Health, Karachi, Pakistan, 2The Aga Khan University, Centre of Excellence in Women and Child Health, Karachi, Pakistan*

Untreated postpartum-endometritis escalates to postpartum-sepsis, with a 17% fatality rate. This study aimed to provide the first population-level data on the epidemiology and microbiology of endometritis in Pakistan. A prospective-observational-cohort-study was conducted in Matiari and peri-urban areas of Karachi. Surveillance-system instituted in the study areas was utilized to recruit women within-14 days of delivery. Participants were followed on postpartum-days 0, 2, 6, 13, 20, 27, 34, 41, 48, and 59 by trained Community-Health-Workers (CHWs) after obtaining informed-consent. All women with physician-confirmed sepsis were referred for endometrial sample collection and treated according to WHO-recommendations. CHWs suspected sepsis in 1762(14.1%) of the 12509 eligible and consenting women. Physicians assessed 1451(82.34%) of the suspected sepsis cases and 1919 healthy women. CHWs identified sepsis with a sensitivity and specificity of 86% and 72%, respectively. Altogether, 466(52.1%) of the 894 women with physician-confirmed sepsis provided endometrial cultures. The most common pathogens were*; E. coli* (40.5%), *G. vaginalis*(15.3%), *S. pyogenes*(11.5%), and *S. aureus* (9.2%). Of the 10 most common pathogens, 67.6% were sensitive to combined clindamycin and gentamycin, 53.2% were sensitive to imipenem, 35.6% were sensitive to combined amoxicillin-clavulanic acid and metronidazole, and 19.4% were sensitive to combined ampicillin and metronidazole. Pakistan's high postpartum sepsis rates necessitate treatment guidelines based on common pathogen susceptibility, preventive strategies are imperative to improve the outcomes of postpartum women and reduce maternal mortality in Pakistan.

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RETROSPECTIVE ANALYSIS OF CHOLERA/ACUTE WATERY DIARRHEA (AWD) OUTBREAKS IN ETHIOPIA FROM 2001 TO 2023: INCIDENCE, CASE FATALITY RATE (CFR), AND SEASONAL AND MULTI-YEAR EPIDEMIC PATTERNS

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Ethiopian government has developed the multi-sectoral cholera elimination plan with an aim of reducing cholera incidence and case fatality rate (CFR). To better understand and monitor the progress of this plan, a comprehensive review of national cholera epidemiology was needed. Reported data on cholera/acute watery diarrhea (AWD) cases in the recent 20 years were extracted from Ethiopian Public Health Institute and World Health Organization databases. Descriptive statistics, Pearson's chi-square, and logistic regression analyses were conducted. From January 2001 to November 2023, total 215,205 cholera/AWD cases, 2,355 deaths with a cumulative CFR of 1.094% (95% CI: 1.092-1.095) and a mean annual incidence rate of 8.9 (95% CI: 6.5-11.3) per 100,000 population were reported. Cholera outbreaks peaked in 2006-7, 2009 and 2016-2017 with over 20,000 cholera/AWD cases per year; followed by the 2020 outbreak (over 15,000 cases). In 2023, nearly 30,000 cases were reported. During

2015-2023, around 54.0% (53,990/99,945) of cases were those aged 15-44 years. In 2019-2022, cholera outbreaks largely hit the southern and eastern regions. Cholera CFR has increased in recent years; highest CFR (3.13%; 95% CI: 2.1-4.5%) in 2022. During the cholera outbreak years, cases sharply increased in major rainy season (June-August). Regional distribution of cholera CFR showed a significant variation during 2015-2023; B/Gumz region (5.2% CFR) with the highest CFR, followed by Sidama (2.3%) region. Cholera cases and attack rates peaked during the El Niño years, indicating the potential impact of climate change on the magnitude of cholera outbreaks. Cholera/AWD patients in older adults (45 years and above), severe dehydration, peak outbreak season, patients treated at outpatient level were associated with higher risk of deaths. Upsurge of cholera cases and deaths in 2023 signals a critical need for reactive and preemptive cholera vaccinations in cholera hotspots. Continued systematic cholera surveillance, early case detection and adequate case management are critical for reducing deaths and controlling cholera transmissions in communities.

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THE TROPICAL MEDICINE IN THE GULF OF MEXICO (TROP-G) NETWORK AS A MODEL TO BRIDGE RESEARCH GAPS, FACILITATE COLLABORATION, AND EMPOWER THE NEXT GENERATION OF NTD SCIENTISTS

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Neglected Tropical Diseases (NTDs) affect people primarily in low- and middle-income regions. The Gulf of Mexico region has been identified as a vulnerable and "hot zone" for emerging NTDs. Amidst these challenges, researchers in global health and NTDs navigate a path full of obstacles, such as scarcity of funding opportunities, limited access to critical samples or data, and lack of public support due to a low priority of global health on the political agenda. To address these challenges, the Tropical Medicine in the Gulf of Mexico (Trop-G) collaborating network (https://trop-g.org/) was established. Trop-G brings together doctoral candidates, postdoctoral scholars, and academics to collaborate on NTD research in the Gulf of Mexico region. The Trop-G goals include A) providing networking opportunities and events to build professional relationships, B) promoting interdisciplinary collaboration between people from diverse backgrounds, C) sharing knowledge by hosting regular discussions and presentations, and D) raising awareness on NTDs by engaging with the academic community and planning public outreach strategies. As part of its activities, Trop-G leads a 'Journal Club' to promote teamwork and networking, increasing awareness of NTDs. Trop-G Journal emerged through collaboration with Universidad Veracruzana, Universidad Autonoma de Yucatan, Baylor College of Medicine, and Tulane University. Today, our community counts 18 PhD students, 2 Postdocs, and eight researchers, with three additional institutions—the University of Florida, the University of Texas at El Paso, John Hopkins University, Universidad Autonoma de Nuevo Leon, and Universidad de Sonora. We have discussed 16 papers, showcased seven research project presentations, and hosted three guest talks. By organizing biweekly gatherings and showcasing the work through seminars and conferences, Trop-G fosters a dynamic forum for discussion and discovery and significantly boosts the visibility of NTDs research. This increased visibility can potentially lead to more opportunities for resources to be allocated toward NTDs research and improved public support.

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VACCINATION EXPERIENCE IMPACTS ON VACCINE CONFIDENCE AND FUTURE VACCINE BEHAVIORS IN KENYA, NIGERIA, AND SOUTH AFRICA

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We conducted large surveys as part of a larger project examining vaccination attitudes in three African countries (Kenya, N=1,545, Nigeria, N=1,557, and South Africa, N=1,588). We examined COVID-19 vaccination experiences & impressions in each country and the spillover of COVID-19 vaccine experiences on confidence in the safety, efficacy & importance of all vaccines approved for use in each country. We also asked about likelihood of self- and child vaccination in the future resulting from COVID-19 vaccine perception spillover. Majorities in all 3 countries indicated that, because of positive experiences with COVID-19 immunizations, they were more confident in the safety of other vaccines (72% in Kenya, 58.9% in Nigeria & 48.6% in South Africa), more confident of vaccine effectiveness (64.3% in Kenya, 55.9% in Nigeria & 49.2% in South Africa), & increased their beliefs that vaccines are important (71.7% in Kenya, 55.6% in Nigeria, 53.8% in South Africa). Other evidence of positive spillover was reflected in an increased likelihood of respondents indicating that they were more likely to vaccinate themselves & their children in the future because of positive experiences with the COVID-19 vaccination process. Among Kenyans, 71.5% were more likely to vaccinate themselves and 78.5% were more likely to vaccinate their children, 60,1% of Nigerians were more likely to get vaccinated in the future, and 64.6% were more likely to vaccinate their children. Fewer South Africans were more likely to vaccinate themselves (60.1%) and 64.6% were more likely to vaccinate their children in the future. In all 3 countries, about 25% of respondents expressed less confidence in vaccine safety and effectiveness after the COVID-19 vaccination process. Multivariate modeling found varying drivers of spillover effects in each country, but misinformation and confidence in government were stable predictors. Personal experiences with the COVID-19 vaccination process appear to be key drivers of generalized vaccination perceptions and predict self- and child vaccination in the future. The discussion will focus on improving vaccine acceptance among varying populations.

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INTESTINAL INFLAMMATION AND ENTERIC PATHOGENS CARRIAGE IN POST COVID-19 PATIENTS

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The COVID-19 pandemic has affected millions of people. As a result of the SARS-CoV-2 infection, a broad array of sequelae have been observed, affecting one or multiple organs, including gastrointestinal inflammation. In developing countries, intestinal inflammation triggered by SARSCOV2 infection should be considered in the context of chronic or recurring infections by enteric pathogens. The main objective of this study was to evaluate the presence of intestinal inflammation and enteropathogenic carriage in post-COVID-19 patients. To this end, a total of 201 fecal samples were collected from post-COVID-19 patients (1-24 years of age) in the period of at least 2-4 weeks following their recovery from the disease. Intestinal inflammation was evaluated by the quantification of fecal calprotectin using an ELISA kit (ORG 580 kit). 14 enteric pathogens were

analyzed by real-time PCR. Pathogens included viruses (rotavirus, norovirus GI and GII, astrovirus, sapovirus, and adenovirus), bacteria (*Salmonella*, *Shigella*, ETEC (estA, eltB) and EPEC (eae, bfpA), *Clostridium difficile* (tcdA, tcdB), *Helicobacter pylori*, and *Campylobacter*), and parasites (*Giardia lamblia* and *Entamoeba histolytica*).In general, levels of calprotectin varied broadly from 6.1 ug/g to 2257.4 ug/g. 94% of the study population displayed levels above the normal range (50 ug/g), and 54% displayed high levels of calprotectin (>200 ug/g), suggesting inflammation. Regarding enteric pathogen infections, 21% carried at least one of the tested pathogens. The most frequently found pathogens were EPEC (34%), ETEC (20%), and *Shigella* (17%). No association was found between COVID-19 severity and inflammation. Overall calprotectin levels correlated positively with a higher number of pathogens (ANOVA, P = 0.012). The data obtained throughout this study indicates that pathogenic bacterial infections and inflammation are common in the study population.

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LESSONS FROM COVID-19 VACCINATION IMPLEMENTATION IN 52 AFRICAN COUNTRIES: IMPLICATIONS FOR FUTURE PANDEMIC PREPAREDNESS

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Driven by the global imperatives to end the COVID-19 pandemic, the WHO set a goal in 2021 to fully vaccinate 70% of the global population by mid-2022. We projected the COVID-19 vaccination trajectory in 52 African countries and compared the projected to the 'actual' or 'observed' coverage as of December 2022. We also estimated the required vaccination speed needed to have attained the WHO 70% coverage target by December 2022. We obtained publicly available, country-reported daily COVID-19 vaccination data, covering the initial 9 months following the deployment of vaccines. We used a deterministic compartmental Susceptible-Exposed-Infectious-Recovered-type model and fit the model to the number of COVID-19 cases and vaccination coverage in each African country using a Markov chain Monte Carlo approach within a Bayesian framework. Only nine of the 52 African countries were on track to achieve full COVID-19 vaccination coverage rates ranging from 72% to 97% by the end of December 2022, based on their progress after 9 months of vaccine deployment. Of the 52 countries, 26 (50%) achieved 'actual' or 'observed' vaccination coverage rates within ±10 percentage points of their projected vaccination coverage. Among the countries projected to achieve <30% by December 2022, nine of them achieved a higher observed coverage than the projected coverage, ranging from 12.3 percentage points in South Sudan to 35.7 percentage points above the projected coverage in Tanzania. Among the 52 countries, 83% (43 out of 52) needed to at least double their vaccination trajectory after 9 months of deployment to reach the 70% target by December 2022. Our findings can guide countries in planning strategies for future global health emergencies and learning from each other, especially those that exceeded expectations and made significant progress towards the WHO's 2022 COVID-19 vaccination target despite projected poor coverage rates.

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UNIQUE AND ADAPTIVE PANDEMIC PREPAREDNESS IN LMIC HEALTH SYSTEM- AN INTEGRATED SURVEILLANCE POTENTIAL OF A RAPID TB AND COVID-19 DIAGNOSTIC IN BANGLADESH

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The COVID-19 pandemic with continuous emergence of its new variants largely affected the aviation system and international travel. Quarantine and proper testing of incoming travelers were considered as the most important preventive strategy. However, many unprecedented challenges were observed at the resource poor settings such as inadequate airport quarantine facilities, lack of highly sensitive but rapid testing and cost-effective management system. In this current study, we present a cost-effective and timely alternative diagnostic and quarantine facility for the incoming impoverished travelers in Bangladesh during the pandemic. We conducted a cross-sectional serosurvey from December 15, 2020 to November 30, 2021 for inbound travelers to Bangladesh. These impoverished travelers (unable to afford hotel quarantine) were quarantined in Hajj camp (a government facility near the airport reserved for muslim pilgrims) with full coverage of food and lodging at subsidized cost and free testing by GeneXpert, which is capable of Nucleic Acid Amplification Test (NAAT) for both COVID-19 and Tuberculosis (TB). Among 1328 participants, SARS-COV-2 positive patients were 106 (7.98%), out of which 72 were male. The highest infection rate was observed in travelers from Singapore (n=16/71, 22.53%) followed by USA and Malaysia. The result processing time was only 1 hour for the NAAT and 1222 participants (92%) were able to travel to their destinations on the same day. The positive cases were kept in quarantine for further assessment. Majority of the participants (95%) were satisfied with the service and processing time. This study is a scalable example of implementation research in resource poor settings which supports the equitable access to COVID-19 diagnostics for disadvantaged group and emergency preparedness for similar pandemics. Due to high sensitivity and specificity, NAAT is also recommended by WHO for diagnosis of acute COVID-19 cases. Our research also emphasizes on the potential to equip hard to reach laboratory facilities by GeneXpert for both TB and COVID-19 diagnostics specially where the double burden exists.

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RAPID RESPONSE MOBILE SUITCASE LABORATORY AS A TOOL FOR COMBATING INFECTIOUS DISEASE OUTBREAKS

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In times of emerging pathogens, point-of-need diagnostics represent the first line of defense. In the last two decades, there have been six pandemics and numerous outbreaks of infectious diseases worldwide. Especially in low- and middle-income countries, healthcare facilities are inadequate to manage and control outbreaks. The Mobile Suitcase Lab (MSL) provides a highly functional minimalist work unit that enables capacity development in remote settings in addition to the ease of delivery and deployment. The molecular methods used in the MSL are isothermal amplification (recombinase-aided amplification or recombinase polymerase amplification assay), rapid real-time PCR, and nanopore sequencing. Nucleic acid extraction can be performed within 15 min using simple and rapid reverse purification extraction methods. The MSL operates with a glove box for working with highly contagious pathogens. All reagents needed are cold chain independent and stable at ambient temperature of tropical areas. Independent power supply is achieved via solar power batteries. Members of the research group have released the first mobile Next Generation Sequencing protocol, where all necessary steps can be performed in a suitcase lab, enabling truly mobile use of this technology including offline data basecalling and analysis.The MSL team is working as an international consortium, consisting of 38 members from 17 countries, including public health, academic and governmental institutions. The MSL has been deployed to outbreaks of Ebola, SARS-CoV-2, Dengue, Zika, Avian Influenza and Marburg. As participants in the WHO's simulation exercise programme for Rapid Response Mobile Laboratories, the team contributed to the establishment of Minimum Operational Standards and the improvement of interoperability with other response forces. The MSL Consortium enables disease outbreak investigation and pathogen detection directly at the point-of-need, while strengthening international collaboration and local capacity building.

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ADAPTING RAPID LABORATORY BIORISK SELF-ASSESSMENTS TO BETTER INCORPORATE CYBER-BIOSECURITY RISKS

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Recent technological advances have highlighted the global catastrophic biological threat that generative AI could pose. A key building block of this threat is the ease of access to sensitive genetic and diagnostic material stemming from laboratories working with high-consequence pathogens. It is vitally important to secure critical high-containment laboratories and biorepositories from physical and digital biosecurity threats that could contribute to heightening AI and biotechnology risks. Since 2017, the Georgetown University Center for Global Health Science and Security has engaged with laboratory systems to identify gaps and strengthen biosecurity and biosafety capacities using the Laboratory Self-Assessment Tool (S-LAT). In light of rising cyber-biosecurity threats, we have developed an adaptation of the S-LAT including components specifically targeted at identifying and mitigating gaps in cyber-biosecurity capacities. The cyber-biosecurity component focuses on building biosecurity capacities across synthetic biology, toxicology, and genomic research communities, especially those deploying biotechnologies. It also establishes measures for biological and genomic data security, including capacities supporting oversight, enforcement, and/or reporting mechanisms. This presentation will examine the process of developing and incorporating the cyber-biosecurity component of the S-LAT, and provide an update on key considerations in mitigating the cyber-biosecurity threat of high-consequence pathogens from a laboratory perspective.

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AGRICULTURAL WORKERS IN GUATEMALA WITH CHRONIC KIDNEY DISEASE ARE AT HIGHER RISK OF ACUTE RESPIRATORY ILLNESS: FINDINGS FROM THE AGRICULTURAL WORKERS AND RESPIRATORY ILLNESS IMPACT (AGRI) STUDY

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Chronic kidney disease (CKD) of unknown origin (CKDu) is a major public health concern in Central American agricultural workers. While CKD is a risk factor for severe COVID-19 and influenza, it is unknown if populations at risk for CKDu, which are typically younger with fewer comorbidities, are also at risk. During 2020-2022, we annually estimated glomerular filtration rate (eGFR) using serum creatinine among banana farm workers in southwest Guatemala enrolled in a longitudinal cohort (AGRI) study. Influenza-like illness (ILI) was defined as ≥ 1 day of cough, fever, or dyspnea reported on weekly symptom surveys. Workers with ILI completed a questionnaire (flu-iiQ), which produced severity scores for 'systemic' and 'respiratory' symptoms, and impact on 'daily activities,' 'emotions,' and 'other people.' We defined moderate and mild renal impairment as eGFR <60 mL/min/1.73m^2 at one measurement, and 60 to < 90 mL/min/1.73m^2 at two measurements, respectively. We assessed the association between renal impairment and ILI using multivariable regression models adjusted for sex, chronic disease, and job type. During 2020-2022, we screened 2,149 workers (2023 data pending); median age was 28.7 years (interquartile range 23.9 – 35.4) and 82% were male. Overall, 77 (3.6%) had moderate and 234 (10.9%) had mild renal impairment. Of the 352 ILI episodes reported, 17 (4.8%) and 32 (9.1%) were among workers with moderate and mild impairment, respectively. Compared to workers without renal impairment, workers with moderate impairment had marginally higher ILI risk (relative risk = 1.43, 95% CI: 0.94-2.16, p = 0.09), while those with mild impairment had marginally lower ILI risk (RR = 0.76, 95% CI: 0.55-1.04, p = 0.09). The flu-iiQ 'Impact on Others' severity score was higher as renal impairment increased (β= 0.15, p = 0.02); other flu-iiQ scores were similar. These preliminary results from farm workers at high risk for CKDu suggest moderate renal impairment may impact the risk and severity of symptomatic respiratory infections. These findings may help public health authorities to prioritize disproportionately affected populations for vaccination campaigns.

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PERFORMANCE OF MALARIA ELIMINATION ACTIVITIES IN SEKE DISTRICT, MASHONALAND EAST PROVINCE, ZIMBABWE, 2023

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Seke district in Zimbabwe became an elimination district in 2022 after achieving an annual parasite incidence <5 cases/1,000 population per year for three consecutive years; a favorable assessment of operational and financial feasibility; and sustainability of the 1-3-7 strategy to report confirmed cases within one day, case investigation within three days, and foci investigation and response within seven days. We conducted a descriptive analysis of malaria surveillance data from Seke District for 2023. Of the 2,409 reported suspected cases passively identified at health facilities, 2,388 (99%) were tested using a malaria rapid diagnostic test or microscopy; of which, 169 (7.1%) tested positive. Through reactive case

detection, 590 household contacts were tested, and 15 (2.5%) tested positive; among whom, 12 (80%) were symptomatic. All 184 confirmed cases (passive and reactive) received appropriate malaria treatment, and 167 (91%) received additional gametocytocidal therapy as single low-dose primaquine. Overall, 172 (94%) cases were uncomplicated, while 11 (6%) were severe cases requiring hospitalization. Among confirmed cases, 60 (33%) were students, 20 (11%) vendors, 14 (8%) farmworkers, and 14 (8%) children <5 years. 88 (48%) of cases sought treatment within 48 hours. Among the 96 cases who sought treatment after 48 hours, 31% were students, 10% vendors, 8% children < 5 years, 8% unemployed, and 41% were other occupations. Overall, 178 (97%) cases were classified as imported; of these, 132 (74%) had a history of travel from malaria high-burden districts, and 11 (6%) from low-burden districts in-country, and 35 (20%) from international locations, mostly from Mozambique (26). All 184 confirmed cases were notified within one day, 156 (85%) of these were investigated within three days, while 12 cases were lost to follow-up, and 16 cases had missing data. No foci investigations were conducted. Case notification and investigation performance was high. Increased capacity for foci investigation and response is needed. Targeted messaging for travelers and students might promote malaria preventive and early care-seeking behaviors.

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UTILIZATION OF PREPOSITIONED RESEARCH LABORATORY CAPABILITIES TO SUPPORT SUDAN VIRUS DISEASE RESPONSE IN UGANDA

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Uganda is prone to outbreaks of high-consequence pathogens including 7 Ebola outbreaks to date. Prepositioning laboratory capability for early detection and effective response is essential for limiting disease spread. The Joint Mobile Emerging Infectious Disease Intervention Clinical Capability (JMEDICC) was established with funding from U.S. Department of Defense and maintained by a partnership across Makerere University Walter Reed Project, the Infectious Diseases Institute and the Austere environments Consortium for Enhanced Sepsis Outcomes. The purpose was to ready a local team to conduct clinical research of medical countermeasures in a filovirus outbreak setting. Laboratory capability development included strategic instrument acquisition allowing for operation inside rapid containment kits, staff competence in Infection Prevention and Control, as well as maintenance of skills through drills/simulation exercises. The Ministry of Health (MoH) leveraged JMEDICC capabilities during the 2022 Sudan virus disease outbreak to offer clinical laboratory testing (biochemistry, hematology and serology) to patients in three Ebola Treatment Units (ETU) for the first time in Uganda. The data generated was crucial for patient care. Prepositioned research capacity and capability enabled safe rapid deployment of mobile clinical laboratories. JMEDICC-MoH collaboration further illustrated the benefits of partnerships to combat global health threats.

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A SURVIVOR CASE OF NEONATAL TETANUS: CASE DESCRIPTION AND SURVEILLANCE SYSTEM EVALUATION IN THE URBAN HEALTH DISTRICT OF EBOLOWA, CAMEROON, MARCH 2023

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Neonatal tetanus (NNT) is a vaccine preventable disease with high lethality rate (80-100%). Cameroon was declared "Maternal and NNT free" in 2012. Elimination strategy of NNT include high vaccination coverage in tetanus toxoid vaccin (≥2 doses) [TT2+] among Women of child bearing age (WCBA) and high-quality surveillance of NNT. On March 9th 2023, the Ebolowa Health District (EHD) was notified of a suspected living NNT case. We aim to investigate to identify exposure factors. A cross-sectional descriptive study was conducted from March 17-26, 2023 in EHD. The case's family was interviewed for case description. Vaccine coverage (VC) and knowledge on NNT evaluation were conducted in the neighbourhood. Health-care workers were interviewed to assess Surveillance system (SS) attributes according to the *2001 CDC guidelines*. Excel (97.2003) software was used for data analysis. Means and proportions were calculated, results presented in tables and figures. The case, female, was born on the floor at home (February 28th, 2023) from a non-vaccinated mother. Umbilical cord was tied with sewing thread and cut using bamboo pestle. The baby presented incessant crying, difficulties breastfeeding, seizures, neck stiffness and spasms 7 days later. Globally 201 neighbours were interviewed. Only 37(18.4%) knew of NNT and 15(7.5%) were aware of its transmission mode. Among the 201 neighbours, WCBA were 85(42%). VC of TT2+ was 21% (18/85) for those WCBA, and 58(68.2%) of them were zero dose for TT2+. A total of 39 health-care workers were interviewed for NNT-SS evaluation, with 16(41%) having at list 3 years' professional experience. The SS was not flexible (51.28%). Completeness (99%), promptness (95%) and usefulness (100%) were satisfactory. Simplicity (70.57%) and acceptability (73.99%) were moderately satisfactory. The EHD recorded the first NNT survivor case in the country. Exposure factors were non aseptic delivery and zero dose mother. VC and knowledge on NNT were very low in the neighbourhood. Utility, completeness and promptness of the NNT-SS were satisfactory. We recommended sensitization, intensive vaccination and training of health-care workers.

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THE IMPACT OF COVID-19 POLICY CHANGES ON RT ESTIMATION IN WEST VIRGINIA, JANUARY 22, 2020-DECEMBER 31, 2020

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Substate-level analysis enables us to better understand geographical variation in COVID-19 transmission and facilitate improvement of prevention efforts with greater granularity. This study analyzes daily cases in West Virginia (data from Johns Hopkins data repository) to estimate the time-varying reproduction number, R_t, in 9 regions across the state. We used the R package EpiEstim to estimate R_t with 7-day-sliding-windows and with non-overlapping-time-windows between 5 policy changes and used

Poisson regression to estimate the incidence rate ratio (IRR) between those 9 regions and West Virginia. Statewide R_t fluctuated throughout the year, with the highest in March 2020 (close to 2) and the lowest R_t (<1) seen in June 2020. The Stay-at-Home Order, Face Mask Mandate, and Virtual Learning Resumes saw 38.7% (95% confidence interval [CI]: 21.9%-57.5%), 10.6% (3.2%-18.9%), and 9.4% (3.2%-15.4%) corresponding decreases in R_t statewide, and varying decreases across the 9 regions. The Eastern region saw no significant R_t changes for all five policy changes. Using the state as the reference group, all regions except Metro-Charleston found significant differences in IRRs. The Northern region had the smallest IRR in 2020 at 0.32 (0.32-0.33), and the Wood-Jackson region had the highest IRR of 1.90 (1.87-1.94). R_t estimates between policy changes showed that policies that isolated people, such as the Stay-at-Home Order and Virtual Learning Resumes, effectively reduced transmission across the state. Geographical variation in case burden is reflected in regions that consistently had IRR >1 or <1 compared to the statewide incidence rate.

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ASSESSING IMMUNIZATION COVERAGE AND POLIO VACCINATION STATUS AMONG CHILDREN AGED 12-23 MONTHS. FINDINGS FROM A CROSS-SECTIONAL SURVEY IN HIGH-RISK UNION COUNCILS OF PAKISTAN

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The current polio epidemiology in Pakistan poses a unique challenge for global eradication as the country is affected by ongoing endemic poliovirus transmission. Across the country, union councils (UCs) that serve as core reservoirs for poliovirus with continuous incidences of polio cases are categorized as super-high-risk union councils (SHRUCs). A cross-sectional survey was conducted in 2023 in 39 SHRUCs over 7 districts using a two-stage stratified cluster sampling technique. 8,011 children aged 12-23 months were covered. A structured questionnaire was used for data collection. Data were analyzed using STATA version 17. Based on both vaccination records and recall, 60% of children were fully-, 34% were partially-, and 6% were non-vaccinated in the SHRUC districts. Among the SHRUC districts, Peshawar in Khyber Pakhtunkhwa (KP) had the highest percentage of fully vaccinated children (83%), followed by SHRUC districts in Sindh (with more than 50%), while the least proportion of fully vaccinated children was found in SHRUC districts of Balochistan. Vaccination cards were available for more than 70% of children in the SHRUC districts of KP and Sindh, and for more than half in the SHRUC districts of Balochistan, except for Killa Abdullah. Results for polio vacancies show that 72.9% of children from the SHRUC districts were vaccinated with at least three doses of OPV and one dose of IPV, while 92.4% were vaccinated with any OPV doses or IPV and 7.6% of children did not receive any polio vaccines. The dropout rate between dose pairs (Penta1 vs Penta3, OPV1 vs OPV3, PCV1 vs PCV3, MCV1 vs MCV2, BCG vs MCV1, and Penta1 vs MCV1) was higher than the WHO-recommended cutoff point of 10% for all vaccine doses in the SHRUC districts except for district Peshawar. To enhance and sustain immunization coverage in the SHRUCs, a multifaceted approach is imperative. This may involve targeted community engagement to dispel misconceptions, enhance vaccine acceptance, and strengthen healthcare systems through training and reliable supply chains.

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THE ACCEPTABILITY OF MINIMALLY INVASIVE TISSUE SAMPLING FOR CAUSE OF DEATH DETERMINATION IN RURAL SOUTH AFRICA: A QUALITATIVE ANALYSIS.

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Minimally invasive tissue sampling (MITS) is increasingly being used to strengthen cause of death data in resource-limited settings. However, information on the acceptability of MITS for community deaths across all ages is scarce, as most studies have focused on child and facility deaths. This qualitative study describes factors influencing the acceptability of MITS for community deaths in a rural South African community and reviews the utility of the theoretical framework for acceptability (TFA). We conducted thematic analysis of 20 in-depth interviews with community members from the Agincourt Health and socio-Demographic Surveillance System site who experienced a death in the last 24 months, and 6 focus group discussions with religious leaders, mortuary workers, healthcare workers, traditional healers, and community members. Most community members had positive attitudes towards MITS as they felt knowing cause of death would provide closure, help prevent further deaths and reduce witchcraft accusations. The participants' belief systems did not forbid participation in MITS, but local traditions dictate that infants and traditional healers be buried within one day of death, which might limit participation of these groups. Rumours of organ-trafficking during autopsies made some participants wary of the MITS. However, MITS was considered more acceptable than standard autopsies as it does not involve the removal of organs from the body. Engaging with local traditional leaders and community members, as well as community education about MITS was considered crucial to improving uptake and building trust. Fieldworkers must empathize with grieving families to facilitate consent, minimize the psychological burden of participating in MITS activities and assist with the grieving process. Our findings were largely in line with the TFA; however, the framework failed to account for trust between providers and participants. Given that this trust influenced the acceptability of our intervention, we propose the modification of the TFA to account for this factor.

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REACHING THE UNREACHABLE CHILDREN FOR ESSENTIAL VACCINATIONS AN OUTREACH APPROACH THROUGH HEALTH CAMP IMPLEMENTATION

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Despite the robust polio eradication efforts, Pakistan remains a polio-endemic nation. To address the persistent poliovirus transmission, the National Emergency Centre for Polio Eradication has initiated integrated health camps in Polio Super High-Risk Union Councils (SHRUCs) as a part of targeted Supplementary Immunization Activities (SIAs) in collaboration with Aga Khan University, Pakistan. The health camps are meant to deliver basic maternal, child health and essential immunization services. This study presents the coverage of priority children for essential vaccinations from the health camps. High-risk union councils are the primary targets of immunization initiatives during SIAs. To reach out to the underserved children who were either missed or inaccessible during the polio campaigns, health camps are systematically organized on a rotational basis post-campaign. Provincial and District EOCs and the Polio Program offices assist in identifying suitable locations for these health camps. Between July 2021 and September 2023, a total of 2,739 health camps were organized in 41 districts with coverage extending to 201 union councils across all four provinces on a rotational basis. During these camps, 80,780 priority children under the age of five received essential vaccinations. Among them, 28,349 were children who had not received any prior doses, and another 28,349 children were those who had been missed or were unavailable during previous immunization campaigns. Within these health camps, 44,934 children who had consistently been missed by previous immunization campaigns were reached, and 11,396 children who had previously refused vaccination were covered. Additionally, the camps provided essential vaccinations to 273,978 more children. The health camp model, as an outreach strategy, is a highly effective approach for delivering vaccination services to underprivileged populations and enhancing immunization to curb the circulation of the polio virus in the country.

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EARLY DETECTION OF CHOLERA OUTBREAKS IN URBAN AND RURAL AREAS OF NAMPULA PROVINCE IN MOZAMBIQUE: PRELIMINARY INTERIM RESULTS OF ENHANCED ACUTE DIARRHEAL DISEASE SURVEILLANCE IN CHOLERA ENDEMIC SETTINGS

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World Health Organization warned in 2023 that one billion people in 43 countries are at risk of cholera with children under five particularly vulnerable. Mozambique is one of the cholera high-risk countries. Coastal areas of North and Central regions, including Nampula province, are periodically affected by cyclones and floodings. This, coupled with poor water, sanitation, hygiene, and weak healthcare systems, leads to frequent cholera outbreaks. A prospective cholera and diarrheal disease surveillance has been set-up in five sentinel healthcare facilities in Nampula city, Monapo and Meconta Districts of Nampula province. Patients with acute diarrheal symptoms were eligible for enrolment. Clinical data and rectal swab samples were collected for cholera rapid diagnostics test (RDT) and laboratory confirmation. Our preliminary interim analysis shows the following findings while surveillance and data cleaning are ongoing. From September 2022 to January 2024, total 904 eligible patients were enrolled, of which 33.5% (183/547) were RDT positive for cholera. 44.6% (332/745) were culture positive for *V. cholerae* and 55.8% (416/745) positive for non-cholera isolates out of total culture positive isolates. Most cholera cases (counted by either RDT or culture positive) were enrolled at Cholera Treatment Center (64.8%; 289/446) and detected among patients in 15+ years age-group (86.8%; 387/446). Most enrolled patients were from Nampula city (88.3%; 798/904), though outbreaks were detected in both urban and rural areas. Overall crude incidence of cholera was 24.9/100,000 person-years (PY); highest in 15+ years (40.8/100,000 PY). Crude incidence of non-cholera diarrheal disease was 25.6/100,000 PY; highest in 15+ years (44.0/100,000 PY). 83.2% (371/446) of cholera patients were hospitalized for treatment; 75.8% (347/458) of non-cholera diarrheal patients hospitalized. Enhanced and sustained surveillance capacity is critical in early detection of cholera outbreaks and case management. Timely planning and pre-positing of cholera RDT and laboratory diagnostics supplies on sites closer to the cholera high-risk areas are critical.

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ANALYSIS AND OPTIMIZATION OF LABORATORY NETWORKS FOR LASSA AND YELLOW FEVER IN NIGERIA: A COMPREHENSIVE APPROACH

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Nigeria faces significant public health challenges posed by epidemic-prone diseases; the National Centre for Disease Control and Prevention (NCDC) has been actively expanding surveillance and diagnostic networks to enhance outbreak detection and response. However, accessibility to testing remains a key challenge. A descriptive and optimization analysis of the Lassa (LF) and Yellow fever (YF) diagnostic networks and associated sample transport systems were conducted to inform NCDC's policy and future strategic planning. The analysis provided valuable insights into the laboratory network and sample referral systems for both outbreak diseases, focusing on turnaround times for sample transport and laboratory procedures during previous outbreaks. Additionally, the study provided valuable insights for designing an optimized diagnostic network capable of promptly detecting and responding to outbreaks. The DNO analysis revealed that while the average transport time for LF samples met NCDC targets at 0.8 days, YF samples experienced a significantly longer transport time of 10.1 days, primarily due to delays during transportation from sample collection to sample hub. This disparity suggests differing specimen management practices at the local government area or health facility level. Implementing mitigative measures such as allowing cross-border transport or expanding hubs could alleviate long distances between health facilities and hubs, potentially reducing transport time. However, addressing variations in specimen management for YF samples would be crucial for optimizing overall transport efficiency. More studies and research are required to include all priority diseases which requires strengthened data systems and sample collection to provide a comprehensive report. DNO has the potential to offer a systematic and evidence-based approach to enhancing laboratory networks for epidemic-prone diseases.

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HEALTH SYSTEM STRENGTHENING THROUGH DATA QUALITY IMPROVEMENTS: A COMPARATIVE ANALYSIS OF HEALTH FACILITY DATA QUALITY PERFORMANCE FROM INITIAL ASSESSMENTS TO SUBSEQUENT VISITS

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Data quality assessments (DQAs) are crucial for ensuring reliable health information and effective healthcare management, aiding stakeholders to understand system strengths and weaknesses. Teams at state and local government levels were trained on malaria DQA processes and conducted routine assessments using the national malaria DQA checklist. The checklist was scripted on KoboCollect, and a PowerBi dashboard was developed to monitor health facility performance. The assessments focused on data availability, consistency, and validity. This study analyzes DQA trends over three years (2021-2023) across four Nigerian states—Benue, Nasarawa, Plateau, and Zamfara. A total of 2,239 HFs were visited, of which 480 (21%) and 70 (3%) received a second and third visit respectively. This aligns with the national DQA guideline that stipulates a minimum of 10% of visited HFs should be revisited. Data availability declined from 84% during the first visit to 82% in health facilities visited for a second time, then increased to 91% among those visited for a third time. The average consistency scores across the first, second, and third visits are 54%, 50%, and 55%, respectively, with a marginal increase observed across the second and the third visit. Consistency scores have been linked to transcription errors from client cards to OPD registers and non-use of client cards due to cost barriers for clients. The validity scores across the first, second, and third visits are 91%, 93%, and 96%, respectively, showing an increasing trend with the highest average score observed in the third visit. Implementation

of improvement plans and maintaining a steady supply of the National Health Management Information System Registers in the HFs are important requirements for data quality. Continuous training to dedicated DQA teams should be adopted to further improve the availability, validity, and particularly the consistency of data to ensure that decision-making, resource allocation, and program adaptation are based on reliable information.

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ETIOLOGY OF INFECTIOUS DIARRHEA IN MADAGASCAR: FINDINGS FROM THE COMMUNITY-BASED SURVEILLANCE SYSTEM FROM 2019 TO 2023

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Diarrhea remains the highest cause of morbidity and mortality among children under five years-old in South Asia and sub-Saharan Africa. Therefore, systematic collection and analysis of data on the etiologies of diarrhea in community settings are needed to prioritize interventions. Our work describes the first laboratory-based surveillance conducted in children under five years, contributing to enrich data on diarrheal etiology in community settings in Madagascar. A pediatric diarrhea surveillance network was carried out from 2019 to 2023 on 21 sentinel surveillance sites of Madagascar. Five children under five-year-old presenting > 3 loose stools in a 24-h period were enrolled weekly. Stool specimens were collected and analyzed by quantitative PCR for a panel of 4 viruses, 4 bacteria and 3 protozoa. Prevalence and seasonal patterns of diarrhea were determined. From 2019 to 2023, the surveillance system captured 1951 diarrhea cases. The median age was 1,3-years old. Of the 1951 stools tested, 1562 (80%) were positive for at least one pathogen. Among positives, 845 (43.3%) were infected with viruses, 1198 (76.7%) with bacteria, 280 (14.3%) with parasites and 947 (60.6%) had co-infections. Enteropathogenic bacteria *Escherichia coli* was detected in 855 (43.8%) stools followed by *Shigella* spp. in 496 (25.4%), *Campylobacter* spp. in 283 (14.7%). Rotavirus was the most prevalent virus detected in 533 (27.7%) stools, adenovirus in 205 (10.5%), astrovirus in 180 (9.2%) and norovirus GII in 101 (5.2%). *Giardia intestinalis* was the most prevalent parasite detected in 202 (10.4%) stools whereas *C. parvum* and *E. histolytica* were infrequent (3.7% and 0.9% respectively). We observed a seasonal pattern where diarrhea occurred during the hot-rainy and the dry-cold seasons. Detection of diarrhea reached its lowest during the inter-season of March and September. This work has, for the first time, described the etiologies of pediatric diarrhea in Madagascar and a sketch of their seasonal circulation. The data highlight the importance of strengthening laboratory capacity for rapid detection and for implementation of diarrhea control and prevention.

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IMPACTS OF BAD OBSTETRIC HISTORY ON ANTENATAL CARE UPTAKE IN SUBSEQUENT PREGNANCIES: INSIGHTS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS), BANGLADESH

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Women who suffer adverse pregnancy outcomes require extra care in subsequent pregnancies to ensure healthy outcomes for mother and baby. To understand whether adverse pregnancy outcomes influence subsequent health-seeking behavior, particularly antenatal care (ANC), we conducted an observational study using the Child Health and Mortality Prevention Surveillance (CHAMPS) data. It includes detailed pregnancy data with ANC histories from all pregnant women in Baliakandi, a rural subdistrict of Bangladesh. We defined a bad obstetric history if a mother had a history of either stillbirth, neonatal death, a child with a congenital anomaly, or ≥2 consecutive miscarriages. Mothers with a bad obstetric history and at least two pregnancy outcomes between January 2018 and January 2024 were included in this analysis. We compared ANC utilization between the pregnancy associated with the bad obstetric outcome and the subsequent pregnancy. A total of 137 mothers were included. In the first pregnancy, 35% received no ANC, increasing to 43% in subsequent pregnancy. However, no difference was found between the first and subsequent pregnancy in the proportion who received the first ANC visit within 12 weeks of pregnancy (31% vs 36%). In spite of an adverse outcome, 43% received ANC from qualified doctors in the first pregnancy, and this decreased to 39% in subsequent pregnancy. Additionally, the proportion completing 4 ANC visits decreased from 17% to 10%. Only 7% mothers in 1st pregnancy and 4% mothers in the 2nd pregnancy took ≥4 ANC from qualified doctors. However, the mean number of ANC visits in the first and subsequent pregnancy remained almost similar (2.4 ± 1.9 vs 2.0 ± 1.3). We have found that mothers with bad obstetric history had less ANC uptake compared to their subsequent pregnancies from qualified health care providers. In addition, few mothers took the recommended 4 ANC visits, which is alarming. Different sociodemographic factors may be responsible for this. However, future research should be directed toward identifying the challenges and developing interventions to encourage mothers to utilize government health facilities to ensure quality ANC.

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DENGUE PREPAREDNESS. FRAMEWORK FOR INNOVATIVE TOOLS AND STRATEGIES FOR SURVEILLANCE AND RESPONSE IN OIL AND GAS COMPANY

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The World Health Organization (WHO) in 2023 reported half of the world's population is at risk of dengue, estimating 100-400 million infections each year. *Aedes aegypti*, one of the main vectors for dengue, has an indoor and outdoor day biting pattern. ExxonMobil (EM) has a global workforce with some resident workers and travelers in remote high-risk areas. EM surveillance and evidence-based driven decision led to the development of a global Dengue Control Program, which includes health risk assessments, increased awareness, bite prevention, prompt diagnosis and treatment. Additional strategy includes pre-travel preparation, preventive measures to minimize disease risk, serious illness events, health costs, and business disruption. A retrospective review of case trends and program implementation allows a multidisciplinary approach of a sustainable dengue control program. Regular clinician training on vector-borne diseases such as dengue fever with ongoing review of suitability and availability of dengue vaccines in high-risk areas to ensure current knowledge for appropriate

guidance to travelers. Optimized pre-travel preparation using an innovative tableau travel health dashboard that shows country specific health risks and travel requirements. GeoSentinel Surveillance Network studies in travelers have found dengue as the leading cause of febrile illness among ill travelers returning from Southeast Asia, Latin America, and the Caribbean. Increased emphasis on awareness has shown a steady use of preventive materials. Global business locations are evaluated by required facility specifications, environmental management, and surveillance to ensure program compliance. The Company pretravel preparation ensures 100% identification of risk locations and documentation of risk reviews in the travel health dashboard for clinicians and employees. Dengue disease burden has expanded globally. A robust surveillance and technology embedded in company dengue control program provides guidance and sustainable mitigation tools to reduce serious illness event and support evidence-based priorities in traveler health.

6948

ADVANCING MALARIA CARE THROUGH VARIED INTERVENTIONS: IMPROVING MALARIA RAPID DIAGNOSTIC TEST (RDT) USE IN FOUR NIGERIAN STATES - BENUE, NASARAWA, PLATEAU, AND ZAMFARA

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Inaccurate malaria diagnosis and treatment increase disease burden and drive potential drug resistance. In 2020, 180,394 (18%) fever cases were clinically diagnosed as malaria by assessing symptoms without a confirmatory parasitological test in four States: Benue, Nasarawa, Plateau and Zamfara. WHO recommends Rapid Diagnostic Tests (RDTs) for malaria diagnosis before treatment in areas with limited access to malaria microscopy due to their simplicity and rapid results. The U.S. President's Malaria Initiative for States (PMI-S) aims to improve malaria case management (MCM) by increasing RDT use through various interventions (training, guidelines, RDT availability and supervision). Data from health facilities' (HFs) mentoring visits at baseline (December 2020) and regular follow-up supervisory visits from August 2022 to December 2023 were analyzed. Through collaboration with the supply chain implementing partner, RDT availability increased from 45 to 512 HFs, and RDT use increased from 152 healthcare workers (HCWs) in 73 HFs to 1008 HCWs in 616 HFs. PMI-S increased the availability of MCM job aids, standard operating procedures (SOPs) and revised national guidelines from 30 HFs to 491 HFs. PMI-S advocated for and supported regular supervisory visits by trained government staff to 614 HFs. The increased use of RDTs reflects better adherence to national guidelines, which call for parasitological confirmation of malaria, and reduced clinical diagnoses, which dropped to 2% in December 2023. The availability of jobs aids, the enhanced competence in utilizing RDTs, and the continuous supervisory visits resulted in better diagnosis, and, therefore, appropriate treatment for confirmed cases.

6949

OPTIMIZING THE END OF CYCLE (EOC) REPORTING FOR SEASONAL MALARIA CHEMOPREVENTION (SMC) CAMPAIGN IN ZAMFARA STATE, NIGERIA

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Zamfara state has been implementing seasonal malaria chemoprevention (SMC) campaigns amidst security challenges which makes reporting and follow ups to facilities with data quality issues difficult, affecting the timeliness of reporting SMC data. The SMC campaign in 2023 included end of cycle (EOC) meetings, occurring 2 days after completion of each cycle of the mass drug administration (MDA). This study aims to assess the effectiveness of introducing a data aggregator system in the EOC meeting to aggregate data across 599 HFs in 14 Local Government Areas (LGAs) of Zamfara State. The Android-based tool enabled LGA data officers to validate SMC MDA data during the EOC meeting, using logical checks. The true figures were confirmed from the primary source document (tally sheet) and corrected. Validated entries were securely transmitted to the central server then exported to the backend view where the data is managed and processed. The system conducted secondary deduplication and data cleaning using unique identifiers. The non-duplicate entries were sorted and displayed on each LGA visualization accessible through a secure web interface. The system generated state and LGA aggregate preliminary reports tables and charts of children reached and treated. Compared to the 2022 cycle 1 baseline of 7% data quality issues requiring retrospective correction, all four 2023 SMC cycles achieved 0% data quality issues upon EOC submission. Reporting timeliness improved from 7 working days (2022) to just 2 days (2023) after each SMC MDA cycle. The EOC meeting approach improved data quality by creating a dedicated time and space close to the end of each SMC cycle, to validate, consolidate, and correct erroneous data discovered during data validation at the EOC meeting. Additionally, the use of an Android tool for the data validation enabled faster correction at the point of validation and reliability of SMC data, reduced security risk and travel to facility costs for correction of data and eliminated human errors typical of paper-based tools. This further exemplifies the potential for automated, real-time EOC reporting and validating tools.

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IMPLEMENTATION OF AN APPROACH TO INTEGRATE COMMUNITY HEALTH INTERVENTIONS INTO COORDINATION, MONITORING AND EVALUATION AT THE HEALTH DISTRICT LEVEL IN CÔTE D'IVOIRE

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In Côte d'Ivoire, the coordination and monitoring of community activities is mainly carried out by civil society organizations (CSOs) under contract with international NGOs. The end of these contracts usually leads to partial or total cessation of activities, and access of populations to basic health care. Since 2021, the PMI Stop Djekoidjo project has initiated an approach aimed at increasing local ownership of the coordination, monitoring and evaluation of community health worker (CHW) activities in 29 health districts. The process encompassed 1) development and validation of an operational document, 2) identifying a Community Activities Coordinator (CAC) in each district, 3) training CACs on their job description and entry of data into DHIS2, 4) support for the supervision of CHWs), and 5) organization of coordination meetings with CACs. From January 2021 to December 2023, CHWs recorded data on fever case management for children under five years of age living in communities beyond five km from a health center. Data from all CHWs in the health area were then compiled into a report and forwarded to the health district and entered DHIS2 by the CAC. Data completeness is the percentage of expected CHWs reports submitted in DHIS2.1,600 CHWs were operational during the 2021 to 2023 period. The completeness of data entered DHIS2 increased from 75.3% to 98.6% between 2021 and 2023. The number of fever cases recorded by these CHWs increased by 57.6%, from 76,269 in 2021 to 120,206 in 2023. In addition, the proportion of fever cases tested by rapid diagnostic test increased from 73% in 2021 to 89% in 2023, and positive cases treated with artemisinin-combination therapy increased from 91% in 2021 to 98% in 2023. Despite the withdrawal of CSOs, there has been a gradual increase in the volume of CHW activities between 2021 and 2023. The completeness of data and management of fever cases improved after the introduction of CACs. Thus, the approach appears to be an efficient strategy for consideration in the context of resource scarcity and sustainability of services to the communities.

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PROJECTING *IXODES SCAPULARIS* DENSITIES OF INFECTED NYMPHS (DIN), IN EASTERN UNITED STATES, 1997-2022

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Ixodes scapularis is the primary vector of *Borrelia burgdorferi* sensu lato (*Bbsl*), the causative agent of Lyme disease (LD) in the United States. Risk for LD can be partly quantified by the densities of infected *I. scapularis* nymphs (DIN), a metric of the ecological hazard across areas. We predicted DIN across parts of the Eastern US using meta-analytic models trained on published data. Two systematic literature searches were conducted in PubMed to identify studies published between 1 Jan 2000 and 23 Aug 2023 that measured density of nymphs (DON) and prevalence of *Bbsl* infection in nymphs (NIP) in the 25 states and DC categorized as high-incidence (>10 LD cases/100,000 population) or neighboring high-incidence jurisdictions in 2022 CDC surveillance data. Studies that reported county-level DIN per unit area and NIP were included. Separate multivariate, linear mixed effects models were fit for DON and NIP. Significant ($p<0.05$) model covariates included latitude and longitude, proportion of wild-urban interface, proportion of forested area, white-tailed deer density, presence of *I. scapularis,* LD incidence, and geographic division (US Census). Best fitting models were chosen via Akaike information criterion and used to predict DON and NIP across all counties in the 25 states and DC. Predicted DIN was calculated as the product of predicted DON and predicted NIP. The literature review yielded n = 934 DON observations (26 studies) and n = 845 NIP observations (57 studies). Most observations for both DON and NIP were in the Northeast and reported by two multi-year, multi-county studies. Observations for DON had wider geographic coverage (96% of jurisdictions) than observations for NIP (81% of jurisdictions). DON was predicted to be highest in parts of NY, NJ, PA, and WI and moderately high in the Mid-Atlantic and East North Central. NIP was predicted to be highest in the Northeast and parts of MN, MI, and WI. DIN was thus highest in the Mid-Atlantic. This study demonstrates the utility of existing published data on *I. scapularis* populations that can be used to inform ecological hazard of LD, but also highlights the spatial and temporal limitations of these data.

6952

A SIMPLE AND SENSITIVE COLORIMETRIC NUCLEIC ACID TEST FOR *BABESIA MICROTI* SURVEILLANCE IN WHOLE BLOOD AND TICK VECTORS

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Human babesiosis is a disease of increasing public health importance resulting from infection of red blood cells by protozoan parasites of the genus *Babesia*. The parasite is primarily transmitted to humans by *Ixodes* ticks and can also be transmitted through contaminated blood transfusion. We have developed a simple and sensitive RT-LAMP assay with colorimetric readout for the detection of *Babesia microti* targeting the 18S rRNA gene. The assay simultaneously detects both RNA and DNA and shows higher sensitivity than published qPCR assay. The assay showed no cross-amplification with DNAs from *Homo sapiens*, *Ixodes scapularis*, *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, or *Plasmodium falciparum*. The visual colorimetric detection of this isothermal LAMP assay eliminates the need for sophisticated equipment. In addition, its high tolerance to inhibitors enabled us to develop a direct blood protocol without the need for nucleic acid extraction. Using this assay, we also conducted surveillance of 332 *I. scapularis* collected at Ipswich in Massachusetts (USA), and New Hampshire (USA) for *B. microti*, in parallel with LAMP-assays detecting *B. burgdorferi* and *A. phagocytophilum.* We found 18% (27 of 152) of Ipswich and 7% (13 of 180) of New Hampshire ticks positive for *B. microti*. Our results demonstrate that this simple colorimetric nucleic acid test is suitable for *Babesia microti* surveillance in whole blood and tick vectors.

6953

DISENTANGLING THE RELATIONSHIP BETWEEN THE DEER TICK MICROBIOME AND TICK-BORNE PATHOGENS

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Tick-borne diseases are a growing threat to public health worldwide, further exacerbated by their range expansions. Aside from known pathogens, ticks also carry a wide variety of other infectious and non-infectious organisms. We aimed to catalog the full spectrum of bacteria present in deer ticks (*Ixodes scapularis*) and the effect of biotic factors such as tick sex, geographic region, and presence of known pathogens on microbiome composition. We sequenced the V4 region of the bacterial 16S rRNA gene from about 300 individual *I. scapularis* ticks from Massachusetts and New Hampshire. A total of 1.63 billion reads were obtained from runs on a Illumina NovaSeq instrument, providing a median depth of 5.6 million reads per sample. Microbiome analysis using the QIIME2 pipeline and Deblur algorithm identified a total of 24,070 bacterial Amplicon Sequence Variants (ASVs) across all samples. A rarefaction curve analysis determined that a minimum sample read count of approximately 125,000 is needed to capture the full spectrum of bacterial diversity in over 90% of our tick samples. Beta diversity analyses and significance testing across all samples indicate that the sex of the tick, geographical region, and *Borrelia burgdorferi* (Lyme disease) infection status are key drivers of tick bacterial microbiome composition. We observed previously unreported correlations between the presence of *Borrelia* and certain microbiome members, including bacteria with pathogenic potential, such as *Mycobacterium* and *Roseomonas*. The microbiome members found to be highly associated with *Borrelia* warrant further study to determine their role in disease.

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COINFECTION OF *ANAPLASMA PHAGOCYTOPHILUM* AND *BORRELIA BURGDORFERI* IN NON-HUMAN PRIMATES. IMPACT ON IMMUNE RESPONSE AND DISEASE SEVERITY

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Anaplasma phagocytophilum (Ap) and *Borrelia burgdorferi* (Bb), the agents of Human Granulocytic Anaplasmosis (HGA) and Lyme disease, respectively, are transmitted by *Ixodes scapularis* ticks. Coinfection has been reported in humans and animals. Ap preferentially infects the neutrophils, which are critical for clearing Bb infection. Severe Combined Immune Deficient (SCID) mice have higher Bb tissue load and pathology and are susceptible to Ap infection, which persists for several months. Nonhuman primates (NHPs) are the most relevant animal models for translational diagnostic and therapeutic intervention due to their susceptibility to both pathogens and reproduction of human disease. Our overarching goal is to study the effect of coinfection in NHPs, but we first investigated concurrent Ap/Bb infections and transmission to uninfected mice. We infected immunocompetent mice with Bb culture and Ap-Infected HL60 (human promyelocytic leukemia) cells via syringe inoculation and confirmed infection of larval ticks. Transmission of both pathogens to uninfected mice through those ticks, post-molt into nymphs, was subsequently demonstrated. We evaluated coinfection using conventional PCR by targeting the *Msp2* gene in Ap, blood smear, immunofluorescence (IFA), and cell culture for Bb. Bb was detected in the ears, heart, skeletal muscle, tibiotarsal joints, spleen, and bladder, while Ap was detected in the blood, liver, and spleen of coinfected and Ap-infected mice. We will propagate Ap in SCID mice and capillary-feed the infected blood to nymphs to generate infected ticks as well. We will use infected ticks to assess coinfection in NHPs by determining pathogen burden in blood and tissues utilizing qPCR, IFA and blood smear. Gross and histopathology, immune responses using flow cytometry, serum cytokine profiles and antibody responses will be assessed. Based on previous studies, we hypothesize that the coinfected NHPs will have a higher bacterial burden, significantly reduced immune response, and more severe tissue pathology than the single-pathogen-infected groups.

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HEMOPLASMA AND PIROPLASM SPECIES IN WHITE-EARED OPOSSUMS (*DIDELPHIS ALBIVENTRIS*) FROM ALAGOAS, NORTHEASTERN BRAZIL - PRELIMINARY DATA

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The presence of marsupials in domestic environments is relevant for public health purposes, with species of hemotropic *Mycoplasma* (hemoplasmas, HM) and piroplasms known to infect domestic and wild animals, including *Didelphis*. This study aimed to molecularly characterize HM and piroplasm species in white-eared opossums (*Didelphis albiventris*) from transitional areas between the Atlantic Forest and Caatinga biomes in the State of Alagoas, northeastern Brazil. DNA was extracted from EDTA-blood samples from 30 (19 males and 11 females) white-eared opossums using a commercial kit. DNA samples were initially screened by a SYBR Green Universal Real-Time PCR (qPCR) targeting the 16S rRNA gene of HM. Samples were also screened by a nested-PCR (nPCR) assay targeting a fragment of the 18S rRNA gene of piroplasms. Four out of 30 (13.33%, 95% CI 5.31-29.62%) animals tested positive for HM and piroplasms, with one animal was co-infected by both agents. Hemoplasma-positive samples were subjected to conventional PCR assays targeting a fragment of the 16S rRNA (~900 bp) and 23S rRNA (800 bp) genes, followed by Sanger sequencing. Sequencing of both the 16S and 23S rRNA genes revealed that the animals were infected by '*Candidatus* Mycoplasma haemoalbiventris'. Piroplasm 18S rRNA gene sequences showed 100% identity with *Babesia* sp. from *D. albiventris* from Brasília, central-western Brazil (MW290046). Phylogenetic analyses using Bayesian inference revealed the detected *Babesia* sp. formed a polytomy with piroplasm sequences detected in marsupials from Brazil, reinforcing the existence of the piroplasmid clade "South American Marsupialia". Our future steps involve sequencing other gene fragments (*cox-1*, *cox-3*, and *hsp70*) to confirm our preliminary findings. This is the first of *Babesia* sp. in white-eared opossums from Northeastern Brazil.

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POTENTIALLY NOVEL *EHRLICHIA* SP. IN WHITE-EARED OPOSSUMS (*DIDELPHIS ALBIVENTRIS*) FROM ALAGOAS, NORTHEASTERN BRAZIL-PRELIMINARY DATA

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The genus *Didelphis*, comprising synanthropic marsupials, is known to host various vector-borne agents, including tick-borne bacteria. Here, we detected a potentially novel *Ehrlichia* spp. in white-eared opossums (*D. albiventris*) in transitional areas of the Atlantic Forest and Caatinga biomes in Alagoas, northeastern Brazil. DNA was extracted using a commercial kit from EDTA-blood samples from 30 (19 males and 11 females) white-eared opossums. DNA samples were initially screened by a nested-PCR (nPCR) assay targeting a fragment of the *dsb* gene of *Ehrlichia* sp. A total of 24/30 (80%; 95% CI: 62.69 - 90.49%) white-eared opossums tested positive for *Ehrlichia* spp. by the *dsb*-nPCR assay. After that, *Ehrlichia*-positive samples were subjected to a PCR targeting a fragment (~844 bp) of the *groEL* gene of *Ehrlichia*, followed by Sanger sequencing. Seven DNA samples were sequenced. *Ehrlichia groEL* gene sequences obtained herein showed 93.77% identity with *Ehrlichia* sp. from *Ornithodoros capensis* of birds from Japan (LC649942). Phylogenetic analyses using Bayesian inference revealed the detected *Ehrlichia* grouped in a single clade, suggesting the white-eared opossums were infected by a putative new *Ehrlichia* sp. species. A total of six/30 white-eared opossums were infested by larvae of *Ornithodoros mimon* ticks at the time of sampling. We report a potentially novel *Ehrlichia* species in white-eared opossums from Alagoas, northeastern Brazil. Our future steps involve sequencing other gene fragments (16S rRNA, *dsb*, *sodB,* and *gltA*) to confirm our preliminary findings.

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HUMAN HEALTH DISPARITIES IN MITE-BORNE ILLNESSES

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Mites transmit bacterial infections, such as scrub typhus and rickettsialpox, and cause chronic infestations, such as crusted and nodular scabies. Secondary infections cause impetigo, rheumatic fever, and glomerulonephritis. Mite-borne allergens cause asthma and anaphylaxis. Some populations are disproportionately affected by mite-borne illnesses. Several Internet search engines were queried to identify the most significant population-level risk factors for mite-borne illnesses. There are several human health disparities in mite-borne illnesses characterized by either reduced host immunocompetency or excessive mite exposures. Immunocompetency levels wane with advancing age, viral infections, especially HIV and HTLV-1, cancer and chemotherapy, corticosteroid and transplant antirejection therapy. Excessive mite exposure levels occur in crowded venues including shelters for refugees, evacuees, and the homeless, chronic care institutions, sexually transmitted disease clinics,

animal shelters and veterinary clinics, and food and fruit-processing workplaces. Some populations may be uniquely predisposed to crusted scabies and secondary infections including patients with Down syndrome, other cognitive disabilities, Australian Aborigines, and the indigenous inhabitants of the Fijian, Samoan, and Solomon islands in the South Pacific. Others may be exposed to animal scabies or plant, insect, and foodborne mite infestations in their workplaces. Targeted interventions to control and prevent mite-borne illnesses should be directed at these neglected populations and excessive exposure groups worldwide.

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A NEW MULTIPLEX SEROLOGIC ASSAY FOR DETECTION OF *BARTONELLA* SPECIES IN IRAQ DEPLOYED MILITARY WORKING DOGS

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Bartonella species seroprevalence was 47.4% in feral dogs in Iraq; blood collected by the U.S. Army Zoonotic Disease Surveillance Program in 2008-9. *Candidatus* Bartonella merieuxii *(C*bm*)* DNA, an uncultured *Bartonella* species, was amplified from 37% of Iraq feral dogs` blood. The objectives of this surveillance study were 1) to define the prevalence of bartonellosis in military working dogs (MWDs) that had deployed to Iraq, 2) to report the species profile. Medical records and paired sera/whole blood samples were obtained from pre and post Iraq deployment for 104 MWDs. Conventional diagnostic testing for *Bartonella* species was performed including Indirect Immunofluorescence Assay (IFA) for *B. bovis, B. henselae, B. koehlerae* and *B. vinsonii berkhoffii* with ≥ 1:64 considered seroreactive. *Bartonella* genus *rpoB* gene qPCR assay was conducted using whole blood DNA, with amplicon sequences compared to GenBank by BLAST analysis. Fifty paired sera were evaluated by Mesoscale/MSD V-PLEX™ platform using a new 10-plex assay with a total of 20 peptides representing B cell linear epitopes predicted by the Bepipred algorithm (Immune Epitope Database iedb.org). The studied population (n=104 MWDs) showed no significant clinical differences in those testing positively for *Bartonella* acquired in Iraq except for a decrease in white blood cells, *p=0.032*. Twelve dogs (12%) were IFA seroreactive for any *Bartonella* spp. including four dogs (4%) IFA seroreactive to the *C*Bm surrogate (*B. bovis)* with titers 1:128 or 1:1024. *Bartonella* genus-specific qPCR assay identified Iraq-related infection of one (1%) MWD with sequencing of *rpoB* gene determined to be *C*Bm with 99.9% sequence homology. In the new Mesoscale assay 15 MWDs (30%) showed statistical differences between pre and post deployment sera (p<0.001), suggesting seroconversion during deployment (luminescence signal post/pre >2). In conclusion, MWDs acquired novel *Bartonella* spp. infections during deployment in Iraq and our newly developed MSD assay can serve as a new diagnostic tool providing an alternative high-throughput assay.

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SEVERE TICK-BORNE DISEASE IN NORTH CAROLINA, A TEN-YEAR REVIEW OF HOSPITALIZED CASES

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Tick-borne diseases such as spotted fever group rickettsiosis (SFGR) and ehrlichiosis are a growing public health concern in the United States. Clinical manifestations are non-specific and include fever, arthralgia, diarrhea, headache, and rash. Delays in treatment are strongly associated with morbidity and death. Yet other demographic and clinical risk factors associated with severe disease remain poorly described. Utilizing a retrospective cross-sectional design, we performed a 10-year review of ehrlichiosis and SFGR cases admitted to the University of North Carolina health system from 2014 to 2024 to identify factors associated with severe disease. A total of 242 admissions from 239 unique individuals with a diagnosis of ehrlichiosis (N=30), SFGR (N=204), or both (N=8) were included in this study. The median age was 55 years (IQR 37-67), with most participants identifying as white (186, 76.9%), non-Hispanic (221, 91.3%), and male (161, 66.5%). Over 88% (N=214) of cases occurred between April and October. Twenty-two percent (N=55) had some form of immunocompromise including asplenia, bone marrow or solid organ transplant, cancer, chronic dialysis, neutropenia, or human immunodeficiency virus. Nearly 15% (N=35) were admitted to the ICU, with 27/35 (77%) having SFGR. Approximately 10% (N=24) required mechanical ventilation. The average number of days from admission to doxycycline administration was 2.2, though the use of doxycycline was not significantly higher among patients requiring ICU care (OR 0.8, 95% CI: 0.3-1.9). Risk factors for ICU admission included underlying pre-existing cardiovascular disease (OR 4.4, 95% CI: 2.1-9.2), diabetes mellitus (OR 2.1, 95% CI: 1.0-4.4), and male sex (OR 2.7, 95% CI: 1.1-6.9). However, older age (e.g. >65 years) and immunocompromised status were not statistically associated with ICU care. Our results show that diabetes and cardiovascular disease may be risk factors for severe
ehrlichiosis or SFGR and there should be a low threshold to administer doxycycline in these high-risk groups when consistent symptoms, laboratory abnormalities and/or exposures are present.

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MINIMUM FEEDING TIME REQUIRED FOR *HAEMAPHYSALIS LONGICORNIS* TO TRANSMIT SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS

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Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV) is an emerging tick-borne bandavirus that can cause disease in humans with a 6-30% mortality rate. The major tick vector of SFTSV is *Haemaphysalis longicornis*, which is native to eastern Asia but recently emerged in the United States. Emerging viruses and invasive tick species highlight the importance of understanding how a virus such as SFTSV associates with and is transmitted by its tick vector. A notable factor in this tick-pathogen association is the minimum tick attachment time required for the tick to successfully transmit a pathogen during feeding. This transmission time is understood for some bacteria but for many tick-borne viruses, including SFTSV, this tick-to-host transmission time is unknown. The objective of this study is to define the minimum feeding time required for *H. longicornis* nymphs to transmit SFTSV to a vertebrate host. Nymphs were infected with SFTSV by transovarial transmission to generate a population of infected ticks to be used in the tick-to-host transmission time experiments. In a pilot study, mice were each infested with 8 - 10 putatively infected nymphs that were allowed to feed for 5 hours. At the 5 hour post-attachment (h.p.a.) timepoint, nymphs were manually removed from mice and screened via q-RT-PCR for SFTSV RNA. Samples of mouse blood and skin biopsies (proximal and distal to the tick feeding site) were also collected at 5 h.p.a. and screened for viral RNA. SFTSV RNA was detected in the proximal skin biopsies from several mice. These preliminary results suggest that after feeding for 5 hours, SFTSV-infected *H. longicornis* nymphs were able to transmit SFTSV to mice; however, detection of infectious virus in the vertebrate host still needs to be assessed. Follow-up studies will assess tick feeding timepoints less than 5 hours. Methods to pre-screen putatively infected nymphs for SFTSV before they are included in the transmission experiment are also being optimized. In upcoming tick-to-host transmission time experiments, this optimized model system will be used to define the minimum feeding time required for *H. longicornis* nymphs to transmit SFTSV to a host.

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INVESTIGATION INTO THE BACTERIOME OF TICKS COLLECTED FROM NINE KENYAN COUNTIES.

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Vector surveillance has become a very important component in public health preparedness. Continuous and rigorous screening of vectors such as ticks allows for up-to-date pathogen situational awareness. This study sought to enhance the knowledge of bacterial pathogens circulating in ticks from Kenya by sampling and screening ticks from nine counties representing major regions in the Country. These are representative of the North-eastern, Coastal, Western, and the Rift Valley region. These were selected to represent a wide variety of climatic and socio-economic zones thus generating a clearer picture of the situation in the country. 16S rRNA metagenomic sequencing on the MinION (Oxford Nanopore Technologies) platform was used to screen the ticks. Bioinformatics analysis involved base-calling, adapter trimming and demultiplexing using Dorado, quality trimming and filtering using Trimmomatic, deduplication, chimaera filtering and OTU clustering using QIIME2-VSearch. Taxonomic classification of the representative sequences was done using a Bayes classifier that was trained on 16S rRNA sequence data from the SILVA 138 database. 1,562 ticks were collected, surface sterilized and pooled into 251 pools with an average of 6 ticks per pool. The ticks collected belonged to 3 genera and 14 species. 237 bacterial species were identified in the ticks and of these, 78 species were identified as pathogens and opportunistic pathogens. The top 5 pathogens with the highest Minimum Infectivity Rate (M.I.R) were *Staphylococcus pseudintermedius* (6.91%), *Staphylococcus aureus* (6.85%), *Rickettsia africae* (3.65%), *Coxiella burnetii* (3.59%) and *Rickettsia japonica* (3.20%). The diverse nature of bacteria identified both pathogens and non-pathogens is proof that ticks are complex arthropod vectors that offer a rich source of emerging and re-emerging infectious diseases. Further investigation needs to be done to determine which of these pathogens are viable and subsequently transmissible. This study greatly contributes to public health awareness within the country.

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HOUSEHOLD INSECTICIDE USE AND REAT FLEA RESISTANCE IN MADAGASCAR: IMPLICATIONS FOR PUBLIC HEALTH

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In Madagascar where bubonic plague, a flea-borne disease, is endemic, there is a gap in knowledge regarding household pest control that may impact health and insecticide resistance in vectors. In this study, we investigated 254 households distributed in seven villages within three districts in plague-endemic areas of Madagascar to understand the pattern of insecticide use in homes and to assess rat flea (*Xenopsylla cheopis*) susceptibility to insecticides. Here we present the results from household surveys and insecticide bioassays. We found that insecticide was the most common means for domestic pest control for 91.66 % of respondents, primarily targeting the house flea (80.11%). Most applied liquid formulations (78.41%),and 62.50% used insecticides without dilution. Bedrooms (90.90%) and floors (89.78%) were primarily treated. Only 46.02% of respondents were satisfied with the treatment results. Products were bought from outdoor market vendors (38.64%) or agricultural stores (31.25%). Retailer advice (55.68%) and neighbors' opinions (21.02%) guided insecticide selection. Retailers provided most (84.65%) information on insecticide usage. Yet, 39.54% of respondents could not recall the commercial name of the insecticide used, given that only 26.13% bought labeled products. Laboratory insecticide bioassay revealed widespread resistance to DDT (mortality rate, MR: 0 - 7.50%) and deltamethrin (MR: 0 - 42.50%) among rat fleas from these villages. Flea populations were tolerant (MR: 82.8 - 95.10%) and susceptible (MR: 97.60 -100%) to fenitrothion, with only fleas from one village showing resistance (MR: 45%). The significant reliance on insecticide to control household pests and limited product knowledge pose a risk for health and may contribute to the development of resistance in non-target insects such as the plague vector, *X. cheopis.* Our findings suggest that interventions focused on retailers (i.e., education, incentives) would equip households with accurate pesticide knowledge. Addressing these challenges is imperative for safeguarding public health and mitigating insecticide resistance.

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*COXIELLA BURNETII*I N RUMINANTSAND DONKEYS *(EQUUS ASINUS)* FROM SOMALIA

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Coxiella burnetii, a zoonotic obligate intracellular bacterium that causes Q fever in humans and coxiellosis in ruminants, may pose significant economic losses and health risks. Understanding its epidemiology is paramount for implementing effective control measures. Our study investigated the presence of *C. burnetii* in ruminants and donkeys in Somalia using serological and molecular techniques. Serum samples from 402 animals (190 goats, 133 cattle, 49 sheep, and 30 donkeys) in the Benadir and Lower Shabelle Regions of Somalia underwent testing using the Indirect Fluorescent Antibody Test (IFAT) against *C. burnetii* strain At12. IgG titers for each *C. burnetii* antigen were determined by diluting the samples in two-fold increments with phosphate-buffered saline (PBS), starting at a 1:64 dilution. DNA was extracted from EDTA-blood samples (199 goat, 131 cattle, and 45 sheep) and screened using a qPCR assay based on the repetitive element IS1111 for *C. burnetii.* A total of 53**/**402 (13.2%) animals (endpoint titer: 64 – 8.192) showed antibodies reactive to *C. burnetii.* Donkeys exhibited seroreactivity 6/30 (20%) (endpoint titer: 64 – 512), goats 40/190 (21.1%) (endpoint titer: 64 – 2.048), and sheep 7/49 (14.3%) (endpoint titer: 64 – 8.192), while cattle showed negative results. Two goats tested qPCR-positive for *C. burnetti*. All other animals tested qPCR-negative. This study confirms the presence of anti-*C. burnetii* antibodies in Somali livestock (goats, sheep, and donkeys). Our data highlighting its potential impact on animal and public health through zoonotic transmission. Further investigation into the epidemiology of *C. burnetii* in Somalia and the development of targeted control measures are needed.

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SEROPREVALENCE OF *RICKETTSIA* SPP. IN CATTLE, SHEEP, GOATS AND DONKEYS (*EQUUS ASINUS*) FROM SOMALIA

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Rickettsia spp. are gram-negative obligate intracellular bacteria, with *Rickettsia africae* being transmitted by *Amblyomma* ticks and posing a zoonotic risk, notably causing African tick bite fever (ATBF). Livestock and donkeys (*Equus asinus*) play vital roles in Somalia's economy, facing tick-borne disease risks. Our study investigates rickettsial exposure in livestock and donkeys across two bioclimatic regions in the country. A cross-sectional study collected 402 (190 goats, 133 cattle, 49 sheep, and 30 donkeys) serum samples from Benadir and Lower Shabelle regions of Somalia. Immunofluorescence assays (IFA) were conducted using crude antigens of *R. africae* and *R. rhipicephali*. Sera were diluted in two-fold increments with phosphate-buffered saline (PBS) starting at a 1:64 dilution, and endpoint IgG titers for each *Rickettsia* antigen were determined. A total of 212/402 (52.7%) (endpoint titer: 64–2.048) samples were seropositive for *Rickettsia* spp. *R. africae* was predominant in 20.9% of cases, while *R. rhipicephali* was detected in 9.9%. Co-reactivity was observed in 21.9 percent of the samples. Cattle showed the highest seroreactivity at 90.2%, primarily with *R. africae* (50.4%), followed by goats at 27.4%, primarily with *R. rhipicephali* (18.9%), and sheep at 28.6%, mainly with *R. africae* (18.4%). Donkeys showed 83.3% seroreactivity, mainly to *R. africae* (23.3%). Co-reactivity was prevalent across species. Cattle, donkeys, and sheep were more likely to be seroreactive to *Rickettsia* spp. than goats (OR: 24.5, 13.2, and 1.1, respectively). This study reveals the first serological evidence of *Rickettsia* sp. in Somali ruminants and donkeys, emphasizing the importance of investigating tick-borne diseases within the One Health framework.

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ELUCIDATING THE TICK MICROBIAL PROFILE IN DISTINCT ECOLOGICAL REGIONS OF EAST AFRICA

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In Africa, where pastoralism is pivotal in the economy, the interaction between ticks and humans may be more significant than initially perceived. Pastoralism contributes to the stability of many African economies, accounting for a significant portion of the Gross Domestic Product (GDP) in countries where it is practiced. These regions are crucial economic hubs and are home to a significant portion of the country's livestock and wildlife. One of the key challenges and threats faced by these pastoralist communities is the increasing risk of animal and zoonotic diseases. This risk poses a significant danger to both the livelihoods of pastoralists as well as their health. To identify habitats with increased transmission of tick pathogens in East Africa, we sampled ticks in six districts of Uganda and four Kenyan counties in high-intense pastoralist farming regions with distinct ecology. We carried out an Illumina sequencing of tick singletons in the 16S V3-V4 hypervariable rRNA region. The microbial abundance and diversity were assessed. Our findings identified diverse microbes of significant public health concern circulating in ticks collected from the East African region. These microbes were not geographically clustered in unique regions but were identified across the different ecological regions. Our findings demonstrate a high incidence of tick-borne pathogens in the East African pastoralist zones. The factors driving tick-borne pathogen transmission in different habitats of East Africa are not well understood. There is a need to better define these factors to prevent tick-borne pathogen epidemics in Africa and global spillover.

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EFFICACY OF TWO DOSES OF IVERMECTIN TABLET IN TREATMENT OF SCABIES IN COMPARISON TO ONCE APPLICATION OF 5% PERMETHRIN LOTION- A RANDOMIZED CONTROLLED TRIAL

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Scabies may cause community outbreaks without early diagnosis and appropriate treatment. Oral ivermectin offsets some challenges associated with topical permethrin 5% application for treating scabies. We aimed to evaluate the efficacy of two doses of oral ivermectin [200 microgram/kg] on day one and day seven compared to 5% [weight/volume] once whole-body application of permethrin lotion in treating scabies. We recruited one hundred participants with mild or moderate scabies and randomized into ivermectin and permethrin arms using computer-generated sequences. Participants and their contacts in the ivermectin arm received two doses of ivermectin [200 micrograms per kg] on days one and seven. The participants and their contacts in the permethrin arm received treatment with 5% [w/v] permethrin application over the whole body. The participants were followed up after four to six weeks of the intervention to determine the cure rate. Institutional ethics approval was obatined from Institutional Ethics Committee of All India Institute of Medical Sciences, Bhubaneswar [IEC reference number: T/IM-NF/CM&FM/21/149]. The trial was registered in ctri.nic.in (CTRI/2022/03/040762) prospectively. We got a similar cure rate (100%) in both arms for the patients after one dose of whole-body application of permethrin or two appropriate doses of ivermectin among mild to moderate cases of scabies. The cost was lower in the ivermectin arm than in the permethrin arm. The cure rate of scabies with one local application of 5% permethrin lotion and two doses of oral ivermectin tablets is similar. Ivermectin has an added advantage regarding lower cost and convenience in its usage.

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CORRECT KNOWLEDGE, ATTITUDES, AND CONFIDENCE FOR APPROACHING RICKETTSIOSIS IN A SAMPLE OF MEDICAL STUDENTS IN CLINICAL SCIENCES FROM ENDEMIC AND NON-ENDEMIC REGIONS OF MEXICO

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Medical diagnosis is commonly guided by clinical and epidemiological evidence and experience. Anamnesis is fundamental to identifying causes and risks for Rickettsiosis. Ticks, mosquitoes, and other vectors may coexist in undeserved regions, and they may relate to unspecific signs and symptoms. Medical education programs vary across Mexico Objective: We aimed at evaluating differences in knowledge about preventing and diagnosing rickettsiosis, personal experience when assisting patients with probable diagnosis and the confidence they self-identify for accurately establishing a diagnosis of rickettsiosis among medical students from endemic and non-endemic regions. In this cross-sectional study, 144 medical students from seven universities. Were invited to participate by responding a 30-item questionnaire. Sample size was obtained for

two-proportion comparison with 95% confidence, p<0.05, considering a difference of 25% between endemic or non-endemic regions. From 144 participants, 50% male, aged 24.2 years, 46.5 were from non-endemic regions, while 53.4% from endemic regions. Students from endemic regions had more knowledge about the vector, transmission, prevention, and risks for rickettsial infections (64% more); 85% of non-endemic region identified differential diagnoses, compared to 100% residing in endemic regions. In regression analysis, those from endemic regions were more likely to correctly consider rickettsiosis (OR:1.34) in differential diagnosis, to revise specific protocols and guidelines (OR:2.74), were more confident of their diagnostic capacity (OR:1.49), more prone to consider themselves as well trained (20.77) and to indicate appropriately the clinical tests (OR:1.34). Rickettsiosis diagnosis is part of general physicians every day's activities. Knowledge is fundamental for medical students from endemic and non-endemic regions of Mexico, even when experience with rickettsioses may depend on the epidemiology of the region.

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EXPLORING TICK VECTOR DYNAMICS IN CRIMEAN-CONGO HEMORRHAGIC FEVER OUTBREAK ZONES OF EAST AFRICA

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Crimean-Congo hemorrhagic fever virus (CCHFV), a member of the Nairoviridae family and Orthonairovirus genus, is a tick borne, negative-sense RNA virus that causes Crimean-Congo hemorrhagic fever (CCHF). This disease, characterized by a severe course, has a case fatality rate of 30% or more. The primary vector for CCHFV is recognized as *Hyalomma marginatum*, and its presence has been closely linked to outbreaks of human disease. In East Africa, Uganda has faced several CCHF outbreaks since 2013, while Western Kenya documented just one case in October 2000. Interestingly, Central and Western Uganda, where most CCHFV cases occurred previously, show very low environmental suitability for *Hyalomma* species. To deepen our understanding of tick species distribution in CCHF high-risk zones across East Africa and the prevalence of CCHFV infection, we conducted field surveys in six districts in Uganda's high-risk regions and four counties in Kenya's intensive pastoralist farming areas. The findings revealed significant variations in tick species diversity and distribution between and within Kenya and Uganda, with minimal overlap. Surprisingly, no *Hyalomma* species were found in Central Uganda's CCHF high-risk zone, whereas the arid North of Kenya was predominantly (over 60%) populated by this species. In Uganda, *Rhipicephalus appendiculatus* emerged as the most prevalent tick species, constituting 62% of the total collection. We successfully isolated CCHFV from pools of *Rh. appendiculatus* collected from Uganda's CCHF high-risk region. These results suggest that CCHF epidemiology in Uganda may be regionally specific and that *Hyalomma* species might not be the primary vector driving CCHFV transmission in all areas. The absence of the main host species in Uganda's high-risk region may indicate a regional variation in CCHFV's host. These findings provide significant implications for tick and CCHFV control strategies in East Africa.

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A DETAILED CHARACTERIZATION OF *RICKETTSIA BELLII* ECOLOGY AND HOST INTERACTIONS

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Vector-borne diseases are a group of ailments transmitted through an arthropod host. One genus of bacteria that falls into this group is *Rickettsia. Rickettsia* are obligate intracellular bacteria that are transmitted to vertebrate hosts through different vectors, specifically ticks, fleas, and human lice. These bacteria present a wide range of phenotypes with some being of medical importance, such as *R. felis,* and others being nonvirulent, such as *R. bellii.* These nonvirulent species often serve as endosymbionts within ticks, bringing on a positive impact on feeding and reproduction. As vector-borne diseases continue to become a growing concern, methods of control are of the utmost urgency. Eliminating vital endosymbiotic species in the tick microbiome has been a discussed method to reduce current tick population size and reproductive capability. *R. bellii* is common throughout the Americas within ticks of multiple genera in their microbiome but its role in tick physiology and immune response to pathogenic *Rickettsia* are not known. The prevalence of other rickettsial agents and the downstream effects of removing them from ticks has been examined yet *R. bellii* has been neglected. Although they share similar genomes, this need of *R. bellii* characterization has not been met. Our long-term goal is to establish the importance of *R. bellii* in influencing the transmission of pathogenic *Rickettsia*. In this study, we examine the presence of *R. bellii* and other endosymbionts within field caught ticks, commenting on their infection rate in ticks. Preliminary data with field-caught *A. amblyomma* ticks in Central Missouri has identified high prevalence of endosymbiont *Rickettisa*, where it appears to dominate the ticks' microbiome. Towards understanding how this may impact the host response, we are characterizing transcriptional and cellular responses to *R. bellii* in vitro. Laboratory studies have highlighted an increase of cytotoxic activity over time, reaching 50% by day 4 post infection. This work will bridge missing gaps in the literature surrounding *R. bellii* while illuminating the role of endosymbiotic bacteria vector-borne diseases control.

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TWO HIGHLY SELECTED MUTATIONS IN THE TANDEMLY DUPLICATED CYP6P4A AND CYP6P4B GENES DRIVE PYRETHROID INSECTICIDE RESISTANCE AND CAUSE LOSS OF INSECTICIDE-TREATED BED NET EFFICACY AGAINST THE MAJOR MALARIA VECTOR *ANOPHELES FUNESTUS* IN WEST AFRICA

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Insecticide-based vector control tools have been crucial in reducing malaria. However, the emergence of insecticide resistance (IR) in malaria vectors is seriously hampering their effectiveness. To address this challenge, National Malaria Control Programs (NMCPs) must apply evidence-based resistance management strategies along with the WHO recommendations for routine genetic monitoring of IR. As such, our study investigated how two genes, *Cytochrome 6P4a* and *Cytochrome 6P4b,* contribute to IR in the major malaria vector *Anopheles funestus*. We used population genetics, molecular biology, *in vitro* insecticide depletion assays, and generation of transgenic Drosophila flies exposed to insecticides to establish the impact of mutations and overexpression of the genes on the resistance phenotype. We further designed two field-deployable diagnostic tools to detect and monitor IR. Our population genetics studies unveiled the striking selection of two mutant gene variants in Ghana between 2014 and 2021. These mutants exhibited a 3-fold greater capacity to deplete pyrethroid insecticides compared to the wild types. Also, overexpression of the mutant alleles in the transgenic flies resulted in significantly higher insecticide resistance compared to the wild-type flies (mortality <50% vs. >80%, respectively), confirming the role of *6P4a* and *6P4b* in causing IR. In addition, using our designed diagnostic tools, a strong association was established between carrying the mutant alleles and the inefficacy of bed nets, where mosquitoes

carrying the mutant alleles resisted exposure to insecticide-treated bed nets like OLYSET® and DURANET® than non-mutants, -hence increased mosquito life-span which leads to higher malaria transmission rates. We also confirmed that the mutations are predominantly found in the West African region. Overall, our study established that *CYP6P4a* and *CYP6P4*b confer highly escalated insecticide resistance in the major malaria vector *An. funestus* and provides two field-applicable resistance diagnostic tools with significant implications for NMCP implementation of vector control strategies in Africa.

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INSECTICIDE RESISTANCE STATUS AND HIGH *KDR* FREQUENCY IN *AEDES AEGYPTI* IN A DENGUE ENDEMIC CITY OF HONDURAS

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Several arboviruses are transmitted to humans through bites from infected *Ae. aegypti*, and insecticide-based interventions are the main strategy for outbreak control. In Honduras, cyclic arbovirus epidemics have led to the intensive use of pyrethroids, leading to the emergence of insecticide resistance. So far, limited data are available about the participation of resistance mechanisms in *Ae. aegypti* in Honduras. Here, we aimed to conduct a phenotypic assessment of insecticide resistance and detect *kdr* alleles in *Ae. aegypti* from the Central District of Honduras. Between May-June 2023, *Ae. aegypti* larvae were collected in 4 localities: Loarque (LO), La Concordia (LC), Rio Abajo (RA) and Altos de Villa Vieja (AV) and reared until F1 as adults for bioassays. Susceptibility bioassays were carried out using the diagnostic doses of deltamethrin, permethrin, malathion and bendiocarb. AS-PCR was employed to detect *kdr* alleles at the 1534 and 1016 positions in mosquitoes randomly selected from each population and phenotype, and allele frequencies were calculated. A total of 1,592 *Ae. aegypti* were bioassayed. Mortality rates for deltamethrin ranged between 86 and 100%, with LC population showing the lowest mortality. For permethrin, the mortality ranged between 1 and 48%, with LC exhibiting the lowest mortality and RA the highest. Similarly, all populations showed malathion resistance, with mortalities between 24 and 74%. All populations were susceptible to bendiocarb. Screening of 275 individuals revealed the presence of *kdr* genotypes at both loci. The allele frequencies for F1534C and V1016I were 1.0 and 0.89, respectively. It is noteworthy that the frequency of the V1016I mutation showed variability between locations. Only the phenotypically resistant mosquitoes to deltamethrin and permethrin, from LC and LO, showed a frequency of 1.0 for the mutant genotype, while the others ranged from 0.48 to 0.97. These findings reveal resistance in *Ae. aegypti* to the pyrethroids used for vector control in Honduras, and resistance to malathion. Additionally, *kdr* alleles were present at high frequencies and were associated with phenotypic resistance.

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RELATIONSHIPS BETWEEN BIOLOGICAL AGE, DISTANCE FROM AQUATIC HABITATS, AND PYRETHROID RESISTANCE STATUS OF *ANOPHELES FUNESTUS* MOSQUITOES IN SOUTH-EASTERN TANZANIA

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Malaria transmission can be highly heterogeneous between and within localities and is influenced by factors such as the survival and biting frequencies of *Anopheles* mosquitoes. This study investigated the relationships between the biological age, distance from aquatic habitats, and pyrethroid resistance status of *Anopheles funestus* mosquitoes, which currently dominate malaria transmission in south-east Tanzania. Female *An. funestus* were collected in houses located 50-100 m, 150-200 m, or over 200 m from the nearest known aquatic habitats. The mosquitoes were exposed to 1×, 5× and 10× the diagnostic doses of pyrethroid (deltamethrin or permethrin), or the synergist, piperonyl butoxide (PBO) followed by the pyrethroids, then monitored for 24 h-mortality. Ovaries of exposed and non-exposed mosquitoes were dissected to assess parity as a proxy for biological age. Adults emerging from larval collections in the same villages were tested against the same insecticides at 3-5, 8-11, or 17-20 days old. Mosquitoes collected nearest to the aquatic habitats (50-100 m) had the lowest mortalities compared to other distances, with a maximum of 51% mortality at 10× permethrin. For the age-synchronized mosquitoes collected as larvae, the insecticide-induced mortality assessed at both the diagnostic and multiplicative doses (1×, 5×, and 10×) increased with mosquito age. The highest mortalities at 1× doses were observed among the oldest mosquitoes (17-20 days). Pre-exposure to PBO increased the potency of both pyrethroids. The proportion of parous females was highest among mosquitoes collected furthest from the habitats. Older An. funestus near the center of the village are more susceptible to pyrethroids than those at the edge of the village. Pyrethroid-based interventions may remain at least moderately effective despite widespread pyrethroid-resistance, by killing the older, less-resistant, and potentially-infective mosquitoes.

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HOUSEHOLD RISK FACTORS ASSOCIATED WITH INCREASED MOSQUITO DENSITIES AND INSECTICIDE RESISTANCE PROFILES OF MAIN MALARIA VECTORS IN KWALE COUNTY, COASTAL KENYA

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The spread of insecticide resistance threatens the efficacy of current malaria control programs which rely heavily on insecticide-based vector control interventions. The aim of this study was to determine the insecticide resistance profiles of the main malaria vector species complex in coastal Kenya (Kwale county) and explore household risk factors leading to increased densities of mosquitoes. Adult mosquitoes and larval sampling were performed in the same sites, collected larvae were reared to F1 for susceptibility tests using WHO tube assay kits. A synergist assay with piperonyl butoxide (PBO 4%) was performed to investigate the possible involvement of metabolic resistance mechanisms. GLMM (negative binomial regression models) were used to identify factors influencing the indoor density of different vector species complex.Approximately 8302 mosquitoes were collected, composed of *An. funestus s.l.* (70%), *An. gambiae s.l.* (17%) and other Anophelines (13%). The presence of ITNs in households significantly reduced *An. funestus s.l.* count by 65% (IRR = 0.35, 95% CI 0.13-0.97, P<0.044). Moreover, palm leaves roof type (IRR = 4.46, 95% CI 2.30-8.64, P<0.001) and mud walls (IRR = 6.74, 95% CI 2.81-16.17, P<0.001) significantly increased *An. funestus s.l.* We did not find statistically significant association between indoors densities of *An. gambiae s.l.* and different house characteristics. *An. gambiae s.l.* exhibited resistance to deltamethrin and permethrin, but was susceptible to DDT, pirimiphos-methyl, and bendiocarb. *An. funestus s.l.* also demonstrated resistance to deltamethrin while DDT remained susceptible. The reversal of resistance was observed during the synergistic assay with PBO in both *An. funestus s.l.* and *An. gambiae s.l*. Resistance to pyrethroids is widespread and likely to involve metabolic mechanisms of resistance. Despite resistance, net usage continues to be associated with fewer indoor mosquitoes.

Household structural characteristics strongly influenced indoors densities of malaria vectors, further confirming the association between built environment and potential exposure to malaria.

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THE IMPACT OF NEXT-GENERATION DUAL-ACTIVE INGREDIENT LONG-LASTING INSECTICIDAL NET DEPLOYMENT ON INSECTICIDE RESISTANCE IN MALARIA VECTORS: RESULTS OF A THREE-YEAR CLUSTER-RANDOMIZED CONTROLLED TRIAL IN BENIN

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To delay the evolution and spread of resistance and alleviate reversals in malaria control gains, long-lasting insecticidal nets (LLINs) incorporating new active ingredients (A.I.s), with distinct modes of action, are urgently needed. Through a three-year, three-arm cluster-randomised controlled trial (cRCT), we assessed the longitudinal impact of dual-A.I. LLINs (chlorfenapyr-PY and pyriproxyfen-PY LLINs) on insecticide resistance, compared to pyrethroid-LLINs (PY-LLINs). Longitudinal phenotypic and genotypic insecticide resistance profiles were measured among 19,292 *An. gambiae* s.l. collected over 39 months (3 months of baseline, followed by three years, post-intervention), using insecticide resistance bioassays and quantitative real-time reverse transcription PCR of metabolic resistance genes, respectively. In all three trial arms, a significant intervention effect was evident, with alpha-cypermethrin resistance intensity decreasing between baseline and twelve months post-LLIN distribution. Over the subsequent two years, alpha-cypermethrin resistance intensity rebounded to comparable or moderately higher levels than at baseline in all three trial arms. In all trial arms, by the third year, the alpha-cypermethrin concentration required to kill 95% of vectors increased to more than fifty times the diagnostic dose. Minimal reductions in chlorfenapyr susceptibility were observed; variable, albeit significant reductions in fertility following pyriproxyfen exposure, with an overall upward trend of increasing susceptibility across trial years was apparent. Several metabolic genes were implicated in resistance selection, including CYP6P4 in the pyriproxyfen-PY arm, and CYP6P3 and CYP9K1 in the chlorfenapyr-PY arm. Study findings indicate that after 24 months of use, chlorfenapyr-PY LLINs no longer mitigated pyrethroid resistance selection in *An. gambiae* s.l., while nets are currently procured every three years. Knowledge about the impact of next-generation LLINs on insecticide resistance selection is crucial for the pragmatic design of prospective resistance management strategies.

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THE E205D MUTATION IN THE P450 GENE CYP6P3 DRIVES PYRETHROID RESISTANCE IN THE MAJOR AFRICAN MALARIA VECTOR ANOPHELES GAMBIAE

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To improve the longevity of malaria control tools, this study pinpoints genetic mutations in the major malaria mosquito that cause pyrethroid resistance, paving the way for simple DNA tests to track resistance in the field. The entire genomes of highly resistant and highly susceptible malaria mosquitoes were compared to identify genetic changes linked to resistance (signatures of selective sweeps). The role of a top candidate was then elucidated using functional validation assays. A DNA-based assay was designed to monitor the pyrethroid resistance in the field and its impact on the effectiveness of long-lasting insecticide-treated bednets using standard WHO cone assays. WGS detected a major P450-linked locus on chromosome 2R beside the sodium channel locus to be linked to pyrethroid resistance in Cameroon. We demonstrated that the E205D mutation in a key metabolic resistance P450 *CYP6P3* drives pyrethroid resistance in *Anopheles gambiae. In vitro* metabolism assays with recombinant *CYP6P3* protein revealed that the catalytic efficiency of 205D was 2.5 times higher than E205 with α-cypermethrin. Overexpression of the 205D allele in transgenic flies confers higher pyrethroids and carbamates resistance, compared to controls. A DNA-based assay further supported that the *CYP6P3*-205D variant strongly correlates with pyrethroid resistance in field populations (OR=26.4; P<0.0001) and that it reduces the efficacy of pyrethroid-only LLINs with homozygote RR genotype exhibiting significantly higher survival following PermaNet 3.0 exposure compared to the SS genotype (OR: 6.1, p = 0.0113). Furthermore, the *CYP6P3*-E205D combines with the *kdr* target-site resistance mechanisms to worsen the loss of bednet efficacy. The 205D mutation is widespread in West and Central Africa, but less common or even absent in East and South Africa with signs of introgression with *An. coluzzii* in Ghana. This study emphasizes the importance of P450-based resistance and designs field-applicable tools to easily track the spread of metabolic resistance and assess its impact on control interventions.

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ACE-1 DUPLICATION AND COPY NUMBER VARIATION ARE CORRELATED TO RESISTANCE TO ORGANOPHOSPHATES IN *ANOPHELES GAMBIAE* FROM CENTRAL AFRICA

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Mosquito resistance to insecticides hinders malaria control. Organophosphates (OPs) and carbamates (CMs) are used in indoor residual spraying (IRS) as a support for pyrethroids, to which many mosquito species are resistant. Unfortunately, West and East Africa see growing resistance to these classes used in IRS, including pirimiphos-methyl (PM), an OP newly recommended by the WHO. Mosquitoes with mutation replacing glycine with serine at position 280 in the acetylcholinesterase enzyme (Ace-1 280S) decrease sensitivity to OPs and CMs. Ace-1 duplications and copy number variation (CNV) enhance resistance, but empirical evidence is scarce in wild *Anopheles* in general, and in Central Africa particularly. We aimed to explore the correlation between specific Ace-1 alleles, the number of duplicated copies, and insecticide resistance levels in *Anopheles gambiae* s.s, *An. coluzzii*, and *An. funestus* s.l, to two organophosphates, PM and malathion (MA) across six Cameroonian localities. Mosquitoes were collected from breeding sites and susceptibility was determined using the WHO assay. Taq-Man and sequencing techniques investigated the Ace-1 gene in dead and surviving

mosquitoes after insecticide exposure. Analysis of 100 clones and qPCR permit to explore gene duplication and relative copy number variations. While *An. funestus* populations exhibited full susceptibility, *An. gambiae* s.l. showed potential or clear resistance to OPs (97%-50% mortality). A significant correlation linked the Ace-1 mutation with resistance in *An. gambiae* s.s. from Nkolondom to the two OPs (PM: OR= 20.33; P=0.04, MA: OR= 98.33; P =0.0019). Analyses revealed for the first time Ace-1 gene duplication and increased CNV correlated with resistant populations to PM and MA in Central Africa. The observed low-frequency (3%) of Ace-1^R mutation in *An. coluzzii* suggests recent selection pressure. These findings highlight the necessity for monitoring susceptibility before effective implementation of IRS in Cameroon. Ace-1 resistance demands long-read sequencing to fully map duplications, ensuring long-term insecticide effectiveness in malaria control.

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MALARIA VECTOR ECOLOGICAL DIVERSITY INFLUENCING TRANSMISSION AND RESISTANCE TO INSECTICIDES

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Prevalence of malaria could be a function of vector density, transmission dynamics and ability for insecticide resistance and ecological variation could play a vital role. In this study, 1,857 adult *Anopheles* mosquitoes were collected from three ecosystems using standard procedures to establish their diversity, indoor and outdoor feeding and biting habits. The specimens were graded according to their abdominal conditions and preserved dry for morphological, molecular identification and ELISA test. Larvae were collected and reared to adulthood. Susceptibility tests conducted on 2-3-day old emerged female adults using standard WHO procedures. Species collected from the rain forest include; *Anopheles gambiae, An. funestus, An. moucheti, An. Arabiensis, An. nili* those from the savannah mosaic include; *An. gambiae, An. funestus, An. moucheti, An. Arabiensis, An. longipalpis, An. nili, An. maculipalpis, An. coustani, An. rhodesiensis* and *An. ziemani* and those from mangrove ecosystem are; *An. gambiae, An. melas* and *An. nili. Anopheles gambiae* abundance was significantly higher, accounting for 81.3% of all the collections and was found in all the localities. Those established to be vector of malaria include; *Anopheles gambiae, An. funestus, An. moucheti, An. Arabiensis* from the forest, *An. gambiae, An. funestus, An. moucheti, An. Arabiensis, An. longipalpis, An. nili* from the savannah and *An. gambiae, An. melas* from the mangrove. The infection rates ranged from 1.2% in the rain forest to 1.0% in the savannah and 0.9% in the coastal zone, this showed no significant difference (P>0.05). The entomological inoculation rates are 2044, 1716 and 1789 infective bites per person per year for the rain forest, savannah and coastal zones respectively, indicating no significant difference (P>0.05). Species from the coastal zone are more susceptible to doses of insecticides tested followed by those from rain forest while savannah mosaic species showed higher level of resistance. This is a baseline information to guide a community-based strategy for malaria control intervention.

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DYNAMICS OF RESISTANCE INTENSITY AND MECHANISMS OF *ANOPHELES GAMBIAE* TO PYRETHROID INSECTICIDES BETWEEN 2021 TO 2023 IN RWANDA

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The prevailing increase of insecticide resistance of *Anopheles gambiae* (s.l) to pyrethroid insecticides represents a crucial threat on the gains achieved from the scaling up of core vector control interventions. This study investigated the dynamics of resistance intensity and mechanisms of *An. gambiae* (s.l) to the pyrethroid insecticides between 2021 and2023 in Rwanda in order to guide the insecticide resistance management strategies. The intensity of resistance was measured at five (5x) and ten (10 x) times to the diagnostic doses for phenotypic resistance tests. The piperonyl butoxide (PBO) as synergist was added to the diagnostic dose to test the detoxification enzymes where the resistance was confirmed per insecticide and surveyed site. Out of the 25 surveyed sites, the high resistance intensity measured at 10 times the concentration of diagnostic dose for *Anopheles gambiae s.l.,* increased from 0% to 12% for Deltamethrin 0.05%, 0% to 7.4% for Permethrin 0.75% and 4% to 44% for Alpha-cypermethrin 0.5%. Therefore, from 2022 to 2023, the usual addition of synergist (PBO) encountered the decrease of susceptibility restoration from 100% (n=18) to 84.6% (n=13) for Deltamethrin 0.05%, 94% (n=20) to 92.6% (n=27) for Permethrin 0.75%, and 92.3% (n=26) to 84% (n=25) for Alphacypermethrin 0.05%. The study demonstrated an incremental increasing of resistance intensity to the pyrethroid insecticides and mainly to alpha cypermethrin. The underlying metabolic resistance mechanism involving detoxification esterase enzymes was detected using PBO and its effect is decreasing overtime. Other potential resistance mechanisms are suspected and require investigations with future projects. The monitoring of insecticide resistance has to be strengthened and integrated into the routine malaria vector surveillance, to guide decision making in deployment and impact evaluation of malaria control interventions in Rwanda.

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INSECTICIDE RESISTANCE PROFILE OF *AEDES* MOSQUITOES IN OGUN STATE, NIGERIA

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Aedes mosquitoes remain important vectors of dengue & yellow fever viruses in Nigeria. We investigated the insecticide resistance patterns of *Aedes* mosquitoes in Ogun State, in southwest Nigeria. Between April & August 2023, larval breeding sites of *Aedes* were identified & immature stages collected from four Local Government Areas, namely Odeda, Abeokuta South, Obafemi-Owode and Sagamu. Emerged females were exposed to four classes of insecticides according to the standard World Health Organization (WHO) protocol: pyrethroids (permethrin 0.75% & deltamethrin 0.05%); organochlorines (DDT 4%); organophosphates (fenitrothion 1.0%) & carbamates (bendiocarb 4%). A total of 2500 female *Aedes* mosquitoes were identified & exposed to insecticides. Of these, 2,297 (91.9%) were *Aedes aegypti,* while 203 (8.1%) were *Aedes vitattus*. *Aedes aegypti* was the sole species collected in Obafemi-Owode & Sagamu, whereas both species were found in Odeda and Abeokuta South. Across all sites, mortality to (DDT) ranged between 82% and 97%, suggesting mild resistance. Mosquitoes from Odeda, Abeokuta South & Obafemi Owode showed full susceptibility to permethrin, while suspected resistance was observed in Sagamu (92%). Mortality to deltamethrin ranged between 91% and 92%, indicating suspected resistance across all sites. Mosquitoes were largely susceptible to bendiocarb, except in Obafemi-Owode, where resistance was suspected (91% mortality). Susceptibility to fenitrothion was recorded in all sites except Sagamu (72% mortality). These findings suggest that resistance to all classes of insecticide is emerging among *Aedes* mosquitoes in southwest Nigeria, highlighting the need for targeted actions to address increased resistance & safeguard public health.

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HIGH SURVIVORSHIP OF *ANOPHELES GAMBIAE* LARVAE TO LETHAL CONCENTRATIONS OF CLOTHIANIDIN, ACETAMIPRID OR IMIDACLOPRID IS CONSISTENT WITH CROSS-RESISTANCE TO NEONICOTINOIDS

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Worldwide, agrochemicals have been effectively repurposed for mosquito control. The effectiveness of this method is challenged by preexisting resistance in larval and adult populations brought about by unintentional pesticide exposure or other cross-resistance mechanisms. Thus, in order to evaluate the effectiveness of repurposed agrochemicals against mosquitoes, understanding of the lethal and sublethal effects of residual pesticide is essential. We reared field-collected mosquito larvae in water that had an agrochemical concentration that, after 24 hours, killed 100% of susceptible mosquitoes (lethal concentration). With the help of this experimental setup, we investigated the effects on mortality rates and life table parameters of third-instar larvae of the two sibling species *Anopheles gambiae* and *Anopheles coluzzii* collected from Yaoundé, Cameroon caused by lethal concentrations of a pyrethroid (deltamethrin), a pyrrole (chlorfenapyr), and three neonicotinoids (acetamiprid, clothianidin, and imidacloprid). We observed that *An. gambiae* and *An. coluzzii* larvae were susceptible to chlorfenapyr and a minimal concentration of 0.10 mg/L killed them in less than 24 hours. In both species, deltamethrin caused low mortality, which is consistent with strong insecticide resistance. In *An. coluzzii* larvae, lethal doses of acetamiprid, imidacloprid, and clothianidin significantly hindered their ability to survive, grow, and emerge. On the other hand, 5 to 60% of *An. gambiae* immature stages were able to grow and emerge in water containing a lethal dose of neonicotinoid, demonstrating cross-resistance to this class of insecticides, depending on the active component and the population examined. These findings corroborate susceptibility profiles observed in adults and suggest that unintentional pesticide exposure or other cross-resistance processes could contribute to the establishment of resistance to neonicotinoids in some *Anopheles* populations.

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DIVERGENCES AND SIMILARITIES ON INSECTICIDE RESISTANCE PROFILES IN WILD POPULATIONS OF *ANOPHELES GAMBIAE SL* BREEDING IN VEGETABLE FARMS IN COTONOU, BENIN

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Pesticide management by vegetable farmers might play a key role in the selection of insecticide resistance in field populations of mosquito vectors. Here, we investigated the distribution of insecticide resistance profiles recorded with populations of *Anopheles gambiae sl* breeding in vegetable farms in the city of Cotonou in Benin, where no harmonization and no regulation is established, leading to uncontrolled use of pesticides. Two field sites were selected, Houeyiho and Seme. Wild Anopheles gambiae sl larval populations were collected and their susceptibility to lambda-cyhalothrin and permethrin was assessed. Synergist bioassays with PBO were conducted and the kdr target-site mutations were investigated. The genetic diversity of An. gambiae sl was assessed by sequencing the exon-20 element of the voltage-gated sodium channel. Overall, Lambdacyhalothrin constituted the main insecticide used by vegetable farmers. Mortalities to lambdacyhalothrin were 63% and 30% of the mortality rate respectively at Houeyiho and Seme. Susceptibilities to permethrin at Houeyiho and Seme were 14% and 42% of the mortality rate respectively. The PBO synergist assays showed a total recovery of the susceptibility to lambda-cyhalothrin in An. gambiae sl (100% mortality rate) at Seme, while this recovery was partial at Houeyiho (80% mortality rate). As to permethrin, the recovery was partial at houeyiho (73% mortality rate) and total in Seme (100% mortality rate). The kdr 1014F mutation was close to fixation in all the sites. In Hoeuyiho, 6 haplotypes were found, the haplotype diversity was 0.18. In Seme 3 haplotypes were found for a haplotype diversity of 0.09. There was a divergence in *An. gambiae sl*, about the resistance profile to pyrethroid, the involvement of cytochrome P50 in the observed resistance and the genetic diversity from one site to another. However, there was a similarity in Kdr mutation distribution. This study suggests that the implementation of vector control strategies should take into account divergences and similarities in mosquito resistance profiles, even at a small field scale for better management of malaria transmission.

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KEY RESISTANCE P450S PROFICIENT PYRETHROID METABOLIZERS, ARE REDUCING NEONICOTINOID EFFICACY IN *ANOPHELES FUNESTUS* WHILE EXACERBATING THE POTENCY OF CHLORFENAPYR

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Novel insecticides were recently introduced to counter pyrethroid resistance threats in African malaria vectors. To prolong their effectiveness, potential cross-resistance from promiscuous pyrethroids metabolic resistance mechanisms must be elucidated. Previous evidences have established that mutations in *CYP6P9a* and *CYP6P9b* (*CYP6P9a/-b*) are the main drivers of pyrethroid resistance in *Anopheles funestus* in Southern Africa. In this study, we used field strain of *An. funestus* from Malawi to assess the impact of *CYP6P9a/-b*, proficient pyrethroid metabolizers, on the efficacy of two novel insecticides, chlorfenapyr and clothianidin, using CDC bottle assay, coupled with extensive *in vivo* and *in vitro* function validation to directly establish the impact of the major pyrethroid resistance P450s on those insecticides. A strong association between the *CYP6P9a/-b* mutations and the ability to survive clothianidin exposure was noted for mutant versus non-mutant (OR=7.5; P=0.001 for *CYP6P9a* OR=7.08; P=0.002 for *CYP6P9b*). However, mutant had significantly higher mortalities upon chlorfenapyr exposure, compared to non-mutant (OR=0.1; P<0.0001 and OR=0.2; P=0.0003 respectively). Transgenic expression of *CYP6P9a/-b* in Drosophila revealed that flies expressing *CYP6P9a* and *CYP6P9b* were significantly more resistant to clothianidin 12h post-exposure than the control flies, with average mortalities of 45.05% ± 7.03 for *CYP6P9a* (P<0.001) and 30.1% ± 2.9 for *CYP6P9b* (P<0.001) compared to the control flies (73.9% ± 3.3). In contrast, experimental flies over-expressing these two P450s were more susceptible to chlorfenapyr 12h post-exposure compared to control flies, with average mortalities of 62.3% ± 4.1 for *CYP6P9a* (P<0.001) and 61.1% ± 5.9 for *CYP6P9b* (P<0.001) compared to the control (37.6% ± 5.6). This phenotype was also confirmed by RNAi knock-down experiments. This study highlights the risk of cross-resistance between pyrethroid and neonicotinoid and reveals that chlorfenapyr-based control interventions such as Interceptor G2 could remain efficient against some P450-based resistant mosquitoes.

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BACTERIA COMMUNITY EXACERBATE PYRETHROID RESISTANCE IN *ANOPHELES FUNESTUS*, MAJOR MALARIA VECTOR IN AFRICA

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The increasing resistance of *Anopheles* mosquitoes to pyrethroids is subjecting many African countries to a high risk of malaria epidemics. An in-depth understanding of the mechanisms associated with this phenomenon is needed to mitigate this growing threat to malaria vector control. Numerous studies have highlighted the involvement of microbiota in mediating insecticide resistance (IR) in agricultural pests. Based on this, our study sought to investigate the potential role of bacteria in the escalation of insecticide resistance in the major malaria vector *Anopheles funestus* Giles (Diptera : Culicidae). Using the sequencing of the 16S rRNA mitochondrial gene, we comparatively characterized the microbiota of a highly pyrethroid-resistant strain (Fumoz-selected) and a normal-resistant strain (Fumoz unselected). This enabled the identification of bacteria strains associated with the escalation of IR. In addition, to further confirm the involvement of bacteria in the phenotype, we performed an antibiotic treatment (penicillin/streptomycin) of Fumoz unselected mosquitoes, proceeded by exposure to insecticides. As findings, lower bacterial diversity was observed in the selected group, suggesting that, insecticide selection pressure reduces bacterial enrichment. Also, we noticed an overabundance of the *Rhanella* genus in the Fumoz-selected strain (Deseq2: Log2FC-15.776, p=4.23E-11), which could argue its involvement in the escalation of IR phenotype. Concerning the antibiotic treatment, we observed a partial recovery of the susceptibility of treated individuals, to insecticides after exposure to varying WHO diagnostic concentrations of pyrethroids: Permethrin 1X ($\chi2 = 46.936$, $p < 0.0001$), Deltamethrin 5X ($\chi2 = 4.102$, $p = 0.04$) and 10X ($\chi2 = 9.706$, $p = 0.0018$). Overall, our findings confirmed the potential role of bacteria in the escalation of IR in *An. funestus*. This study, therefore, lays the initial groundwork for understanding microbial mechanisms that exacerbate pyrethroid resistance in malaria vectors while jeopardizing vector control efforts.

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SEX PEPTIDE RECEPTOR IS NOT REQUIRED FOR REFRACTORINESS TO REMATING OR INDUCTION OF EGG LAYING IN AEDES AEGYPTI

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Aedes aegypti is a major vector of arboviruses worldwide. Understanding major reproductive pathways in males and females is essential for development and success of novel control tools that can reduce human infection risk. Across diverse insect taxa, the behavior and physiology of females dramatically changes after mating – processes largely triggered by the transfer of seminal proteins from their mates. In the vinegar fly *Drosophila melanogaster*, the seminal protein sex peptide (SP) decreases the likelihood of female flies remating and causes additional behavioral and physiological changes that promote fertility including increasing egg production. Although SP is only found in the *Drosophila* genus, its receptor, sex peptide receptor (SPR), is the widely conserved myoinhibitory peptide (MIP) receptor. To test the functional role of SPR in mediating post-mating responses in a non-*Drosophila* dipteran, we generated two independent *Spr*-knockout alleles in the yellow fever mosquito, *Aedes aegypti*. Although SPR is needed for post-mating responses in *Drosophila* and the cotton bollworm *Helicoverpa armigera*, *Spr* mutant *Ae. aegypti* show completely normal post-mating decreases in remating propensity and increases in egg laying. In addition, injection of synthetic SP or accessory gland homogenate from *D. melanogaster* into virgin female mosquitoes did not elicit these post-mating responses. Our results demonstrate that *Spr* is not required for these canonical post-mating responses in *Ae. aegypti*, indicating that other, as yet unknown, signaling pathways are likely responsible for these behavioral switches in this disease vector.

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MICRO-SPATIAL PARTITIONING INFLUENCES THE DIVERSIFICATION OF MOSQUITO-ASSOCIATED VIRUS PROFILES AMONG *AEDES AEGYPTI* MOSQUITOES IN PUERTO RICO

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Mosquito-borne arboviruses remain a major global health burden. The mosquito's microbiome, particularly, its virome can influence its life ability to transmit arboviruses. However, little is known about the intrinsic diversity of the virome across mosquito populations at smaller spatial scales. *Aedes aegypti* is the primary vector for dengue virus, Zika virus, and Chikungunya virus globally. We hypothesized that micro-spatial factors shape the mosquito core-virome and influence the diversification of mosquito-associated virus (MAV) profiles in *Ae. aegypti.* To test this hypothesis, we used RNA-Seq to characterize the diversity of MAVs among *Ae. aegypti* populations from urban and rural habitats on the main island of Puerto Rico and compared MAV diversity among *Ae. aegypti* collected from 2 urban and 2 rural habitats. Metatranscriptomic analysis identified 15 different viruses in this study that partitioned to rural vs. urban sampling sites. Of these, the most represented families were *Totiviridae* (3 viruses) and *Partitiviridae* (2 viruses). Phasi Charoen-like phasivirus (PCLV), Humaita-Tubiacanga virus (HTV) had the highest viral sequences overall. Of the 15 viruses detected, seven viruses were common to both rural and urban sites; however, six were present in urban *Ae. aegypti* but absent from the rural samples. Also, HTV had the most viral reads (>80%) among rural *Ae. aegypti,* whereas PCLV had very low viral reads (<2%). In contrast, PCLV (>80%) predominated in urban *Ae. aegypti*, while HTV reads were low. Phylogenetic analysis of the PCLV, HTV, and Guadeloupe mosquito virus strains revealed that our strains are quite unique, barely clustering with others from different geographical origins. We further compared MAV prevalence and vector competence for DENV-1 between urban and rural mosquito populations, and discuss how these results not only support our prevailing hypothesis but impact our understanding of arbovirus transmission at local scales. We anticipate that future studies will help assess the generalizability of the observed phenomena in other DENV-endemic regions.

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HOST-SPECIFIC DYNAMICS OF MICROBIOTA ASSEMBLY IN *AEDES AEGYPTI* MOSQUITOES AFTER RECIPROCAL TRANSPLANTATION OF CRYOPRESERVED WHOLE GUT-DERIVED MICROBIAL COMMUNITIES

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As in other animals, the mosquito gut is colonized by a diverse consortium of microbes that contributes to host traits including survival, fecundity, insecticide resistance, and vector competence. Accordingly, manipulation of the mosquito microbiome via the introduction of bacteria that reduce

mosquito vector competence and/or fitness is a promising avenue for controlling the transmission of mosquito-borne pathogens. However, many pathogen studies are conducted in laboratory-reared mosquitoes with gut microbial communities that are distinct from field-collected mosquitoes. Here, we describe a new method to isolate, cryopreserve, and transplant whole microbial communities from donor mosquitoes into axenic (germ-free) recipient mosquitoes. A reciprocal swap was conducted between *Aedes aegypti* Liverpool strain mosquitoes reared in isolation for 50 years at the University of Wisconsin-Madison (UW) and Liverpool School of Tropical Medicine (LSTM). Notably, mosquito hosts from each colony reacted differently to microbiome transplantation: UW mosquitoes experienced a shift in community composition after transplantation, but LSTM mosquitoes did not, suggesting host filtering of microbes may differ between geographically isolated mosquito strains. Fidelity of transplanted microbial communities further varied based on initial composition of the donor pool and recipient host genotype, though patterns of assembly were conserved across the mosquito life cycle. Altogether, these results highlight the value of this method for studying mosquito-microbe interactions and lay the foundation for future efforts to identify bacterial candidates for use in mosquito and mosquito-borne disease control. They also provide a critical next step toward the standardization of pathogen infectivity experiments to include laboratory-reared mosquitoes colonized by microbial communities isolated from mosquitoes in disease endemic areas in the field.

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INVESTIGATING THE EFFECTS OF TEMPERATURE CHANGE ON OVIPOSITION AND PROGENY VIABILITY OF *AEDES AEGYPTI* AND *CULEX TARSALIS* MOSQUITOES

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Temperature is known to affect the transmission efficiency of mosquito-borne viruses, particularly those spread by *Aedes aegypti* and *Culex tarsalis* mosquitoes. Investigating how environmental changes impact *Ae. aegypti* and *Cx. tarsalis* fecundity will inform future action for vector control and subsequent disease mitigation. Our preliminary data has shown impaired egg deposition when Rift Valley fever virus- adult *Ae. aegypti* mosquitoes were exposed to temperatures varying from typical environmental conditions. It is unclear if this behavior is due to infection or altered temperatures. Therefore, we are investigating the relationship between altered temperatures, oviposition rates, and progeny viability within uninfected blood-fed *Ae. aegypti* and *Cx. tarsalis* mosquitoes. We hypothesize that temperature variation will negatively impact egg viability, deposition rates, and offspring development. Blood-fed female mosquitoes (n=50) will be housed individually at lower (18°C), standard (28°C), or higher (32°C) rearing temperatures. Egg production will be assessed by quantifying deposited eggs in comparison to withheld eggs, obtained by ovarian dissection. Deposited egg hatch rates will be recorded to determine offspring viability. Data collection is ongoing. Preliminary trials showed increased developmental rates in *Ae. aegypti* at 32°C when compared to standard temperature. In contrast, *Cx. tarsalis* mosquitoes showed impaired egg-laying behavior and developmental rates at 32°C. Understanding the relationship between mosquito fecundity and temperature is of great importance for anticipating infectious disease dynamics in a complex and shifting global environment.

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A SINGLE-CELL ATLAS OF THE *CULEX TARSALIS* MIDGUT DURING WEST NILE VIRUS INFECTION

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The mosquito midgut functions as a key interface between pathogen and vector. However, studies of midgut physiology and associated virus infection dynamics are scarce, and in *Culex tarsalis* - an extremely efficient vector of West Nile virus (WNV) in the contiguous United States - nonexistent. We performed single-cell RNA sequencing on dissociated *Cx. tarsalis* midguts to define cell types comprising and associated with the midgut, and determine whether specific cell types are more permissive to WNV infection. We identified 15 midgut cell populations comprised of 7 distinct cell types, consistent with existing descriptions of *Drosophila* and *Aedes aegypti* midgut physiology. We found that all midgut cell populations were permissive to WNV infection. However, higher levels of WNV RNA, relative to other cell types, were present in enteroendocrine cells and cells enriched for mitochondrial genes, suggesting enhanced replication in these populations. In contrast, we observed the lowest levels of WNV RNA in proliferating intestinal stem cell (ISC) populations, a finding consistent with previous studies suggesting ISC proliferation in the midgut is involved in viral control. Notably, we did not detect significant upregulation of canonical mosquito antiviral immune genes (e.g., AGO2, R2D2, etc.) associated with WNV infection at the whole-midgut level. Rather, we observed a significant positive correlation between immune gene expression levels and WNV RNA level in individual cells, suggesting that within cells, high levels of WNV RNA may trigger antiviral responses. Our findings describe the cell types that comprise the midgut of *Cx. tarsalis*, and provide insight into the midgut infection dynamics of WNV in this highly efficient WNV vector by characterizing cell-type specific enhancement of, and immune response to, infection at the single-cell level.

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THE CONTRIBUTION OF SPECIFIC PROPHENOLOXIDASES TO PLASMODIUM MELANIZATION IN ANOPHELES GAMBIAE MOSQUITOES

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Anopheles gambiae mosquitoes rely on their innate immune responses to fight against *Plasmodium* infection. Among these responses is the melanization immune response, characterized by the deposition of melanin on the parasite's surface preventing it from gaining nutrients and thus triggering its death. Melanization involves a set of biochemical reactions that require the active phenoloxidase (PO), which is secreted into the hemolymph as prophenoloxidase (PPO) zymogen. A cascade of CLIP serine proteases is required for the cleavage and activation of PPO. The classical organization of this cascade in insects starts with the autoactivation of an upstream modular serine protease that integrates the signal from an activated pattern recognition receptor (PRR) into a downstream CLIP serine protease cascade constituted of several members. The most downstream CLIP in this cascade, known as the prophenoloxidase activating proteases, cleaves PPO into active PO which initiates the melanin biosynthesis pathway. Nine different PPOs have been identified in the *Anopheles gambiae* genome. Here, we attempt to identify the PPOs involved in *Plasmodium* melanization. We found that two different prophenoloxidases (PPOs) act together to mediate *Plasmodium* ookinete melanization, and our future aim is to generate transgenic mosquitoes that overexpress both PPOs to be used later in different functional infection assays.

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KINETICS OF MAYARO VIRUS INFECTIONS OF NEW WORLD AND OLD WORD *ANOPHELES* VECTORS

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The Mayaro virus (MAYV) is an *Alphavirus in the family Togaviridae*. The virus has been classified into three genotypes (D, L, and N); genotype D has the greatest geographical distribution in the Americas. The primary vector for MAYV in the sylvatic transmission cycle are *Haemagogus* mosquitoes. However, the virus can also be transmitted in urban cycles by *Aedes aegypti*. MAYV infections can cause long-term debilitations in afflicted countries. It has been shown that mosquitoes of the genus *Anopheles* can transmit the MAYV. To understand the potential expansion of the virus eastward to Africa, we tested if MAYV (genotype D) infection kinetics differs between Old World (*Anopheles gambiae*) and New World (*Anopheles albimanus*) anophelines, as compared to infections in *Aedes aegypti* (Orlando) mosquitoes from Florida. We observed that MAYV disseminated infection of *An. albimanus* was rapid, wherein *virus was found in saliva* after only 2 days post infection (dpi), at a 26.6% infection prevalence. This translated to a higher prevalence of infection, increasing to 80% after 7 dpi as compared to *Ae. aegypti. Importantly, we also* detected the virus in ovaries, wherein ovary infection rates increased from 80% (2 dpi) to 100% (7 dpi), indicating a high potential for vertical transmission and persistence in the environment. At 2, 7, and 14 dpi, *An. gambiae* had a 100% midgut infection. Although the virus was not detected in saliva at 2 dpi, infection prevalence in saliva increased from 20% (7 dpi) to 60% (14 dpi); suggesting transmission in the Old World is possible. We also observed that *An. albimanus* infection with MAYV impacts lifespan and have profiled the mosquito host response to infection at 7 dpi to gain insight into the mechanisms affected by MAYV. Since the virus can already be transmitted as early as 2 dpi, *An. albimanus* are indeed competent in transmitting MAYV within a shorter extrinsic incubation period and should be considered as potential targets for vector control during local outbreaks.

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OPTIMIZATION OF ANTIMALARIAL DRUGS DELIVERY AND EVALUATING THEIR EFFECTS ON THE SURVIVAL AND FECUNDITY OF LABORATORY REARED ANOPHELES GAMBIAE MOSQUITOES

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WHO global technical strategy for malaria control targets to reduce malaria cases by 90% by the year 2030. While the up scaling of control strategies in the initial years led to significant reduction in global malaria cases, malaria burden has plateaued in the last five years. Recent studies have demonstrated the potential of using standard antimalarials to block the development and transmission of pre-erythrocytic stages within the vector. This study aimed to determine the maximal tolerable doses and the efficacy of the antimalarial drugs (artemether, lumefantrine, primaquine and tafenoquine) on the fecundity of the reared *An. gambiae s.s* mosquitoes. *An. gambiae s.s* Kisumu strain were reared in the insectary by maintaining standard insectary conditions. Fifty, 3–5 days old, blood naive and starved mosquitoes were introduced into ten labelled paper cups. Eight doses consisting of serial dilutions of each antimalarials drug in 10% glucose solution. Mosquitoes were allowed to feed on cotton wool soaked in different concentrations of antimalarials and mortality monitored for ten days. To monitor fecundity, a fresh batch of mosquitoes were fed with human blood and subjected to the highest tolerable drug doses. The number of eggs laid was monitored over 8 days period. Controls were fed 10% glucose without drugs. Kaplan–Meier survival analysis was performed to estimate the tolerable drug doses while Chi- square method was used to assess the fecundity of *Anopheles* mosquitoes. The highest tolerable doses were 700 ng/ml for artemether and lumefantrine and 5000 ng/ml for tafenoquine and primaquine. The number of eggs did not differ between the mosquitoes exposed to the different drugs and control groups. The mosquitos tolerated doses of artemether and lumefantrine, tafenoquine and primaquine that were equivalent to doses recommended for use in human host. These doses do not seem to have an effect on mortality or on mosquitos' fecundity hence can be recommended for future use as potential transmission blocking compounds.

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ENTEROBACTER CLOACAE AND *SERRATIA MARCESCENS* METABOLITES MINIMIZE *PLASMODIUM* GAMETOCYTE DEVELOPMENT *IN VITRO.*

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Bacteria belonging to the family Enterobacteriaceae proliferate in the *Anopheles* mosquito midgut following a blood meal, and two members; *Enterobacter cloacae* and *Serratia marcescens* limit *Plasmodium* infection within the vector. As candidates for transmission-blocking strategies, it remains uncertain which will be more effective in targeting parasites: the increase in bacterial cell numbers in the vector and/or introduction of the vector to bacterial metabolites. We have already shown that metabolites from a 4hr spent media from *E. cloacae* and *S. marcescens* has varied effects on oocyst numbers in *Anopheles* mosquitoes. This current study aims to determine the concentration-dependent effect of bacterial metabolites on *Plasmodium*. Spent media following 6 different time-points culturing of two isolates each of *E. cloacae* (*EspG1*, *EspG3*) and *S. marcescens* (*SmG5*, *SmG6*) were lyophilized and reconstituted at 3mg/mL. *P. falciparum* 3D7 and Dd2 gametocyte stages IV-V were obtained with sorbitol synchronization, and incubated with bacterial metabolites for 72 hours. We have also begun to investigate the properties of the metabolites by applying heat (56ºC) and proteinase K treatments. Viable parasites were assessed with SYBR Green I and absorbances were read using a fluorescence plate reader. The overall treatment effect of the metabolites across all time-points differed between *SmG6* and *EspG1* (P= 0.003). There was evidence of interaction between the metabolites and parasite strains suggesting that the killing effect was stronger in some metabolite-parasite combinations than others. *Plasmodium* intensity reduced across all time-points with the highest effect at 4 and 6hrs for 3D7 and, 1hr for Dd2. Heating reduced the efficacy of *E. cloacae*-derived metabolites only (P=0.02) while proteinase K treatment had no effect. Our data provides preliminary results on studies that aim to understand the mechanisms, potential applications and feasibility of mosquito midgut symbiont-based approaches for mosquito/disease control.

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ELIZABETHKINGIA ANOPHELIS MSU001 ISOLATED FROM *ANOPHELES STEPHENSI*: MOLECULAR CHARACTERIZATION AND COMPARATIVE GENOME ANALYSIS

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Elizabethkingia anophelis is an aerobic, non-fermenting, non-motile, non-spore-forming gram-negative rod that readily colonizes the mosquito gut, forms part of the gut microbiome, and offers potential for control of mosquito-borne pathogens via paratransgenesis. However, it also is an opportunistic pathogen of humans. This study involved characterization of a new strain, E. anophelis MSU001, isolated from *Anopheles stephensi* (JHU strain) in the laboratory, and characterized by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-ToF/MS), biochemical testing, and genome sequencing. The strain was isolated by

dissecting a gut of An. stephensi and plating contents onto Luria-Bertani agar medium with erythromycin. Average nucleotide identity analysis revealed 99% identity of MSU001 with the type species E. anophelis R26. Phylogenetic placement revealed a clade with mosquito-associated strains separate from a clade of clinical isolates. Comparative genome analysis showed that it shared at least 98.6% of genes with mosquito-associated isolates (except E. anophelis As1), while it shared at most 88.8% of common genes with clinical isolates, suggesting divergence between strains adapted to the mosquito gut and clinically-significant strains. Metabolites from MSU001 inhibited growth of E. coli but not mosquito gut symbionts Serratia marcescens and Asaia sp. strain W12. Mosquito-associated E. anophelis strains carried glycoside hydrolase- and auxiliary activities-encoding genes distinct from those of clinical isolates, indicating their potential role in reshaping chitin structure and other components involved in larval development or formation of the peritrophic matrix. Like other Elizabethkingia, MSU001 also carried genes encoding two-component system proteins, transcription factor proteins, DNA-binding proteins, and a diverse repertoire of antibiotic resistance genes and several virulence factors. Its potential for opportunistic infections in humans should be further evaluated prior to implementation as a paratransgenesis agent.

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REPRODUCTIVE STRATEGIES ASSIST THE BIOLOGICAL INVASION PROCESS OF *AEDES ALBOPICTUS*

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The success of biological invasions depends on a species ability to survive and reproduce in a new environment, traits which mediate the effective establishment and persistence in new habitats. The arboviral vector *Aedes albopictus* is a successful invasive mosquito, which conquered tropical and temperate areas of the world in less than 100 years. The rapid spread of *Ae. albopictus* has been ascribed to its ecological plasticity, its ability to overwinter through photoperiodic diapause and produce desiccation resistance eggs. Whether *Ae. albopictus* reproductive capacity has contributed to its invasive success has not thoroughly investigated yet. Here, we compared the phenotypic variations and reproduction potentials of several *Ae. albopictus* populations. We observed extensive phenotypic variations between invasive and native populations with invasive mosquitoes being statistically bigger in size and having a higher reproductive output. To investigate the biological underpinnings of these differences, we visualized ovaries during their development and analyzed their physiology and protein profile in a comparative manner including mosquitoes of an invasive population with respect to those of the laboratory Foshan reference strain. We observed that females of the invasive population better allocate the energy reserves acquired during the larval stage and that from a blood meal resulting in higher production of fertile eggs than Foshan mosquitoes. Proteomic analyses and ovarian micrographs showed a delay in oogenesis in invasive mosquitoes which correlated with a higher fecundity and fertility. We further performed reciprocal crosses between mosquitoes of Foshan and the invasive population which highlighted a potential contribution of males on the reproductive success of invasive mosquitoes. Overall, our findings show reproductive strategies assisted the biological invasion process of *Ae. albopictus*.

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CHARACTERIZING RESIDUAL MALARIA TRANSMISSION IN THREE SELECTED HIGH BURDEN DISTRICTS OF WESTERN PROVINCE, ZAMBIA

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Zambia remains a highly malaria-endemic country, with infection risk highest in rural regions such as Western Province. The primary vectors responsible for transmission vary by region and include *Anopheles funestus s.s.*, *An. gambiae s.s.*, and *An. arabiensis*. Since 2002, implementation of standard vector control interventions, namely insecticide treated nets and indoor residual spraying, has contributed substantially to reducing the malaria burden in Zambia: between 2002 and 2018 national-level malaria prevalence in children under 5 dropped from 22% to 9%, while inpatient malaria cases and deaths each declined by approximately two-thirds. However, in Western Province malaria burden remains high, with 2021 estimates of under 5 prevalence near 50% and all-ages case incidence at 785/1000 person-years at risk. This consistently high burden despite quality implementation of effective malaria control programming shows that residual transmission persists, and underscores the need to better understand key entomological drivers of residual transmission to guide targeted scale up of complimentary interventions and to inform development of new tools and approaches. This study aimed to characterize, for the first time, the full breadth of *An. funestus* biting behaviors in four high burden communities of Western Zambia. Longitudinal vector surveillance was conducted from January to April 2024 using human landing catches (HLC) conducted over 24 hours, indoors and outdoors, at households and at schools and markets. Results indicate biting occurs both indoors and outdoors with a peak in the early morning from 01:00 - 6:00, but substantial potential for malaria transmission also exists in the later morning hours - particularly indoors at schools, where more than 1 bite per person was recorded between 6:00 and 11:00 each collection day. Future work should expand 24-hour vector surveillance activities year-round, explore sporozoite positivity by time and location of human biting, and overlay vector and human behaviors to map a fuller understanding of community-wide malaria transmission risk and identify gaps in current vector control approaches.

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FOREST EDGE LANDSCAPE CONTEXT AFFECTS MOSQUITO COMMUNITY COMPOSITION AND RISK OF PATHOGEN EMERGENCE

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Forest edges, where humans, mosquitoes, and wildlife interact, may serve as a nexus for zoonotic arbovirus exchange. Although often treated as uniform interfaces, the landscape context of edge habitats can greatly impact ecological interactions. Here, we investigated how the landscape context of forest edges shapes mosquito community structure in an Amazon rainforest reserve near the city of Manaus, Brazil. Between July 2021 and June 2022, we sampled diurnally active mosquitoes using hand-nets at ground level and on 5 m platforms at three distinct forest edge types bordering urban land cover, rural land cover, and natural treefall gaps, while sites in continuous forest served as controls. Mosquito communities differed considerably between forest edges and continuous forest. Urban edges had the most distinct communities, dominated by ground dwelling *Aedes albopictus* and *Limatus durhamii*, followed by rural edges, and treefall gaps where *Haemagogus*, *Psorophora*, and *Sabethes* species were common. Rural edges supported the highest species diversity, providing suitable habitat for both urban and forest specialists, including key arbovirus

vectors. *Haemagogus janthinomys* was notably abundant at ground level at treefall gaps, where there is a high risk for interaction between this species and ground dwelling wildlife and humans. Our findings emphasize the importance of landscape context in assessing pathogen emergence risk at forest edges.

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MOLECULAR XENOMONITORING FOR POST-VALIDATION SURVEILLANCE OF LYMPHATIC FILARIASIS IN BANGLADESH: EVIDENCE TO SUPPORT LYMPHATIC FILARIASIS (LF) ELIMINATION AS A PUBLIC HEALTH PROBLEM

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Bangladesh achieved validation of elimination of lymphatic filariasis (LF) in 2023. To cement this achievement and sustain elimination, the program must continue emphasis on post validation surveillance and response measures to prevent recrudescence of infection. Tailoring a sensitive surveillance strategy by combining host- and vector-directed surveillance tools is imperative to track the transmission of LF at this phase. Since molecular xenomonitoring (MX) is a non-invasive and sensitive means for surveillance, we used this technique to detect any *Wuchereria bancrofti* (Wb) DNA. We included 62 villages under Gangachara Upazila, spanning in two evaluation units (EU) in Rangpur district, in the cross-sectional survey. We applied an index-based approach to collect mosquitoes from residences of LF clinical patients (n=83) and their neighboring households (n=315) within a≈50 m radius. Mosquitoes were collected Jun 2022-Nov 2023 using CDC gravid traps placed in each household for three consecutive nights. Mosquitoes were identified morphologically using a standard taxonomic key and placed into pools of up to 25 mosquitoes. Female Culex quinquefasciatus (fed and gravid) were tested for Wb DNA using previously described real time PCR pool screening method. We collected 47,611 *Cxulex quinquefasciatus* mosquitoes including 44,785 females; 1.6% were fed and 72.9% were gravid. In total, 1,225 mosquito pools (15-25 mosquitoes per pool), comprising either blood-fed or gravid females, were tested. We detected Wb DNA in four pools corresponding to estimated prevalence rates of 0.03% (95% Confidence Interval (CI): 0.01-0.07%) or 0.03% (95% CI: 0.01-0.07%) using maximum likelihood estimation and Bayesian estimation, respectively. These data indicate the persistence of low levels of Wb infection in the EUs below the provisional threshold (<0.25%) set by WHO and are consistent with results of previous transmission assessment surveys. Our findings support the adoption of MX by the national LF elimination program to monitor transmission of infection in combination with host surveillance data, which could help prevent the recrudescence of LF.

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DETECTION OF *AEDES ALBOPICTUS* IN DISTRICT 3 OF MANAGUA, NICARAGUA

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The Asian tiger mosquito, *Aedes albopictus* (Skuse), is an invasive mosquito species that has established itself in all continents of the globe, except for Antarctica. It is the vector of over 30 arboviruses, serving also as a bridge vector for diseases such as West Nile virus and Eastern equine encephalitis virus. Entomological larvae, pupae and adult surveys were conducted during the rainy and dry seasons of 2022 and 2023 in a rural (Nejapa) and urban (Camilo Ortega) sector of District 3 of Managua, Nicaragua. We randomly selected 500 households from a parent arboviral clinical and serological cohort study as well as 65 key sites, all in the catchment areas of our study health posts. All mosquito life stages were transported to our main facilities in Managua for classification and separation by stage (unfed and bloodfed), sex and species. We found only 2 larvae of *Ae. albopictus* in each survey of the dry season of 2022 (Camilo Ortega) and 2023 (Nejapa), with no *Ae. albopictus* found in the rainy season of 2022. However, in the 2023 rainy season, we collected 557 *Ae. albopictus* larvae-pupae and 223 adults in both communities. A total of 415 immature aquatic forms and 76 adult mosquitoes (65 females) were collected in households. In key sites, we collected 142 larvae/pupae and 137 adults (79 females). We observed that in >60% of households and >40% of keys sites, the preferred habitat for immature forms was "other container" (*i.e.,* boot, toy, plastic bottle, etc). Our results reveal the introduction of *Ae. albopictus* into communities of District 3 of Managua over the past two years. Further surveillance is required to determine if *Ae. albopictus* will displace *Ae. aegypti* in the area or if co-habitation will occur. Additionally, this ecological displacement is critical to determine in the context of novel vector control activities targeting *Ae. aegypti* in Managua.

6999

GLOBAL ANALYSIS OF *ANOPHELES STEPHENSI* BIONOMICS AND CONTROL APPROACHES THROUGH A SYSTEMATIC LITERATURE REVIEW

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Anopheles stephensi is a mosquito endemic to South Asia and the Arabian Peninsula that has recently expanded its range into Africa, posing a significant threat to global malaria control efforts. This study investigates the efficacy of trapping methods and larvicides and larvivorous fish in controlling *An. stephensi* mosquitoes through an analysis of global literature, identified by searching all relevant databases (PubMed, Web of Science, and Google Scholar) for studies focused on *An. stephensi*'s behavior and biology. Data from 83 articles revealed that host-seeking human-baited traps improve collection efficiency significantly when compared to mechanical baited traps, with no difference observed between human-baited and animal-baited traps. However, mechanical unbaited traps outperform mechanical baited traps. *Anopheles stephensi*'s indoor and outdoor biting and resting behaviors exhibit no significant difference, and its breeding habitats include discarded household utensils and vegetative areas. *Bacillus thuringiensis israelensis, Beauveria bassiana* and temephos are the most effective larvicides among those considered. Comprehensive surveillance programs covering both larval and adult populations are crucial for assessing intervention impacts and quantifying resistance levels. Increased use of biolarvicide control tools is recommended to control *An. stephensi*, since

resistance to traditional chemical insecticides is confirmed in adults. Understanding historical surveillance and control approaches is essential to the advancement of invasive *An. stephensi* mitigation efforts in Africa and the reduction of impacts on malaria morbidity and mortality.

7000

ASSESSMENT OF TWENTY-FOUR HOURS BITING PATTERNS AND HUMAN EXPOSURE RISK TO BITES OF *ANOPHELES* MOSQUITOES IN SOUTH-EASTERN TANZANIA

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Over the past two decades, Tanzania has made remarkable progress in reducing the malaria burden, instilling hope for its elimination by 2030. This success is attributed to the large-scale implementation of core vector control interventions such as LLINs and IRS. However, persistent transmissions from 24 hour exposure to infective mosquito bites remain a challenge to current elimination efforts. This study aimed to assess the 24-hour biting patterns and human exposure risk to bites of *Anopheles* mosquitoes in Ulanga district South-eastern Tanzania to inform strategies for addressing persistent transmissions. Hostseeking mosquitoes were collected hourly using a miniaturized double net trap over 24 hours both indoors and outdoors. Pooled hourly collections were morphologically and stored as dried samples for subsequent laboratory analyses Data analysis was done using R statistical software and all tables charts and graphs were generated using grammar for graphics R package. *An. arabiensis* and *An. funestus* were found to be the major vectors in the study area, accounting for 94% and 4% of the entire collections respectively. Interestingly, both species exhibited a shift towards day-biting behavior and their aggressiveness was not just limited to morning and evening hours but widely distributed across the entire daytime period. There was no difference between indoor and outdoor biting rates of the two species except only during daytime for the case of *An. arabiensis*. More than half of the mosquitoes collected during the daytime were unfed, a probable indicator of daytime host-seeking behavior. More than 65 percent of the dissected mosquitoes were parous potentially indicative of an older population with high malaria transmission potential. The suddenness of the day-biting behavior of malaria vectors may potentially increase the risk of malaria transmission This highlights the need for novel tools to supplement the existing interventions and intensive community engagement to increase awareness regarding day-biting mosquitoes and their associated malaria transmission risk.

7001

CHARACTERIZATION OF THE SPECIFIC COMPOSITION, TROPHIC AND RESTING PREFERENCES AS WELL AS THE LEVEL OF INFECTION OF MALARIA VECTORS IN THE CITY OF OUAGADOUGO, BURKINO FASO

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Malaria in urban areas is a scourge whose importance is increasing with the increase in immigration to urban areas. Urban malaria remains a public health problem whose fight relies on better knowledge of vector biology. The objective of this research was characterize the specific composition, trophic and resting preferences as well as the level of infection of malaria vectors in the city of Ouagadougo. Adult mosquitoes were collected during the rainy season from July to October 2023 in the city of Ouagadougou. A total of 31 neighborhoods across three health districts (Baskuy, Bogodogo and Nongremassom) were visited. The choice of neighbourhoods in the three districts was 10 neighborhoods per district and was done randomly. Mosquitoes were collected outside and inside houses. The distance between the houses is 100 meters. Collections were made using electric vacuum cleaners. Collections were carried out in the morning between 6 a.m. and 9 a.m. and in the evening between 4 p.m. and 5 p.m. to increase the chances of collecting resting mosquitoes. PCR was used to identify the members of Anopheles gambiae complex, as well as the origin of the blood meals. The ELISA method was used to determine the infection of mosquitoes by *P. falciparum*. Approximately thirty-nine thousand seven hundred and twenty-seven (39,727) mosquitoes including 1,304 *Anopheles gambiae* s.l females were collected. After molecular identification, 1261 (96.7%) was *Anopheles arabiensis* and 43 (0.03%) from *Anopheles coluzzii*. Five hosts were identified as the source of blood meals, 108 (43.37%) human blood meals, 93 (37.65%) blood meals in cattle, 24 (9.71%) in pigs, 18 (7. 28%) on dogs and 04 (1.61%) on goats. The majority, 66.41% of *Anopheles gambiae* s.l were collected outside homes. A total of 10 mosquitoes infected with *P. falciparum* sporozites were identified, representing an infection rate of 0.7%. Anopheles represent 5.6% of the number of mosquitoes collected in the different areas. Despite this relatively low infection rate, the exophilic behavior of these mosquitoes, associated with rapid urbanization, deserves specific attention in the fight against malaria.

7002

DEVELOPMENT OF ENVIRONMENTAL DNA (EDNA) SAMPLING FOR ARBOVIRUS VECTOR SURVEILLANCE IN SOUTHERN NEVADA

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Accurate, rapid, and cost-effective surveillance of arbovirus mosquito vectors is critical for monitoring species distribution and infection prevalence and ultimately mitigating transmission risk. Vector surveys conducted by the Southern Nevada Health District (SNHD) are limited to a few productive sentinel sites, with considerable infrastructure and logistical requirements. New vector surveillance methods that are simple and unbiased at the sampling stage are needed. One potential method to increase efficient vector sampling capacity may be to exploit detection of environmental DNA (eDNA), shed by vectors breeding in aquatic environments. In this study, we first designed and optimized a novel multiplex TaqMan qPCR assay, based on SNPs in COXI, for simultaneous detection of the three major regionally important arbovirus vector species: *Culex* (*Cx.*) *quinquefasciatus*, *Cx. tarsalis,* and *Aedes* (*Ae.*) *aegypti*. 50ml water samples were collected from across Clark County using sterile plastic syringes and 0.22µm filters. Collection sites included water bodies that were adjacent to overnight gravid traps and BG sentinel traps, set by the SNHD, to compare vector species composition between sampling methods and additional aquatic environments in local public parks, golf courses, and drainage ditches. eDNA was extracted from filter membranes and screened for vector species presence using our qPCR assay. eDNA deposited by co-occupying *Cx. quinquefasciatus* and *Ae. aegypti* was detected in water samples, without observable larvae breeding, from multiple drainage ditches. *Cx. tarsalis* was identified in water samples from stormwater runoff and drainage channels in a public park. eDNA surveillance has the potential to be implemented as a field-friendly, arbovirus vector surveillance tool for expanded entomological monitoring capacity in southern Nevada, to detect changes in dispersal patterns of arbovirus vector species as well as the spread of new invasive vector species. eDNA amplicon-seq is ongoing to characterise vector population dynamics and insecticide resistance mechanisms to inform potential regional control initiatives.

7003

UNDERSTUDIED MALARIA VECTORS MAY DRIVE RESIDUAL MALARIA TRANSMISSION IN CHOMA DISTRICT, AN AREA OF LOW MALARIA TRANSMISSION

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Choma District in southern Zambia continues to measure low rates of malaria transmission despite very low counts of f what have been recognized as the primary vectors, *Anopheles funestus* and *An. arabiensis.* This altered vector landscape may create opportunities for understudied secondary vectors to subsequently act as sources of residual malaria as demonstrated by the recent presence of *Plasmodium falciparum* sporozoites in *An. squamosus, An. coustani* and *An. rufipes*. This study investigated understudied malaria vectors; species composition, relative abundance, and sporozoite infectivity as measures of potential malaria transmission. The study was conducted in three catchment areas of Choma district; Macha, Simaubi and Mapanza, which together recorded a parasite prevalence of less than 1% from October 2022 to February 2024. Forty-eight sentinel households in historical malaria hotspots were recruited. Monthly, Center for Disease Control and Prevention Light Traps were set indoors (sleeping area), the peri domestic area (outdoor kitchens) and near animal shelters (goat pens and/or cattle kraal). In 1,991 trap night-traps, 11,114 *Anopheles* mosquitoes were collected. *Anopheles squamous* was the dominant species (*n*=5,190; 58.6%). Other species were *An. gambiae* s.l., *An. coustani* s.l., *An. rufipes*, *An. pretoriensis*, *An. funestus* group, *An. Pharoensis* and most mosquitoes were collected from goat pens (n=8,112; 73.0%). There was a statistically significant higher mean count of anopheline mosquitoes outdoors in the peri domestic area (mean=1.44, 95% CI 1.22-1.65) and outdoors near goat pens (mean=23.8, CI 22.7-24.9) than indoors (mean= 0.78, CI 0.68-0.89) (t-test, $t_{(1483)} = 8.38$, $P > 0.001$ and $t_{(1483)} = 4.88$, $P > 0.001$ respectively). Sporozoite infectivity rates in *An. coustani, An. squamosus* and *An. rufipes* were 0.52%, 0.58% and 0.10% respectively. High outdoor counts of understudied malaria vectors present a potential risk to sustaining residual malaria transmission.

7004

THE ESCALATING BIOLOGICAL THREAT: OBSERVATIONS FROM TEN YEARS OF MAPPING INSECTICIDE RESISTANCE IN MALARIA VECTORS.

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Insecticide resistance remains a key biological threat recognized by World Health Organization (WHO) as a key biological threat to the stagnating gains in malaria control and elimination. Insecticide Resistance Management (IRM) is important to identify areas where resistance has been reported and understand the associated resistance mechanisms. IR Mapper has offered insecticide resistance mapping support since 2012. IR Mapper collates insecticide resistance information reported in peer reviewed, published literature, with monthly updates. These are loaded onto a cloud database, then visualized on the mapping platform developed using ArcGIS API. Partnerships and collaborations have been focal in the IR Mapper process. Growing from a platform that maps phenotypic resistance and resistance mechanisms, to addition of malaria endemicity layers and modelled surfaces that predict the probability of resistance to cover scarcity of resistance data due to monitoring constrains. This analysis gives a view of pyrethroid resistance trends between the years 2000-2015, when pyrethroid LLINs offered the greatest impact against malaria, and 2016-2023 when gains stagnated, focusing on sub-Saharan Africa which holds more than 90% of global malaria cases and deaths. By the main vector species, pyrethroid resistance in *Anopheles gambiae* s.l., increased 1.3-fold, from a median mortality of 59 (IQR: 30-78) between 2000-2015 to a median mortality of 45 (IQR: 16-72) between 2016-2023. In *An. funestus*, pyrethroid resistance has grown from a median mortality of 54 (IQR:23-74) in 2000-2015 to a median mortality of 60 (IQR: 40) in 2016-2023. The most reported resistance mechanism are knock-down resistance gene mutations and over expression of mixed function monooxygenases. Regions with the highest malaria burden also show high levels of pyrethroid resistance. IR Mapper continues to be a valuable tool in aiding vector control decisions by being a point of reference for up-to-date insecticide resistance data. With ever changing needs, IR Mapper is getting an update to encompass additional molecular resistance mechanisms such as the P450 gene family data.

7005

QUANTIFYING FEW, FIXED, AND FINDABLE: A DIGITAL, STRATIFIED SURVEILLANCE APPROACH TO ASSESS LARVAL SOURCE MANAGEMENT FEASIBILITY IN MOZAMBIQUE'S CAPITAL CITIES

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Malaria remains a major health challenge in Mozambique. Insecticide-treated nets and indoor residual spraying face issues such as rising insecticide resistance and outdoor biting, and depend on community compliance. Larval source management (LSM) offers a supplementary method, especially in urban and semi-urban areas. To evaluate the feasibility of Larval Source Management (LSM) and its alignment with the "few, fixed, and findable" criteria set by the WHO, we assessed the density, types, positivity, and permanency of water bodies in the 11 provincial capital cities of Mozambique. To ensure unbiased sampling, we combined stratified and random sampling methods, enhancing the representativeness of our data. All areas of the cities were stratified based on factors such as population density, topography, and proximity to rivers. Sectors were randomly selected for surveillance from each strata. Field officers were assigned to walk through the selected sectors and report water bodies using the Zzapp mobile app. Water bodies were reported, categorized (e.g., swamp, agricultural), and sampled for larvae. In all cities, the density of water bodies was below 200 per square kilometers, making LSM feasible. With over 50 houses per water body, the cost per person for LSM is projected to be low ("Few"). Most water bodies were classified as permanent or semi-permanent ("Fixed"). Field workers thoroughly mapped the area, and we report related quantitative measures for area coverage and community acceptance ("findable"). In total, an area of 34.3 sq km was scanned, revealing 3,168 water bodies. Among all sampled water bodies across 11 cities, positivity rates for Anopheles and non-Anopheles larvae were 3% and 11%, respectively, with regional variations for Anopheles between 2-5%. Water bodies hosting Anopheles larvae included ponds (8%), swamps (4%), and other sites like puddles, agricultural, and construction sites (~2%), while pools and tires were not conducive to Anopheles larvae. The study provides a quantitative evaluation of the "few, fixed, and findable" criteria and suggests that all cities included in the study meet the WHO standards for LSM.

7006

HOW DOES BEDNET USE AFFECT FEMALE *ANOPHELES* EXPOSURE IN COTE D'IVOIRE: ASSESSING VECTOR-HUMAN INTERACTION USING ENTOMOLOGICAL SURVEILLANCE AND ACCELEROMETER-BASED BEDNET MONITORING

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The timing of bednet use may not correspond with the timing of vector exposure in malaria-prone households leading to continued transmission of malaria despite wide-scale distribution of long-lasting insecticide treated bednets. Surveys about bednet use provide only a snapshot of bednet use the previous night, whereas remote monitors can provide objective measurements of whether a bednet is in use over longer time periods. This observational study deployed accelerometer-based bednet monitors in Cote d'Ivoire to assess how exposure to female *Anopheles* mosquitoes overlapped with patterns in bednet use. Bednet use monitors were attached to the side of one bednet in each of 50 households from 3 regions representing different malaria transmission settings: urban Yamoussoukro (20 households), peri-urban Tiassalé (20) and rural Korhogo (10). Accelerometer data was classified using a previously trained random-forest machine learning algorithm (Koudou et al. 2022). Entomological surveillance was performed using window traps. Mixed-effects regression models were employed to account for multiple measures per household. Negative binomial regressions were used to assess the biting rate, defined as the number of fed *Anopheles* mosquitoes retrieved from the window traps per night. Fifty households were followed for a mean of 115 nights each (5,749 total nights), and mean bednet use was 10.3 hours per night (95% CI: 9.8 - 10.9). Each additional hour of bednet use per night was associated with a 4.0% decrease in the nightly biting rate (95% CI: 0.0% to 7.5%; p=0.03), which is equivalent to 29.4% decreased rate of mosquito biting for each hour of additional bednet use averaged over a month. There were differences between regions, with peri-urban Tiassalé (+83%; p=0.05) and urban Zatta (+94%; p=0.07) having higher rates of fed mosquitoes compared to Korhogo. These findings suggest that bednets provide variable protection between regions based on differences in vector and human behaviors. Further work characterizing these differences by vector species and the timing of biting could shed light on better ways to prevent malaria in the future.

7007

ADVANCES IN ARTIFICIAL INTELLIGENCE FOR VECTOR IDENTIFICATION AND MONITORING

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Recent advances in artificial intelligence and machine learning, such as the use of convolutional neural networks (CNNs) for image recognition, have emerged as a promising modality with the capability to visually differentiate between mosquito species. Here we present the first performance metrics of IDX, Vectech's system for AI mosquito identification, as part of Maryland's mosquito control program in the USA. Specimens were collected over 14 weeks in 2023 from 12 CDC gravid trap collection sites in Anne Arundel county, identified morphologically by an entomologist, and imaged using the IDX system. By comparing entomologist identification to the algorithm output by IDX, we are able to calculate the accuracy of the system across species. Over the study period, 2,591 specimens were collected and imaged representing 14 species, 10 of which were available in the identification algorithm on the device during the study period. The micro average accuracy was 94.9%. Of these 10 species, seven consisted of fewer than 30 samples. The macro average accuracy when including these species was 79%, while the macro average when excluding these species was 93%. In the next iteration of this technology, Vectech is optimizing the vector identification capabilities of IDX to handle high-accuracy identification of both primary and secondary malaria vectors including *Anopheles gambiae s.l., An. funestus, An. stephensi, An. coustani, An. pharoensis* and others that will allow public health organizations in malaria endemic countries to increase entomological surveillance capability. These advances demonstrate the utility of artificial intelligence in contemporary entomological practice and its potential to support current vector surveillance and control programs around the world.

7008

DOES DOMESTIC USE OF INSECTICIDAL SPRAYS UNDERMINE PUBLIC HEALTH CONTROL STRATEGIES?

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Despite the ongoing threat of evolving insecticide resistance to anti-mosquito campaigns worldwide, insecticide-based intervention remains the primary strategy for preventing vector-borne disease (VBD) transmission. Untangling the drivers of mosquitoes' evolving resistance to insecticides is critical for resistance management and interventions' effectiveness. Meanwhile, public health and agriculture-related insecticide use have been suggested as primary drivers of increased mosquito resistance, although the role of household insecticide use for self-protection remains an unappreciated contributing factor. Herein, we aimed to assess the level of household insecticide usage in VBD-endemic countries through a literature review and determine mosquito resistance to pyrethroid-based domestic insecticides. Our findings indicate that using household insecticides for self-protection has been commonplace over the past decade in all 19 studied countries across the Americas, Africa and Asia, with ≈60% of homeowners surveyed using insecticide-based products. Our results also suggest that the widespread use of domestic insecticides may impose heterogeneous insecticidal selection pressure, driven by a vast spectrum of pyrethroid blends identified worldwide within 67 distinct insecticidal aerosol products. Aerosolized household formulations may vary in effectiveness - our susceptibility results for 10 *Aedes aegypti* populations from three Brazilian Northeastern states (PB, PE, RN) revealed mortality rates from 30% to 100%, which aligns with susceptibility profiling against public health pyrethroid insecticides. Furthermore, genotypic-phenotypic inferences indicate that ≈100% of surviving *Ae. aegypti* mosquitoes exposed to two aerosolized insecticides were triple-resistant homozygotes (*Kdr* - 410Leu/016Ile/1534Cys), which are also known to impact public health insecticides efficacy. Together, this evidence highlights the need to re-scrutinise the impact of private use of domestic insecticides on public health programmes to ensure the sustainability of current and novel vector control interventions.

7009

APPLICATION OF PREDICTIVE MODELLING OF DENGUE CASE NUMBERS USING METEOROLOGICAL DATA IN PERU

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Climate change is anticipated to increase the frequency and magnitude of extreme weather events during the El Niño Southern Oscillation (ENSO), intensifying meteorological determinants that compound mosquito-borne diseases. In 2023, Peru experienced its highest-ever dengue burden after surpassing 270,000 cases, and the situation is expected to worsen with ENSO continuing from June 2023 into 2024. The objective of this study is to assess the accuracy and applicability of a meteorological predictive model for dengue cases in Peru amidst varying scenarios during ENSO, with potential adaptability to other ENSO-affected countries. Weekly dengue cases for Peru and meteorological data from January 2014 to July 2023 were aggregated monthly. Using a linear model with a five-month lag

applied to meteorological variables, we forecasted dengue cases from July 2023 to July 2024. Forecast accuracy was assessed by the percentage error between forecasted and actual case counts. ENSO projection scenarios of an increase in the ten-year monthly precipitation average of 10%, 20%, and 50% were evaluated. Monthly dengue cases correlated with precipitation, but not temperature. Forecasting projected 292,337 cases (CI: 213,256-400,742) by the end of 2023 and 188,455 (CI: 135,815-261,497) dengue cases for the first half of 2024. Forecasts were accurate to +/- 7% difference for the last half of 2023 and February 2024, while a difference of -52.7% was observed for January 2024, likely exaggerated by small numbers due to reporting year recalibration. ENSO projections for increases in the ten-year monthly precipitation average for the first half of 2024 ranged from 223,530 (CI: 160,164-311,967) to 442,437 (CI: 308,735-634,039). The forecasting success demonstrates the potential of this methodology as an early warning system for dengue-endemic countries increasingly affected by weather events brought on by climate change. Projection scenarios can be used to better target existing vector control interventions as dengue vaccination capacity is further developed.

7010

SEMI-FIELD EVALUATION OF AQUATIC PREDATORS FOR THE CONTROL OF *ANOPHELES FUNESTUS* IN RURAL SOUTHEASTERN TANZANIA

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Biological control is a promising alternative or complementary approach for controlling vector populations in response to the spread of insecticide resistance in malaria vectors. This study evaluated the efficacy of three selected potential predators on the density and fitness parameters of *Anopheles funestus* larvae in rural Tanzania. Common predator families (Aeshnidae, Coenagriondae, and Notonectidae) and *An. funestus* group larvae were collected from natural aquatic habitats in rural south-eastern Tanzania. Predators were starved for 12hours while *An. funestus* larvae were given fish food before starting the experiment. *Anopheles funestus* larvae were placed into artificial habitats containing predators, exposing them to potential predation. The number of surviving *An. funestus* larvae was counted every 24hours. An emergence trap was placed at the top of artificial habitats to capture emerging mosquitoes. Emerged mosquitoes were monitored until they died. Female wings were measured and used as a proxy for body size. Generalized linear mixed models (GLMM) with binomial variates at 95% CI and Cox proportional hazard models were used to assess the proportion of dead mosquitoes and the daily survival determined. There were significant differences in the number of emerged mosquitoes between the treatment and control groups ($p<0.001$). Thus, all predator species played a significant role in reducing the density of *An. funestus* mosquitoes ($P<0.001$). Furthermore, these predators had notable effects on the fitness parameters and survival of emerged mosquitoes ($P<0.001$). Among the three predators studied, Coenagrionidae were most efficient followed by Notonectidae, with Aeshnidae being the least efficient. Selected aquatic predators have the potential to reduce the survival and density of *Anopheles funestus* larvae. They might eventually be included within an integrated malaria vector control strategy, ultimately leading to a reduction in malaria transmission.

7011

NAVIGATING THE EVALUATION OF NOVEL IRS PRODUCTS: LESSONS LEARNED FROM ASSESSING RESIDUAL EFFICACY WITHOUT SUSCEPTIBLE MOSQUITO COLONIES

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Novel, longer-lasting insecticidal products are now on the market that can help countries extend IRS protection and combat resistant mosquitoes. However, residual efficacy varies widely from setting to setting. While the need to measure the residual efficacy of such products prior to their implementation is paramount to appropriately targeting them, justifying their higher price point, and sometimes even for registering the product, many countries lack the susceptible mosquito colonies required to do so. One such example, Honduras, was in search for a longer-lasting product capable of addressing resistant vector populations, yet did not have a susceptible colony to measure its local residual efficacy. With support from CHAI and Envu, the country embarked on a study to evaluate the residual efficacy of Fludora® Fusion on local surfaces using local wild mosquitoes. This session presents the findings of the study conducted in Honduras, highlighting the challenges encountered in the absence of a susceptible mosquito colony and because of the specific post-exposure holding times required for assessing this innovative product. The lessons learned will support other countries that, like Honduras, are interested in introducing novel IRS products and need practical solutions to overcome a lack of susceptible mosquito colonies to measure their residual efficacy.

7012

DEVELOPMENT AND EVALUATION OF A NOVEL, MULTI-ACTIVE INGREDIENT ATTRACTIVE TOXIC SUGAR BAIT FOR MOSQUITO CONTROL

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The continuingly high burden of disease caused by mosquito-borne pathogens highlights the need to develop novel tools to suppress mosquito populations. Attractive toxic sugar baits seek to exploit mosquito nectar-feeding behavior through a lure-and-kill approach, coaxing mosquitoes to feed on baits containing a lethal products. To be viable, these products must retain their efficacy for weeks or even months after their initial deployment. Declines in activity over time could potentially mediate resistance amongst exposed mosquitoes. To address this issue, we have developed a novel attractive toxic sugar bait that contains several different chemical and microbial active ingredients. Each active ingredient mediates adult mosquito mortality through a distinct mechanism, potentially mitigating issues of insecticide resistance. Our data demonstrate high efficacy of this bait as an attractant. We observed rapid, and significant mortality amongst pyrethroid-susceptible and -resistant, adult *Aedes aegypti* and *Culex quinquefasciatus* mosquitoes after feeding on the bait under laboratory conditions. We also demonstrate synergistic mortality effects accrued when the different active ingredients were tested in combination. Semi-field trials highlight that the bait retains high mosquitocidal activity under environmental heterogeneity. Further testing of the bait is ongoing, but these initial findings highlight a promising new tool for mosquito control.

7013

HOW FREQUENTLY DO WE NEED TO TREAT BREEDING SITES WITH *BACILLUS THURINGIENSIS ISRAELENSIS* (*BTI*)? EVIDENCE FROM LARGE-SCALE LARVAL SOURCE MANAGEMENT ON BIOKO ISLAND

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Larval source management (LSM) is one of the few vector control interventions available to target indoor and outdoor biting mosquitoes. In 2023, due to increasing evidence of residual biting both indoors and outdoors, the Bioko Island Malaria Elimination Project (BIMEP) expanded LSM in urban Malabo as a complement to indoor household interventions. The larvicide *Bacillus thuringiensis israelensis* (*Bti*) in granular form was used due to it being available, affordable and easy to apply. A critical aspect of the product is the required frequency of treatment of breeding sites to maximize impact. The manufacturer recommends a 7-to-14-day frequency of application, however there is limited field evidence about the effect size of different frequencies. Here, we investigate the effect of treatment frequency over four months (85 field days) in urban Malabo. At varied frequency bins, daily data on prospective breeding sites detected, verified positive sites, and sites treated were utilized to estimate positivity rate (sites positive/sites found/day). The median frequency of field teams visiting target areas was 10 days. Initial findings reveal a 7-day revisit frequency considerably lowers positivity rates than longer intervals. Visit frequency bins of 8-10, 11-14, and 15-20 days had similar effects on positivity, while frequencies longer than 20 days did not significantly reduce positivity relative to baseline. These findings may be context specific, and suggest that on Bioko, shorter than longer intervals did maximize the impact of LSM. This represents an operational challenge as shorter revisit intervals demand more resources. Moreover, the fact that medium intervals (between 8-20 days) appear to provide similar results in positivity that remain significantly below baseline levels gives some implementation flexibility. As part of the BIMEP's approach to adaptive malaria control, this information will prove useful to inform LSM targeting strategies whereby places with higher larval densities could be revisited at the highest operationally feasible frequency while others can be visited at the longer intervals resulting in impact.

7014

ASSESSING THE SUSCEPTIBILITY AND EFFICACY OF TRADITIONAL NEUROTOXIC (PYRETHROID) AND NEW GENERATION INSECTICIDES (CHLORFENAPYR, CLOTHIANIDIN, AND PYRIPROXYFEN), ON WILD PYRETHROID RESISTANT POPULATIONS OF *ANOPHELES GAMBIAE* FROM SOUTHERN BENIN

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This study aimed to determine the susceptibility of wild *Anopheles gambiae* sensu lato (s.l.), the main malaria vector in southern Benin, to chlorfenapyr (CFP), pyriproxyfen (PPF), clothianidin (CTD), and three pyrethroids insecticides (alpha cypermethrin, deltamethrin, and permethrin). Additionally, the efficacy of ITNs containing CFP, PPF and alpha-cypermethrin (ACM) was assessed with wild *An. gambiae* s.l. reared to adults from larvae and the susceptible laboratory strain, *An. gambiae* sensu stricto (Kisumu). Wild *An. gambiae* from the communes of Allada, Ifangni, Akpro Missérété, and Porto-Novo were tested for susceptibility to CFP and PPF using the WHO bottle test and to the pyrethroids and CTD using the WHO tube test. WHO ITN efficacy tests using standard plastic cones were used to evaluate the efficacy of ACM only, (CFP, ACM), and (PPF, ACM) nets. The ovaries of blood fed *An. gambiae* from Ifangni and the susceptible laboratory strain, *An. gambiae* (Kisumu) exposed to a PPF treated net were dissected, and egg development status was examined using Christopher's stages to determine the fertility status. Using a standardized protocol, the oviposition rate and oviposition inhibition rate were calculated from live blood fed *An. gambiae* placed in oviposition chambers after exposure to PPF. In resistance bioassays, the mosquito populations from the four communities, pyrethroid mortality ranged from 5% to 80%, while CFP and CTD mortality ranged from 98% to 100%. At Ifangni, all mosquitoes exposed to nets with (PPF, ACM) were infertile while most (74.9%) of mosquitoes exposed to nets with ACM only had fully developed their eggs to Christopher's stage five. The oviposition inhibition rate after exposure of the mosquitoes to the PPF was 99% for the wild population of *An. gambiae* s.l. and *An. gambiae* (Kisumu). Pyrethroid-resistant *An. gambiae* from the selected communes in southern Benin were susceptible to CFP, CTD, and PPF. Furthermore, nets with (PPF, ACM) and (CTD, ACM) insecticides were effective against pyrethroid resistant mosquitoes from Ifangni. Continued monitoring for insecticide resistant *An. gambiae* is needed in Benin.

7015

SPECIES-SPECIFIC SALIVARY ANTIGEN ELISAS AS BIOMARKERS OF EXPOSURE TO LA CROSSE VIRUS VECTORS IN NORTH CAROLINA

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La Crosse virus (LACV) is the leading cause of pediatric arboviral neuroinvasive disease in the United States. Three mosquito species are likely responsible for the majority of LACV transmission – *Aedes triseriatus*, the primary, endemic vector and two invasive, secondary vector species: *Ae. albopictus* and *Ae. japonicus*. The risk of LACV disease is geographically persistent in North Carolina; however, current estimates of disease risk do not accurately reflect exposure risk or the genuine burden of disease. Furthermore, low incidence and poor detection rates grossly limit the evaluation of potential public health interventions. We seek to use mosquito salivary gland ELISAs to measure LACV vector exposure as a proxy for exposure/disease risk. Here we share the development of salivary gland (crude extract) IgG ELISAs for *Ae. triseriatus*, *Ae. albopictus* and *Ae. japonicus*. Using convenience human sera (n=41 individuals) from North Carolina, we compared optical density (OD) values for all three species. Pairwise comparisons (ANOVA, Tukey's HSD comparisons) detected higher mean OD values for *Ae. albopictus* as compared to *Ae. triseriatus* ($P = 0.013$). This is consistent with prior knowledge that *Ae. albopictus* is the more common peridomestic container *Aedes* in the areas where the human samples were obtained (Piedmont NC). Field and colony OD values of *Ae. triseriatus* were highly correlated ($r=0.88$) suggesting homologous immunogenic proteins are present in divergent species strains. The results of ongoing western blot and peptide sequence analyses will be shared. The application of these novel methods will be further demonstrated using field collected human sera from ongoing epidemiological studies in western NC (Summer 2024).

7016

IMPACT OF INDOOR RESIDUAL SPRAYING WITH SUMISHIELD® 50WG ON ENTOMOLOGICAL DRIVERS OF TRANSMISSION IN KIGOMA REGION NORTHWEST TANZANIA

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Despite the deployment of insecticide-treated nets (ITNs), indoor residual spraying (IRS), and artemisinin-based combination therapy (ACT), the population in Tanzania's Lake Zone remains at high risk of malaria transmission. PMI VectorLink Tanzania has supported IRS implementation in the region since 2015. The impact of IRS on transmission drivers was assessed through routine entomological surveillance. The IRS campaign with SumiShield® 50WG took place from October 5th to November 4th, 2022, in Kasulu and Kibondo districts. Monthly entomological surveillance, using various methods, was conducted before and after spraying in three sentinel sites: Kagerankanda and Minyinya (sprayed) and Murufiti (unsprayed). *Anopheles* species collected included *An. gambiae* (25.1%), *An. funestus* (29.8%), *An. arabiensis* (44.9%), and *An. parensis* (0.2%) in sprayed sites, with *An. funestus* predominating (75.1%) in unsprayed sites. Indoor resting densities were generally higher in Minyinya and Murufiti than in Kagerankanda. IRS led to reduced human biting rates in sprayed sites compared to unsprayed ones. Annual Entomological Inoculation Rates (EIR) varied, with the lowest in Kagerankanda (0 i/b/p) and the highest in Minyinya (39 i/b/p) and Murufiti (19.5 i/b/p). IRS with SumiShield® 50WG reduced human biting rates in sprayed areas, suggesting its effectiveness. However, varied impacts on indoor resting densities and EIR were observed, with reduced transmission noted in one sprayed site.

7017

COMPARISON OF UNTREATED AND TREATED INSECTICIDE-TREATED NETS TO DETERMINE THE VALIDITY OF WHO TUNNEL ASSAYS

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The WHO has established guidelines that provide specific, standardized procedures for testing Insecticide-Treated Nets (ITNs) for personal protection and malaria vector control. In these guidelines, the tunnel test is recommended for the evaluation of bio-efficacy of Insecticide treated nets against malaria transmitting mosquitoes. The laboratory bioassays results are an indicator of the bioavailability of the active ingredient of the tested product samples. In standard tunnel test a restrained bait (guinea pig or rabbit) is exposed to 50-100 mosquitoes for 12-15h overnight. According to animal welfare regulations, restraining laboratory animals for prolonged periods should be avoided unless it is not possible to achieve research objectives by other means. Here, three tunnel assays: 3-hours daytime, 6-hours daytime with sedated guinea pigs and 15h overnight with un-sedated bait were conducted. Firstly, untreated net was used to determine the feeding success. Then treated net material (unwashed Olyset) was evaluated and the main outcome measure was mortality and blood feeding success (BFS) which are determinants of a WHO tunnel assay validity. Both pyrethroid resistant and susceptible mosquito strains were used in the assay. The control experiments all replicate of both Kisumu and Muleba KisKis strains passed the WHO criteria of blood feeding success > 50%. In the treatment arm using susceptible Kisumu strain the % mean mortality at 24 hours was 90%, 84% and 98% for 3h day, 6h day and 15h overnight respectively while blood feeding inhibition was 87%, 73%, 92% for 3h day, 6h day and 15h overnight respectively. For the resistant strain Muleba Kis the %mean mortality at 24 hours was 8%, 35% and 23% for 3h day, 6h day and 15h overnight respectively, the blood feeding inhibition was 51%,30% and 27% for 3h day, 6h day and 15h overnight respectively. The results suggest that it is possible to avoid restraining laboratory animals for prolonged period of time by replacing the traditional method with the modified tunnel and achieve the recommended WHO research objectives.

7018

LATE MORNING BITING BEHAVIOUR OF *ANOPHELES FUNESTUS* IS A RISK FACTOR FOR MALARIA TRANSMISSION IN SCHOOLS IN SIAYA, WESTERN KENYA

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Children in Kenya spend a substantial amount of time at school, including at dawn and dusk when mosquitoes are often active. With changing vector behaviour towards early morning biting, it is important to determine whether there is an additional risk of transmission in schools. This study sought to understand whether late morning biting by *Anopheles funestus* previously documented in households in western Kenya was replicated in schools. From the 4th to the 6th of August 2023, human landing collections were conducted hourly in four schools in Alego Usonga Sub-County, Siaya County. The collections were conducted inside and outside five classrooms in each school and ran for 17 hours, starting at 18:00 until 11:00 hours the next morning. *Anopheles funestus* was the predominant species collected, accounting for 93.2% of the 980 mosquitoes collected, with peak landing between 06:00 and 07:00 hours and continuing until 11:00 hours. All *An. funestus* were identified as *An. funestus* sensu stricto by PCR. More than half of the collected *An. funestus* were either fed or gravid, potentially indicative of multiple bloodmeals within each gonotrophic cycle, and had a sporozoite rate of 2.05%. Other species collected included *An. gambiae* sensu lato (n=49; 6.3%), *An. coustani* (n=2, 0.26%), and *An. ziemanni* (n=2, 0.26%). Of the 49 *An. gambiae* s.l., 48 were identified by PCR as *An. arabiensis*. None of the *An. gambiae* s.l. tested positive for sporozoite infection. School children spend up to 10 hours per day at school, reporting between 06:00 and 07:00 hours and often staying in school until 17:00 hours, meaning that they are potentially exposed to infectious mosquito bites while at school. Targeting vector control approaches to schools and other peridomestic spaces in the morning hours when *An. funestus* is active may help control malaria in school-aged children.

7019

KNOCKING OUT TO KNOCK IN: IMPACT OF LOSS OF END JOINING FACTORS ON HOMOLOGY DIRECTED REPAIR INCIDENCE IN THE DISEASE VECTOR MOSQUITO, *AEDES AEGYPTI*.

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Aedes aegypti mosquitoes are vectors for a number of viruses of public health concern. Homing-based gene drives offer an intriguing tool to combat these disease vectors. Many homing-based gene drives leverage the Double Strand Break (DSB) repair pathway, Homology Directed Repair (HDR), to convert wild type genes to the engineered drive gene. However, another DSB repair pathway, Non-Homologous End Joining (NHEJ), is antagonistic to HDR and can even result in resistance alleles that prevent further super-Mendelian inheritance from the gene drive. Here, we utilize

previously generated *Aedes aegypti* strains with key NHEJ factors knocked out to evaluate the impact of loss of NHEJ efficiency on the incidence of HDR. The key NHEJ factors and associated knockout strains are *Ku80* (Ku80$^{-/-}$ strain), *DNA-PKcs* (DNA-PKcs$^{-/-}$ strain), and *Ligase IV* (Lig4$^{-/-}$ strain). We initiated site-specific DSBs utilizing CRISPR/Cas9 and guide RNA targeting a locus in the *kmo* gene (which is involved in eye pigmentation to allow for facile phenotype screening of results). Our data suggest that a loss of NHEJ efficiency in the germline cells of *Aedes aegypti* is compensated for by an increase in the incidence of HDR. Knockout of *DNA-PKcs* and *Ligase IV*, but not *Ku80* elevates the rate of HDR over that observed in the NHEJ wild type strain. Therefore, gene drive approaches that rely on HDR could potentially be made more efficient by incorporating some method of NHEJ down-regulation into the overall strategy. Such approaches could prove useful in vector control.

7020

ANTIBODIES TO *AEDES AEGYPTI* D7L SALIVARY PROTEINS AS A NEW SEROLOGICAL TOOL TO ESTIMATE HUMAN EXPOSURE TO *AEDES* MOSQUITOES

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Aedes spp. are the most prolific mosquito vectors in the world. Found on every continent, they can effectively transmit various arboviruses, including the dengue virus which continues to cause outbreaks worldwide and is spreading into previously non-endemic areas. The lack of widely available dengue vaccines accentuates the importance of targeted vector control strategies to reduce the dengue burden. High-throughput tools to estimate human-mosquito contact and evaluate vector control interventions are lacking. We propose a novel serological tool that allows rapid screening of human cohorts for exposure to potentially infectious mosquitoes. We tested 563 serum samples from a longitudinal pediatric cohort study previously conducted in Cambodia. Children enrolled in the study were dengue-naive at baseline and were followed biannually for dengue incidence for two years. We used Western blotting and enzyme-linked immunosorbent assays to identify immunogenic *Aedes aegypti* salivary proteins and measure total anti-*Ae. aegypti* IgG. We found a correlation (r_s=0.86) between IgG responses against AeD7L1 and AeD7L2 recombinant proteins and those to whole salivary gland homogenate. We observed seasonal fluctuations of AeD7L1+2 IgG responses and no cross-reactivity with *Culex quinquefasciatus* and *Anopheles dirus* mosquitoes. The baseline median AeD7L1+2 IgG responses for young children were higher in those who developed asymptomatic versus symptomatic dengue. The IgG response against AeD7L1+2 recombinant proteins is a highly sensitive and *Aedes* specific marker of human exposure to *Aedes* bites that can facilitate standardization of future serosurveys and epidemiological studies by its ability to provide a robust estimation of human-mosquito contact in a high-throughput fashion.

7021

THREE YEARS OF ENTOMOLOGICAL SURVEILLANCE IN HOUSES RECEIVING TARGETED INDOOR RESIDUAL SPRAYING (TIRS) AGAINST *AEDES AEGYPTI* IN MEXICO

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Targeted indoor residual spraying (TIRS) is a novel approach for *Aedes aegypti* control that uses adult female mosquito resting behavior to target insecticide applications and has the advantage of being deployed preventively (before the peak transmission season). We report the preliminary entomological findings of the TIRS trial, a two-arm, parallel, cluster randomized controlled trial conducted in Merida, Mexico. The protocol involves one preventive application of TIRS during each of three consecutive years (May-June 2021-2023) on a total ~27,900 houses. Indoor adult *Ae. aegypti* collections using Prokopack aspirators on a sub-sample of 1,500 houses were monitored monthly for a period of 6 months post-TIRS application, covering the peak arbovirus transmission season. Before TIRS, house infestation rates and female mosquito abundance were similar for both study arms. After TIRS, the strongest impact was observed during the first three months for both infestation (OR=0.18-0.41, P<0.05) and mosquito abundance (IRR=0.08-0.37, P<0.05). Significant reductions were maintained throughout the 6 months post-intervention in Year 1. Average treatment coverage increased from 60.2% in 2021 to 74.9% of target households per cluster in 2023. Intervention clusters (central and external blocks) were categorized according to TIRS coverage: 1= >75% of coverage in both central and external blocks; 2= <75% central/external blocks (n=10); 3= >75% central/<75% external blocks; 4= <75% central/>75% external blocks. Significant reduction in *Ae. aegypti* abundance was observed between houses in clusters with higher than 75% versus below 75% TIRS coverage (IRR=0.55, P<0.005); we observed significant increases in density (IRR=3.14 and 2.11, P<0.005) and positivity (OR=2.4 and 2.6, P<0.005) in the central vs external blocks when external blocks had <75% TIRS coverage. These promising results on entomological impact emphasize the importance of maintaining broad coverage to ensure better effectiveness of TIRS in the real world setting.

7022

TESTING A COMBINED IIT-SIT APPROACH TO CONTROL *AEDES AEGYPTI* AND URBAN ARBOVIRUS TRANSMISSION IN YUCATAN, MEXICO

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Due to the successful implementation of the sterile insect technique (SIT) in area-wide control of several insect pests of agricultural and

veterinary importance, significant efforts have been made to develop analogous techniques for mosquito control. One of them is Incompatible Insect Technique (IIT), in which males carrying the maternally inherited endosymbiotic bacteria *Wolbachia* are released to induce incompatible mating with target females who either do not carry *Wolbachia* or carry different *Wolbachia* strains. We present baseline and preliminary results from a two-arm cluster randomized controlled trial to evaluate the entomological and epidemiological impact of *Aedes aegypti* population suppression via IIT-SIT on arbovirus transmission in urban neighborhoods of the city of Mérida, Mexico. The intervention includes integrated control activities structured in two phases: 1) an Attack phase (~1-2 months prior to the transmission season) with area-wide ULV adulticide spraying to control Aedes adults in four weekly applications followed by 2) Male *Aedes aegypti* releases (2,000 male mosquitoes per hectare twice a week). We present information of the overall study design, baseline epidemiological and entomological data, and preliminary results of entomological impact. Findings from this study will allow establishing a link between epidemiologic, entomo-virological, and entomological indicators to determine the effectiveness of IIT-SIT in real world conditions. Built on the successful field trial and existing mosquito mass rearing capacity established in Merida, scaling-up this innovation is not only logical but also feasible. Successful findings from this study will pave the way for future expansions of the technology to the entire city and nationwide using a rolling-carpet strategy, which has been successfully demonstrated for area-wide control of screwworm and medfly in Latin America.

7023

NON-HOUSEHOLD ENVIRONMENTS PROMOTE DENGUE TRANSMISSION: IMPLICATIONS FOR VECTOR CONTROL

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Aedes-borne pathogens have been increasing in incidence despite vector control activities implemented in endemic settings. Vector control for *Aedes*-transmitted arboviruses typically focuses on households because vectors breed in household containers and bite indoors. Yet, our recent work shows a high abundance of *Aedes* vectors in public spaces. We used field-collected data on the distribution of vectors in different urban environments in Kenyan cities of Kisumu and Ukunda along with movement data to create an agent-based model. The model quantified the number of infections happening in both household (HH) and non-household (NH) environments. We additionally modeled the outcome of vector control activities implemented in different environments in preventive (before an outbreak) and reactive (after an outbreak commences) scenarios. We estimated that more than half of infections take place in NH environments, where the main spaces for transmission are workplaces and markets. Accordingly, a greater reduction of cases was estimated when control activities targeted only NH as opposed to when targeting only HH. As expected, greater control effectiveness is achieved when activities are implemented earlier and at higher levels of coverage. Additionally, we included spatial variables to study how the movement of individuals affects the dengue burden of both environments under three different urban conformations of NH: randomly distributed, centered, or clustered. According to the model, the number of cases is slightly higher when NH are randomly distributed, suggesting a role as spreaders of disease toward nearby HHs. Also, we discovered that the number of people visiting NH is an important factor determining dengue burden. At very low movement of people, transmission decreases and the number of infections in both environments becomes roughly even. Together, these results lead us to rethink the way urban transmission is understood, which is often placing HH as the main transmission environment. Accordingly, new control guidelines and risk factors estimation methods should be developed to render control and prevention truly effective.

7024

VERTICAL AND HORIZONTAL TRANSMISSION OF *MICROSPORIDIA MB*: A *PLASMODIUM* INHIBITING NATURAL SYMBIONT OF *ANOPHELES*

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Microsporidia MB, a naturally occurring symbiont in *Anopheles arabiensis* inhibits *Plasmodium* development and is avirulent. *Microsporidia MB* is transmitted vertically, from mother to offspring, and horizontally through mating. Transmission is expected to promote its spread through mosquito populations, enhancing the potential of *Microsporidia MB* as a candidate for the development of a symbiont-mediated malaria transmission-blocking strategy. In-depth understanding of *Microsporidia MB* transmission patterns is required for mass production of mosquitoes, a pre-requisite for mosquito release, and robust estimates from theoretical models on *Microsporidia MB* spread in the natural populations following release. Iso-female lines originating from field-collected *Microsporidia MB*-infected and uninfected females were compared for various life history traits from the egg to adult stage. Bioassays were conducted on first filial-generation mosquitoes to determine effect of diet type and quantity on *Microsporidia MB* prevalence and density. *Microsporidia MB* -infected and uninfected males were compared individually and in groups for mating competitiveness. Larval development time of *Microsporidia MB* -infected *An. arabiensis* is shorter compared to uninfected mosquitoes. Diet type and quantity influence density of *Microsporidia MB*. *Microsporidia MB* -infected adults have a higher mating rate compared to uninfected mosquitoes. In general, *Microsporidia MB* -infection has a positive effect on the development of *An. arabiensis* mosquitoes. *Microsporidia MB*-infection is influenced by diet type and quantity, therefore, diet can be manipulated to rear highly infected mosquitoes. *Microsporidia MB* is inherently able to spread in mosquito populations due to higher mating rate making it a promising candidate for malaria transmission-blocking strategy.

7025

DATA-DRIVEN TARGETING OF MALARIA AT-RISK POPULATIONS FOR DISTRIBUTION OF TOPICAL REPELLENTS IN ZIMBABWE

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Reported annual malaria incidence in Zimbabwe ranged from 9 to 32 cases per 1,000 population over the past five years, with 14 cases per 1,000 population reported nationally in 2023. Over 75% of malaria cases nationally are reported from three of the country's ten provinces. Despite consistently reporting indoor residual spraying (IRS) coverage of >85% of the population, prevention gaps remain, particularly among farmers whose livelihoods require outdoor nighttime activities and time away from home-based vector control strategies. To address residual transmission resulting from protection gaps among these farmers, we explored criteria for topical repellents as a supplementary protective intervention. Wards (administrative unit 3) considered eligible for a topical repellent-based intervention included those with a reported annual parasite incidence >100 cases per 1,000 population, an IRS population coverage >85%, and a large population of agricultural workers engaged in outdoor nighttime activities during peak malaria season. Of the country's 396 wards, we identified seven (1.8%) meeting these criteria using descriptive and spatial analyses of routine surveillance, and malaria programmatic, socioeconomic, and 2022 census data. A bottom-up approach through stakeholder engagement was used to target communities and healthcare authorities at the sub-national and national-levels to gather insights on priority populations to be covered by topical repellents. A ward with approximately 6,000 people will be prioritized for distribution and monitoring of topical repellents commencing in July 2024. This data-driven approach with key informant input was essential to tailor malaria interventions at the subnational level and address these unique drivers of malaria transmission.

7026

TWO MOSQUITO SALIVARY ANTIGENS DEMONSTRATE PROMISE AS BIOMARKERS OF RECENT EXPOSURE TO *PLASMODIUM FALCIPARUM* INFECTED MOSQUITO BITES

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Measuring malaria transmission intensity using the traditional entomological inoculation rate is difficult. Antibody responses to mosquito salivary proteins such as SG6 have previously been used as biomarkers of exposure to *Anopheles* mosquito bites. Here, we investigate four mosquito salivary proteins as potential biomarkers of human exposure to mosquitoes infected with *P. falciparum*: mosGILT, SAMPSP1, AgSAP, and AgTRIO. AgSAP and AgTRIO are transcriptionally upregulated in *P. falciparum*-infected mosquitoes, and all four proteins have either a prior reported association with sporozoites or could be secreted into *An.* saliva. We tested population-level human immune responses to these proteins in longitudinal and cross-sectional plasma samples from individuals with known *P. falciparum* infection from low and moderate transmission areas in Senegal using a multiplexed magnetic bead-based assay. AgSAP and AgTRIO were the most closely associated with recent exposure to infected mosquitoes. Antibody responses to AgSAP, in a moderate endemic area, and to AgTRIO, in both low and moderate endemic areas, were significantly higher than responses in a healthy non-endemic control cohort ($p = 0.0245$, 0.0064, and <0.0001 respectively). Antibody responses did not significantly differ between the low and moderate transmission area for any of the four proteins, or between equivalent groups during and outside the malaria transmission seasons. For AgSAP and AgTRIO, reactivity peaked 2-4 weeks after clinical *P. falciparum* infection and declined 3 months after infection. Since reactivity to both AgSAP and AgTRIO peaked after infection and did not differ seasonally, nor between areas of low and moderate transmission, the data suggest reactivity is likely reflective of exposure to infectious mosquitos or recent biting rather than to general mosquito exposure. Kinetics suggest reactivity is relatively short-lived. AgSAP and AgTRIO are promising candidates to incorporate into multiplexed assays for serosurveillance of population-level changes in *P. falciparum*-infected mosquito exposure.

7027

DEPLOYMENT OF ATTRACTIVE TARGETED SUGAR BAITS IN WESTERN ZAMBIA: INSTALLATION, MONITORING, REMOVAL, AND DISPOSAL PROCEDURES DURING A PHASE III CLUSTER RANDOMIZED CONTROL TRIAL

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Attractive Targeted Sugar Baits (ATSBs) offer a complementary vector control strategy to interventions targeting blood feeding or larval control by attacking the sugar feeding behavior of adult mosquitoes. Western Zambia was the first location to receive and deploy ATSB Sarabi v1.2 stations, in a Phase III cluster randomized control trial (cRCT). The cRCT was implemented in 70 study clusters (35 intervention and 35 control) across three districts, representing a population of 23,466 households at baseline. The trial measured epidemiological and entomological outcomes during a two-year seasonal deployment of ATSB stations (November 2021-June 2022; November 2022-June 2023). Two ATSB stations were installed on eligible structures in intervention clusters through planned installation campaigns. During deployment, ATSB monitoring was conducted to maintain high coverage of ATSBs and to assess their condition. Damaged ATSBs required replacement per pre-defined criteria for holes, leaks, mold, depletion, and dirt. Annual cross-sectional household surveys measured ATSB coverage. ATSBs were removed from all structures at the end of each transmission season and transported to Lusaka for incineration. A total of 67,945 ATSBs were installed in Year 1 (41,695 initially + 26,250 during monitoring) and 69,494 ATSBs were installed in Year 2 (41,982 initially + 27,512 during monitoring). The primary reasons for ATSB replacement were holes and mold. Cross-sectional surveys documented high coverage of ATSB stations across both years with 93.1% of eligible structures having ≥2 ATSB stations in any condition; however, only 71.5% of eligible structures had ≥2 ATSB stations not meeting the replacement criteria, demonstrating the high volume of ATSB damage. Additional research is needed to better understand the impact of damage on ATSB effectiveness, including the thresholds below which holes and mold are associated with reduced product efficacy. This presentation will describe the Zambia trial ATSB station installation, monitoring, removal, and disposal methods, quantify ATSB station coverage, and report reasons for ATSB station replacement.

7028

MATRIX-ASSISTED LASER DESORPTION/IONIZATION TIME-OF-FLIGHT (MALDI-TOF) MASS SPECTROMETRY AS A RELIABLE APPROACH FOR THE SURVEILLANCE OF CHIKUNGUNYA VIRUS IN MOSQUITO VECTORS

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Since its first outbreak in Africa, Chikungunya virus has spread to South Asia, the Indian Ocean islands, and the Americas, affecting over 100 countries. Quick identification of vector species and determination of infection status is critical for accurate vector-borne disease surveillance. Mosquito identification is often performed through morphological criteria and/or molecular methods, which can be time-consuming and expensive. Here, we use MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight) mass spectrometry to simultaneously identify mosquito species and infection status with CHIKV, which is more accessible, quicker, and cheaper than the current methods. Experimentally infected and non-infected *Aedes aegypti* and *Aedes albopictus* were dissected to obtain either legs or combined head and thoraxes for spectra generation. Spectra were grouped according to body part, species, and infection status. Spectra were assessed for quality using FlexAnalysis software and for reproducibility and specificity using pseudo-gel and PCA analyses with ClinProTools software. Leg spectra from infected and non-infected mosquitoes clustered separately in PCA analyses, while significant overlap was observed with cephalothorax spectra, indicating leg data were more suitable for differentiation. A database was created with high-quality reference spectra for each species. Samples were queried against this database, and all were correctly identified to the species level. Additionally, all non-infected mosquitoes were recognized as such while 97% of infected mosquitoes were correctly detected as infected. MALDI-TOF MS has been a critical development in the clinical and surveillance field for rapid and sensitive testing of microbial and arthropod samples. The present study

demonstrates the use of MALDI-TOF MS in the concurrent identification of mosquito species and infection status with CHIKV. The continual addition of quality spectra to the database and modifications to the current protocol will aid in the quick and accurate identification necessary for the surveillance of this spreading arboviral disease.

7029

LANDSCAPE PREDICTORS OF *AEDES AEGYPTI* ABUNDANCE IN A DENGUE-ENDEMIC LOCALITY IN MANAGUA, NICARAGUA

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Dengue has been traditionally recognized as an urban disease where urban centers are thought to provide ample habitat for *Aedes aegypti* reproduction and susceptible human hosts to drive dengue virus (DENV) transmission. Increasing evidence of DENV infections in rural populations challenges this narrative. DENV transmission is driven by various spatial, environmental, and anthropogenic factors, often summarized by a dichotomous urban-rural variable. However, this urban-rural dichotomy overlooks underlying drivers of spatial spread, many of which can be captured by landscape features. As such, this study proposes to quantify the landscape structure and composition of two characteristically urban and peri-urban neighborhoods in Managua, Nicaragua, a dengue endemic locality. Elucidating differences in landscape composition between peri-urban and urban sites will facilitate a more nuanced analysis of DENV epidemiology among heterogeneous spatial patches. We approached this analysis using remote sensing and landscape structure characterization techniques and household level *Ae. aegypti* abundance data that were systematically collected within 500 households across both neighborhoods using manual aspiration and container inspection. We employed high resolution multispectral WorldView 3 imagery and a machine learning Random Forests model to classify land types of the two study sites. Using FRAGSTATS software, we computed landscape metrics to spatially assess patch connectivity, geometry, and aggregation for each land type across the two study sites. To assess the relationship between landscape metrics and *Ae. aegypti* abundance we will also integrate ancillary environmental and climatic data and generate DENV transmission risk estimates using spatial regression and spatial clustering techniques. This landscape scale analytic framework provides a more mechanistic understanding of spatial risk patterns and moves beyond the urban-rural dichotomy concept for risk mapping and will allow us to delineate specific urban features and typologies that sustain dengue transmission within urban- or rural-like landscapes.

7030

THE POTENTIAL USE OF DIGITAL TOOLS FOR LARVAL SURVEYS IN VECTOR CONTROL: EXPERIENCE FROM ANAMBRA AND ONDO STATES OF NIGERIA

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Malaria Consortium is conducting studies to assess the entomological and epidemiological impacts of insecticide-treated net (ITN) campaigns in 2021 and 2022 in Ondo and Anambra states respectively. These studies involved the use of a digital questionnaire completed alongside the collection of mosquito larvae for resistance tests. We report observations from using the digital tool, and explore its potential use for mapping larval habitats to inform the targeting of vector control interventions. The digital tool was developed using SurveyCTO, a customisable application, and deployed on mobile devices. The tool facilitated the collection of data on breeding sites capturing various attributes of the habitats. *Anopheles* larvae were collected alongside images of the sites and their geocoordinates, type and characteristics, and the timestamps of collection. Data were submitted in real time which allowed research staff to monitor field activities in progress and immediately map survey sites. Although the primary use of the digital data was to locate the sources of mosquitoes used in resistance tests, the findings indicated the potential use of the tool to link species- after rearing and identification of adult mosquitoes - with the collection sites to deploy larval source management (LSM) and other measures. Digitization of larval surveys for resistance monitoring or other entomological studies could allow mapping of important breeding sites for vector control, beyond the primary purposes of the sample collections. Insecticide resistance monitoring activities in several African countries are based on larval collection and rearing. If during such activities information is gathered on larval habitats employing similar digital tools, this could allow real-time monitoring of transmission foci by integrating into the surveillance system. A similar approach could also be used at community levels for mapping of breeding sites for wider geographic coverage of LSM measures.

7031

STRATEGIES FOR ALTERING THE FREQUENCY AND COVERAGE OF INSECTICIDE-TREATED NET MASS CAMPAIGNS WITH DIFFERENT NET TYPES TO MAXIMIZE CASES AVERTED UNDER FIXED BUDGETS

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Mass campaigns of insecticide-treated nets (ITNs) are recommended every three years to control malaria. However, evidence indicates most nets do not last this long, and those that do may have impaired effectiveness in areas of pyrethroid resistance. The availability of pyrethroid-only, pyrethroid-PBO and dual-active ingredient (AI) ITNs with differing costs and durability means it is unclear whether biennial distribution of a cheaper net may be more cost-effective than triennial distribution of other more costly but more effective ITNs. It is also unclear whether distributing fewer but better pyrethroid-PBO and dual-AI nets through mass campaigns will be more cost-effective than larger quantities of pyrethroid-only nets under fixed budget constraints. Here we fit retention curves to Demographic and Health Survey data to estimate sub-national mean net retention times in Burkina Faso, Ghana, Malawi, Mali, Mozambique and Senegal. Central estimates of mean retention times were less than 2 years for 68.8% of regions investigated. Models indicate considerable sub-national heterogeneity, with mean retention ranging from 0.95 years (95% CrI: 0.92-0.97) in urban Maputo, Mozambique, to 3.04 years (95% CrI: 2.84-3.23) in urban Est, Burkina Faso. By accounting for sub-national heterogeneity in net retention, in addition to transmission intensity and pyrethroid resistance, we generate projections of cases averted for biennial vs triennial mass campaigns for pyrethroid-only, pyrethroid-PBO and dual-AI nets under different costed strategies using a transmission-dynamics model. Results highlight distribution strategies for administrative-one level regions investigated where biennial distribution with pyrethroid-pyrrole nets could be more cost-effective than triennial pyrethroid-only campaigns under fixed budget constraints. As policymakers look to move towards distributing pyrethroid-pyrrole nets in the face of increasing pyrethroid resistance, our findings highlight increased distribution frequencies could also be considered concurrently in some regions for optimal cost-effectiveness.

7032

MODELLING THE POTENTIAL OF GENE DRIVE MOSQUITOES FOR MALARIA CONTROL IN SETTINGS WITH MULTIPLE VECTOR SPECIES IN MAINLAND TANZANIA

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Malaria persists as a significant global health challenge especially in regions such as mainland Tanzania where multiple vector species mediate transmission dynamics. This study aims at evaluating the potential of gene drive (GD) modified mosquitoes to combat malaria with such complex eco-epidemiological settings. Focusing on the Kilombero Valley – a well-documented site for malaria endemicity with predominant *Anopheles funestus* and *Anopheles arabiensis* mosquito populations, we propose a multifaceted approach to understanding the impact of deploying GD mosquitoes as part of an integrated vector management (IVM) strategy. Through mathematical modelling and scenario analysis, we will simulate the release of GD mosquitoes into local vector population and assess the efficacy of replacement drive strategies in diminishing the rate of malaria transmission. The study will determine the necessary scale of GD mosquito releases required for substantial reduction, factoring in the variation in epidemiological conditions specific to Kilombero Valley. We will also investigate the integration of GD mosquitoes with current control measures, such as insecticide treated nets (ITNs) to discern potential synergistic or antagonistic outcomes on malaria control. A critical component of our research includes the identification of thresholds for escaped GD mosquitoes that could present ecological or health concerns. In here, we aim to develop a comprehensive monitoring plan to address the risks associated with escape and unintended establishment, contemplating both full-drive (super-mendelian inheritance) and effector-only (mendelian inheritance) constructs to enable robust risk management strategies. The study's results will provide strategic insights into the operational feasibility of incorporating GD mosquitoes within broader malaria elimination initiatives, paving the way for novel, sustainable approach to vector control in settings challenged by the presence of multiple vector species.

7033

VALIDATION USING ATTRACTIVE SUGAR BAITS (ASBS) CONTAINING A FLUORESCENT DYE IN SIAYA, WESTERN KENYA: AN EVALUATION OF ANOPHELES FEEDING RATES

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Vector control is an essential component of malaria prevention. Additional mosquito control tools like Attractive targeted sugar baits (ATSBs) are urgently needed to further suppress malaria transmission worldwide. Prior to epidemiological trials on ATSBs, validation studies were conducted to assess the levels of mosquito feeding on attractive sugar baits (ASBs) with uranine fluorescent dye and to evaluate whether the deployment of two versus three bait stations per building structure led to a significantly different daily feeding rate in local malaria vectors as a proxy for ATSBs. The study followed a cross-over design in twelve clusters of Siaya western Kenya. Either two or three ASBs were deployed to all structures and switched over at two months' time point so that clusters which initially received two ASBs were given three and vice versa. ASB monitoring was done for four months from initial deployment then an additional four months for extended monitoring of ASBs. Mosquitoes were collected using UV light traps and Prokopack aspiration indoors and outdoors then screened for morphological characteristics and fluorescence due to the uranine dye. Samples of mosquitoes collected were processed by PCR and sporozoite infectivity. Data analysis was performed using R statistical software. *An. funestus* s.s. was the dominant malaria vector with overall dye feeding of 11.2% followed by *An. gambiae* s.l. at 3.5%, translating to daily feeding rates of 4.8% in *An. funestus* and 1.2% in *An. Gambiae*. No significant difference was detected between two or three ASB stations. *An. funestus* s.l. comprised 82% *An. funestus* s.s. and 6.3% *An. leesoni* while *An. gambiae* s.l. constituted 68% *An. arabiensis* and 21% *An. gambiae* s.s. Sporozoite positivity rate was 2.28% and1.00%. in *An. funestus* s.l. and *An. gambiae* s.l. respectively. *Anopheles funestus* s.s. demonstrated higher rates of feeding on ASBs compared to *An. gambiae* s.l. No significant difference was detected between deploying two or three bait stations per structure. The study provided important information utilized in the subsequent deployment of ATSBs in epidemiological trials.

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COMPARISON OF SEASONAL MOSQUITO POPULATIONS ACROSS A DIVERSIFYING SEMI-PASTORAL LANDSCAPE IN LOITOKITOK SUB-COUNTY, KENYA

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Ecological variables have a profound impact on mosquito populations and micro-environments suitable for proliferation of certain species can result in disease transmission hotspots. Rift Valley fever virus (RVFV), a priority zoonotic arbovirus, is transmitted by a wide range of mosquito species, and endemic transmission is poorly understood. A subset of randomly sampled households in different ecozones and land use types (cropland, grassland, and shrubland) were used to capture outdoor mosquitos associated with livestock using Biosentinel (BG) traps baited with CO_2 set for 48-96 hours. We trapped in three seasons, the August 2023 dry period, the rains at the end of November into December 2023, and in February 2024 after the El Niño phenomenon prolonged the short rains. Total mosquitos were adjusted for trapping time and transformed for analysis. We caught 323 mosquitos over 30 trapping events, lasting on average 54.5 hours. The majority, 94%, of mosquitos were *Culex spp.* We caught *Anopheles spp*. at one trapping event in a cropland household at 1,497 meters elevation, and eight of the ten total *Aedes spp.* were captured in shrubland. We had similar mosquito totals in shrubland and grassland landcover (β=1.01, SE=0.06, *p=0.89*) and caught more mosquitos in cropland households (β=1.10, SE=0.05 *p=0.10*) but did not identify a significant association with the elevation or ecozone. The greatest impact was seasonality, with significantly fewer mosquitos in the August dry period (β=*0.84,* SE=0.06, p=0.005), and catches were only slightly higher in February (β=1.04, SE= 1.04, *p=0.41*) compared to December. Furthermore, in December, we repeated trapping at three households and caught significantly more mosquitos six weeks after our weather station recorded the first major rainfall event compared to three weeks after (β =1.12, SE=0.03, *p=0.01*). We captured very few mosquitos during the dry season and demonstrated that following the first major rainfall event after a dry period, mosquito abundance continues to increase significantly. We also caught more in cropland and, as this land use type continues to expand, could increase total mosquito abundance.

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THE USE OF INSECTICIDE TREATED EAVE RIBBONS AS A PROTECTION TOOL AGAINST POPULATIONS OF MOSQUITOES THAT TRANSMIT MALARIA AND DENGUE

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Mosquito-borne diseases such as malaria and dengue continue to pose a significant public health challenge in disease-endemic communities worldwide. While insecticide-treated nets and indoor residual spraying have been successful in preventing these diseases, they face challenges such as insecticide resistance, high costs, logistical difficulties, and limited durability. Therefore, there is a need for simpler and affordable interventions that can be used on a large scale in endemic communities to supplement current approaches. This study evaluated the efficacy of insecticide-treated eave ribbons as a potential tool for complementing the current vector control methods. Eave ribbons are pieces of hessian fabric placed around the eave spaces of houses to kill or repel mosquitoes. Laboratory cone bioassays were conducted to assess the efficacy of eave ribbons treated with the organophosphate, pirimiphos-methyl, for killing the malaria vectors, *Anopheles funestus* and *Anopheles arabiensis*, and the dengue vector, *Aedes aegypti*, under varying exposure durations and insecticide doses. A semi-field experiment was done to assess the efficacy of eave ribbons treated with pirimiphos-methyl against the malaria vectors. The findings revealed that treated eave ribbons resulted in higher mosquito mortality than the untreated ribbons, but the impact increased with increased exposure duration or dose. The semi-field study indicated moderate levels of bite prevention and mortality of the mosquitoes. At the doses of 1g a.i./m^2 and 2g a.i./m^2 pirimiphos-methyl, there was no significant protection against *An. arabiensis*, but at the dose of 4g a.i./m^2 pirimiphos-methyl, there was a significant protection in outdoor biting *An. arabiensis* (RR = 0.80, 95% CI: 0.71-0.91, $p < 0.001$), but not *An. funestus*. In conclusion, while insecticide-treated eave ribbons may have potential for controlling malaria and dengue vectors, further research is needed to validate their efficacy in field settings and to identify suitable insecticides or insecticide combinations that are highly effective, particularly against pyrethroid-resistant vectors.

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MALARIA TRANSMISSION RISK IN THE CITY OF ACCRA, GHANA

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Unplanned urbanization in sub-Saharan Africa is altering urban malaria transmission dynamics, challenging existing control methods such as indoor residual spraying (IRS) and long-lasting insecticide-treated nets (LLINs). Therefore, understanding these dynamics is crucial for tailored control strategies. This study investigated the vector densities, bloodmeal sources and infectivity rate of malaria vectors in Accra, Ghana. Biting and resting mosquitoes were collected in ten sites within the city of Accra, Ghana using human landing catches (HLC) and Prokopack aspirators (PPA) during the dry and rainy seasons in 2023. Sites were selected and categorized into five sectors (two sites per sector): Irrigated Urban Farming (IUF), Lower (LS), Middle (MS) and High (HS) socioeconomic status, and Peri-urban (PU) sites. Vector speciation, sporozoite infection and blood meal analysis were determined using PCR. Overall, a total of 42,331 mosquitoes were collected over the entire sampling period; Culicine = 17,820 [HLC = 16,742, PPA = 1,078], Anopheline = 21,520 [HLC = 20,931, PPA =589], Aedine = 1,708[HLC = 1491, PPA = 217]. Significantly high biting activity was observed in the late evening (LE) for both seasons [Dry (69.93%, 2,925/4,183); Rainy (70.44%, 8,367/11,878)] [F (2, 27) = 6.03, $P = 0.019$, 95% CL 135.2691 - 1388.731]. High biting activity (HBR = 352.9) and entomological inoculation rate (EIR) 0.409 (ib/m/n) were observed in IUF site categories compared to other sectors. Vectors preferred to feed on humans (HBI = 86.30%, 359/416). Higher sporozoite infection rate (Tuba = 77.27%) was found in indoor resting mosquitoes. The L1014F mutations were detected at higher frequencies (0.98 - 1) in all sites, followed by G119S (0.86 – 0.89). L1014S was detected at very low frequencies (0.15 – 0.5). The study highlights the importance of adopting novel approaches to complement existing strategies in controlling urban malaria vectors.

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UNDERSTANDING THE ECO-EPIDEMIOLOGY OF MOSQUITOES IN HOUSTON, TEXAS: INFORMING PUBLIC HEALTH STRATEGIES

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Mosquito-borne diseases present a significant challenge to public health, particularly in regions like Harris County, Texas, characterized by a humid subtropical climate and dense population. Effective disease surveillance and control strategies necessitate a comprehensive understanding of mosquito community dynamics, including species composition, abundance, and distribution. To address this need, we extensively analyzed routine mosquito surveillance data collected from 2018 to 2022, comprising nearly 4 million female mosquitoes collected over 55,000 trap nights using three trap types. Our analysis revealed *Culex quinquefasciatus* (the primary vector for West Nile virus in the southern United States) as the predominant species (88%), alongside *Aedes albopictus, Culex salinarius, Aedes taeniorhynchus,* and *Aedes aegypti.* Biodiversity analysis indicated variations in species richness and diversity among trap types and years, with BG-sentinel traps capturing the highest diversity in 2018. To investigate variation in female *Culex quinquefasciatus* abundance, global and local spatial autocorrelation analyses were performed to identify high-abundance neighborhoods surrounded by similar high-abundance neighborhoods (hotspots) for 2020 to 2022. Interestingly, we observed the highest abundance of female *Culex quinquefasciatus* in some of the oldest communities in Harris County, characterized by a higher median home age. Our findings underscore the importance of understanding population dynamics and species composition for targeted disease surveillance and control efforts. Furthermore, these results emphasize the interconnectedness of humans, mosquitoes, and the built environment in a large metropolitan region. Continued monitoring and research efforts are essential for effectively implementing public health interventions, safeguarding both human and animal populations against vector-borne illnesses.

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URBAN VECTORIAL TRANSMISSION OF MALARIA IN KOULIKORO DISTRICT, MALI

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The rapid but unplanned urbanization occurring in several African countries and the global warming could lead to an increase in malaria burden through the proliferation of mosquitoes breeding sites in specific areas of the cities. The study aimed to determine the species composition of malaria vector population during the transmission season from August to November

2021 in an urban area of Mali, Koulikoro. Mosquitoes were collected each month in 60 randomly selected rooms using Pyrethrum spray catches. Specification of vectors was done using molecular techniques while other entomological indicators such as blood meal sources and infection rates were determined by ELISA techniques. A total of 2106 Culicidae specimens were collected and among which 30.1% were *Anopheles gambiae s.l.* and 69.9% were Culex sp. Three species composed of the *Anopheles gambiae s.l.* population: *Anopheles coluzzii* (84.2%), *Anopheles arabiensis* (11.6%), and *An. gambiae sensu stricto* (4.2 %). The mean density of *An. gambiae s.l.* was 2.7 individuals per room. The mean human blood index was 98.1% and the infection rate was 0.50%, with 0.1 infected bites per person per month. This study not only reported the presence of the three main vector species in the Koulikoro urban area but also a significant human and vector contact enough to sustain malaria transmission. The observed adaptation of the main malaria vectors to the urban environment calls for more attention in terms of vector control specific to this environment. **Keywords :** Malaria, Anopheles; Urban, Mali.

7039

THE IMPACT OF CLIMATE CHANGE ON MOSQUITO ENTOMOLOGY AND SPATIOTEMPORAL DENGUE TRANSMISSION

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Dengue disease is caused by four serotypes (DENV- 1-4). Infection confers lifelong immunity to a homologous serotype, but only temporary immunity against a heterologous serotype. Secondary infection drastically increases the likelihood of disease. Dengue's primary vectors, *Aedes aegypti* mosquitoes, display high sensitivity to climate. Therefore, climate change has the potential to markedly affect the spatiotemporal dynamics and disease burden of dengue, by increasing disease incidence (and the frequency of secondary infections) in traditionally low transmission settings. Here we infer the relationship between temperature and rainfall and dengue transmission intensity. We then use these inferred relationships to investigate the impact of projected climate change-driven shifts in temperature and rainfall on dengue transmission. We developed an age-structured, stochastic transmission model that captures human infection history. Where possible, the model further represents mosquito entomology parameters (e.g. fecundity, carrying capacity, extrinsic incubation period, mortality and biting rate) mechanistically as functions of temperature and rainfall. UNWPP population data is used to model non-stationary demography. Previously estimated laboratory-derived relationships between temperature and mosquito parameters are used as model prior distributions. Using approximate Bayesian computation, we calibrate our model against multiple epidemiological data streams, including large, historical and spatiotemporally resolved incidence, prevalence and seroprevalence datasets. We reproduce climate-driven seasonal and inter-annual dengue disease incidence, and our analysis shows that the majority of inter-annual variation in dengue incidence is climate-driven. Together with the World Climate Research Programme (WCRP) Coupled Model Intercomparison Project Phase 6 (CMIP6) high resolution climate projections, we project potential changes in dengue transmission. Our work will inform ongoing dengue vaccination and control policies.

7040

TRENDS IN ORGANOPHOSPHATE RESISTANCE AMONG *AEDES AEGYPTI* IN TAPACHULA: IMPLICATIONS FOR VECTOR CONTROL FROM 2018 TO 2021

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In Tapachula, Mexico, the exclusive deployment of pyrethroids (PYRs) for 15 years in *Aedes aegypti* control programs resulted in substantial PYR resistance and subsequent failures in dengue prevention. In response, PYRs were phased out in 2013 in favor of organophosphates (OPs), which have a different mechanism of action. However, the extensive application of OPs since then has raised the risk of developing resistance mechanisms in field populations of *Ae. aegypti*. Therefore, ongoing surveillance of mosquito susceptibility to OPs is crucial to mitigate resistance development. This study used the bottle bioassay to track changes in susceptibility from 2018 to 2021, determining the lethal concentration 50 (LC_{50}) for two OPs—malathion and chlorpyrifos—at 24 collection sites throughout Tapachula. The results showed a slight but significant increase in resistance to both insecticides over time. Mosquito populations showed moderate to high resistance to chlorpyrifos and low resistance to malathion. Given that OPs and PYRs constitute two of the three insecticide classes used in public health, it is essential to develop more sensitive bioassays and molecular markers to detect early signs of OP resistance.

7041

INNOVATIONS RESULTING FROM THE USE OF CULTURED *ANOPHELES* CELL LINES

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Research involving *Anopheles* cell culture systems represents an accessible, cost-effective, versatile approach to support *in vivo* experiments. Molecular biology approaches that can both inform, or themselves constitute, novel interventions to block pathogen transmission can be first elucidated in cell culture. Our particular focus is cellular secretion mechanisms. We first provide a summary of available *Anopheles* cultured cell lines, then describe past successes resulting from work in these lines. Cellular secretory pathways may hold key information about the contributions of mosquito secretions to pathogen infectivity in human hosts immediately following a transmission event, as was shown previously for ticks. We then offer a comprehensive approach to molecular characterization of *Anopheles* cellular secretion, including an efficient cDNA-based method for determining the sex of an Anopheles cell line, and provide preliminary data. In summary, we hope to leverage cellular secretion to develop new methods of preventing the spread of mosquito-borne diseases. This work highlights the importance of molecular processes, including cellular secretion, in the transmission of mosquito-borne diseases.

7042

HYBRIDIZATION BETWEEN *AEDES AEGYPTI* AND *AE. MASCARENSIS* MOSQUITOES LEADS TO DISRUPTION OF MALE SEX DETERMINATION

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Understanding the sex determination pathway and its disruptions in mosquitoes is critical for the effective control of disease vectors through genetic manipulations based on sex separation. When male hybrids of *Aedes aegypti* females and *Ae. mascarensis* males are backcrossed to *Ae. aegypti* females, a portion of the backcross progeny manifests as males with abnormal sexual differentiation. We discovered a significant correlation between the abnormality of pupae and the feminization of subsequent adults exemplified by the relative abundance of ovarian and testicular tissues. All intersex individuals were genetic males as they expressed a male determining factor, *Nix*. Further, our analysis of the sex-specific splicing of *doublesex* and *fruitless* transcripts demonstrated the presence of both male and female splice variants indicating that sex determination is disrupted. A comparative transcriptomic analysis revealed similar expression levels of the majority of female-associated genes in reproductive organs and carcasses between intersexual males and normal females. Moreover, intersexes had largely normal gene expression in testes but significant gene downregulation in male accessory glands when compared with normal males. We conclude that evolving hybrid incompatibilities between *Ae.*

aegypti and *Ae. mascarensis* is due to the disruption of sex determination and is accompanied by changes in gene expression associated with sexual differentiation.

7043

CHROMATIN ARCHITECTURE OF THE MALARIA VECTOR, *ANOPHELES COLUZZII*

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Transcriptional enhancers are non-coding regulatory elements that are responsible for most gene expression above basal levels in eukaryotes. Through their regulation of gene expression, enhancers likely play a role in natural *Anopheles* vector susceptibility phenotypes such as behavior, ecological adaptation, insecticide resistance, and an intrinsic resistance to *Plasmodium falciparum* infection. To better characterize the chromatin architecture of a major African malaria vector, Micro-C approaches were used on an *An. coluzzii* hemocyte cell line to comprehensively identify enhancer-promoter physical interactions. Downstream analyses were performed on the high-resolution enhancer-promoter contact matrices to identify open/closed chromatin domains (A/B compartments), topologically associating domain (TAD) boundaries, and chromatin loop interactions. Results will be presented on chromatin architecture data coupled with gene expression data focused on the previously characterized *Plasmodium* resistance island (PRI) and well characterized immune genes, such as LRIMs, TEPs, and APLs. A molecular understanding of endogenous gene regulation is crucial for a functional understanding of mosquito immune biology and for use in the generation of genetically modified mosquitoes.

7044

HEAD-SPECIFIC TRANSCRIPTOMIC STUDY REVEALS KEY REGULATORY PATHWAYS FOR WINTER DIAPAUSE IN MOSQUITO *CULEX PIPIENS*

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The primary vector of West Nile virus, *Culex pipiens*, undergoes reproductive dormancy during the adverse winter season. Although there is much documentation on the correlation between phenotypic shifts and global transcriptome modifications, there is still a lack of information concerning tissue-specific transcriptomic changes. This knowledge gap is a major challenge in interpreting the regulatory mechanisms at the tissue level. To examine the transcriptome dynamics particular to different tissues that contribute to the diapause phenotype, the present work used RNA-seq technology to analyze the regulatory mechanisms of head-specific genes. RNA samples were obtained from the heads of diapausing and nondiapausing female mosquitoes at two specific time intervals, namely ZT0 and ZT16, and then subjected to sequencing. The findings revealed significant variations in the number of differentially expressed genes between ZT0 and ZT16 under diapause (912) and non-diapause (767) conditions. Additionally, there were differences in the number of differentially expressed genes between diapause and non-diapause at ZT0 (499) and ZT16 (1106) periods, indicating the presence of circadian and seasonal variations in gene expression. In addition, eleven genes associated with the diapause phenotype were chosen, and the abundance of transcripts at six different periods for 24 hours was determined. qRT-PCR analysis showed similar up- and down-regulation of transcripts between the diapause and nondiapause phenotype thus validating the results of RNA-seq. In summary, our findings reveal crucial genes and their corresponding regulatory pathways that play a vital role in the diapause phenotype and are regulated by the circadian clock. The newly presented information here will significantly enhance our comprehension of insect diapause and may provide novel opportunities for vector control strategies

7045

SUPPRESSION OF H3K27ME2 DEMETHYLASE DISRUPTED DIAPAUSE FORMATION IN MOSQUITO *CULEX PIPIENS*

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The northern house mosquito, *Culex pipiens*, undergoes diapause to endure the harsh winter environment. Diapause triggers a cascade of transcriptional and physiological changes, enhancing stress resistance, promoting fat storage, arresting ovarian development, and prolonging lifespan. Understanding of the basis of diapause can help in uncovering potential targets for genetic or biological control methods. Epigenetic regulation, known to influence developmental and behavioral traits in some mosquito species, has attracted attention to researchers. Our previous study revealed a significant reduction in H3K27me2 levels in the fat body of diapausing female *Cx. pipiens* upon diapause onset, suggesting a link between histone methylation and diapause initiation. However, the exact mechanism of the regulatory pathways remains elusive. Here, we inhibited histone demethylases responsible for H3K27 methylations using the histone demethylase inhibitor GSK-J4. Mosquitoes injected with GSK-J4 exhibited elevated H3K27me2 levels, accompanied by reduced lipid conservation and shortened lifespan, ultimately disrupting diapause. Our findings highlight the involvement of H3K27me2 in diapause formation, suggesting potential for targeting histone methylation in novel mosquito control strategies.

7046

MOLECULAR DIVERSITY OF *ANOPHELES* SPECIES OVER THREE YEARS OF INSECTICIDE-TREATED DURABILITY MONITORING IN KAYES, WESTERN MALI.

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Local Anopheles species' composition and bionomic characteristics are drivers of insecticide-treated nets (ITN) effectiveness. This study aims to investigate the diversity of Anopheles mosquitoes during understudied low-density periods towards evaluating species-specific drivers of residual transmission after universal coverage of ITNs. From 2018 to 2020, adult Anopheles were collected in Western Mali using indoor and outdoor CDC light traps, outdoor BG-Pro traps, and indoor Prokopak aspirator collection methods. Morphological identification was performed using taxonomic keys. Molecular identification was performed using specific PCR protocols, and the phylogenetic analysis of rDNA-ITS2 was conducted to identify specimens that could not be identified. Circumsporozoite enzyme-linked immunosorbent assay was used to estimate mosquitoes' *Plasmodium falciparum* infection rate. Of 308 adult female Anopheles sampled, five species were identified morphologically, including *An. gambiae* s.l. (53.6%), *An. rufipes* (15.2%), *An. funestus* s.l. (3.9%), and non-identified specimens (22%). With molecular identification, eight species were identified *An. gambiae* ss (45.8%), *An. coluzzii* (15.6%), *An. arabiensis* (1.3%), *An. funestus*, *An. rufipes* (16.9%), *An. pretoriensis* (2.9%), *An. ziemannii* (4.2%), *An. pharoensis* (1%) and non-identified specimens (6.8%). *An. gambiae* sl was the predominant species with endophilic behavior. Only *An. gambiae* ss was infected with *P. falciparum* sporozoites (0.7%; n = 141). Consensus ITS2 sequences were aligned to construct a phylogenetic tree. The sequence of the novel species clustered within Series Myzomyia. This study highlights the complexity of Anopheles mosquitoes. Detecting a novel and unidentified species suggests potential underreported Anopheles diversity and a potential vector of malaria transmission during the low transmission season. This points to the importance of continuous surveillance and

advanced molecular identification techniques to understand the drivers of malaria towards reducing residual malaria transmission effectively on the road to malaria eradication.

7047

MOLECULAR SURVEILLANCE OF ANOPHELINE VECTORS TO SUPPORT MALARIA ELIMINATION IN BRAZIL

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In 2022, the Brazilian Ministry of Health launched a Malaria Elimination Plan for Brazil. To support malaria elimination, rapid and cost-effective monitoring of the country's main malaria vectors is fundamental for understanding mosquito dynamics and planning timely vector control actions. The primary objective of this project is to establish a practical protocol for molecular analysis of *Anopheles* mosquitoes. This protocol will be used to develop a large-scale implementation strategy for entomological surveillance, specifically for identifying *Anopheles* species in various water collections. In this study, we will analyze the changes in mosquitoes, both spatially and temporally, before and after the application of the VectoMax biolarvicide in fish farming ponds in a malaria-endemic area in Juruá Valley, Acre State, Amazon region, Brazil. Our approach involves the use of metabarcoding of the D2 rDNA marker. Sampling and molecular pipelines were used to verify the species that were using the fishponds as habitats using mass identification of *Anopheles* species. Preliminary results showed that in the pre-intervention period, 2,016 monthly collections of *Anopheles* immature forms were carried out in 170 fishponds, with the presence of approximately 32,210 different larval stages (L1 to L4). The average density of larvae before the fishpond intervention was 0.467 (95% CI, 0.444 to 0.490) anopheline larvae per dip. There was a decrease in the density of larvae to an average of 0.046 (95% CI, 0.041 to 0.051) larvae per dip after implementing larvicide. For analyses and sequence processing, we used MOTHUR v.1.36.1 to analyze the sequence data obtained from the Illumina MiSeq platform. Metabarcoding of immature stages could confirm the temporal and spatial distribution of *Anopheles* species in different water collections in a malaria endemic area. It is expected to translate scientific evidence into a practical metabarcoding protocol to apply at state and municipal level to support entomological surveillance of Anopheline vectors.

7048

POPULATION STRUCTURE OF THE *AEDES ALBOPICTUS* VIROME IN SUFFOLK COUNTY, LONG ISLAND, NY

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Aedes albopictus is an invasive mosquito species known to vector several arboviruses worldwide and was recently detected in Suffolk County, Long Island, NY. Advances in next-generation sequencing have fundamentally shifted our understanding of viruses worldwide and revealed a variety of symbiotic viruses with no known pathogenicity that infect a range of hosts, including *Ae. albopictus*. However, little is known about the distribution of these viruses, their ecology, and how they interact with each other and their hosts. Additionally, given that many of these viruses are likely species-specific, viral phylogenetic structure likely reflects their host's population dynamics and structure. Using georeferenced individual *Aedes albopictus* sampled across Suffolk County, between May 2022 and October 2023, we describe how virome composition varies between individuals and how diversity shifts across seasons and environments. We additionally use phylogeographic models based on whole genomes of select viruses to estimate *Ae. albopictus* population structure in the region. By comparing these results to those predicted by models, we test for the relative impact of active (flight) and passive (human-mediated) dispersal on *Ae. albopictus* population structure. This work will not only help inform future vector control in the area by identifying possible source and sink populations and routes of invasion, but also serve as a proof-of-concept that can be applied to other vector species.

7049

RADIATION EXPOSURE INDUCES GENOME-WIDE ALTERNATIVE SPLICING EVENTS IN *AEDES AEGYPTI* MOSQUITOES

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The sterile insect technique (SIT) is a radiation-based method to control arthropod pest populations. Ionizing radiation, used to sterilize the pests, affects gene transcription patterns, including alternative splicing events in irradiated cells. In this study, we investigated the effect of radiation on alternative splicing in male *Aedes aegypti* mosquitoes. *Ae. agypti* is a major vector of dengue, Zika, and other arboviral diseases. Analyzing RNA sequencing data, we found that radiation altered the splicing of genes involved in a variety of biological processes, including signal transduction, phosphorylation, and metabolism. Specifically, we observed changes in the expression of splicing factors and alternative splicing events in transcript-coding genes. Our results suggest that radiation damage produced by ionizing radiation can alter the splicing of genes involved in important biological functions in male *Ae. aegypti* mosquitoes. Understanding the impact of radiation on alternative splicing may prove critical for improving mosquito Sterile-Insect-Technique and to prevent the transmission of mosquito-borne diseases.

7050

HYBRID ASSEMBLY AND ANNOTATION OF TWO GEOGRAPHICALLY DISTINCT STRAINS OF THE MALARIA VECTOR *ANOPHELES ALBIMANUS* REVEALS LOW INTRA-SPECIFIC DIVERGENCE

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Anopheles albimanus is one of the principal malaria vectors in the Americas and exhibits phenotypic variation across its geographic distribution. High-quality reference genomes from geographically distant populations are essential to deepen our understanding of the biology, evolution and genetic variation of this important malaria vector. In this study, we applied long-read PacBio and short-read Illumina sequencing technologies to assemble the complete genomes of two reference strains of *An. albimanus*, Stecla (originating from El Salvador), and Cartagena (originating from Colombia); and investigated the structural features of these genomes, including gene content, transposable elements (TE) genetic variations, and structural rearrangements. Our hybrid assembly approach generated reference-quality genomes for each strain and recovered ~96% of the expected genome size. The genome assemblies of Stecla and Cartagena consisted of 109 and 149 scaffolds, respectively, with estimated genome sizes of 167.5 Mbp (N_{50}=88 Mbp) and 167.1 Mbp (N_{50}=87 Mbp), respectively. They exhibited a high level of completeness and contained a smaller number of gaps and

ambiguous bases than either of the two previously published reference genomes for this species, suggesting a considerable improvement in the quality and completeness of the assemblies. A total of 12,082 and 12,120 protein-coding genes were predicted in Stecla and Cartagena, respectively. TE analyses indicated more repetitive content was captured in the long-read assemblies. The assembled genomes shared 98.12% pairwise identity and synteny analyses suggested that gene position was primarily conserved between both strains. These genome assemblies will serve as an important resource for future research in comparative genomics, proteomics, epigenetics, transcriptomics, and functional analysis of this important malaria vector

7051

PHOSPHOPROTEOMICS ANALYSES OF *AEDES AEGYPTI* FAT BODY REVEAL BLOOD MEAL-INDUCED SIGNALING AND METABOLIC PATHWAYS

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The mosquito fat body is the principal source of yolk protein precursors (YPP) during mosquito egg development in female *Aedes aegypti*. To better understand the metabolic and signaling pathways involved in mosquito reproduction, we investigated changes in the mosquito fat body phosphoproteome at multiple time points after a blood meal. Using LC/MS, we identified 3,570 phosphorylated proteins containing 14,551 individual phosphorylation sites. We observed protein phosphorylation changes in cellular pathways required for vitellogenesis, as well as proteins involved in primary cellular functions. Specifically, after a blood meal, proteins involved in ribosome synthesis, transcription, translation, and autophagy showed dynamic changes in their phosphorylation patterns. Our results provide new insight into blood meal-induced fat body dynamics and reveal potential proteins that can be targeted for interference with mosquito reproduction. Considering the devastating impact of mosquitoes on human health, worldwide, new approaches to control mosquitoes are urgently needed.

7052

PREVALENCE OF MALARIA AND LONG-COVID AMONG INDIVIDUALS PREVIOUSLY INFECTED WITH THE SARS-COV-2 VIRUS IN ETHIOPIA AND UGANDA: A CASE CONTROL STUDY

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By 15th April 2024, more than 12 million patients had recovered from SARS-CoV-2 infection across Africa. Although most patients fully recover after acute infection, a proportion experience long-term complications and symptoms referred to as long COVID. The potential interplay between any such post-COVID syndromes and the risk of other infectious diseases like malaria is largely unknown. We determined the prevalence of malaria and long COVID among individuals with previous SARS-CoV-2 infection in a case-control study in Uganda and Ethiopia. Detailed clinical evaluation was conducted using a standardized clinical tool and malaria was diagnosed using rapid diagnostic tests, microcopy and molecular methods. Previous *Plasmodium falciparum* exposure was assessed using serologic responses to a panel of *P. falciparum* antigens using a multiplex bead assay. Additional evaluations including radiological investigations were carried out as needed. Of 3,251 individuals enrolled between 15th September 2022 and 30th March 2024, 1700 (52%) were female and median age (SD) was 35 (15.3) years. Preliminary findings show an overall prevalence of malaria infection was 9.5% (197/2076, 95% CI 8.3 to 10.8), with a higher prevalence among controls (16.7%, 150/898) compared to cases (4.0%, 47/1178), 95% CI 10.1% to 14.5%, p<0.0001. Overall, the prevalence of long COVID was 62.2% (1119/1800, 95% CI 59.9 to 64.4). The commonest manifestations of long COVID included mental health issues, headache, memory loss, brain fog, muscle/joint/bone pains, chest pain/dyspnea and suicidality. Some symptoms persisted up to 24 months post-acute illness. No clear healthcare pathways for the management of these long-term complications were reported. Additional findings will be presented. The burden of long COVID in these settings is significant and defining treatment strategies and recommendations for African patients with long COVID is critical.

7053

EMERGENCE OF CRIMEAN CONGO HEMORRHAGIC FEVER VIRUS IN EASTERN SENEGAL IN 2022

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Crimean-Congo hemorrhagic fever (CCHF), the most widespread tick-borne viral human infection, poses a threat to global health. In this study, clinical samples collected through national surveillance systems were screened for acute CCHF virus (CCHFV) infection using RT-PCR and for exposure using ELISA. For any CCHF-positive sample, livestock and tick samples were also collected in the neighborhood of the confirmed case and tested using ELISA and RT-PCR, respectively. Genome sequencing and phylogenetic analyses were also performed on samples with positive RT-PCR results. In Eastern Senegal, two human cases and one *Hyalomma* tick positive for CCHF were identified and a seroprevalence in livestock ranging from 9.33% to 45.26% was detected. Phylogenetic analyses revealed that the human strain belonged to genotype I based on the available L segment. However, the tick strain showed a reassortant profile, with the L and M segments belonging to genotype I and the S segment belonging to genotype III. Our data also showed that our strains clustered with strains isolated in different countries, including Mauritania. Therefore, our findings confirmed the high genetic variability inside the CCHF genotypes and their introduction to Senegal from other countries. They also indicate an increasing CCHF threat in Senegal and emphasize the need to reinforce surveillance using a one-health approach.

7054

INVESTIGATING THE EMERGING BURDEN OF DENGUE IN THE KATHMANDU VALLEY, NEPAL THROUGH A LONGITUDINAL POPULATION-BASED SEROSURVEY

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Dengue, an arthropod-borne infection by *Aedes aegypti* and *Ae. albopictus*, is intensifying globally due to climate change. In Nepal, dengue was previously limited to lower elevations, but recent clinical reports indicate transmission is now occurring at higher altitudes. This study aimed to characterize the population-level risk of dengue in the Kathmandu Valley, Nepal's densely populated region. We enrolled a geographically representative, stratified random sample of individuals between the ages of 1 and 25 residing in Kathmandu and Kavrepalanchok districts. We collected dried blood spot (DBS) samples from participants between 2019-2021 and collected a follow-up sample in 2023. We tested samples for IgG responses against dengue-derived recombinant antigens using commercial ELISA kits. We determined seropositivity cut-offs using Gaussian mixture models, then calculated seroincidence as the number of individuals who seroconverted

from negative to positive divided by their person-time. We enrolled 843 participants (352 in Kathmandu and 491 in Kavre) and analyzed 2091 blood samples. The median age at baseline was 11 years (IQR: 6-17); 47% (396/843) were female. Dengue seropositivity rose from 1.9% (15/792) in 2019 to 12.4% (44/354) in 2023 and was highest in Kathmandu, where it rose from 4.1% (11/271) to 34.0% (36/106). Seroincidence was highest in Kathmandu (99.2 per 1000 person-years, 95% CI: 69.8-136.7). In Kavre, seroincidence ranged from 0 in Panauti to 31.0 (95% CI: 8.5-79.5) in Panchkal. Across all regions, seroincidence increased with age, peaking among 15-25-year-olds at 47.7 infections per 1000 person-years (95%CI: 31.2-70.0). In conclusion, this study reveals a significant rise in dengue incidence in Kathmandu Valley between 2019 and 2023, which may be linked to warming temperatures. The findings indicate an urgent need for interventions to mitigate dengue's rise in Nepal's higher altitudes and contribute to the broader understanding of climate change on vector-borne diseases worldwide.

7055

DETECTION OF ANTIBODIES TO POSSIBLE FILOVIRUS-LIKE PATHOGENS IN RURAL COMMUNITIES IN SARAWAK, MALAYSIA

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Ebolaviruses (EBOV) are zoonotic pathogens that have the potential to cause severe morbidity and mortality. They are deemed to be viruses with high pandemic potential. During our analysis of samples from rural communities in Sarawak, Malaysia, we note the presence of antibody signatures against EBOV in the high throughput serological platform, Phage Immunoprecipitation Sequencing VirScan. We followed up these results using commercially available ELISA for verification. Here, we present preliminary data that shows detection of EBOV glycoprotein (GP) antibodies in several communities in the rural forests of Sarawak, Malaysia.Samples from the rural communities and urban controls were ran on commercially available ELISA with a variety of EBOV GP (Bundibugyo, Tai Forest, Reston, Sudan and Zaire GP) as antigens. Manufacturer recommended cutoff determination was used to interpret the results and the individuals' ELISA results to different EBOV GP was then assessed. Antibody responses were primarily detected against Bundibugyo, Reston, Sudan and Zaire EBOV GP, with a cross-reactive pattern noted in individuals with positive results. Of the EBOVs studied, Sudan and Reston responses are predominant. We observed that individuals residing in the rural community yielded higher ELISA ZEBOV results compared to their urban counterparts.
While known to be lethal and highly pathogenic in most cases, there are certain EBOV (e.g., Reston) that causes asymptotic infections in humans. Given that there were no reports of unidentified illness and there have been no known Filoviruses circulating in the locale, it is possible that a novel zoonotic Filovirus-like pathogen may be the cause of these antibody signatures. Further work - such as neutralization tests - are required and are being conducted to verify our results.

7056

RE-EMERGENCE OF RIFT VALLEY FEVER VIRUS LINEAGE H IN SENEGAL IN 2022: *IN VITRO* CHARACTERIZATION AND IMPACT ON ITS GLOBAL EMERGENCE IN WEST AFRICA

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Rift Valley Fever (RVF) is an re-emerging vector-borne zoonosis causing major epidemics and huge losses in livestock production. In West African countries, the lineages A, C and N were previously detected but since 2020, mainly the lineage H from South Africa were detected in Senegal. In this study, clinical samples collected through national surveillance system were screened for RVF virus (RVFV) acute infection by RT-PCR and exposure by ELISA. Molecular and *in vitro* phenotypic characterization were also performed on RT-PCR positive samples. Four human cases were detected RVFV positive by RT-PCR (2) and ELISA (2) in four regions in Senegal. Phylogenetic analyses revealed that these strains belonged to lineage H and clustered with West African strains, specifically found in Senegal and Mauritania in 2020. The *in vitro* characterization showed that the lineage H had significant higher replication than lineage C. Our findings showed a re-emergence of the lineage H in Senegal in 2022 and showed its higher replication compared to previous lineage C identified in West Africa. This study gives new insights on the biological properties of the lineage H and will be useful for the implementation of control strategies of RVF in Senegal and neighboring countries.

7057

MPOX VIRUS SEROPREVALENCE AMONG INDIVIDUALS VULNERABLE TO INFECTION IN EAST AFRICA

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Endemic in Central and West Africa as a zoonotic infection, mpox has recently been associated with human-human transmission in many non-endemic countries. No mpox cases have been reported in East Africa, but asymptomatic or mild cases in conjunction with limited mpox testing capacity could underestimate disease spread. Results from a mpox seroprevalence study among individuals in East Africa vulnerable to infection during the 2022-23 global outbreak are presented. The African Cohort Study (AFRICOS) is a prospective cohort of adults and adolescents living with, or vulnerable to HIV in four African countries. Cohort participants in Kenya, Tanzania, and Uganda were identified as vulnerable to mpox by meeting one of the following criteria per their study enrollment questionnaire: men or transgender women who have sex with men, HIV pre-exposure prophylaxis use, alcohol/recreational drug use during sex, four or more sex partners in the past six months, sexually-transmitted infection in the past month, or transactional sex. A participant's most recently collected plasma/

serum was tested for anti-clade IIb mpox antibodies using the Meso-Scale Discovery (MSD) Orthopoxvirus panel 1 MULTI-SPOT kit. Mpox seropositive participants' most recent demographic and social behavior data were described. Of the 618 participants identified as vulnerable to mpox, 50 (8.1%) were seropositive. Median age was 53 (interquartile range: 44-63) and 13 (26%) were female. Ten reported recent behaviors associated with mpox vulnerability (eight men who have sex with men and two reporting transactional sex). The high seroprevalence observed in these participants with relatively low mpox vulnerability per their recent behavior data suggests prior infection with other orthopoxviruses or cross-reacting immune responses to Vaccinia virus vaccination may be contributing. However, these results may also indicate previously unrecognized human mpox in East Africa and highlight the need for expanded seroprevalence studies and prospective surveillance to address the persistent knowledge gap in mpox epidemiology in Africa.

7058

FOLLOWING A 50-YEAR HIATUS TAMANA BAT VIRUS (TABV) IS DETECTED AGAIN IN IQUITOS, PERU

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Tamana Bat Virus (TABV) is a putative flavivirus first identified and isolated in 1973, from the salivary glands, saliva and spleen of *Pteronotus parnellii*, an insectivorous bat collected in the Tamana bat caves of Trinidad, in South America. At the time, the authors showed serological evidence of TABV infection in bats (72/850, 8.5%) of several species (15), as well as in humans (21/172, 12%), suggesting this novel flavivirus could potentially be a pathogen of concern. The complete TABV genome of the original isolate was sequenced 30 years later, in 2002, but in the 50 years since its original discovery in Trinidad there have been no further reports of TABV anywhere, until now. As part of ongoing metagenomic investigations of the virome of various bat species residing at the human-animal interphase in the Amazonian Region of Peru, we used unbiassed NGS to identify partial genomic sequences matching TABV in a feces sample from a pale spear-nosed bat (*Phyllostomus discolor*) collected within the city of Iquitos. Given that the genomic sequences initially identified covered only ~46% (4,587 of 10,053 total bp) of the complete TABV genome, we used this information in combination with the previously published TABV whole genome to design TABV-specific primers for tiling amplification, and we further supplemented 5'- and 3'-UTR sequences using 5'- and 3'-RACE. With this approach we have generated a complete TABV genome from Peru, which in turn has enabled other downstream analyses, including a basic phylogeny. Here, we report complete genomic characterization of TABV from a sample collected from a city-dwelling omnivorous bat known to feed on insects, fruit, pollen, nectar and flowers. Further, we report on ongoing efforts to test additional samples for this relatively novel flavivirus to further characterize its little-known epidemiology.

7059

METABOLOMIC BIOMARKERS IN DENGUE VIRUS INFECTION FOR PREDICTING SEVERE DISEASE

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Dengue virus (DENV) infection results in a range of clinical outcomes, spanning from self-limited febrile disease known as dengue fever (DF) to severe disease characterized by hemorrhage and vascular leakage called dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). While diagnostic tools aid in identifying infections, the triage of those at risk of progression to DHF/DSS relies on clinical and hematological parameters. Here, we aimed to identify prognostic biomarkers by analyzing the metabolome of DENV-infected children early after infection (≤3 days post-symptom onset). Using liquid chromatography/mass spectrometry, we analyzed the serum metabolome of children from the prospective Pediatric Dengue Hospital-based Study and the Pediatric Dengue Cohort Study in Nicaragua. To control for potential confounders, children who progressed to DHF/DSS (n=14) were matched with DF cases (n=81) using propensity score full matching. We used a multivariate regression with regularization to identify discriminant features between both clinical groups. The dataset (n=95) was split into training/testing subsets (50:50) for parameter estimation of the model via cross-validation (n=10). The median age was 10.6 years (interquartile range 7.9-12.6, female 52.6%). From a total of 3850 metabolomic features that were extracted, filtered, and normalized, only 56 were discriminant between children who developed DHF/DSS vs. DF during follow-up. Fifty-four were enriched in DF, while only two were enriched in DHF/DSS. Interestingly, a molecular feature with mass to charge 780.5538 was associated with DHF/DSS in primary and secondary infections (OR 3.66, 95%CI 1.39 to 14.42 and OR 3.59, 95%CI 1.38 to 13.89, respectively), while a molecular feature with mass to charge 777.695 was associated with DF in both primary and secondary infections (OR 0.07, 95%CI 0.01 to 0.42). Further analysis will identify metabolites associated with DF vs DHF and will explore metabolic pathways during the acute, critical and recovery phases of disease. Our results suggest that specific metabolomic markers may serve as early prognostic indicators during DENV infection.

7060

PREVALENCE AND PREDICTORS OF PERSISTENT SYMPTOMS POST-ACUTE COVID-19 INFECTION AMONG A COHORT OF FRONTLINE HEALTHCARE WORKERS IN BANGLADESH

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Despite evidence of a wide range of persistent symptoms among COVID-19 survivors, commonly known as long COVID, their frequency, clinical spectrum and risk factors are not well characterized. We assessed the prevalence and predictors of long COVID among healthcare workers (HCWs) in Bangladesh. Between July 2021-December 2023, we enrolled a cohort of HCWs from purposively selected 10 hospitals across Bangladesh to prospectively record COVID-19 illness. At enrolment, we captured data on HCWs' demographics, co-morbid conditions and COVID-19 illness. The study physician followed the participants biweekly to record any new and persistent symptoms following acute illness. We used the WHO case definition for long COVID (symptoms occurring 3 months from the acute COVID-19 infection and persisting for at least2 months). We performed a multivariable logistic regression to identify the predictors of long COVID. The analysis included 875 HCWs with lab-confirmed SARS-CoV-2 infection: 30% (261) doctors, 53% (468) nurses, and 17% (146) support staff. Themedian age of the HCWs was 35 (IQR, 29-44), and 69% (601) were female. Of the 875 HCWs, 462 (53%) reported persistent symptoms, with fatigue being the most common (83%), followed by brain fog (14%), cough (5%), breathing difficulties (4%),and joint pain (4%). HCWs with co-

morbidities (aOR 3.39, 95% CI 2.32-4.95; p=0.0001), breathing difficulty during the acute phase (aOR 2.84, 95% CI 1.77-4.55; p=0.0001), and those who required hospitalization during acute infection (aOR 2.25, 95% CI 1.53-3.04; p=0.0001) were more likely to develop persistent symptoms than HCWs without a history of co-morbidities, respiratory symptoms, or hospitalization. Nurses (aOR 1.36, 95% CI 1.01-1.85; p=0.04) were more likely to develop persistent symptoms than doctors. More than half of the HCWs in our cohort experienced long-term symptoms of COVID-19, with a greater risk observed among nurses and those with the co-morbid condition. These findings underscore the pressing need for long-term care and rehabilitation strategies with a standardized guideline to enhance the post-acute recovery of COVID-19 patients.

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VIRAL CLEARANCE IN COVID-19 PATIENTS WITH AND WITHOUT COMORBIDITIES IN BAMAKO, MALI.

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Coronavirus Disease 2019 (COVID-19) rapidly spreading to the rest of the world afteridentification. Comorbidities have increased morbidity and mortality rates and have been linkedto more hospitalization and intensive care unit (ICU) admissions. Thus, the aim of our study wasto determine the duration of the positivity of SARS-CoV-2 in COVID-19 patients with and withoutcomorbidities at the University Teaching Hospital (UTH) of Point-G, Bamako, Mali. A Crosssectional study was conducted between March 2020 and December 2022 enrolling SARS-CoV-2 RT-PCR positive patients in IRB approved protocol after written consent. Treatment was donein accordance with the national protocol combining Chloroquine, azithromycin, and vitamin C for7 days. Clearance was defined as anyone with two consecutive negative RT-PCR results within24 hours on nasopharyngeal swabs. One hundred and twenty-eight patients were included, andthe sex ratio was 1.6. While most patients had no symptoms, some had a wide range of symptomsfrom mild complaints to hospitalization at ICU. Among the 128 patients, 91 had comorbidities ofwhich 13.3% had critical symptoms. The average duration of viral clearance was 11.76days±4.48. The difference between age groups (years) was not statistically different, 14 days±0for [8-17], 11.5±3.54 for [18-60], and 12.6 ±6.39 for those aged greater than 60 years respectively(p= 0.24). In addition, we didn't find a difference on gender based with 12.3±5.31 for women and11.4±3.85 for men respectively (p=0.43). On the other hand, the average time to clearance ofpatients without comorbidities was higher than those with comorbidities, 13 days±3 vs. 11.30days±3.85 respectively (p = 0.007). The most common comorbidities identified were high bloodpressure (N=61), diabetes (N=36), sickle cell disease (N=8) and HIV (N=5). Viral RNA frompatients without comorbidities persists for a somewhat long period than those on patients withcomorbidities. A complete monitoring of these patients including the check for long COVID-19together with some immunological factors will determine the impact of COVID-19 on Human hostfactors.

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CLINICAL AND RISK FACTOR PROFILE OF OROPOUCHE VIRUS DISEASE DURING AN ONGOING OUTBREAK IN THE PERUVIAN AMAZON: FINDINGS FROM THE RIVERA ACUTE FEBRILE ILLNESS SURVEILLANCE STUDY.

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Oropouche fever is an emerging arthropod-borne zoonotic disease caused by the Oropouche virus (OROV) and leads to undifferentiated acute febrile illness (AFI) symptoms. OROV transmission is endemic among wild animal hosts in the forests and jungles of Central and South America, with occasional spillover to humans in the bites of midges and mosquitoes resulting in sporadic outbreaks. Incidence is increasing with over 500,000 cases and >30 outbreaks reported in the Americas, likely underestimated due to surveillance limitations. An outbreak of OROV is currently underway in Amazonian Brazil and Peru. RIVERA is an ongoing surveillance study of AFI etiology with a case-control design. AFI patients and matched controls are enrolled at urban and rural health facilities in and around Iquitos, in the Peruvian Amazon. Blood samples are tested for 32 locally relevant endemic and emerging pathogens using multiplex PCR. Using a nested case-control approach, OROV-positive AFI patients from the parent study were identified, and symptomatic AFI cases negative for all pathogens (unattributed AFI) were treated as controls. Relevant risk factors, signs and symptoms were compared, and logistic regression models fitted to the OROV positive/unattributed AFI binary outcome. From 8/25/2021, through 3/31/2024, 24 cases of OROV attributable AFI were identified, with 18 (75%) occurring in 2024. 1,012 unattributed AFI controls were recruited in the same period. The odds ratio for joint pain in the prior two weeks in cases compared to controls was a statistically significant 12.4 (2.89, 53.33). 16.7% (4) of OROV cases reported having traveled in the preceding 15 days compared with 7.2% of controls, giving a statistically significant odds ratio of 3.11 (1.12, 8.60). As the outbreak plays out, we will prospectively add new cases of OROV attributable AFI to the analysis, eventually giving large enough numbers for confounder matching and adjustment. OROV disease is characterized by muscle and joint pain, malaise, and headache in this study population in the Peruvian Amazon. Those contemplating travel within Amazonia, should take precautions against OROV insect vectors.

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THE GLOBAL HEALTH BURDEN OF CHIKUNGUNYA FROM 2011 TO 2020: A MODEL-DRIVEN ANALYSIS ON THE IMPACT OF AN EMERGING VECTOR-BORNE DISEASE

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Chikungunya is a mosquito-borne arboviral disease posing an emerging global public health threat. Understanding the global burden of chikungunya is critical for designing effective prevention and control strategies. However, current health estimates caused by chikungunya remain limited and are potentially underestimated. Considering the increasing risk of large-scale outbreaks driven by climate change and globalization, it is crucial to have a thorough understanding of the health burden of chikungunya. Therefore, we aimed to estimate the global and regional burden of chikungunya from 2011 to 2020 based on a data-driven simulation model. Based on worldwide case numbers from several publicly available sources, we estimated the disability-adjusted life years (DALYs) for the acute and chronic phase of chikungunya per country, super-region, and globally over a ten-year time period. Because the true burden of chikungunya is likely underreported due to misdiagnosis amongst others, we included an underreporting

factor for the reported case numbers. DALYs were calculated using the GBD methodology and represent the sum of the years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs). Our model revealed 17.5 million chikungunya cases in 110 countries between 2011 and 2020, causing 1.8 million DALYs lost in this ten-year timeframe. The majority was driven by long-term chronic illness, accounting for 1.4 million DALYs lost. YLDs take up most of the total DALYs, with 77%. YLLs in the acute phase were 426,000. In 2014, the highest DALY burden was recorded, with 640,000 DALYs. This aligns with the significant case numbers reported in the Latin American and Caribbean super-region that year. These results show that the burden of chikungunya should not be neglected. The disease's unpredictable nature in combination with the emerging spread due to climate change poses a significant threat to public health and can cause a substantial health burden for individuals affected.

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RAPID ALTERNATIVE DETECTION ASSAY OF SARS-COV2 RNA USING A ONE-STEP RT-FAST-MULTIPLEX PCR AND LATERAL FLOW IMMUNOASSAY

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COVID-19 pandemic has put emphasis on diagnosis and surveillance, and the subsequent shortage of diagnostics reagents and kits. It is strategic for the countries to be able to access, expand diagnosis, and acquire capacity to deploy alternative rapid accurate nucleic acid tests that are at lower costs. Here, we propose a visual SARS-CoV-2 detection using a one-step RT-fast-multiplex PCR amplification coupled to lateral flow immunoassay detection on a generic PCRD dipstick. Simplex fast-PCRs were developed by screening 17 primer pairs. They include 12 designed primer pairs targeting genes encoding the S protein (N=6 pairs), the N protein (N=2 pairs), the E protein (N=2 pairs), and the Open Reading Frame ORF1ab (N=2 pairs), and 5 other primer pairs selected from the published and validated WHO quantitative (q) RT-PCR protocols. For PCRD detection, labelled primers with Fam/Biotin or Dig/Biotin were used in fast RT-PCR protocols using RNA isolated from patients' nasopharyngeal swabs. Two primer pairs were selected based on their specificity, sensitivity, stability and absence of background to noise in the PCRD, and were used to set up a multiplex assay targeting two different viral genomic regions, N and E genes. The selected assay was then evaluated on 98 samples including 46 SARS-CoV+ with Ct values varying from 15 to 38, and 48 SARS-CoV-, comparing the performances to those of the RT-qPCR used to diagnose the patients by the virology lab of IPT. Our one step RT-fast-multiplex PCR coupled to PCRD showed a sensitivity of 86,96% (40/46) and a specificity of 97,75% (47/48). All patients presenting Ct values lower than 33 were positive with our assay. Patients with Ct values higher than 33 showed negative results. Our results brought proof of principle on the usefulness of the one step RT-fast-multiplex PCR assay coupled to PCRD for specific, sensitive, and rapid detection of SARS-COV-2 without requiring costly laboratory equipment, and thus at reduced costs and prone to be deployed when resources are limited. This new method of SARS- CoV2 detection appears as a good alternative for Covid19 diagnosis or screening at points of need.

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FIELD EVALUATION OF VALIDITY AND FEASIBILITY OF PAN LASSA RAPID DIAGNOSTIC TESTS FOR LASSA FEVER IN ABAKALIKI, NIGERIA: A PROSPECTIVE DIAGNOSTIC ACCURACY STUDY

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Background Lassa fever is a viral haemorrhagic fever with few options for diagnosis and treatment. A point-of-care bedside test diagnosing Lassa fever,adhering to REASSURED criteria, is not currently available but is urgently needed in west African regions with high Lassa fever burden. We aimed to assess the validity and feasibility of a rapid diagnostic test (RDT) to confirmLassa fever in people in Nigeria.Methods We estimated the diagnostic performance of the ReLASV Pan-Lassa RDT (Zalgen Labs, Frederick, MD, USA) as a research-use-only test, compared to RT-PCR as a reference standard, in 217 participants at a federal tertiary hospital in Abakaliki, Nigeria. We recruited participants between 2022 and 2023. The RDT was performed using capillary blood at the patient bedside and using plasma at the laboratory. The performance of the test, based on REASSURED criteria, was assessed for user friendliness, rapidity and robustness, sensitivity, and specificity.ResultsParticipants were aged between 0 and 85 years, with a median age of 33 years (IQR 22·0-44·3), and 24 participants were younger than 18 years. 107 (50%) participants were women and 109 (50%) were men. Although the specificity of the Pan-Lassa RDT washigh (>90%), sensitivity at bedside using capillary blood was estimated as 4% (95% CI 1-14) at 15 min and 10% (3-22) at 25 min, far below the target of 90%. The laboratory-based RDT using plasma showed better sensitivity (46% [32-61] at 15 min and 50% [36-64] at 25 min) but did not reach the target sensitivity. Among the PCR-positive participants with Lassa fever, positive RDT results were associated with lower cycle threshold values. Personnel conducting the bedside test procedure reported being hindered by the inconvenient use of full personal protective equipment and long waiting procedures before a result could be read.ConclusionThe Pan-Lassa RDT is not currently recommended as a diagnostic or screening tool for suspected Lassa fever cases. Marked improvement in sensitivity and user friendliness is needed for the RDT to be adopted clinically. There remains an urgent need for better Lassa fever diagnostics in low-resource settings.

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COMPARATIVE ANALYSIS OF NS1/IGM RAPID DIAGNOSTIC TESTS WITH NS1 AND IGM ELISA FOR DENGUE CASES AND ITS POSSIBLE CORRELATION WITH UNDER-REPORTING OF DENGUE CASES IN INDIA.

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According to the guideline of National Center for Vector Borne Diseases Control (NCVBDC), Government of India, IgM Antibody Capture ELISA kit (MAC ELISA) is provided for definitive diagnosis of dengue infection in the network of sentinel surveillance laboratories, established across the country. Therefore, a negative IgM ELISA result concludes to a dengue negative result. However, most patients with dengue infection get tested by Rapid Diagnostic Kit (RDT) during the first 4 days of the febrile illness

when IgM are not usually formed. This could be a possible factor behind under-reporting of Dengue cases in India. Our study aims to compare the results of the rapid test for dengue with NS1 and IgM ELISA and find the possible correlation that IgM negative NS-1 Antigen (NS1Ag) positive cases have with under-reporting of Dengue cases and to formulat an efficient combination of serological tests which could bring the "missed-out" Dengue cases in the fold of reported cases. Blood samples (n=264) from patients diagnosed with dengue with RDT in CCI Lab, SSL Hospital, BHU were used in our study from September 2023 to November 2023. We performed NS-1 ELISA and IgM ELISA by DENV NS-1 ELISA kit and IgM Antibody Capture MAC ELISA kit, respectively in all the samples. RDT of 264 samples, showed NS1 Ag positive in 251 sample out of which 239 were NS-1 positive and 12 were NS-1/IgM co-positive while 13 were IgM positive. Out of the 239 samples solely positive for NS-1Ag by RDT, we detected 237 sample to be positive through NS-1 ELISA and from the co-positive samples, we found 10 to be positive from NS-1 ELISA. Similarly, IgM positive samples via RDT were 25 in which 13 were solely positive for IgM out of which 12 were found positive by IgM ELISA while all 12 positive for both NS-1/IgM by RDT was positive by IgM ELISA. Overall, out of 264 samples, 257 (97.34%) were found positive for NS-1Ag via NS-1 ELISA and only 54 (20.45%) were positive for IgM via IgM ELISA. This shows almost 80% of the cases will be missed if only IgM ELISA is used for definitive diagnosis of Dengue. Our study suggests revision of guidelines, recommending NS1-ELISA alongside IgM for accurate dengue case reporting in India.

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DETECTION OF ANTI-MARBURG VIRUS IGG ANTIBODIES IN WATSA, DEMOCRATIC REPUBLIC OF THE CONGO: 25 YEARS AFTER OUTBREAK

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Marburg virus (MARV) is a rare, but potentially fatal, zoonotic pathogen responsible for Marburg virus disease (MVD) among humans and non-human primates. As a member of the *filoviridae* family of viruses, and close relative of *Ebolavirus*, historic outbreaks of MARV have almost been exclusively in Sub-Saharan Africa, with six alone reported between Uganda and the Democratic Republic of the Congo (DRC). The most recent MARV outbreak in DRC was reported in the Watsa/Durba region of Haut Uele province from 1998-2000-near recent reported MARV outbreaks in Uganda in 2022. With limited outbreaks of MARV and no available clinically approved MARV vaccines, this study sought to elucidate the prevalence of anti-MARV antibodies (Ab) among a mixed cohort of Watsa/Durba residents enrolled in 2023. This cohort (n = 370) included known MVD survivors of the 1998 outbreak (n = 6), close contacts (n = 29) and healthcare workers (n=318). Among this group, 6.8% of respondents reported recent travel to Uganda, and 9.5% were under 24 years of age - thus, born after the 1998 outbreak. Additionally, a small sample of the cohort (n = 3) indicated that their primary occupation was gold-panning - an activity shown to be a significant risk factor for MARV exposure. Using a multiplex bead-based immunoassay, the seroreactivity to MARV antigens was compared among the Watsa/Durba cohort with the cut-off for seroreactivity calculated at 6711 Median Fluorescence Intensity (MFI) for MARV glycoprotein (GP) and 11491 MFI for viral matrix protein 40 (VP40). In this comparison, the seroreactivity to MARV GP was 3.5% and 1.2% to MARV VP40. Interestingly, none of the seroreactive individuals were known survivors of the 1998 outbreaks. There were no associations between travel to Uganda and seroreactivity, nor employment as a goldminer. When using a less stringent cut-off to determine seroreactivity, all known survivors were classified as reactive for both MARV GP and VP40 - with 42.9% and 39.4% seroreactivity among the entire Watsa cohort. This high seroprevalence may indicate exposure to MARV or MARV-like antigens despite no active outbreak declared in the area.

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DETECTION AND PARTIAL GENOMIC CHARACTERIZATION OF ROTAVIRUS A STRAINS CIRCULATING IN DIARRHEAL OUTBREAKS IN LLAMA AND ALPACA FLOCKS FROM BOLIVIA

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In marginal agricultural areas of the Bolivian highlands, South American camelids (SAC) often constitute the indigenous farmer's only resource for food, clothing, and extra income. Acute diarrheal diseases affecting llama and alpaca newborns constitute major annual financial losses for farmers due to high levels of mortality. The objective of this study was to report the preliminary genomic analysis of two RVA strains affecting llama and alpaca flocks with diarrhea during March–June 2018 using an NGS-based approach. For this purpose, seven fecal samples were selected out of twenty five from animals with diarrhea in two highland regions. Following viral RNA extraction, cDNA library construction, and sequencing on an Iseq100 platform (Illumina), the genotype of each RVA gene was determined using the RotaC v2.0 tool. Sequences were compared to those of RVA strains obtained from GenBank. For each gene, multiple alignments were carried out using MAFFT 7.0, and phylogenetic trees were constructed using neighbor-joining in MEGA-X. Two samples isolated from alpaca and llama revealed the presence of two different genotypes: G8-P[14] and G3-P[14] that were partially classified as: G8-P [14]-I2-Rx-C2-M2-A11-N2-Tx-E3-H3 and G3-P [14]-I2-R2-C2-M2-A17-N2-T6-E3-H3, respectively. The isolated segment genotypes G8, P[14], I2, C2, M2, A17, E3, and T6 were closely associated with RVA strains isolated from vicuñas, guanacos, and alpacas, while R2, N2, and H3 were related to bovine-RVA strains, and G3 and A11 to strains identified in humans. This data suggests complex reassortment events among rotaviruses from diverse host species, which may have contributed to the genetic constellation of llama and alpaca RVA strains, highlighting the need for monitoring the potential emergence of novel rotavirus strains in the region.

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COMORBIDITIES AND HOSPITALIZATION RISK FROM DENGUE, CHIKUNGUNYA, AND ZIKA, PUERTO RICO, 2012-2023

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Previous research has established links between comorbidities and severe arbovirus infections, but there is limited research on how specific comorbidities impact hospitalization risk for each arbovirus. We analyzed data from 2012–2023 from the ongoing Sentinel Enhanced Dengue Surveillance System in Puerto Rico, focusing on adults aged ≥18 years diagnosed with dengue, chikungunya, or Zika virus infection via RT-PCR or serology. Mixed-effects logistic regression was used to evaluate associations between each comorbidity and arbovirus, adjusting for age group, sex, days post onset, previous dengue infection, respiratory viral coinfection, pregnancy, other comorbidities, and hospital site. To account for potential confounding by disease management practices, including admission for dengue warning signs, we additionally adjusted the dengue analyses for severe dengue status. Of 18,941 adults with acute febrile

illnesses, median age was 40 years [IQR: 26-57] and 52.6% were female. From these, 1,359 (7.2%) had Zika, 1,250 (6.6%) had chikungunya, and 594 (3.1%) had dengue. The most frequent comorbidities were obesity (Zika: 39.5%, chikungunya: 20.0%, dengue: 22.7%) and hypertension (Zika: 26.6%, chikungunya: 29.4%, dengue: 22.1%). Logistic regression showed increased odds of hospitalization among adults with hypertension and Zika (OR: 2.28, 95% CI: 1.21–4.28), diabetes and chikungunya (OR: 2.11, 95% CI: 1.28–3.48), and cancer and chikungunya (OR: 2.97, 95% CI: 1.27–6.95) compared with patients without those comorbidities. No associations were found between any comorbidity and hospitalization for dengue. No associations were found between asthma, congenital heart disease, high cholesterol, obesity, thyroid disease, or hospitalization for any arbovirus. While null findings for dengue may reflect the lower case count compared with Zika and chikungunya, future analyses leveraging the ongoing PR dengue epidemic could strengthen this investigation. These findings underscore the importance of understanding comorbidities for arbovirus management.

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TRANSMISSION DYNAMICS OF RIFT VALLEY FEVER AND CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUSES IN THREE DIFFERENT ECOLOGICAL REGIONS IN SENEGAL

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Rift Valley Fever (RVF) and Crimean Congo Hemorrhagic Fever (CCHF) are 2 emerging diseases with great economic, medical and veterinary impact. Humans can be infected through arthropod bites or contact with fluids or tissues from infected animals. As a result, livestock workers are at high risk of contracting these diseases. In the absence of specific treatment and licenced vaccines for humans, their epidemiology needs to be better understand for the implementation of preventive measures. Here we sampled humans, animals and arthropods in Kedougou (South) Barkedji (Center), and Podor (North) to analyze the circulation dynamics of RVF and CCHF. Indeed, at-risk and low risk healthy humans as well as cattles, sheep and goats from transhumant and sentinel herds were sampled. Ticks were collected by extirpation while mosquitoes were collected using different traps. Animal and human samples were tested by IgM and IgG ELISA while arthopod samples were tested by RT-PCR and virus isolation. In humans as in animals, the seroprevalence rates varied by virus, sex, locality, age and exposure level to animals for humans. RVF and CCHF were not detected in arthropods but a North-South gradient of relative abundance of their main vectors has been found. The data showed different transmission modes for these two viruses according to the area. Indeed, in the North and Center, RVF is circulating in at-risk and low risk populations, while CCHF is mainly detected in at-risk populations. However, in the South, a different transmission pattern has been observed with RVF circulating only in at-risk populations while CCHFV is circulating in both at-risk and low risk populations. These data suggest the enzootic and regular circulation of these viruses in Senegal with different transmission modes. This emphasize the need to reinforce surveillance and to consolidate data to identify risk factors in order to better prevent and control the spread of these viral infections.

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UNRAVELING THE TRANSMISSION DYNAMICS OF RIFT VALLEY FEVER : INSIGHTS FROM EAST AND CENTRAL AFRICA

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In East Africa, outbreaks of Rift Valley Fever (RVF), a vector-borne viral zoonosis, follow a 5-10-year cycle, with periods of quiescence in between. Although RVF outbreaks in animals are known to precede human cases, some human outbreaks may go unnoticed and are difficult to predict. A multi-country initiative of the Center for Research on Emerging Infectious Diseases-Eastern and Central Africa (CREID-ECA), undertook surveillance of acute febrile illness (AFI) and community human-animal linked seroprevalence studies to unravel the dynamics of cryptic RVF transmission. In Kenya, the Democratic Republic of the Congo (DRC) and Uganda, a 2-year longitudinal health facility-based study enrolled AFI cases while the human-animal serosurveys is assessing RVF burden in communities in direct contact with animals. Human and animal sera are analyzed for anti-RVF virus antibodies (ELISA) and viral RNA (PCR). Demographic, behavioral and environmental factors and RVF knowledge were assessed by questionnaires. In the health facility-based study, 4,755 subjects (median age 31 years, IQR 22-44, female 57.4%) were enrolled. In Uganda, 77 (4%) participants tested positive for IgM/PCR, documenting unusual sustained cases, in contrast to Kenya and DRC where no acute cases were detected. A total of 232 (4.9%) participants tested positive for total RVF antibodies: DRC 1.5%, Kenya 2.0%, and Uganda 9.5% ($p< 0.001$). At multivariable analysis, male participants (OR: 1.73; 95% CI 1.29, 2.32), age ≥50 years (OR: 1.64; 95% CI 1.16, 2.27), low schooling (OR: 1.49; 95% CI 1.05, 2.16) and sheep contact (OR: 1.6; 95% CI 1.00, 2.52) were significantly associated with RVF seropositivity. No significant association was found between RVF knowledge and previous RVF exposure. The community serosurvey in Kenya detected 1.8% (5/282) RVF IgG in humans and 4.4% (31/706) in livestock with goats significantly less affected than cattle (OR = 0.29 CI 0.12, 0.65). A substantial exposure to RVF was identified in the three countries with significant differences among them. Complete findings from this study will provide important insights for understanding the epidemiology of RVF in ECA.

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DENGUE VIREMIA AMONG FEBRILE PERSONS IN GRENADA, WEST INDIES

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Dengue virus (DENV) is endemic in Grenada, a small island developing state in the Caribbean, and circulates at low levels causing sporadic outbreaks during rainy seasons. However, the incidence of DENV is likely underestimated, as the gold-standard diagnostic test, reverse transcription polymerase chain reaction (RT-PCR), is not routinely available on the island. To more accurately determine the incidence of DENV infection in Granada, we performed febrile illness surveillance among adults and children in Grenada using serum RT-PCR for DENV, Zika virus (ZIKV) and chikungunya virus (CHIKV). Participants also provided demographic, symptom and mosquito behavioral data to evaluate factors associated with infection. Enrollment is ongoing, but to date 214 participants have been enrolled and tested from June 2023 through February 2024. Most participants are female (66%), with median age of 32 years (IQR 24-44) and were enrolled from private clinics throughout the country (66%). To date we have identified 27 positive DENV cases, an incidence of 12.6%, and one case of CHIKV, an incidence of 0.5%. No cases of ZIKV have been identified. The peak DENV incidence rate occurred in July 2023 (21.7% of samples tested positive). In interim univariate analysis comparing DENV positive and negative persons, those with DENV were less likely to live in a house (56 vs 85%, $p<0.01$), more likely to report use of window screens (63 vs 36%, $p=0.02$), and more likely to endorse controlling mosquito breeding sites around the home (100 vs 81%, $p=0.03$). We do not currently observe statistically significant differences between age, sex, education, income, subjective reporting of mosquitoes or reported symptoms. Our results show a relatively high incidence of DENV among febrile persons in Grenada. Possible epidemiologic risk factors are observed, but analyses will be ongoing as we continue to enroll additional participants.

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SURVEILLANCE OF CORONAVIRUS IN WILD MAMMALS SEIZED AND RESCUED BY THE NATIONAL FOREST AND WILDLIFE SERVICE OF LIMA, PERU

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Coronaviruses are pathogens that cause respiratory or enteric diseases in humans and animals. They exhibit high genome plasticity and replication errors, allowing them to change host range. The illegal trafficking of wildlife is a key factor in the emergence of infectious diseases, as it can lead to long-distance circulation and outbreaks of viruses in areas other than their usual environment. The aim of this study was to detect coronaviruses in mammals seized and rescued by the National Forestry and Wildlife Service from tracheal and rectal swabs using a pancoronavirus PCR assay that amplifies the RNA-dependent RNA polymerase (RdRp) gene. Ninety mammals were collected, of which 11.11% (10/90) tested positive by molecular analysis of the collected tracheal swabs. The species that tested positive were *Aotus* sp. (n=1), *Sapajus apella* (n=3), *Saimiri sciureus* (n=2), *Procyon cancrivorus* (n=1), and *Otaria flavescens* (n=3). Sequencing analysis of the ten positive PCR products indicated that nine of them shared 98% similarity with porcine epidemic diarrhea virus (PEDV) from GenBank. In addition, all of them were 100% identical to each other. The remaining sample showed a 95.52% similarity to feline coronavirus (FCoV). Both belonged to the genus Alphacoronavirus. We constructed a phylogenetic tree using sequences from this study and a large set available from GenBank. The maximum likelihood phylogenetic tree supports the hypothesis that PEDV sequences form a monophyletic clade, and FCoV sequence was found to be closely related to other FCoV from different countries. Notably, we only detected the viral RNA in the respiratory tract, despite the enteric nature of these viruses. This discovery confirms airborne transmission, a recently proposed alternative pathway. This study represents the first report of PEDV and FCoV in animals other than their natural hosts, highlighting the importance of epidemiologic surveillance.

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ASSESSING CORRELATIONS IN SEROLOGICAL STATUS TO MULTIPLE VACCINE-PREVENTABLE DISEASES: A CASE-CONTROL STUDY IN ZAMBIA, 2016

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Novel methods for assessing immunization system performance could provide additional insights on opportunities for improvements to reach unvaccinated children. One method to examine gaps in vaccination programs or assess the likelihood of recent infection history is to conduct serologic analyses measuring antibody responses to multiple vaccine-preventable diseases (VPDs), such as measles, diphtheria and tetanus. This study aimed to assess correlations in serological status across VPDs by testing whether individuals who are measles seronegative were more likely to have also missed diphtheria and tetanus vaccination. Nationally-representative samples stored in a biorepository collected during the 2016 ZAMPHIA study were previously tested for measles and rubella IgG serostatus. Paired measles seronegative and seropositive samples from this biorepository among children aged 2-to-10-years-old were identified by exact matching on gender, age, province (i.e., first-administrative unit) and HIV status and proximity matching for district (i.e., second-administrative unit), such that samples from districts closer together were more likely to be matched. Additional paired samples were identified by exact matching on gender, province and HIV status with proximity matching for age, such that samples with similar ages were more likely to be matched. For all selected samples (n = 1298), plasma sera were tested for diphtheria and tetanus IgG antibodies using enzyme-linked immunosorbent assays. Antibody concentrations were standardized using a four-point logistic regression and seropositivity was determined using internationally recognized thresholds. Serologic results for diphtheria and tetanus were analyzed based on underlying measles serostatus using conditional logistic regressions controlling for age and province. Results suggest differential titers over age and varying associations across measles serostatus. More broadly, this study illustrates a key use case of serological data on VPDs to identify the geographic and demographic reach of vaccination programs.

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A SYSTEMATIC LITERATURE REVIEW OF COMMUNITY ACUTE RESPIRATORY INFECTIONS (ARI) AND ACUTE GASTROENTERITIS (AGE) INCIDENCE RATES: A SYSTEMATIC LITERATURE REVIEW OF COMMUNITY-BASED OBSERVATIONAL STUDIES

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Acute respiratory infections (ARI) and acute gastroenteritis (AGE) are major causes of global morbidity and mortality. Most estimates of ARI and AGE incidence emphasize medically attended disease. Such data can severely underestimate true disease burden, especially in low- and middle-income countries (LMIC) where access to healthcare is limited. A systematic literature review of community-based observational studies was conducted to estimate community incidence rates of ARI and AGE. A PubMed search conducted in January 2024 identified 205 studies published between 1965-2017. Studies were included if sampling was performed at the community level with prospective monitoring for ARI or AGE. Studies of single pathogens, and those with follow-up of <12 months or insufficient data to calculate incidence were excluded. Weighted averages of incidence (cases per 1000 person-years (PY)) were calculated by age group from studies using similar case definitions. Meta-regression methods were conducted to identify differences in ARI/AGE incidence by study design characteristics. Eighteen studies of ARI incidence including 26,504 participants were identified, with 13 conducted in LMIC. Eleven studies of AGE incidence among 8,812 participants were identified, all from LMIC. The average all-age incidence rate was 1701 per 1000 PY (95% CI 1680-1723) for ARI and 320 per 1000 PY (95% CI 312-328) for AGE. Children under 5 had the highest incidence of both ARI (3188 per 1000 PY; 95% CI 3150-3227) and AGE (1349 per 1000 PY; 95% CI 1302-1398). ARI incidence was also elevated among adults ≥60 years (2405 per 1000 PY; 95% CI 2359-2453). ARI incidence rates were lower when symptom screening was performed virtually versus through in-person interviews (aIRR=0.30, 95% CI=0.13-0.68). In summary, this systematic literature review of community-based observational studies estimated a high incidence of ARI and AGE, particularly among young children and older adults. Accurate measurement of these conditions is vital to understand their burden and impact, and to help inform proper design, evaluation and implementation of related interventions.

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MARBURG VIRUS DISEASE OUTBREAK PREPAREDNESS AND RESPONSE IN THE SOUTH REGION OF CAMEROON, FEBRUARY - APRIL 2023

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Since the declaration of the first Marburg Virus Disease (MVD) outbreak in Equatorial Guinea on February 13, 2023, several neighboring countries have been implementing preparedness efforts to prevent MVD cross-border transmission and respond in case of confirmation. We described the experience of the South region, Cameroon, bordering Equatorial Guinea, in MVD preparedness activities. We conducted a descriptive study of preparedness from February to April 2023. We collected data from activity reports and from the regional staff involved in MVD preparedness. Preparedness activities were organized into 7 key pillars: coordination, epidemiological surveillance, specimen transportation and biologic diagnostic, case management and infection prevention and control, risk communication, emergency supply, continuity of essential care and services. The regional Incident Management System (IMS) was activated on February 13, 2023 with the Regional Delegate of Public Health as incident manager. Case definitions were developed and disseminated in the community and health facilities. We defined a suspected case as any resident or visitor in the region with sudden fever (T°≥38°c) or anyone with unexplained bleeding or any unexplained death since January 18, 2023. A total of 120 community health workers were recruited to strengthen rapid detection. At the 6 points of entry, 4272 passengers were screened to detect suspected MVD cases. A total of 159 alerts were investigated with 7 validated as suspected case and samples, collected and transported to Centre Pasteur Cameroon; all came negative. About 62283 persons were sensitized on MVD and prevention methods through radio spots and communications in gathering places. Three isolation and treatment units were established in the districts and protective equipment, disinfection and decontamination provided. A total of 14 biweekly meetings were organized and 11 situation reports developed. No MVD case was confirmed while the Region activated its IMS. The aim was to strengthen MVD preparedness activities. It is important to sustain preparedness efforts, not only for MVD but also for other epidemics.

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INVESTIGATING THE EPIDEMIOLOGY AND RISK FACTORS FOR DENGUE VIRUS AND CHIKUNGUNYA VIRUS INFECTIONS IN KARACHI, PAKISTAN

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Dengue virus (DENV) and chikungunya virus (CHIKV) are spread by *Aedes* species mosquitos that can thrive in pooled fresh water and have recently caused outbreaks across south Asia. Pakistan has endured recent outbreaks of DENV in addition to CHIKV, which can present similarly. Concurrently, Pakistan has also suffered repeated periods of severe flooding with some of the worst floods in history occurring in 2022, when approximately one-third of the country was under water. Given the ongoing climate crisis, this trend is likely to continue and worsen. With this reported re-emergence of infection we hypothesize there is a substantial burden of DENV and CHIKV in Karachi that can be linked to the built environment, human behavior, and other elements like surrounding litter. With shifting of vector proliferation to newer communities it is critical to better understand the epidemiology and transmission of these arboviruses in the region and the links to climate, especially in densely populated cities like Karachi. Through this cross-sectional pilot study of children we evaluated risk factors for dengue and chikungunya infection in the peri-urban setting in Karachi, in relation to the environmental impact, behavior, and demographics associated with infection. We recruited 500 children from two demographic and health survey program sites Karachi, Pakistan. In a single visit, participants are undergoing phlebotomy and survey administration to identify risk factors for exposure to these pathogens. All serum samples will be tested for DENV IgG and CHIKV IgG by enzyme-linked immunosorbent assay (ELISA) to determine seroprevalence. Within the cohort, 100 children had prior serum collected two years prior and will be evaluated for interval DENV/CHIKV seroconversions. This study is ongoing with active data collection and will be completed by mid-2024. Initial preliminary data suggests a high burden of DENV compared to CHIKV with majority of participants testing positive for DENV. With active data collection ongoing, we anticipate to continue to delineate the burden of DENV exposure in this cohort and will link to potential risk factors for the community.

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CLINICAL CHARACTERISTICS ASSOCIATED WITH DENGUE SEROTYPES IN AMAZONAS, PERU

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Dengue represents a major public health challenge worldwide. In Peru, a significant rise in dengue cases has particularly impacted the region of Amazonas, reporting a total of 24 981 cases and 28 deaths until the epidemiological week 7th of 2024, almost double the amount reported in 2023. In this study, we analyzed the clinical and epidemiological characteristics associated with the circulating serotypes in Amazonas by using 591 serum samples from dengue-confirmed patients collected in five provinces between 2021 and 2024. Serotype detection was conducted with a multiplex reverse transcription polymerase chain reaction (RT-PCR) assay. Statistical analysis was performed using R software v.4.3.1. Results revealed that 250 patients were infected by DENV-1 and 341 by DENV-2. According to our results, these serotypes have co-circulated across all affected provinces. For instance, DENV-1 caused the majority of infections in Bagua (13.6%) and Bongará (24.8%), while DENV-2, in Chachapoyas (9.4%), Condorcanqui (18.5%) and Utcubamba (59.8%) ($p < 0.001$). Additionally, dengue infections with warning signs were more frequent in patients with DENV-2 compared to DENV-1 ($p = 0.005$), and severe cases were exclusively reported in DENV-2 infections, highlighting its association with the severe form of the disease. Fever (DENV-1: 93.20% and DENV-2: 91.50%) and headache (DENV-1: 88.80% and DENV-2: 87.68%) were the most prevalent symptoms. Nausea (prevalence rate: 1.28, 95% CI: 1.02-1.62), conjunctivitis (prevalence rate: 1.78, 95% CI: 1.04-3.03), and abdominal pain (prevalence rate: 2.71, 95% CI: 1.35-5.45) showed a significant association with DENV-2. Its enhanced pathogenicity could be due to its faster replication, resulting in a higher viral load that could lead to severe cases. In conclusion, this study emphasizes the widespread circulation of DENV-1 and DENV-2 in Amazonas, highlighting the necessity to understand its transmission dynamics. Furthermore, it underscores the importance of real-time molecular surveillance that could provide an early prognosis of the disease severity.

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SEROPREVALENCE OF CHIKUNGUNYA VIRUS INFECTION IN SURAT THANI PROVINCE, THAILAND

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Chikungunya virus (CHIKV) infection is characterized by an abrupt onset of high fever, profound joint pain, and although low mortality, often lasting morbidity due to joint pain. Although globally distributed, there are multiple gaps in our understanding of CHIKV epidemiology, which pose challenges for the evaluation of CHIKV vaccines and countermeasures. CHIKV epidemics are frequently explosive, emerging unpredictably and waning to low levels after high levels of population immunity achieved. In 2008-2009 a large-scale outbreak of CHIKV occurred in 47 of 76 provinces in Thailand including Surat Thani province in southern Thailand. Despite a second outbreak in 2018-2019, little is known about the distribution of disease in the area. This study examined the seroprevalence and patterns of CHIKV transmission and persistence in communities within Surat Thani stratified by age. Investigators enrolled 1,700 participants aged 2 years and older to collect the blood for CHIKV serological testing in 10 rural, semi-urban and urban communities of Surat Thani province. Seropositivity was determined by CHIKV IgM/IgG (positive ≥40 EIA units) and CHIKV PRNT80 (NT80). The median age of enrollees was 25.0 years (IQR 9.3-39.9) with 62.5% of female gender. The primary occupation was student (49.6%). Overall, the seropositive rate for CHIKV IgM and IgG was 0.12% and 16.06%, respectively. Female had significantly higher levels of CHIKV IgM ($p=0.034$) and IgG ($p=0.007$) than male participants. Seropositive data by age group indicated that subjects between 18-50 years old had significantly higher IgM ($p=0.053$) and IgG ($p<0.0001$) levels than other groups. CHIKV IgG seropositive rate increased in an age dependent manner (from 4.6 years to 88 years old). The CHIKV NT 80 showed good correlation with all positive CHIKV IgG. The 2 urban community sites showed significantly higher seropositivity by CHIKV IgG than rural and semi urban sites ($p=0.048$ and 0.006 respectively) but was not significant based on CHIKV NT80 level. This data identifies CHIKV seroprevalence in the study area and will be crucial for future vaccine and countermeasure studies.

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FACTORS ASSOCIATED WITH DEATH IN PATIENTS ADMITTED WITH EBOLA VIRUS DISEASE TO EBOLA TREATMENT UNITS IN GUINEA, SIERRA LEONE, AND LIBERIA DECEMBER 2013 TO MARCH 2016

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The 2013-2016 West African Ebola Virus Disease (EVD) outbreak resulted in 28,600 cases and 11,300 deaths officially reported to the World Health Organization. Previous studies investigating factors associated with death had conflicting findings, interventions showing promising outcomes had small sample sizes, studies were often single- or dual-country based and most focused on laboratory-confirmed EVD and not on clinically-suspected EVD. We used the Ebola data platform of the Infectious Disease Data Observatory (IDDO) to review individual patient records to assess factors associated with death, and particularly whether there were differences between laboratory-confirmed and clinically-suspected cases. This was a cohort study involving analysis of secondary data in the IDDO database. The study population included all patients classified as having either clinically-suspected or laboratory-confirmed EVD, admitted to 22 Ebola Treatment Units (ETU) in Guinea, Liberia and Sierra Leone between December 2013 and March 2016. Baseline characteristics and treatments were documented along with ETU exit outcomes. Factors associated with death were investigated by multivariable modified Poisson regression. There were 14,163 patients, of whom 6,208 (43.8%) were laboratory-confirmed and 7,955 (56.2%) were clinically-suspected. Outcomes were not recorded in 2,889 (20.4%) patients. Of the 11,274 patients with known outcomes, 4,090 (36.3%) died: 2,956 (43.6%) with laboratory-confirmed EVD and 1,134 (18.8%) with clinically-suspected EVD. The strongest risk factor for death was confirmed disease status. Patients with laboratory-confirmed disease had 2.9 times higher risk of death compared to clinically-suspected patients. Other factors significantly associated with death included a higher risk for patients aged ≥60 years and a lower risk for patients in Sierra Leone. Although laboratory-confirmed patients admitted to ETUs fared worse than clinically-suspected patients, the latter still had a substantial risk of death and more attention needs to be paid to this group in future EVD outbreaks.

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MODELING DENGUE FORCE OF INFECTION AMONG EXPATRIATES LIVING IN THAILAND

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Dengue fever virus (DENV) is a mosquito-borne illness that causes as many as 96 million cases of dengue fever annually. Two dengue vaccines are now licensed for use in several countries, but a vaccine that confers sustained tetravalent protection in DENV-naive individuals remains aspirational. Travelers from non-endemic regions have unique viral exposure histories and associated immunological profiles. The WHO recommends Takeda's Qdenga® vaccine for populations with at least 60% DENV seroprevalence but does not make specific recommendations for travelers. Models of dengue force of infection in children suggest that most people born in dengue endemic areas (DEA) will be DENV seropositive by age 6; whether non-locals share this exposure profile is a critical epidemiological question in the recommendation of novel dengue vaccines for travelers. In this analysis, we use catalytic models of force of infection (FOI) to estimate time to 60% DENV seropositivity for a cross-section of expatriates in Thailand. Demographic and risk history data was collected using a short survey. Blood specimens were tested for neutralizing antibody titers against all four DENV serotypes, Japanese encephalitis, and Zika, using plaque reduction neutralization tests. Our full model adjusted for average daily time outside, years not exposed to DENV, gender, living setting, and four mosquito prevention strategies: repellent, nets, long sleeves, and air conditioning. We estimated an adjusted average FOI of 0.016 (95% CI: 0.004-0.069) per year spent in DEA (approx. 55.7 years to 60% seropositivity). Urban living setting was significantly associated with DENV seropositivity (OR = 2.66; 95% CI: 1.18-6.00) in the adjusted model. These findings suggest that expatriates have a dengue exposure profile unique from locals, which is characterized by a lower force of infection. With the current need to deprioritize vaccination of dengue-naive individuals, this suggests that even long-term travelers will require separate vaccine recommendations.

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TRENDS IN MORTALITY CAUSED BY VIRAL HEPATITIS IN THE UNITED STATES POPULATION: A RETROSPECTIVE CROSS-SECTIONAL STUDY USING THE CDC WONDER DATABASE.

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In this retrospective cross-sectional study, spanning from 1999 to 2023, we examined mortality trends using national mortality datasets among individuals infected with hepatitis virus. Our aim was to analyze these trends in mortality among US residents by demographic characteristics including age, gender, race/ethnicity, and geographic characteristics like urbanization and census region. The national mortality data from the multiple causes of death files in the CDC WONDER Database were queried by applying the ICD-10 codes as B15-B19 for viral hepatitis to identify deaths among the US population from 1999 to 2023. Trends in age-adjusted mortality rate (AAMR) were assessed for age groups, gender, race/ethnicity, urbanization, and census region using state-level data. Results were expressed as annual percentage changes (APC), average annual percentage changes (AAPC), and 95% confidence intervals (CI). The data was analyzed on statistical software i.e., the Joinpoint regression by National Institutes of Health (NIH version 5.0.2). The county-level data was analyzed according to the National Center for Health Statistics [NCHS] urbanization classification scheme 2013. The crude mortality rate for viral hepatitis from 1999-2023 was found to be 4.4 per 100,000 US population and AAMR was 3.4 per 100,000 US population. Mortality rates for viral hepatitis were found to be highest for the male gender, age group 55-74 years, American Indians or Alaskan Natives, Census Region West, and metropolitan suburban areas (although rural areas showed the highest upgoing trends with AAPC: +2.64). Geographically, states in the top 90th percentile for viral hepatitis-associated mortality included the District of Columbia, Oklahoma, Oregon, California, New Mexico, and Washington. These findings provide valuable insights into age-adjusted mortality patterns among the United States population with these diseases. Mortality rates among the US population with viral hepatitis were noted to slightly decrease overall from 1999 to 2023 (AAPC -0.61, p=0.002), and certain subgroups with specific demographic and geographic characteristics had high AAMR.

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DENGUE SEROPREVALENCE AND FORCE OF INFECTION IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Introduction: There is limited knowledge on dengue transmission in the Democratic Republic of Congo (DRC). However, recent publications highlight an increasing dengue prevalence among individuals presenting with febrile symptoms in Kinshasa, the capital of DRC. The extent of dengue circulation in the country is unknown, which poses questions around the burden of dengue infection and the potential impact of new interventions. The objective of our analysis was to assess the age-stratified dengue seroprevalence and estimate the force of infection (FOI, per-capita risk of dengue infection for a susceptible subject) in Kinshasa and Matadi. Methods: By leveraging samples collected from individuals aged 0 to 94 years in a SARS-CoV-2 serosurvey, we assessed the age-stratified dengue seroprevalence using a combination of two Enzyme-Linked Immunosorbent Assay (ELISA) IgG antibody tests, respectively a purified dengue particles test (ELISA-1) and a recombinant non-structural protein 1 (NS1) (ELISA-2) assay and a serotype-specific Plaque Reduction Neutralization Test (PRNT) for all 4 dengue serotypes. We employed a Bayesian framework to estimate the FOI for each location and reconstruct the results obtained across each testResults: Overall, 3580 plasma samples were tested by IgG ELISA-1 and a subset of 202 samples was also tested by IgG ELISA-2 of which 70 were also tested by PRNT. Our findings reveal endemic dengue circulation in DRC, with an average FOI of 2.9% (95% CrI: 2.2-3.9) in Kinshasa and 1.4% (95% CrI: 0.9-2.0) in Matadi and an overall population seroprevalence of 41% (95% CrI: 34-48) in Kinshasa and 23% (95% CrI: 17, 32) in Matadi respectively. Conclusion: These results confirm endemic dengue transmission in different regions of DRC and highlight the dengue transmission differences between the two cities. These findings underscore the importance of establishing dengue surveillance in the country, to monitor prevalence and changes in transmission in a changing climate.
1

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A MULTICENTER STUDY TO ASSESS THE EFFECTIVENESS OF AN INACTIVATED COVID-19 VACCINE AGAINST HOSPITALIZED COVID-19 IN THE PHILIPPINES

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There is limited information on the protection conferred by Coronavac (Sinovac, China), an inactivated COVID-19. We conducted a multi-center, hospital-based test-negative case control study to determine the vaccine effectiveness of a complete CoronaVac regimen with or without a homologous or heterelogous booster dose against hospitalized and critical COVID-19.

Between 9 November 2022 and November 2023, we enrolled adult patients experiencing acute respiratory illness (ARI) admitted to three government referral hospitals. We collected clinical and socio-demographic data, vaccination histories, and oro/nasopharyngeal swabs for SARS-CoV-2 RT-PCR testing from eligible patients who consented to participate. Patients testing positive in at least one SARS-CoV-2 RT-PCR test were classified as cases while those testing negative served as controls. Critical COVID-19 was defined as having either respiratory failure, acute respiratory distress syndrome, sepsis/shock or multi-organ failure. We enrolled 2,365 participants, and 165 (7.0%) were SARS-CoV-2 positive. More than a year after the last vaccine dose, unmatched analysis showed that full vaccination of CoronaVac did not protect against hospitalized and critical COVID-19 (VE:0.69%,CI: -23.7%-20.3%, p=0.9511 and VE:5.4%, CI:17.8%-24.0%, p=0.6201 respectively), but conferred 31.3% (CI: 9.5 - 47.9, p=0.0077) protection against death. The protection against death increased to 45.8%(CI:18.6%-63.8%, p=0.0031) with a booster dose. Cases were significantly older than the controls (mean age±SD: 58.12±20.15 vs. 53.41±17.60, p=0.001). An age-matched analysis showed that a full regimen of CoronaVac provided 61.3% (CI:5.3% - 84.2%,p=0.0376) protection against critical COVID-19, and 27.1% (CI:-25.3%-57.6%, p=0.2528) against death, which increased significantly to 91.2% (CI: 30.7% - 98.9%, p=0.0210) and 60.1% (CI:16.4%-81.0%, p=0.0150) with a booster dose, respectively. Our findings show that a primary series of inactivated COVID-19 vaccination provided protection against critical outcomes over time, which was enhanced by booster vaccination.

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MOLECULAR EPIDEMIOLOGY IMMUNOLOGICAL RESPONSES TO SARS-COV-2 OTHER RESPIRATORY VIRUSES IN SELECTED URBAN RURAL AREAS OF GHANA

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Ghana implemented non-pharmaceutical interventions and vaccination campaigns to mitigate the impact of COVID-19. However, the effectiveness of these interventions has not been fully evaluated. Understanding the prevailing levels of exposure and immunity in different sociodemographic settings offers an important overview of the epidemiology of respiratory viruses in these populations. This study seeks to determine the prevalence of SARS-CoV-2 and other respiratory viruses (RVs) in selected areas in Ghana, using Kumasi Metropolis as a case study. Nasopharyngeal swabs and blood (serum) samples of 109 participants above 10 years in Kumasi were collected with consent. Their socio-demographic data, clinical symptoms, and vaccination status were taken with structured questionnaires. Viral RNA was extracted and tested with multiplex real-time RT-PCR detecting respiratory viruses including SARS-CoV-2, Influenza A, Human Rhinovirus (HRV), Adenovirus, Picornaviruses, and common cold coronaviruses. Samples with Ct ≤ 30 will be sequenced and analysed. Results from 109 participants from Kumasi who were aged 10-55 years, mostly females (62.4%) showed an RNA positivity rate of 1.0% for both SARS-CoV-2 (n =1) and HRV (n = 1). Both positive cases were females aged 35 and 37 with headache and fever as common symptoms, traders, not living alone, married and both cases were detected in the Manhyia study site. None of these characteristics was found to have a statistically significant association to respiratory virus positivity as determined by a Fisher's exact test (P < 0.05). We observed a low circulation of RVs in Kumasi. The collected serum samples will be tested for SARS-CoV-2 antibodies, their longevity and new seroconversions by ELISA. Further sampling will be done in urban and rural areas represented by Tamale, Buoyem, Forikrom, and Obuasi to estimate the prevalence of SARS-CoV-2 and other respiratory viruses circulating in Ghana. The mean IgG levels will be analyzed using R to determine the difference in seroprevalence for rural and urban areas. Individuals with a positive ELISA result will be sampled again after one year.

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BEYOND RAINFALL: ENVIRONMENTAL DRIVERS OF HISTORIC RIFT VALLEY FEVER OUTBREAKS IN KENYA

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Rift Valley fever (RVF) is a viral vector-borne zoonosis of the *Phlebovirus* genus, causing widespread abortion in livestock with potential to cause severe disease in humans. RVF was first identified in Kenya in 1931 and has since led to numerous outbreaks that have resulted in loss of life and livelihoods. Several environmental variables have been linked to cases in some areas, but these efforts have not considered ecologically relevant spatial heterogeneity on a national scale. Here, we collated a database of historic cases in Kenya by expanding methods described in previous systematic reviews. To account for underreporting, we transformed RVF as a binary outcome variable for a specific year and geographic regions divided according to existing Agro-Ecological Zones (AEZ) in all models. We selected scaled temperature, precipitation, potential evapotranspiration, Palmers Drought Severity Index (PDSI) and soil moisture as environmental predictors. Linear relationships were tested using Linear Mixed Models (LMM), with AEZ and species as random effects. Non-linear relationships were tested using General Additive Models (GAM), fit to datasets subset by AEZ. The best fit LMM included precipitation and PDSI which showed precipitation to have a strong positive effect and PDSI a slightly negative effect on RVF occurrence in Kenya, with AEZ significant as a random effect. Including AEZ as a random effect produced the top 17 LMM models and the non-linear relationships (in the GAMs) varied in magnitude and shape depending on AEZ, suggesting the relationships between the environment and RVF are distinct among regions. These findings support the hypothesis that heavy rainfall after drought, which decreases soil permeability, is an environmental risk factor for RVF transmission, and this effect is more significant in some AEZs potentially due to varying soil types. The results of this study will contribute to ongoing national efforts to map the risk of RVF in Kenya. We conclude the drivers of historic RVF outbreaks extend beyond solely rainfall and further climate extremes, such as drought and flooding, may lead to more frequent outbreaks.

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CAN'T START A FIRE WITHOUT A SPARK: HIGHLY VARIABLE VIRUS IMPORTATION RATES UNDERLIE THE UNPREDICTABLE TIMING OF CHIKUNGUNYA OUTBREAKS

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The epidemiology of chikungunya virus (CHIKV) is notoriously sporadic. Outbreaks of this mosquito-borne pathogen are often intense and short-lived and, in many populations, are not repeated for years, or even decades. This unpredictability presents a major challenge to public health preparedness and intervention trial planning. Epidemiological theory suggests three primary drivers of the frequency of outbreaks of a pathogen such as CHIKV. Two of those drivers, the basic reproduction number (R_0) and population immunity, are commonly estimated. The third—the importation rate of the pathogen itself—remains elusive and poorly quantified, although for CHIKV this importation is believed to occur mainly through the movement of infected humans. To address this gap, we performed a model-based analysis of age-stratified serological data that yielded joint estimates of R_0, population immunity, and the importation rate of CHIKV infections for each of 35 populations affected by CHIKV between 1950 and 2020. Our approach leverages the fact that some imported infections may not have resulted in chikungunya outbreaks due to population immunity or stochastic fade-out. Estimated annual CHIKV importation rates spanned orders of magnitude across the populations considered, with posterior means ranging from one imported infection per 4.5 to 80 million residents. Combining these values with R_0, immunity, and growth rate estimates for each population results in highly variable expected inter-epidemic periods for chikungunya, ranging from as few as eight years between outbreaks or as many as 100. This variability highlights the significance of the CHIKV importation rate as a driver of chikungunya's sporadic epidemiology. More broadly, these results demonstrate the value of better understanding pathogen importation rates for enhancing public health preparedness.

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RISK FACTORS FOR LASSA FEVER VIRUS INFECTION IN A POPULATION-BASED COHORT STUDY IN SIERRA LEONE

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An improved understanding of Lassa fever virus (LASV) epidemiology is needed to inform efficacy trials for LF vaccines. Investigators at Kenema Government Hospital (KGH) in Sierra Leone, Tulane University, and IAVI implemented a prospective study (X100) to characterize risk factors for incident LASV exposure. Participant data and blood was collected using finger sticks and dried blood spots (DBS) at two time points (baseline and 18-24 months later). DBS were tested by pan-LASV-NP IgG ELISA (Zalgen Labs, MD, USA). Re-exposures were defined as seropositive at baseline, with a ≥4x antibody titre at follow up. Independent predictors of incident exposure were characterized with a mixed effects model to control for cases clustering within households. Between April 2021 and May 2022, 8,237 residents aged ≥2 years were enrolled; baseline and follow-up data were available for analysis for 6,447 (78.3%) participants, our analysis set for this abstract. Of the 6,447 participants, 655 (10.2%) had evidence of incident exposure to LASV. While controlling for other covariates, we found that residing in Kenema district, a traditionally "higher risk" geographic area, was associated with incidence (incidence rate ratio IRR 1.73, 95% CI: 1.41-2.11) as was being seronegative at baseline (IRR 2.26, 95% CI: 1.82-2.78). Children ages 2-10 were less likely to become LASV positive compared to other ages (IRR 0.72, 95% CI: 0.59-0.88). Efforts to store food securely from rodents, perhaps as a proxy for known rodent infestations, was associated with incidence (IRR 1.74, 95% CI: 1.26-2.39) as was having cleared all bush within 5 meters of the dwelling, suggesting rodents moved into the house rather than into foliage that was >5 meters from a home (IRR: 1.55, 95% CI: 1.27-1.89). We observed multiple individual and household characteristics associated with high rates of LASV seroincidence in this rural, population-based cohort of Sierra Leonians at risk of LASV infection. These data improve our understanding of LASV epidemiology and will inform clinical trial design, recruitment, and conduct.

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MOLECULAR DIAGNOSIS AND CLINICAL CHARACTERISTICS OF CHIKUNGUNYA VIRUS INFECTIONS IN THE PERUVIAN JUNGLE, 2020-2023

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Chikungunya virus (CHIKV) infections cause acute febrile illness associated with unspecific symptoms that can progress to joint pain and arthritis over time. In 2015, Peru reported its first autochthonous case, followed by an outbreak nationwide. Peruvian Andean and jungle regions report prevalence rates ranging between 2.4% and 9.4%, sometimes surpassing dengue as the primary cause of AFI. In high-risk areas, it is important to differentiate CHIKV infection from other arboviruses due to its concurrent circulation. To evaluate the prevalence and clinical manifestations of CHIKV in Peruvian patients, we conducted a study in the Peruvian jungle. AFI patients were enrolled if they had a 38°C axillary temperature and a source of infection that was unknown. Infection signs and symptoms were recorded using a standardized format after they were evaluated. Blood samples were collected for the detection of CHIKV infection by qRT-PCR and/or IgM detection using ELISA assays. During the study period (2020 through 2023), a total of 4413 patients with AFI were enrolled. 256 (5.80%) CHIKV cases were identified by qRT-PCR, and 472 (10.69%) were identified by IgM detection. Most infected patients were adults aged between 18-39 years (52.73% for qRT-PCR positive and 49.15% for IgM positive), with females being the predominant affected gender (54.69% for qRT-PCR positive and 62.92% for IgM positive). The most common clinical symptoms in CHIKV qRT-PCR and IgM positive patients were headaches (87.85% and 90.16%), myalgias (77.33% and 74.14%), and arthralgias (74.90% and 78.95%). The highest number of positive cases occurred in July 2021 (10.45%). In conclusion, our study underscores the substantial burden of Chikungunya virus (CHIKV) in the Peruvian jungle, revealing notable prevalence rates among patients with acute febrile illness. In regions where CHIKV co-circulates with other arboviruses, robust surveillance and diagnostic efforts are particularly important. It is crucial to understand the epidemiology and clinical presentation of CHIKV infection in order to develop effective disease management and control strategies.

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UNVEILING THE PATH TO POLIO ERADICATION: INSIGHTS FROM CONSECUTIVE SEROPREVALENCE SURVEYS AMONG PAKISTANI CHILDREN

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After the cessation of the trivalent oral poliovirus vaccine (tOPV), Pakistan has maintained immunity to type 2 poliovirus by administering inactivated polio vaccine (IPV) in routine immunization alongside monovalent OPV

type 2 (mOPV2) and IPV in supplementary immunization activities (SIAs). This study assesses the poliovirus type 2 immunity change after tOPV cessation and due to SIAs with mOPV2 and IPV among children aged 6-11 months. Three cross-sectional sequential serological surveys were conducted in 12 polio high-risk areas of Pakistan. Twenty-five clusters from each geographical stratum were selected using probability proportional to size. Seroprevalence of type 2 poliovirus was 49%, with significant variation observed among surveyed areas; <30% in Pishin, >80% in Killa Abdullah, Mardan & Swabi, and Rawalpindi. SIAs with IPV improved immunity from 38% to 57% in Karachi and 60% to 88% in Khyber. SIAs with IPV following mOPV2 improved immunity from 62% to 65% in Killa Abdullah, and combined mOPV2 and IPV SIAs in Pishin improved immunity from 28% to 89%. Results also reflected that immunity rates for serotypes 1 and 3 were consistently above 90% during all three phases and across all geographical areas. The study findings highlight the importance of implementing effective vaccination strategies to prevent the re-emergence of poliovirus. Moreover, the results provide crucial information for policymakers working towards achieving global polio eradication.

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ADDRESSING CHALLENGES IN WASTEWATER EPIDEMIOLOGICAL SURVEILLANCE IN TROPICAL REGIONS: COSTA RICAN EXPERIENCE

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The increasing recognition of wastewater-based epidemiology (WBE) as an invaluable tool for public health surveillance has prompted the initiation of a comprehensive program in Costa Rica. This study focuses on a pivotal wastewater treatment plant (WWTP) in the Great Metropolitan Area, serving approximately 10% of the Costa Rican population. Commencing in June 2023 and concluding a year later, the program systematically monitors the presence of various viral pathogens, including hepatitis A, enterovirus, rotavirus A, norovirus G1 and G2, Influenza A, Monkeypox, and SARS-CoV-2. This monitoring involves a concentration step followed by RNA extraction, one-step reverse transcription, and quantitative polymerase chain reaction (RT-qPCR) amplification with TaqMan probes. Despite observing an increasing viral pathogen load in wastewater and reported cases, particularly during the rainiest months of October and November, we noticed a reduction in the pathogen viral load. This reduction was confirmed by values obtained for our internal controls: PMMoV and somatic coliphages, suggesting external factors such as rainfall that can affect detection efficiency. Nevertheless, the program successfully identified the presence of hepatitis A in wastewater, coinciding with a significant outbreak of Hepatitis A in the Great Metropolitan Area. Additionally, Influenza and SARS-CoV-2 were concurrently detected with a noticeable increase in reported cases of respiratory diseases. This approach enhances our understanding of the dynamics of infectious diseases and strengthens the overall public health surveillance system in Costa Rica.

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HIGH CIRCULATION OF AVIAN INFLUENZA H9N2 SUBTYPE IN LIVE BIRD MARKETS: A NEW EMERGING THREAT IN SENEGAL

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Avian influenza virus (AIV) of the H9N2 subtype has gained increasing attention in recent years due to its widespread circulation in poultry populations and sporadic zoonotic transmission to humans. In Senegal, only one human case of H9N2 infection has been reported so far, despite ongoing influenza surveillance since 1996. However, until now, this surveillance was only focused on humans and the country has never experienced documented H9N2 infection in poultry even though unusual poultry outbreaks associated with mortalities are occasionally reported. So here, we present results of an active influenza surveillance effort focusing on live-bird markets (LBM). The Senegalese National Influenza Center initiated in December 2023 an active influenza surveillance in two LBM in Dakar. Each week, fresh feces, water troughs, carcass washing water and cloacal swabs from birds are collected in each market. Samples are examined by RT-PCR for the presence of, among others, AIV H9, H7 and H5 subtypes, which are then characterized further by next-generation sequencing. In total, 205 samples have been collected so far. Overall, AIVs were detected in 100 of the 205 poultry samples analyzed (48.8%). AIVs were most frequently detected in birds drinking water (32%), carcass washing water (28%), fecal samples (28%), and less frequently in cloacal swabs (12%). All influenza A-positive isolates were H9N2 subtypes. Genome sequences were obtained for 22 isolates and the phylogenetic analysis revealed that Senegalese H9N2 viruses belong to the G1-like lineage and are closely related to H9N2 viruses identified in Burkina Faso, Niger and Tunisia. Furthermore, H9N2 viruses from Senegalese poultry clustered with the H9N2 human case detected through the national influenza surveillance, and possessed multiple molecular markers associated with an increased potential for zoonotic transmission and virulence. Results of this study contribute to our understanding of the epidemiology and genetic characteristics of H9N2 in Senegal and highlight the need to strengthen surveillance and control of AIV in live poultry markets to mitigate public health threats.

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THE PHAGE FACTOR IN ANTIBIOTIC RESISTANCE SPREAD IN THE HOSPITAL AND URBAN SEWAGE SYSTEMS IN GREATER ACCRA REGION, GHANA

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Phages, which are recognized for their endurance and resistance, play an important role in spreading antibiotic resistance genes (ARGs) throughout the environment. This study aimed to assess the prevalence of ARGs in viral fractions of hospital wastewater and urban wastewater sampled from various sites in Greater Accra, Ghana. Whole genome sequencing was performed on DNA isolated from the samples, which was then assembled using the MetaViral SPADES platform. Subsequently, ABRicate was utilized to identify ARGs from the viral contigs. The findings revealed a wide array of ARG classes such as cephalosporin, macrolide, Carbapenem, aminoglycoside, and tetracycline antibiotics prevalence across hospitals, with notable prevalence of the *bla* genes, *mcr-1* genes, and *mecA* genes. Remarkably, ARGs detected in hospital wastewater were concomitantly detected in raw urban wastewater, indicating potential contributions from multiple sources. The study emphasizes the significance of exploring the carriage of ARG genes in the viral fraction and the role of hospital

wastewater in ARG dissemination. These findings offer valuable insights into the dynamics of antibiotic resistance in wastewater systems, thereby guiding strategies to mitigate its spread and impact on public health.

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COMET: A DATABASE TO UNTANGLE VIRAL, MOSQUITO, AND ABIOTIC DRIVERS OF VECTOR COMPETENCE

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Many recent emerging pathogens are arthropod-borne (arbo-) viruses, with over one-third of the world's population at risk for infection. Responding to "the next Zika" and forecasting future risks of vector-borne disease requires laboratory-based studies of mosquito infection. These experiments are often the best way to measure vector competence, and are critical to understanding outbreak risk. While hundreds of these studies have been conducted in the last few decades, their data is rarely shared or readily available. Further, there are numerous challenges to interpreting and comparing different studies. These include inconsistent terminology, insufficient experimental/methodological detail, and differences in reported outcomes. In collaboration with arbovirology labs at several institutions, we therefore compiled, cleaned, and standardized data on the infection, dissemination and transmission of mosquito-borne viruses, from published experimental studies into a database called COMET (vector competence experimental testing). We have thus far compiled over 100,000 measurements of mosquito vector competence for human-infective viruses from over 100 published studies. Using these data we will perform meta-analyses and modeling to decompose and predict extrinsic (temperature, humidity, other unaccounted-for experimental variability) and intrinsic (mosquito-omics, viral-omics) drivers of vector competence. In addition to its role in supporting research on vector-virus interactions and arboviral evolution, we anticipate that COMET will be an invaluable resource for public health agencies interested in contextualizing risk from local vectors during future disease outbreaks.

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CO-OCCURRENCE OF VIRAL PATHOGENS IN CHILDREN: INVESTIGATING RESPIRATORY AND GASTROINTESTINAL SYMPTOMS IN SÃO PAULO, BRAZIL, 2021

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Pneumonia and diarrhea are leading causes of death in children under 5 worldwide. This study investigates viral agents causing respiratory illness in ≤ 3 years old patients with diarrhea in São Paulo, Brazil, during spring 2021. Twenty paired samples (oropharyngeal swab and feces) were screened for viruses including HBoV, HAdV, RVA, EV, PeV-A, NoV, SARS-CoV-2, Influenza A/B, RSV and HAstV. Positive samples for HAdV, HBoV, EV, NoV and PeV-A underwent sequencing and phylogenetic analysis. HBoV and NoV were detected in 75% (15/20) of cases, with co-infections in 65% (13/20), suggesting their involvement in respiratory illness with gastrointestinal symptoms in children. HAdV, EV, PeV-A and RSV were each found in two cases (10%; 2/20), with Flu A identified in one case (5%; 1/20). A substantial number of co-infections involving respiratory and enteric viruses were observed (75%; 15/20), notably HBoV+NoV (40%; 8/20) and NoV+PeV-A (5%; 1/20). Triple infections occurred in 7 cases: HBoV+NoV+RSV (10%; 2/20), HBoV+NoV+HAdV (10%; 2/20), HBoV+NoV+EV (5%; 1/20), and NoV+EV+PeV-A (5%; 1/20). All samples tested negative for RVA, HAstV and SARS-CoV-2. Among the NoV samples, GII.4 Sydney[P16] predominated (69.2%; 9/13), followed by GII.2[P16] (27.1%; 3/13) and one GII.4 Sydney[P31] strain (7.7%; 1/13). HBoV was identified as HBoV-1, EV as Coxsackievirus A6 (CVA6), HAdV as type 6 (HAdV-C6) and PeV-A as PeV-A1. Phylogenetic analysis revealed no evidence of a community outbreak, with HBoV-1 strains forming distinct clusters and NoV strains showing diverse genotypes, indicating independent origins. Similarly, molecular analysis of HAdV-C6, CVA6 and PeV-A1 strains suggested distinct genetic sources. Our findings underscore the co-occurrence of respiratory and enteric diseases, an often-neglected epidemiological scenario, and despite the small sample size, highlight local viral diversity and significant exposure to enteric viruses. These results underscore the complexity of conducting differential diagnoses when symptoms overlap and emphasize the crucial role of syndromic surveillance.

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CO-CIRCULATION OF TWO LINEAGES OF OROPOUCHE VIRUS IN THE AMAZON BASIN, COLOMBIA, 2024

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Oropouche virus (OROV) is a reemerging vector-borne orthobunyavirus with a three-segmented genome that causes acute fever and has spread silently across Latin America since its identification in 1955 in Trinidad and Tobago. In February 2024, the PAHO/WHO began to issue epidemiological alerts because of the dramatic increase in OROV cases in the Amazonian states of Brazil that have more recently extended to bordering Peru and Bolivia. A pre-publication showed that the OROV strain causing the large-scale outbreak in Brazil is a new viral lineage with reassorted genome segments (OROV BR-2009-2018). We have previously established surveillance programs for acute fever illness in several clinics across Colombia and collect blood samples to screen for arboviruses and other pathogens at our One Health Center located in Medellin, Colombia. This center is a consortium established between the Global Health Institute at the University of Wisconsin-Madison and the National University of Colombia-Medellin and is also a member of the Abbott Pandemic Defense Coalition (APDC). Our newly designed OROV RT-qPCR assay and NGS sequencing enabled the confirmation of OROV infection in 22 febrile individuals from the Leticia municipality, Colombian Amazonas department, from January to March 2024. Nine of these individuals were infected with the new reassortant, BR-2009-2018 OROV, while 13 cases were infected with PE-CO-EC/2008-2021 OROV identified previously by our group in Colombia (Ciuoderis et al, Emerg Microbes Infect. 2022). No medical complications or hospitalizations have been reported in the OROV-infected patients during this outbreak. The co-circulation of different OROV strains in this Colombian arboviral hotspot raises concerns about new reassortments and the emergence of new lineages with more severe clinical phenotypes and enhanced vector competence. This ongoing investigation highlights the complex arbovirus dynamics in South America and is a demonstration of the challenges of preventing and controlling the reemergence of arboviruses in the Americas.

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SEROPREVALENCE OF DENGUE VIRUS IN THE TAMPA BAY REGION OF FLORIDA AMONG HOSPITALIZED PATIENTS WITH RESPIRATORY SYMPTOMS IN 2020 AND 2021

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Dengue Virus (DENV) is a flavivirus vectored by Aedes mosquitoes that is suspected to cause over 400 million human infections and 40,000

estimated deaths annually. Since 2010, the United States has seen over 45,000 reported cases, 34,000 of which were locally acquired. Florida has the highest number of DENV cases in the nation with 3,182 reported infections as of 2023. The state has seen multiple DENV outbreaks due to imported cases from the Caribbean and being home to two major competent vectors, *Aedes aegypti* and *Aedes albopictus.* All four serotypes of DENV have been found within the state, although serotype 4 has only been found in mosquitoes pools. The Tampa Bay region is particularly at risk due to having a large tourism industry and immigrant population. Hillsborough county, where Tampa Bay resides, does not have passive surveillance measures for DENV and the main form of mosquito management is through nontargeted air and ground adulticide spraying. To test prevalence of DENV in the Tampa Bay region of Florida, our study utilized enzyme linked immunosorbent assays (ELISAs) for IgG antibodies to test 334 serum and plasma samples collected at Tampa General Hospital during 2020 and 2021. As we tested for IgG antibodies to indicate a previous exposure, current respiratory status of patients would not impact DENV status. We found that over forty percent of samples were positive for serotypes 1/3 and over sixty percent of samples were positive for serotypes 2/4 by ELISA. DENV serotypes were separated into two groups, 1/3 and 2/4, for ELISAs as they are serologically similar to one another. Plaque reduction neutralization tests (PRNTs) were performed to confirm positive results with each serotype being tested individually. While we cannot determine if the cases in this study are locally or travel acquired, we can say that seroprevalence of DENV is higher than reportable cases suggest.

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EFFECT OF PRIOR DENGUE INFECTION AND SINGLE-DOSE DENGUE VACCINATION ON THE RISK OF SUBSEQUENT VIROLOGICALLY CONFIRMED DENGUE: A FIVE-YEAR PROSPECTIVE COHORT STUDY IN CEBU, PHILIPPINES

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In 2015, a three-dose dengue vaccine (CYD-TDV,Dengvaxia) was licensed for those 9 years and older in dengue-endemic areas. The World Health Organization (WHO) recommended that CYD-TDV would be used in settings with at least 70% seroprevalence. The Philippines Department of Health (DOH) implemented a three-dose dengue vaccination program in high dengue burden regions targeting children aged 9 to 14 years old. In June 2017, the program was expanded to Cebu province. A follow-up analysis of the CYD-TDV Phase 3 trials showed that vaccination conferred protection among dengue-seropositive but increased risk for severe dengue among dengue-seronegative participants, the dengue vaccination program was halted with children in Cebu offered only one dose. We conducted a prospective community-based cohort study in Cebu to evaluate the effect of baseline dengue serostatus and a single dose of CYD-TDV on the subsequent risk of virologically-confirmed dengue (VCD). We enrolled 2,996 healthy children 9 to 14 years of age in May 2017. Baseline sera were collected and batch tested by indirect IgG ELISA and focus reduction neutralization test (FRNT). Out of 2,996 sera, 320 (10.7%) was dengue naïve, 292 (9.7%) had one previous dengue infection (monotypic profile) and 2,384 (79.6%) had >2 previous dengue infections (multitypic profile). From June to August 2017, 1,790/2,996 (59.7%) children received a single dose of CYD-TDV. Active surveillance for an acute febrile illness (AFI) was conducted from November 2017 to October 2023. Those who developed AFI were identified, data were collected, and blood drawn for confirmation of dengue by RT-PCR. Cumulative incidence for VCD was 1.02 cases per 100 person-years and the incidence varied by baseline DENV serostatus. Crude and adjusted analyses showed that a single dose of CYD-TDV did not confer protection against VCD in children who were dengue naïve or had a monotypic profile at baseline. One dose conferred significant protection against hospitalized VCD among participants who had a multitypic profile at baseline: at first 3 years, 70% (95% CI 20-88; p=0.017), 5-year follow-up period, 67% (95% CI 19-87; p=0.016).

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MORPHOLOGICAL AND MOLECULAR IDENTIFICATION OF *AEDES* MOSQUITO POTENTIAL VECTOR OF ARBOVIRUS IN KATI FALADIE, MALI

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In Mali *Aedes* vectors and arbovirus coexist, several patients have been seropositive for these five arboviruses. However, given the *Aedes* vector species diversity across various ecoclimatic settings, which *Aedes* species is specific vector for which arbovirus remains to be determined. Precise identification of Aedes mosquitoes will help to differentiate between vectors and non-vectors. In addition, understanding the repertoire of *Aedes* mosquito species that are responsible for sustaining any specific arbovirus transmission at any specific ecoclimatic setting would target vectors fighting. We hypothesize that the new distribution of *Aedes* mosquitoes could contribute to the emergence of arboviruses in Mali. This project aims to identify the *Aedes* mosquito potential vector of arbovirus in Kati-Faladie rural aera from Mali using molecular tool. This study carried out in Faladie, a rural village in Kati, 80 kilometers from Bamako in Mali. Mosquitoes were captured by aspiration and biogents sentinel in Faladie. Collected specimens were identified using morphological dichotomies keys of Culicidae, PCR and sequencing. Circulating arbovirus was characterized from captured mosquitoes by RT-PCR for non-structural protein 5 NS5 gene and sequencing. 287 *Aedes* mosquitoes collected were morphologically identified as: *Aedes aegypti* 82,22% (N=287), *Aedes aedimorphus* 1,74% (N=287), *Aedes mucidus* 0,35% (N=287), *Aedes Aedimorphus hirsutus* 0,35% (N=287) and *Aedes* spp. 15,33% (N=287). With sequencing *Aedes* mosquitoes were identified as: *Aedes aegypti 73,87% (*N=287*), Aedes Aedimorphus hirsutus* 0,35% *(*N=287*), Aedes furcifer* 0,70% *(*N=287*), Aedes albopictus* 0,70% *(*N=287*), Aedes vitattus* 0,70% *(*N=287*) and Aedes spp 23,70% (*N=287*).* 56.44% (n=162) of our samples tested by RT-PCR were positive for arbovirus and 43.55% (n=125) negative. Sequencing of the positive arbovirus samples (n=162) and *Aedes spp* (68). This study will shed light on the *Aedes* species that transmits arboviruses in Mali.

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PRELIMINARY EVIDENCE OF SILENT CIRCULATION OF *ORTHOFLAVIVIRUS NILENSE* IN EQUIDAE POPULATION IN PIAUI STATE, NORTHEAST BRAZIL

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The West Nile virus (WNV; *Orthoflavivirus nilense*) is an arbovirus that belongs to the *Flaviviridae* family, *Orthoflavivirus* genus. Considered an emerging pathogen in South America, WNV can cause encephalitis in animals and humans. Until recently, Piaui state was the only Brazilian state reporting West Nile fever in humans and one of the few states reporting WNV infections in animals that could be used as sentinel animals. Aiming at detection of WNV circulation in animals of the Equidae family from Piaui state, a cross-sectional epidemiological study was conducted from 2019 to 2021, in eight municipalities with confirmed cases of West Nile fever in humans. Three-hundred seventy-seven whole blood samples collected

in the field were centrifuged and frozen in liquid nitrogen until tested. Epidemiological data collection was obtained by interviewing animal owners using a personalized questionnaire. Antibodies to several arboviruses were detected by the Hemagglutination Inhibition test in 75.86% (286/377) of the samples and 63.92% (241/377) were specific for the *Orthoflavivirus* genus. Until now, Plaque Reduction Neutralization Test (PRNT) was performed in 30 samples and, in a preliminary analysis, the presence of neutralizing antibodies to WNV ($PRNT_{50}$) was detected in 66.66% (20/30) of the samples. These preliminary results indicate that, in this northeastern Brazilian state, WNV has infected animals of the Equidae family even though there have been no reports of epizootic events by the public health officials of this state, despite the need for a compulsory reporting of any epizootic event to the Ministry of Health. To our knowledge, this is the first report of detection of neutralizing antibodies to WNV in the Equidae population in Brazil, and these results evidenced a high seroprevalence of neutralizing antibodies to WNV in animals that could serve as sentinel animals to an early detection of a WNV outbreak. Although only a small fraction of the samples was tested, these preliminary results detected the silent circulation of WNV leading to an underestimated prevalence and underreporting of a virus with zoonotic and encephalitogenic potential.

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CHARACTERIZATION OF KOUTANGO VIRUS FROM PHLEBOTOMINE SANDFLIES COLLECTED IN ISIOLO AND BARINGO COUNTIES OF KENYA.

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Koutango virus (KOUTV), a lineage of West Nile Virus, is highly neuroinvasive in animal models and has been associated with human disease. Recent studies in parts of Africa, including Kenya, have identified KOUTV among phlebotomine sandfly populations. However, our understanding of this virus remains limited. The present study aimed to characterize KOUTV from Kenyan phlebotomine sandflies. Sandflies were sampled from selected sites in different geographical regions of Kenya between 2021 and 2023 using CDC light traps. Female sandflies were taxonomically identified and pooled based on genus. Virus isolation was performed in Vero cells. The viral genome was determined using next-generation sequencing on illumina Iseq 100. Phylogenetic and molecular clock analyses were done to decipher the virus's evolutionary relationships. Comparative analyses of amino acid sequences were performed to determine variations. Protein modeling in Pymol was conducted to elucidate variations in key protein regions. Evolutionary pressure analysis was used to investigate both point and episodic selection pressure. In vitro cell growth experiments were used for virus growth kinetics in vero-E6 and C6/36 cells. We report two KOUTV isolates one each from Baringo and Isiolo counties in Kenya. The current KOUTV isolates clustered in a single clade with previously identified KOUTV from Kenya. Comparative analysis revealed alanine amino acid at NS5 653. Diversifying pressure was acting on NS3 267 of the KOUTV lineage. There was no significant difference in the growth rates of KOUTV in Vero-E6 and C636 cells when compared to West Nile virus Lineage 1a. The isolation of KOUTV in two disparate sites in sandflies suggest circulation of the virus amongst sandfly population. The growth of the virus in Vero-E6 may point to the ability of the virus to infect primates. Similarly, growth in C6/36 cells points to amenability of the virus to mosquitoes, hence potential vectors. The close genetic relationship of KOUTV strains between East and West Africa may be enabled by the bird migratory route between the two regions.

7102

DISSECTING ANTIGEN-SPECIFIC T CELL RESPONSES TO MPOX IN VACCINATION AND INFECTION BY GENOME-WIDE ANTIGEN SCREENING

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The mpox epidemic in July 2022 caused by Monkeypox virus (MPXV) prompted a public health emergency. Even after the epidemic peak, cases of mpox are still being reported both within and outside traditional endemic areas. The smallpox vaccine, Dryvax®, which successfully eradicated smallpox, comprises a live replicating vaccinia virus (VACV) and provides robust protection against MPXV, but poses safety concerns for immunocompromised individuals. In response, a non-replicating modified vaccinia Ankara (MVA) vaccine, JYNNEOS, was developed for smallpox and mpox, which is associated with the deletion of numerous open reading frames (ORFs). Recent data obtained during the 2022 mpox epidemic indicate that JYNNEOS may induce less immunogenicity and protection than Dryvax®. T cells play a pivotal role in controlling and terminating pox-virus infections, yet there is limited information on the antigen targets recognized by T cells following VACV vaccinations (Dryvax® and JYNNEOS) and/or MPXV infection. To fill this gap of knowledge, our study focuses on identifying the antigens and epitopes recognized by T cells in donors who have been vaccinated and/or infected. First, we classified the ORFs present in the two VACV vaccine strains and MPXV by their ortholog determination. We then measured T cell responses induced after JYNNEOS vaccination with pools of predicted peptides spanning the entire MVA proteome. Employing our deconvolution strategy, 113 CD4 and 83 CD8 MVA-derived epitopes were identified, exhibiting an unbiased recognition between structural and non-structural proteins. Among the recognized antigens, we identified the top 10 immunodominant antigens for CD4+ and CD8+ T cells with five antigens recognized by both populations of T cells. This comprehensive antigen identification provides a valuable understanding of T cell responses following JYNNEOS vaccination during the mpox epidemics, enabling comparison with responses post-Dryvax® vaccination and MPXV infection. Ultimately, these insights into potential protective antigen targets contribute to the development of next-generation pox vaccines with enhanced efficacy.

7103

PRIOR ZIKA VIRUS INFECTION RESTRICTS DIVERSITY OF SUBSEQUENT ACUTE-PHASE PLASMABLAST RESPONSE TO DENGUE VIRUS SEROTYPE 2 AND PREFERENTIALLY SELECTS A SINGLE CLONE

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Zika virus (ZIKV) and dengue virus serotypes 1-4 (DENV 1-4) co-circulate in the tropics, such that people are exposed to multiple viruses. DENV causes febrile illness ranging from mild to severe disease with vascular leak. We have shown that prior ZIKV infection is associated with increased the risk of subsequent severe DENV2 infection. Plasmablasts rapidly peak in the acute response to DENV infection and secrete antibodies. We hypothesized that prior ZIKV vs DENV1 infection selects for different antibody specificities in the acute immune response to subsequent DENV2 infection. Using single-cell transcriptomics and antibody variable heavy (VH) and light (VL) chain gene annotation, we compared the acute plasmablast (PB) response to DENV2 infection in peripheral blood mononuclear cells (PBMCs) from children with primary DENV2 (n=1), secondary DENV1-DENV2 (n=2), or

secondary ZIKV-DENV2 (n=3). A mean of 1,383 B cells were analyzed per child. The acute ZIKV-DENV2 PB clonal diversity (Shannon Diversity Index, H=5.6) was lower than that of DENV1-DENV2 (H=6.63), suggesting more selection pressure in ZIKV-DENV2 PBs. Surprisingly, a single clonotype of VH3-23_VK1-39, with a 17- or 18-amino acid VH hypervariable region, predominated (33-50%) in ZIKV-DENV2 PBs of all 3 children. We did not find this clone in acute DENV2 or DENV1-DENV2 PBs. In contrast, the most frequent clone in the DENV1-DENV2 group was only present in 1.7-6% of PBs. Monoclonal antibodies (mAbs) representing the VH3-23_VK1-39 clone potently neutralized ZIKV (Neutralizing titer; NT_{50}=0.012µg/mL) but not DENV1-4 (NT_{50}>10 µg/mL). In contrast, most mAbs (6-7) of a set of 8 representative clones from the DENV2 and DENV1-DENV2 PBs neutralized DENV1-4 (NT_{50} in µg/mL: DENV1=0.4-40, DENV2=0.4-20, DENV3=0.6-7, DENV4=0.3-20) but not ZIKV (NT_{50}>10 µg/mL). Thus, the acute PB response to ZIKV-DENV2 demonstrates less diversity and a preference for a single clone that does not neutralize DENV2. This supports that prior ZIKV immunity may not elicit effective immunity in the acute phase of a subsequent DENV2 infection and may partly explain increased risk associated with this infection history.

7104

BLOOD BIOMARKERS THAT PROSPECTIVELY PREDICT HIV-1 INFECTION IN HIGH RISK ADULTS.

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High heterogeneity in HIV-1 transmission is observed with individuals in sub-Saharan Africa exhibiting a nearly 4-fold elevated risk of male-to-female HIV-1 transmission per sexual contact compared to higher income countries. It is possible that environmental exposures may predestine one to becoming more susceptible to HIV-1 acquisition, for example by affecting host constitutive defence mechanism. We recently explored potential blood biomarkers predictive of HIV-1 acquisition using a retrospective case-control study nested in an HIV-1 high-risk longitudinal cohort. Plasma samples taken 3 months prior to HIV-1 infection were used for transcriptional analysis of the RNA encapsulated in small extracellular vesicles (sEVs) circulating in plasma. Preliminary data of the host and pathogen transcripts revealed distinct gene expression patterns 3 months prior to HIV acquisition, in individuals who 3 months later acquire HIV (cases) compared to those who remain HIV negative (controls). Notably, dampening of immunological pathways important for inducing antiviral immunity were associated with HIV-1 acquisition. Interestingly, significantly higher Pegivirus C RNA was observed in those who became HIV-1 positive compared to those who remained negative. Although this was contrary to the protective role of Pegivirus C in slowing HIV-1 disease progression to AIDS, our results suggest that Pegivirus C infection might dampen the immune system and predispose high risk adults to HIV-1 acquistion.

7105

SURVEILLANCE OF ACUTE FEBRILE ILLNESSES IN THE COUNTRY OF GEORGIA: INSIGHTS FROM A HOSPITAL-BASED STUDY

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Understanding the pathogens causing acute febrile illness (AFI) is crucial to address global and militarily health challenges. AFI-related morbidity and mortality remain significant concerns in Georgia. The service members operating in the country are at high risk of exposure to AFI agents. We initiated a hospital-based surveillance study in Georgia to determine infectious causes of undifferentiated febrile illnesses. The study enrolled patients aged 4 years and older who exhibited persistent fever (≥38°C for ≥48 hours) without definitive diagnoses and collected samples for testing. We utilized an enzyme-linked immunosorbent assay (ELISA), serum agglutination test and immunoblotting to detect antibodies against regionally relevant pathogens, including *Leishmania* spp., *Leptospira* spp., Crimean-Congo Hemorrhagic Fever Virus, *F. tularensis*, West Nile Virus, *R. typhi*, Spotted Fever, *Brucella* spp., *C. burnetii*, Tick-borne Encephalitis virus, *Borrelia* spp., and Hantavirus. From February 2023 to March 2024, we enrolled 196 outpatient subjects with a mean age of 46 years (range 13-81 years) of which 60% were female and 40% were male. Testing results indicated *R. typhi* as the predominant pathogen, with IgM positives in 60% of the samples followed by *Leptospira* spp. (29%), *F. tularensis* (15%), *Brucella spp*. (14%), *Borrelia spp.* (11%) and Spotted Fever (9%). In addition, 43% of the samples demonstrated the presence of IgM antibodies against 2 or more pathogens. In attempt to identify the agent causing the illness, samples were also subjected to polymerase chain reaction-based assay using the BioFire Global Fiver Panel. However, no positive AFI pathogens were obtained. The results of our study indicate presence of various AFI agents in the country and highlights the need of continued surveillance and research to develop region-specific diagnostic methods and analyses. The latter is essential to control and mitigate the spread of these infectious agents in the region.

7106

HUMAN *IN VITRO* MODELING CHARACTERIZES MECHANISM OF ACTION OF ADJUVANTATION SYSTEMS DEFINING SCALABLE AND AFFORDABLE PRECISION VACCINE FORMULATIONS FOR EARLY CHILDHOOD

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Children demonstrate distinct immunity in early life including diminished Th1-polarizing cytokine production contributing to high susceptibility to infections caused by intracellular pathogens such as respiratory viruses. This challenge also pertains to pediatric vaccine discovery and development, and could be overcome by developing precision adjuvantation systems with well characterized mechanisms of action (MOA) tailored to enhance age-specific immunogenicity. To this end, we employed novel age-specific human *in vitro* assays to characterize cellular and molecular activities of a selection of adjuvants in children aged between 2-4 years in soluble, oil-in-water and liposomal formulations, including several developed for global open access. In a whole blood assay, which predicts the reactogenicity potential of adjuvants, formulations containing the TLR4 agonist, monophosphoryl lipid A (MPLA), potently induced an innate immune response with primary activation of monocytes, and liposomal formulations were more selective in inducing cytokine production compared to soluble and oil-in-water formulations in children as well as adults. In a monocyte-derived dendritic cell (MoDC) assay, which dissects the mechanism by which adjuvants activate differentiation of T helper (Th) cell subsets, liposomal formulations activated MoDCs to produce Th1-polarizing cytokine response, which is important for anti-viral host defense, with more robust TNF induction observed in children than adults. In a DC-T cell interface assay that demonstrates antigen processing and presentation, activation of influenza-specific $CD4^+$ T cells was driven by MPLA-containing formulations and that of $CD8^+$ T cells was induced by the adjuvant QS-21 with greater variability observed in children than in adults. Insight into the MOA of adjuvanted vaccine formulations via age-specific human *in vitro* modeling may advance global health by accelerating and de-risking development of affordable and scalable precision-adjuvanted vaccines.

7107

SEROLOGICAL PROFILING OF RESPONSES TO VACCINATION AND/OR INFECTIONS CRITICAL TO UNLOCK IMMUNE CORRELATES OF PROTECTION

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Pathogen-specific antibodies are commonly used to assess immunity to various pathogens. Serological readouts often rely on measuring antibodies to a single antigen and, in many cases, inform on disease exposure rather than immunity to the respecting pathogen. Attempting to correlate protection with a single point serological measurement, have shown that depending on the study population, pre-existing immunity and vaccine-induced immunity, such direct relationship between antibodies and protection is highly variable. This has led to the increasing reluctance of conducting serological analysis as they may fail to expand our knowledge in immune mechanisms conferring protection.In this study we showcase the power of serological profiling, specifically, establishing the antibody profiles to SARS-CoV2 and mapping the functional activity (isotype, neutralization) of various study populations. The study populations include male and female donors with/without mRNA vaccination, pregnant women, and neonatal cord blood. The results have led to several conclusions that the single assessment of antibody titers to just SARS-CoV2 spike or nucleocapsid would not have revealed: (1) antibodies to SARS-CoV2 nucleocapsid waned in our study populations over time thus increase the uncertainty on determining immune individuals; (2) distinct antibody profiles in neonatal cord blood vs. maternal blood; (3) distinct functional antibody profiles between the study populations; and (4) vaccination compared to disease induces a distinct functional profile and cross-reactivity with other SARS-CoV2 variants than the original strain. Our results show a clear need to advocate for enabling a full assessment of immunity by profiling both fine specificity and function, to potentially identify immune correlates of protection.

7108

CYTOKINE PROFILING REVEALS DISTINCTIVE IMMUNE RESPONSES IN DENGUE, ZIKA, CHIKUNGUNYA AND MAYARO VIRUS INFECTIONS

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Arboviruses, including Dengue virus (DENV), Chikungunya virus (CHIKV), Zika virus (ZIKV), and Mayaro virus (MAYV) are important causes of acute febrile illness (AFI) in high-risk regions in Peru. Differential diagnosis based on clinical manifestations is challenging due to overlapping symptoms. We conducted a pioneering study to compare cytokine profiles among these arboviruses, aiming to elucidate distinct immunological features for diagnostic and therapeutic insights. We conducted a cross-sectional study in patients with acute febrile illness from Cajamarca, Peru. Blood samples were collected for the diagnosis of arboviruses and the quantification of cytokines. Diagnosis of Dengue, Zika, Chikungunya, and Mayaro virus infections relied on specific IgM antibody detection via enzyme-linked immunosorbent assays (ELISA). Cytokine quantification was carried out by ELISA assays for IL-2, IL-6, IL-10, TNF-α, and IFN-γ. Comparative analysis of cytokine levels was performed between all viruses and controls. A total of 20 patients were recruited for each arbovirus and control group. Our study revealed similarities in clinical symptoms across arboviral infections, with headaches, myalgias, and arthralgias as the predominant symptoms. IL-2 levels were similar across the arboviruses; however, DENV and ZIKV patients had higher levels compared to controls. Elevated IL-6 levels were associated with CHIKV and ZIKV, while IL-10 levels were highest in DENV as compared to other arboviruses. TNF-α and IFN-γ were significantly elevated in DENV and ZIKV, and they were significantly higher in DENV compared to MAYV. Our findings provide valuable insights into the unique cytokine profiles of arboviral infections. We found similar levels of IL-2 across the arboviral groups, IL-6 was predominantly elevated in CHIKV and ZIKV, while IL-10 showed the highest levels in DENV. TNF-α and IFN-γ showed a similar pattern, with DENV and ZIKV patients expressing the highest levels. Understanding the distinct immunological signatures of these arboviruses is crucial for effective diagnostic and therapeutic approaches in high-risk regions.

7109

SERUM INTERLEUKIN-6 AND ZINC LEVELS ARE ASSOCIATED WITH SEVERITY IN COVID-19 PATIENTS FROM LIMA, PERU

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The individual's immune system can determine the progress of SARS-CoV2 infection and lethality. The modulation of the inflammatory response through various molecules, such as cytokines and trace elements, is crucial during the disease. In this context, the objective of the present study was to determine the serum levels of IL-6 and zinc and their association with the severity of the disease in patients with COVID-19 from Lima, Peru. Four groups of patients were analyzed. Hospitalized patients were divided into two groups: 26 admitted to ICU and 26 who did not require ICU. The other two groups included 36 patients who did not require hospitalization, 24 of which belonged to the outpatient group and 12 to the control group. Sixty-four and eight percent (64.8%) of the patients were male. The lowest IL-6 values were obtained in the outpatient group (2pg/mL) and the highest values in the ICU group (168.5 pg/mL). On the other hand, the highest zinc values were also obtained in the UCI group (3402.5 µg/dL).

7110

SERUM SPIKE SPECIFIC IGG3 SERVES AS A DISTINGUISHING IMMUNOLOGICAL MARKER BETWEEN SARS-COV-2 INFECTION AND VACCINATION

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Both SARS-CoV-2 infections and COVID-19 vaccines elicit immunological responses. However, it is difficult to distinguish the responses generated either from vaccination or infection. Here we have investigated SARS-CoV-2 spike receptor-binding domain (RBD)-specific IgG subclasses (IgG1, IgG2, IgG3 and IgG4) responses using ELISA in four different groups; (1) COVID-19 patients (n=39) with varying disease severity and (2) COVID-19 vaccinated individuals (n=30, adenovirus/mRNA based) (3) vaccinated after infection (n=39) (4) patients experiences breakthrough infection (n=19), in Bangladesh. We observed distinct IgG subclass responses in COVID-19 patients compared to COVID-19-vaccinated individuals. Specifically, COVID-19 patients exhibited elevated levels of both IgG1 and IgG3, with IgG3 dominating in the early phase (days 1-7) followed by a subsequent increase in IgG1. Conversely, COVID-19 vaccination predominantly induced IgG1 responses without a concurrent rise in IgG3. This effect was more evident when a significant rise of IgG1 but not IgG3 was observed

in patients who received COVID-19 vaccines after 90 days of infection. However, following breakthrough infection, we observed an increase in both IgG1 and IgG3. All of these findings collectively indicate that COVID-19 vaccination predominantly induces IgG1, whereas natural infection can elicit both IgG1 and IgG3 subclasses. These findings identify the importance of serum spike-specific IgG3 as an important distinguishing marker that can differentiate individuals based on their vaccination and natural infection history. More studies with larger sample size might be needed to establish this marker. This marker can be used as an important tool for longitudinal monitoring of vaccinations and for establishing SARS-CoV-2 correlates of protection.

7111

NO DISTINCT CYTOKINE, CHEMOKINE AND GROWTH FACTOR (CCG) BLOOD PROFILE ASSOCIATED WITH MONKEYPOX VIRUS CLADE IIB INFECTED PATIENTS

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Previous literature, in particular on related orthopoxviruses, suggested a cytokine storm association with overt mpox disease. To date, only a handful of studies have investigated the modulation of circulating cytokine, chemokine and growth factor (CCG) profiles in monkeypox virus (MPXV)-infected patients with limited panels. The sole study on CCGs in clade I MPXV infections in 19 mpox patients showed that cytokine modulation correlated with disease severity. It remains unknown if a similar CCG profile is associated with clade II infections, as patients exhibit different clinical manifestations to both clades. We used a 65-plex CCG panel to analyze serum samples of 100 acute mpox patients from the 2022 outbreak and 26 pre-outbreak healthy controls. All 100 patients were men, median age 40 years (interquartile range: 33-46). Cluster analyses indicated no strong CCG profiles in mpox patients compared to healthy controls, but a trend towards certain cytokine modulations. Individual CCG analyses showed MIF, CXCL10, CCL8, CD30, IL2R, CXCL13, IL18, APRIL, CCL4, TNFRII, VEGFA, CXCL12, CXCL9, and CXCL11 to be significantly elevated in mpox patients, while TWEAK, CCL11, CCL2, CXCL5, and SCF were significantly suppressed. We did not detect significant differences in the expression of key pro-inflammatory cytokines such as IL-1α, IL-1 β, IL-6, IL-8 or anti-inflammatory cytokines such as IL-4, IL-10 and IL-13. Comparing with pre-outbreak samples of 10 mpox patients living with HIV before mpox infection, confirmed an increase in BLC, IL18, and MIF during mpox disease. A higher number of lesions correlated positively with BLC and TSLP expression, and negatively with CCL2. Presence of proctitis was associated with an increase in CD30 and LIF. Presence of systemic symptoms or ongoing fever were associated with an overexpression of IL2R, LIF, and CXCL11 and suppression of CCL24. In addition to well-known differences in clinical manifestations, clade I and clade IIb MPXV infections evoke marked differences in blood CCG profiles. The absence of discriminatory CCG profiles in mpox patients suggests limited clinical applications.

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MODULATION OF THE SPP1 GENE BY CHIKUNGUNYA VIRUS INFECTION *IN VITRO* AND ITS POSSIBLE IMPLICATION IN INFLAMMATION AND DISEASE SEVERITY

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The SPP1 gene is responsible for encoding the osteopontin protein, which has several natural functions in our body, such as bone remodeling, angiogenesis, and tumor migration, in addition to play a role in chronic inflammatory and autoimmune diseases. Furthermore, this protein may also act as a Th1 cytokine on the regulation of the immune response by T cells, contributing as an inhibitor of the anti-inflammatory cytokine IL-10 and increasing the Th1-mediated (pro-inflammatory) response. In this study, expression of the SPP1 gene in monocytes that were infected *in vitro* with the Chikungunya virus (CHIKV) was compared to CHIKV infection of another co-circulating alphavirus in Brazil, Mayaro virus. Although the diseases caused by these viruses bear a strong resemblance, Mayaro disease typically results in a milder clinical presentation than Chikungunya, with less frequent recurrence of joint inflammation. Our transcript analysis revealed that the expression of the SPP1 gene was approximately 12-fold higher at early times after Chikungunya virus infection when compared either to the Mayaro virus and uninfected cells. Later in the infection, SSP1 gene was also observed to be positively modulated, although the expression showed a progressive decrease at later hours post-infection. In the case of Mayaro virus infection there was no significant difference in the SPP1 expression when compared to uninfected cells. This increased gene expression correlated positively with the levels of inflammatory cytokines and chemokines, such as IL-6, IL-15, and eotaxin. Our findings suggest that interventions in the production and secretion of osteopontin could attenuate the inflammatory effects induced by the Chikungunya virus, thereby presenting a potential target for development of drugs that counteract osteopontin functions. Also, therapy strategies for the Chikungunya disease, such as CRISPR-Cas9 and RNAi methodologies, may target the SSP1 gene to reduce the severe chronic manifestations of this disease.

7113

INFLUENCE OF COUNSELLING ON POSITIVE STATUS DISCLOSURE AND VIRAL SUPPRESSION AMONG PEOPLE LIVING WITH HIV IN GHANA

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Counselling is a key gateway to major HIV/AIDS services. Silence on HIV positivity non-disclosure remains dire, encouraging increase disease transmission and death. This study assessed the influence of counselling on HIV positive status disclosure and antiretroviral therapy (ART) adherence among people living with HIV (PLWHIV) at the Korle Bu Teaching Hospital (KBTH) in Ghana. The mixed-methods study design involved 423 participants. A semi-structured questionnaire with both close and open-ended questions was used to collect data from PLWHIV presenting at the Fevers Unit of KBTH. STATA 15.1 was used for data analysis. For open ended questions, thematic data analyses in Nvivo software were used to explore transcripts and appropriate themes generated. HIV positive status disclosure among the 49.3 ± 12.2years mean-aged population was 92.4%. Majority (61.5%) disclosed their status in the symptomatic phase of disease and disclosure to sexual partner was only 51.8%. Prevalence of HIV viral suppression (target not detected) was 52.2% with 68.4% high medication adherence. Having HIV pre-test counselling [aOR = 2.18, 95% CI 1.05 - 4.55, p=0.04] and age on ART (aOR = 0.94, 95% CI 0.89 - 1.00, p = 0.04) were associated with status disclosure. Not having HIV pre-test counselling (aOR = 2.17, 95% CI 1.28 - 3.67, p = 0.004), having enhancement counselling, rural residence, not having a partner/spouse as social support and not having assistance in taking medication were associated with increased odds of not having viral suppression. Qualitatively, counselling "educated", "encouraged", and "supported" ART adherence and status disclosure among PLWHIV, and gave them "hope" to cope with life. Status disclosure served as avenue for "financial assistance", "emotional support" and "reminders to take one's medication" towards attaining viral suppression. We found enough evidence to support the influence of counselling on HIV positive status disclosure, and the duo leading to ART and medication adherence - a call for their enhancement towards reduction of the disease transmission, and improving the quality of life of PLWHIV.

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PERSISTENCE OF ANTI-YELLOW FEVER VIRUS IMMUNOGLOBULIN M ANTIBODIES POST-VACCINATION AND ITS REACTIVITY TO THE ENVELOPE DOMAIN III ANTIGEN OF THE YELLOW FEVER VIRUS

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Yellow fever (YF) is a vaccine-preventable, mosquito-borne viral infection endemic to tropical and subtropical parts of South America and Africa. In these parts, a live attenuated YF vaccine is routinely administered to children at 9-12months of age. If an infant vaccinee develops fever and jaundice years post-vaccination and anti-YF IgM antibodies are detected in their serum, it becomes unclear what these results represent. Does the IgM detection suggest a recent natural YF virus infection indicating vaccine failure or does it suggest the persistence of YF-IgM antibodies years post-vaccination? To better understand YF IgM sero-positivity post-vaccination, we tested archived sera from the ANRS 12225/12140-PEDIACAM study- a prospective observational cohort study of infants born alive to HIV+ and HIV- mothers enrolled from 3 hospitals in Cameroon. The infants were followed from birth to present and received the YF vaccine at 9-12months. To determine the presence and persistence of anti-YF IgM antibodies, we tested samples collected pre-vaccination, at 2-6months and 1-2years post-YF vaccination using the CDC YF IgM antibody capture 72hrs ELISA. We found that at 2-6months post-YF vaccination, 18/352(5.1%) of infants had anti-YF IgM antibodies while, 10/433(2.3%) of infants still had anti-YF IgM antibodies by 1-2years post-vaccination. Our results indicate that, YF IgM is rare by 6 months post-vaccination in infants who receive the YF vaccine at 9-12months. However, IgM persistence years post-YF vaccination could be observed in a minute proportion of infants. To further maximize the insight we could obtain from these samples, we assessed and compared the reactivity of YF IgM-positive vaccinee sera and YF natural infection sera to 3 recombinant YF antigens (Envelope protein, Envelope Domain III protein (EDIII), non-structural protein 1) using the multiplex immunoassay which makes use of antigen-coupled beads. The IgM antibodies from both sera groups exhibited stronger reactions to the YFV DIII envelope protein compared to other proteins, hence could serve as a more specific and sensitive marker for detecting IgM in both cases.

7115

AEDES AEGYPTI MOSQUITO SALIVA INHIBITS HUMAN T CELL PROLIFERATION: IMPLICATIONS FOR ARBOVIRAL DISEASE OUTCOME?

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Dengue fever is one of the most rapidly spreading mosquito-borne viral diseases in the world and is caused by the bite of an infectious *Aedes* mosquito. To facilitate the blood feeding process, the mosquito salivates into the host skin, releasing several compounds known to limit host vasoconstriction, inhibit coagulation processes, and suppress pain receptors. Previous murine studies showed saliva of *Ae. aegypti* to be implicated in enhanced viral dissemination and increased pathogenesis of viral infections, while epidemiological studies have suggested a protective role for anti-*Ae. aegypti* saliva antibodies against symptomatic dengue. Here, we investigate the response of human peripheral blood mononuclear cells (PBMCs) to *Aedes* saliva, to better understand how anti-saliva immune responses influence dengue disease outcome. Preincubation of human PBMCs with salivary proteins of *Aedes* for three hours prior to being stimulated with Concanavalin A, a lymphocyte mitogen, inhibited CD3+ T cell proliferation by 30.8% and reduced IFN-γ and IL-2 secretion by 42.5% and 93.4%, respectively. Repeating this experiment with either denatured (30min at 70ºC) or digested (proteinase K) salivary proteins, abrogated the phenotype (7.1 and 3.6% inhibition of proliferation; 2.95% and 0% reduced IFN-γ secretion; and 41.6% and 14.2% reduced IL-2 secretion, respectively), supporting the hypothesis that saliva has a direct effect on T cell proliferation. Ongoing experiments using a SARS-CoV-2 peptide pool as stimulus on PBMCs of individuals with confirmed high neutralization titers against SARS-CoV-2, will elucidate whether saliva inhibits antigen-specific T cell proliferation. This is the first time that *Aedes* saliva is shown to have an inhibitory effect on human lymphocytes. Future mechanistic studies will uncover the implicated salivary components and potential differences between highly *Aedes* exposed vs. unexposed individuals. We aim to test if anti-saliva antibodies neutralize this saliva-induced inhibition, which will help characterize whether host differences in immune inhibition are associated with dengue disease outcome.

7116

HUMORAL IMMUNITY FOLLOWING VACCINATION IS SUFFICIENT TO PROTECT AGAINST RIFT VALLEY FEVER VIRUS ENCEPHALITIS

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Prevalent in Africa and the Arabian Peninsula, Rift Valley fever virus (RVFV) is a mosquito-borne virus that infects humans and livestock. In humans, RVFV infection typically presents as a self-limiting febrile illness. However, in a subset of individuals severe complications such as hepatitis, retinitis, encephalitis, or death can occur. While there are no RVFV vaccines currently licensed for human use, previous work using promising live attenuated vaccine candidates demonstrated that humoral immunity was sufficient to confer vaccine-mediated protection from lethal *hepatic* disease in C57/BL6 mice. Here, we investigated whether vaccination was effective in preventing lethal *central nervous system* (CNS) disease. Unlike traditional inbred mice such as C57BL6, CC057/Unc mice develop uniform late-onset encephalitis between 8 to 12 days post infection (dpi) when challenged with wild-type (WT) RVFV by foot pad injection. Attenuated RVFV vaccine candidates (DelNSsRVFV and DelNSs/DelNSmRVFV) were safe and immunogenic in CC057/Unc mice. Vaccinated mice also survived subsequent WT RVFV challenge and were fully protected from CNS disease. Furthermore, naïve mice that received passive transfer (PT) of serum from vaccinated animals 2 days post WT challenge were also protected against late-onset encephalitis, indicating that humoral immunity is sufficient for protection against RVFV encephalitis. Notably, protection through humoral immunity was dependent on PT dose and timing of PT administration. A decline in animal survival was observed when PT was administered 2 dpi at lower doses or when PT was given on days 3 to 6 post WT challenge. Overall, these data demonstrate that humoral immunity following vaccination is sufficient to protect against RVFV encephalitis and highlight the utility of attenuated RVFV vaccines in preventing diverse disease manifestations.

7117

DEFINING INNATE IMMUNE MEDIATORS REQUIRED FOR THE EFFECTIVE RIFT VALLEY FEVER VIRUS ANTIVIRAL RESPONSE

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Rift Valley fever virus (RVFV) is an arthropod-transmitted virus affecting humans and ruminants. RVFV infection most frequently manifests as an acute self-limiting disease, but in a subset of cases involves severe manifestations including hepatitis, encephalitis, and/or hemorrhagic fever. The determinants of infection severity are largely unknown. The NSs protein of RVFV is a critical mediator of virulence and is thought to exert its effects through antagonizing the host interferon response, suggesting a key role for innate immunity in controlling RVFV infection. When mice are infected with strains of RVFV that are deleted for the NSs protein they do not develop clinical illness; in contrast, 100% lethal hepatitis is observed in mice infected with WT RVFV. To evaluate the role of specific innate immune sensors and signaling mediators in modulating in vivo RVFV pathogenesis, we infected various immune mediator knockout mice with strains of RVFV that are deleted for the NSs gene. These attenuated NSs-deleted strains

were lethal in MAVS, STAT1, and IFNAR knockout mice. No lethality was observed in TLR3, TLR7, MyD88, TRIF, NLRP3, or TNF knockout strains, suggesting unique functions of MAVS, STAT1, and IFNAR in the RVFV antiviral response. Future investigations will aim to elucidate the contribution of hematopoietic versus stromal compartments of these innate immune mediators in protection from RVFV hepatitis.

7118

IDENTIFICATION OF EPITOPE-SPECIFIC T CELL RESPONSES TO LASSA BY GENOME-WIDE ANTIGEN SCREENING AND CONSERVATION ACROSS ARENAVIRIDAE

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CD4 and CD8 T cells play a key role in clearing Arenaviridae infections, even before the appearance of neutralizing antibodies. Thus, while vaccine strategies that would generate a rapid and durable neutralizing antibody response are desirable, a vaccine also inducing a rapid and durable T cell response would be of significant interest, especially if the T cell response could broadly target different viral species and isolates. Studies performed on Lassa survivors also show a robust and durable T cell response able to cross-recognize different Lassa lineages. Human data is however limited, and most studies so far focused on specific domains or immunodominant epitopes for GPC and NP. We have initiated a systematic study of all Lassa proteins (including GPC, N and L proteins), in terms of which epitopes are immunogenic in humans using a de-novo in-vitro stimulation approach. This approach will also determine the degree of conservation of Lassa human epitopes in other viruses of the Arenaviridae family (Old World and New World arenaviruses alike) Our approach re-reidentified epitopes previously shown in convalescent Lassa human samples and greatly expand the immunogenic regions induced by this virus in GPC, N and L proteins and identify several immunogenic and conserved regions, thus allowing to assess the feasibility of a panArenaviridae vaccine approach.

7119

FILOVIRUS VIRUS GLYCOPROTEIN - EPITOPE MAPPING, AND PSEUDOTYPING

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Recent disease outbreaks highlight the need to characterize the immune response to filoviruses to develop vaccines and therapies. We have used extensive GP mutation libraries to map the epitopes for >200 monoclonal antibodies (MAbs) targeting the EBOV surface glycoprotein, GP. We have extended these studies to Marburg virus (MARV) by generating an Ala-scan library of MARV Δmucin GP (Uganda strain). Initial maps of anti-MARV MAbs include those of two non-neutralizing MAbs MR228 and MR235, targeting the wing region of MARV GP, that showed therapeutic protection in animal models (MR228) or that increased binding (MR235) by neutralizing MAbs. The variety of EBOV MAbs mapped, many from survivors of ebolavirus infection, include cross-neutralizing MAbs targeting the GP membrane-proximal external region (MPER); a broadly cross-reactive MAb that blocks GP interaction with its endosomal receptor Niemann-Pick C1; and MAbs who synergistically transform a non-neutralizing MAb into a potent neutralizer. The epitope maps have expanded our understanding of how the immune system recognizes EBOV GP, and allow correlation of epitopes with MAb neutralizing capabilities, to develop anti-EBOV therapeutics and vaccines. Mapping also identified mutations that increase the exposure of neutralizing epitopes, impacting future anti-ebolavirus vaccine strategies. To provide critical reagents for analyses of antibody or serum immune responses to ebolaviruses, we have developed a pseudotyped lentiviral reporter virus (RVP) system for EBOV and MARV, expressing bearing the appropriate viral GP. These replication-incompetent RVPs perform one round of infectivity and enable safe (BSL-2) and reproducible virus neutralization assays with luminescent or fluorescent readout.

7120

INHIBITORY EFFECTS OF PLANT-DERIVED COMPOUNDS ON ROTAVIRUS PATHOGENESIS

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Acute diarrhea due to Rotaviruses remains a public health concern among newborns worldwide. Despite efforts to develop efficacious vaccines, the morbidity and mortality associated with rotavirus infections persist and this has necessitated the need for alternative therapeutic options. This study sought to investigate the inhibitory effects of specific terpenoids on rotavirus replication, with the goal of identifying potential candidates for antiviral therapy. Rotavirus infections manifest as acute gastroenteritis, characterized by symptoms such as fever, vomiting, abdominal pain, diarrhea, and dehydration, posing significant challenges to healthcare systems globally. Rotavirus infections represent a formidable challenge in pediatric healthcare, particularly in resource-limited settings where access to medical care and sanitation infrastructure may be limited. The burden of rotavirus-associated morbidity and mortality underscores the urgency of advancing strategies for prevention and treatment. Natural compounds such as Terpenoids provides a therapeutic alternative and presents an appealing avenue for the development of novel antiviral therapies. Fresh samples of avocado and guava leaves were assessed for their antiviral activity with crude extracts compared for their efficacy. Phytochemical analysis confirmed the presence of active compounds in both leaf extracts with the former exhibiting the highest inhibition percentage. This study provides compelling evidence for the potential utility of plant-derived phytochemicals as a source of pharmacologically active compounds. The superior inhibitory activity of Avocado leaf extract against rotavirus underscores its promise as a candidate for further investigation in the development of novel antiviral therapies.

7121

THE ARYL HYDROCARBON RECEPTOR/AXL PATHWAY AT THE CROSSROADS BETWEEN POLLUTION AND VIRAL INFECTIONS

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There is still a big gap in our knowledge regarding the molecular mechanism by which anthropogenic pollutants contribute to pathogenesis. Our laboratory has recently published data proving that the aryl hydrocarbon receptor (AHR), a ligand activated transcription factor that acts as an environmental sensor of xenobiotic chemicals, has a pro-viral role during infections with dengue (DENV), Zika (ZIKV), Junín (JUNV) and coronaviruses. AHR can regulate the expression of numerous genes, including some involved in the antiviral cellular response. In this work we aim to study the effect of AHR pharmacological modulation on Axl, a member of the TAM receptor family of proteins. Axl is a well-known entry co-receptor for different viruses and in vivo studies have shown that its expression is altered in rats exposed to secondhand smoke. We hypothesize that an AHR/Axl pathway plays a key role during viral infections. To study the effect of AHR modulation on Axl transcript and protein levels we pre-treated A549 cells with AHR endogenous agonist (L-Kynurenine) or with an AHR antagonist (CH223191) and then carried out the infection with DENV-2. We observed a 4-fold change increase and a 0.6-fold change decrease in Axl transcript levels respectively, measured by RT-qPCR. In concordance, we observed a 17% increase in Axl protein levels measured by flow cytometry in kynurenine-treated and infected cell cultures relative to the untreated

infected control. Finally, we carried out plaque forming unit assays to determine the effect of Axl modulation on the related arboviruses DENV-2 and ZIKV and the unrelated JUNV arenavirus replication. To do this, we pretreated A549 and Huh-7 cell cultures with a specific Axl inhibitor (R428) for 3 hours prior to infection. We observed a significant inhibition of viral replication, following a dose dependent response. Furthermore, we treated cell cultures with Gas-6, an Axl activating ligand, and observed a dose-dependent increase in viral titers. In conclusion, this work proposes an AHR/Axl pathway with a key role during viral replication and highlights the relevance of these pollutant receptors during viral infections.

7122

SARS-COV-2 MAIN PROTEASE: MOLECULAR DYNAMIC STIMULATION WITH COMPOUNDS FROM AFRICAN NATURAL PRODUCTS

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The fast growth of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing a major threat to global public health, requiring the most urgent research for potential therapeutic agents. New targeted drugs are necessary to address the problem of resistance. The use of molecular dynamics (MD) simulations allows us to investigate the conformational details of biological systems as well as the interactions between proteins and ligands. In this work, we use molecular dynamic stimulation to validate some compounds from African Natural Products databases which have shown high affinity score with the main protease of SARS-CoV-2 by virtual screening. **Results:**Gypsogenic acid and Maslinic acid have revealed to have a high affinity with the main protease of SARS-CoV-2 by molecular dynamic analysis. Among the seven compounds used, two were shown very strong affinity for the SARS-CoV-2 main protease and those compounds are more likely to have anti-SARS-CoV-2 activities.

7123

PROMISING EFFECT OF SILYMARIN IN AN ANIMAL MODEL OF ARTHRITIS AND MYOSITIS INDUCED BY ALPHAVIRUS MAYARO AND CHIKUNGUNYA VIRUSES

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Mayaro virus (MAYV) and Chikungunya virus (CHIKV) are both members of the *Togaviridae* family causing similar diseases such as severe joint/muscle pain and fever. Our research group is focused on investigating factors contributing to the pathogenesis of MAYV and CHIKV, as well as identifying natural substances with potential antiviral activity. In a recent study, we demonstrated that silymarin, a complex of antioxidants obtained from *Silybum marianum*, exhibited antiviral activity against MAYV in cells. Subsequently, in animal model, we observed that silymarin displayed outstanding hepatoprotective, antioxidant, anti-inflammatory, and antiviral properties in liver of infected animals. Given that joint and muscle pain are prominent symptoms in Mayaro and Chikungunya fevers and that literature shows a potent antiviral activity of silymarin against these viruses, this study aims to evaluate in an animal model of arthritis and myositis induced by MAYV and CHIKV whether silymarin can reverse the damage to joints and muscles post-infection. To achieve this, 6-week-old BALB/c mice were infected with MAYV or CHIKV in the right hind paw pad (10^6 PFU) and the treated groups received 100 mg/kg/day of silymarin every 12 hours by gavage. Preliminary results from infected animals showed paw edema and inflammation, both of which were reduced in animals treated with silymarin. Euthanasia was performed on 7- and 12-days post-infection (dpi), and various organs/tissues including liver, spleen, brain, footpad, quadriceps, tibial, soleus, and extensor digitorum muscles were collected. CHIKV presence was assessed by qRT-PCR; in the quadriceps, tibial, and extensor digitorum muscles, no virus was detected in any of the groups. However, in the infected group that received silymarin, viral load was reduced in the liver, spleen, brain, and footpad at 7dpi, and in the liver, spleen, brain and soleous at 12dpi. The qRT-PCR results for MAYV are currently undergoing processing by our study group. These findings support further investigation into the potential benefits of silymarin in treating MAYV and CHIKV infections.

7124

DISCOVERY OF NOVEL HENIPAVIRUS INHIBITORS

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The prototype species of henipaviruses, Hendra virus (HeV) and Nipah virus (NiV), are zoonotic, negative sense, single stranded RNA paramyxoviruses capable of infecting at least 18 species across seven orders of animals and are considered a serious pandemic risk by the CDC. Following an incubation period of 5-14 days, NiV infection in people will often present as a severe respiratory, vascular, and neurological disease. Outbreaks of NiV, in Bangladesh and Malaysia have led to high rates of human mortality (40->90%) with significant morbidity in survivors. Transmission of infection to people can be through contact with natural hosts (*Pteropus* fruit bats), excreta-contaminated food, or infected virus-shedding livestock or people. There are no currently approved vaccines or therapeutics to prevent or treat NiV or HeV infection for human use. Work with authentic NiV requires BSL-4 containment which represents a substantial challenge to drug discovery efforts. Here we report the successful application of recombinant Cedar henipavirus encoding nano-Luciferase (rCedV-nanoLuc), a BSL-2 approved surrogate system, to screen for compounds that inhibit NiV and HeV replication. We screened 1.7 million compounds and processed hits through a hit-finding flow chart which includes secondary assays such as a novel BSL-2 NiV minigenome reporter and a biochemical assay probing the polymerase activity of the NiV L-protein. Several counter-screens were also included to filter out hits that prevent viral replication through inhibition of host cell roles. Compounds that passed all filters were subsequently tested for inhibitory activity against authentic NiV. Finally, in order to further accelerate henipavirus antiviral drug discovery and enable structure-based approaches, we solved the cryo-EM structure of the L polymerase in complex with the P protein. Here, we present a comprehensive approach that uses a combination of cell-based NiV surrogate systems, high throughput biochemical assays and structural biology analyses to identify new direct-acting antiviral candidates for the treatment of highly pathogenic henipaviruses.

7125

ASSAY DEVELOPMENT OF FLAVIVIRUSES CELL-BASED LUCIFERASE REPORTER SYSTEM TO ENABLE HIGH THROUGHPUT DRUG DISCOVERY

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There is an urgent need for antiviral therapies against flaviviruses. More than 1 billion people are at risk and disease burden is rapidly rising due to climate change. To prepare for future pandemics, the flavivirus program within UTMB-Novartis Alliance for Pandemic Preparedness (UNAPP) was established to find broad spectrum inhibitors targeting RNA-dependent RNA polymerase (RdRp), protease and NS4B. We have developed and validated high throughput cell-based assay on an automation platform to screen and prioritize compounds for Structure Activity Relationship (SAR) optimization enabling novel drug discovery. Using various *in vitro* transcribed recombinant stable nanoluciferase flaviviruses (Dengue, Zika, YF and JEV), >1500 compounds were tested in duplicates. The protocol was optimized for MOI, signal window and robustness in 384-well format, with robust Z' score of >0.5 for all flaviviruses. Viral replication was measured at 3dpi via luminescence readout. A chain-terminator adenosine analogue, a potent RdRP inhibitor, was used as active control, showing consistent activity and robust correlation with historical high-content image-based data. We have optimized the assay on an integrated automated screening platform in a BSL2 enclosure with robotic arms enabling movement of 384-well plates between various pieces of equipment, improving assay quality, reproducibility and throughput. The transfer of compound into an infected assay plate was possible using an acoustic liquid handler. With the current capacity to test 90 compounds per week in concentration-response in all 4 dengue serotypes, we enabled compound optimization towards increased pan-serotype activity with minimal cytotoxicity for our second-generation dengue NS4B project. In addition, similar cellular nanoluciferase assays were developed for Zika, YF and JEV to enable broad spectrum flavivirus profiling of protease and RdRP inhibitors. These established assays provide a critical opportunity to identify a novel broad-spectrum lead candidates that can be developed into a promising therapy, thereby alleviating the disease burden in future outbreaks.

7126

ESTABLISHMENT OF A BSL-2 NIPAH MINIGENOME SYSTEM FOR ANTIVIRAL DRUG DISCOVERY.

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Nipah virus (NiV) is a deadly and highly contagious zoonotic virus that emerged first in Malaysia and has a high mortality rate of 40 to 75% with severe morbidity in survivors. Nipah virus consists of a negative sense RNA strand (18.2 kb) consisting of L protein, an RNA-dependent RNA polymerase which forms a complex with phosphoprotein P. This complex is encapsidated by nucleocapsid N proteins allowing for viral replication. Owing to its high pathogenicity, NiV is classified as a BSL-4 virus. To enable work in a BSL-2 set up, we developed a noninfectious Nipah minigenome system as a valuable tool to identify potential inhibitors of Nipah replication for drug development. Utilizing only the minimum essential genetic elements required for viral replication, our current transient system is a 5-plasmid system consisting of N, P and L proteins and a minigenome construct that contains the NiV specific leader and trailer sequences flanking a nanoluciferase reporter gene and a T7 promoter. A T7 polymerase-encoding plasmid is co-transfected to generate the negative strand RNA mini genome. We successfully established a 384 well-plate transient assay in human host cells measuring luciferase expression 48hrs post transfection along with a parallel cytotoxic assay. We observed an AC_{50} as reported in literature for the tool compound in our NiV minigenome assay. Using this assay, we assessed NiV specific activity of inhibitors that were identified in a recombinant Cedar virus high throughput screen. To enhance assay robustness and decrease variability, also we developed and characterized a novel cell line stably expressing NiV N, P and L proteins that can be used to screen for novel inhibitors and support structural activity relationship (SAR) studies for Nipah drug development.

7127

RAPID-RESPONSE RNA-FISH ASSAY PLATFORM FOR CORONAVIRUS ANTIVIRAL HIGH-THROUGHPUT SCREENING

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Over the past 25 years, the global community has faced the challenges posed by three distinct outbreaks of coronaviruses. The first of these outbreaks was the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic, which occurred from 2002 to 2004 and tragically resulted in over 700 deaths. Following this, the Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic emerged in 2012, causing over 2600 infections with a case-fatality rate of 36%. More recently, the world has become severely impacted by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of the COVID-19 pandemic, responsible for causing nearly 7 million deaths worldwide. It is crucial to note that the threat of further coronavirus outbreaks continues to be a significant concern, as evidenced by the recent identification of the novel canine coronavirus CCoV-HuPn-2018 in several patients with pneumonia in Malaysia. The threat of the ever-evolving nature of viral infections as well as the lingering health and socioeconomic effects of the recent SARS-CoV-2 pandemic emphasize the urgent need for advanced antiviral drug screening tools to strengthen preparedness and preventive measures against future outbreaks. Here, we present the development and validation of a novel RNA-fluorescence *in situ* hybridization (FISH) assay as a high-throughput rapid response platform for antiviral drug discovery. The flexibility of RNA-FISH probe sets allows for synthesis to for any RNA viral genome, enabling detection of any viral replication inhibition of compounds within cells. Screening of 170 antiviral compounds in concentration-response demonstrates a strong R^2 correlation between the results obtained from our RNA-FISH assay and an immunofluorescence assay (IFA) in both human coronaviruses OC43 and 229E. Additionally, we successfully applied this methodology in the context of CCoV 1-71, opening new avenues for the evaluation of antiviral drugs to future emerging threats.

7128

UNVEILING THE ANTIVIRAL POTENTIAL OF WEDELOLACTONE AGAINST THE OROPOUCHE VIRUS

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Oropouche virus (OROV), belonging to the *Orthobunyavirus oropoucheense* specie and *Peribunyaviridae* family, induces dengue-like febrile illness transmitted by the midge *Culicoides paraensis* and some mosquito species. Despite its typically mild symptoms, it can lead to severe complications such as neurological symptoms. With diagnostic challenges, particularly in impoverished endemic regions, OROV poses a potential threat for new epidemics, akin to other arboviruses like Dengue, Yellow Fever, and Zika virus. Exploring natural molecules for antiviral properties offers a promising avenue for therapies with minimal or no side effects. Wedelolactone (WDL) has shown significant inhibitory effects on viral proteins and replication,

positioning it as a promising candidate across various viruses. Our study delves into WDL's antiviral activity against OROV. In Vero cells, WDL exhibited an EC_{50} value of 18.92 ± 9.4 μM under post-infection treatment condition, showcasing its inhibitory effect against OROV infection. Additionally, *in silico* analyses shed light on WDL's potential inhibitory action on the N-terminal polymerase of OROV, suggesting its effectiveness at multiple stages of viral infection in mammalian cells. These findings underscore WDL's potential as a promising inhibitor against OROV infection.

7129

2-PYRIMIDONE COMPOUND SERIES PREVENTS ACUTE VIREMIA AND CHRONIC CHIKUNGUNYA VIRUS IN A MOUSE MODEL OF INFECTION

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Alphaviruses are arthropod-transmitted RNA viruses, including the NIAID Category B priority pathogens Eastern equine encephalitis (EEEV), Venezuelan equine encephalitis (VEEV) and chikungunya (CHIKV) viruses. In November of 2023, the first chikungunya virus vaccine became FDA approved for use in individuals 18 years of age and older who are at increased risk of exposure to CHIKV, although no FDA-licensed antiviral therapeutics are available to treat alphavirus infection or disease, thus demonstrating a need in the field of public health. We identified a small molecule antiviral hit using a screen against CHIKV. Derivatives of the hit were made by medicinal chemistry, and we identified a first-in-class, orally available, non-nucleoside small molecule (SRI-42718) that targets a conserved region in nsP4-RdRp. The SRI-42718 chemical series blocks both gRNA and sgmRNA synthesis as well as viral protein production. The compound has shown no adverse toxicity in mice as repeat dosing at 40 mg/kg, TID, is a well-tolerated treatment for up to 10 days. *In vivo* PK analysis indicates that the compound has good bioavailability by oral delivery in mice and nonhuman primates, and the compound was distributed to several mouse tissues including joints and muscles. Importantly, oral administration of the compound prevents viremia at a dose of 40 mg/kg three times per day (TID) in acutely infected mice. Viral tissue burden and virus-induced foot/ankle swelling (tissue disease) are also significantly reduced in treated animals compared to vehicle controls. A seven-day treatment of mice beginning at 28 days post infection during the persistent phase reduced the viral RNA level in joint-associated tissue. Combined, our data indicate that SRI-42718 is capable of blocking CHIKV replication *in vivo* during both the acute and persistent phases, which increases the therapeutic potential for this compound. SRI-42718 promises to be an important preclinical candidate and the compound has entered early drug development studies.

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IN VITRO ANTI-SARS-COV-2 ACTIVITY OF CPM01 HERBAL TINCTURE AND ITS FRACTIONS

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The recent COVID-19 pandemic posed a significant challenge to public health worldwide and continue to threaten many lives. While vaccines are instrumental in curbing the spread of the virus, the need for effective treatment remains crucial in managing severe cases and emerging variants. CPM01, an herbal tincture developed by the Centre for Plant Medicine Research in Ghana as an immunomodulatory agent has garnered attention for its clinical efficacy in alleviating COVID-19 symptoms and expediting patient recovery without complications. The study sought to evaluate the anti-SARS-CoV-2 activity of CPM01 and its partitioned fractions *in vitro* in Vero E6 TMPRSS2 cells. The effect of CPM01 and partitioned fractions on SARS-CoV-2-induced cytopathy and virus inhibition was determined by crystal violet staining and fluorescence assay targeting the ORF3a protein of the virus respectively. The phytochemical content of CPM01 and fractions were quantified by colorimetry. The findings indicate that CPM01 and its chloroform fraction exhibited remarkable efficacy in preventing virus-induced cytopathic effect with a minimum inhibitory concentration of 0.31 μg/ml. The hexane and ethyl acetate fractions displayed promising virus inhibition, with minimum concentrations of 1.20 and 20.00 μg/ml respectively. The effective concentrations required to inhibit 50% (EC_{50}) of viral ORF3a were 5.55, 5.20 and 6.22 μg/ml respectively for CPM01, chloroform and hexane fractions. The total phenolic content (TPC) of CPM01 was determined to be 9.006±1.075 mg/100 mg GAE, while the total flavonoid content (TFC) was found to be 16.741±1.386 mg/100 mg QE. Even though the ethyl acetate fraction showed the lowest inhibition, it had the highest TPC and TFC, implying the anti-SARS-CoV-2 activity of CPM01 may not be dependent on its phenolic content alone. The findings highlight CPM01 as a potent anti-SARS-CoV-2 candidate with promising therapeutic potentials against COVID-19. However, further research involving mechanistic investigations and clinical trials, is imperative to comprehensively understand its role in managing COVID-19 and its evolving variants.

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GENERATION OF ANTIVIRAL RECOMBINANT PROTEINS TO OVERCOME MOSQUITO-BORNE VIRUS INFECTION

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Mosquito-borne virus infections impact more than 400 million people annually. With limited therapeutics available, the main control mechanism is vector control, however mosquitoes have become resistant to some insecticides. Other mechanisms to control arbovirus transmission include transgenic mosquitoes; however, the current methods are virus-specific or mosquito population replacement with lethal genes. Both control methods are insufficient because they are not broadly active against multiple viruses or long-lasting due to the ability for mosquito populations to rebound. Thus, alternative strategies that are broadly acting against multiple arbovirus families are needed. Host restriction factors are a large category of antiviral immune proteins, some of which can inhibit multiple virus families. For example, PKR and RNase L antiviral pathways are both activated by double stranded RNA (dsRNA), which is produced during the replication cycle of most viruses. However, viruses have evolved multiple strategies to evade these pathways to promote productive infection. To obtain broad antiviral activity, we generated recombinant enhanced antiviral restrictor (REAVRs) proteins containing the virus-sensing domains of PKR fused with the effector domains of RNase L. REAVRs showed high antiviral activity against dengue, Zika, and chikungunya virus when stably expressed in mammalian cells. Transgenic REAVR-expressing mosquitoes showed strong resistance against Zika virus infection and reduced virus dissemination. To improve efficacy of REAVRs, we have constructed a second generation of REAVRs with different vertebrate RNase L sensor domains and replacing PKR double-stranded (ds) RNA-binding domain with other sensor domains to further increase the breadth of viral families inhibited by REAVRs. We are currently characterizing the antiviral activities of these new REAVRs against a panel of arboviruses.

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USE OF AN INSECT CELL EXPRESSION PLATFORM FOR THE PRODUCTION OF NIPAH AND CRIMEAN-CONGO HEMORRHAGIC FEVER VIRAL FUSION, GLYCO-, AND NUCLEOPROTEINS

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Development of recombinant production methods characteristic antigens of priority pathogens, such as Nipah Virus (NiV) and Crimean-Congo Hemorrhagic Fever Virus (CCHFV), are critical for public and global health research. Recombinant proteins have numerous research and biopharmaceutical applications including the use in surveillance of potential outbreaks, studying immunological responses to infection, and the development of vaccines and serological assays. NiV has caused over 600 human infections between 1998 and 2023 in Singapore, Malaysia, Bangladesh, and India with case fatality rates up to 70%. CCHFV has resulted in over 450 human cases since its identification in the mid 1900s, throughout Africa and Southeast Asia overlapping with NiV endemic countries, CCHFV has case fatality rates between 5% and 30%. Currently, it is suspected that cases of CCHFV are largely underreported with several epidemiological studies showing a seroprevalence around 11% in endemic countries. This underreporting can be due to the lack of affordable multianalyte assays available in these areas. There is an urgent need to develop more cost-effective multianalyte serological assays to assess human and animal seropositivity to NiV and CCHFV. High quality recombinant protein production using a scalable *Drosophila* S2 expression system and affinity purification offers an avenue for the development of affordable multiplex immunoassays in both high and low resource settings. Here we present first results of the production of NiV (pre)fusion (pf/F), attachment (G), and nucleocapsid (N) proteins as well as CCHFV receptor recognition glycoprotein (Gc and Gn) and nucleocapsid (N) proteins using our proprietary expression vector and *Drosophila* S2 cells. Recombinant proteins were purified using metal ion affinity chromatography. This research allows for production of antigens to be further used in the development of multiplex serological assays. These can then be used to better understand the prevalence of infection in humans and livestock in endemic and co-endemic areas of NiV and CCHFV, as well as other priority pathogens.

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INITIAL CLINICAL CHARACTERIZATION OF EGT710, A NOVEL CORONAVIRUS MPRO INHIBITOR, FOLLOWING ORAL ADMINISTRATION TO HEALTHY ADULTS

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EGT710 is a low molecular weight inhibitor of the coronavirus main protease (Mpro). It has activity against 8 coronavirus genera Mpro enzymes and potent cellular activity against SARS-CoV-2 variants. It has also shown efficacy in vivo in a mouse infection model. The safety, tolerability, and pharmacokinetics of EGT710 were investigated in a randomized (3:1), blinded, placebo-controlled study of healthy adults at a single center using a conventional single and multiple ascending dose design. Each cohort was 8 study participants (6 receiving EGT710; 2 receiving placebo). A relative bioavailability and food effect study were also included to evaluate the performance of a capsule and liquid (suspension) formulation in a separate cohort of 18 study participants using a Williams crossover design. A total of 70 received EGT710 and 18 received placebo across all parts of the study. Single doses up to 1100 mg and multiple doses up to 700 mg once daily for 7 days were safe and well tolerated. The most common adverse events involved general disorders and administration site conditions, none of which was considered related to the study treatment. There were no evident dose-dependent or dose-limiting adverse effects. Systemic exposure increased with dose. The two formulations showed comparable bioavailability. Administration of the suspension formulation with food modestly increased exposure to EGT710 and delayed the Cmax, suggesting EGT710 may be taken with or without food. The dose range investigated included therapeutic and supratherapeutic exposures, thus generating sufficient data to support dose and regimen selection for subsequent investigations of clinical efficacy in patients with acute coronavirus disease (using established antiviral PK/PD relationships). The data support once or twice daily administration of EGT710 without the need for a pharmacokinetic booster (e.g., ritonavir). The results support continued development of EGT710 as a treatment for coronavirus disease. The liquid formulation provides a unique option for patients who are unable to swallow or have difficulty swallowing.

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INVESTIGATION OF ANTIVIRAL ACTIVITY OF MEK INHIBITORS AGAINST YELLOW FEVER VIRUS USING IN VIVO MODEL

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Yellow fever virus (YFV) causes an acute viral hemorrhagic disease, varying from very mild infection to severe and life-threatening illness, with mortality rate of 20-50%. YFV is endemic in tropical areas of Africa, and Central and South America, with massive outbreaks causing thousands of deaths in recent years, showing that YFV is still a serious public health concern despite the vaccination. To date there is still no specific antiviral treatment for YF. Here, we established the lethal dose (LD) of wild type YFV_BR_2018, a new YFV lineage, in knockout mice for interferon type 1 receptor (IFNAR $1^{-/-}$), and evaluated the potential activity of Selumetinib and Trametinib using this in vivo model. Four-weeks-old male and female C57BL/6 IFNAR$1^{-/-}$ mice were infected with 1.6 x 10^3 to 5.75 x 10^3 PFU of YFV_BR_2018, and monitored for 14 days. Mice infected with the higher dose had survival rates of 60% (females) and 40% (males). They clinical signs, as piloerection, hunched back, conjunctivitis, edema, paralysis, tremors, or penis inflammation. Infectious particles were found in the testicles of convalescent males. The deaths occurred between 8 and 11 days post infection. Then, 4- weeks-old male and female C57BL/6 IFNAR$1^{-/-}$ mice were infected with YFV_BR_2018 and treated with Selumetinib (50 mg/kg/day) or Trametinib (3 mg/kg/day) for 8 days. Neither Selumetinib nor Trametinib showed protection against mortality. It was possible to establish an infection model for the wild YFV_BR_2018 strain, with a mortality rate close to 50%. Although, antiviral effect against orthoflaviviruses have been shown for Selumetinib and Trametinib preliminary results do not indicate antiviral effect of tested inhibitors against YFV, based on mortality rate. Further analyses will be performed to address the effect of treatment on experimentally infected mice.

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EX VIVO ANALYSIS OF AN IL2/ANTI-IL2 COMPLEX FOR THE TREATMENT OF CHRONIC CHIKUNGUNYA ARTHRITIS IN A COLOMBIAN COHORT

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Chikungunya virus (CHIKV) is an alphavirus that causes chronic arthritis in one-fourth of patients. No standard treatments exist for CHIKV chronic

arthritis. Our Colombian cohort is the largest longitudinally followed CHIKV patient cohort in the Americas. Immune analysis from this cohort revealed that low IL2 during acute infection predicted chronic joint pain. Chronic CHIKV arthritis is associated with altered gene pathways in regulatory T cell (Treg) function, decreased interleukin (IL)-2 production, and CD4+ effector T cell (Teff) synovial infiltration. Novel low-dose IL2 therapies preferentially activate Treg IL2 receptors with no apparent side effects reported in rheumatoid arthritis patients who received this treatment. Our previous studies in a CHIKV arthritis mouse model demonstrated that treatment with a complex containing low-dose IL2 and anti-IL2 monoclonal antibody (mAb) expanded and activated Tregs more than IL2 or the IL2 mAb alone, but also expanded Teffs and did not impact tarsal joint inflammation. The IL2 mAb alone amplified activated Tregs, increased expression of Treg suppression marker FoxP3, and improved histologic markers of inflammation, perhaps by augmenting the activity of endogenous IL2. To understand the mechanism of these IL2-related therapies in human CHIKV arthritis, PBMCs collected from our Colombian cohort of chronic CHIKV arthritis patients and a small group of healthy Colombian volunteers will be exposed to low doses of IL2 or the IL2/anti-IL2 mAb complex for 5 days. Flow cytometry of Treg populations, functional Treg suppression assays, and cytokine analysis will then be performed. This will be the first study to use an IL2/anti-IL2 mAb complex ex vivo using PBMCs from healthy donors or CHIKV arthritis patients. We hypothesize that IL2/anti-IL2 mAb complex treatment will significantly increase Treg immunosuppressive function via enhanced FoxP3-mediated CTLA4 suppression of Teff cells. This study is an important step toward determining the feasibility and safety of low-dose IL2-based treatments for CHIKV arthritis. This investigation is underway, and data will be available by August 2024.

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NOVEL IL2 FUSION PROTEIN FOR THE TREATMENT OF CHIKUNGUNYA VIRUS-INDUCED CHRONIC ARTHRITIS IN A MOUSE MODEL

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Chikungunya virus (CHIKV) is an alphavirus that causes persistent arthritis in one-fourth of patients. There are no standard treatments available for CHIKV chronic arthritis. Our preliminary data suggest that alteration of regulatory T cell (Treg) function and low IL2 levels play a role in CHIKV arthritis pathogenesis. Low-dose recombinant IL2 (rIL2) is an effective therapy for the treatment of autoimmune disease and may be of use in CHIKV arthritis flares. When rIL2 is complexed with an anti-IL2 monoclonal antibody (mAb), enhanced Treg differentiation is present in animal models. The mouse model for post-CHIKV arthritis involves footpad inoculation of wild-type C57BL/6 mice, which causes localized swelling and systemic infection. We previously treated CHIKV-infected mice with rIL2, anti-IL2 mAb, or rIL2/anti-IL2 complex. The complex increased peripheral IL2 and expanded and activated Tregs more than the other treatments, but also expanded effector T (Teff) cells and did not improve histological scores. We hypothesize that using a novel IL2 fusion protein in place of the complex will improve the outcomes by decreasing off-target Teff cell stimulation and improving histological inflammation markers. A fusion protein of IL2 and mouse IL-2Rα (CD25) joined by a non-cleavable linker extends the IL2 half-life and improves in vivo efficacy for Treg expansion and control of autoimmunity than rIL2. Mice infected with CHIKV or saline will be confirmed positive or negative by PCR. After the virus is cleared, mice will be treated with saline, rIL2, or the fusion protein for 5 days, at which time blood will be collected for cytokine analysis, spleen tissue harvested for flow cytometry analysis of T cell populations, and synovial tissue fixed for histology. This research provides a pre-clinical evaluation of fusion protein therapy for CHIKV arthritis and insights into using this novel therapeutic for alphavirus arthritis. This investigation is scheduled to begin in May 2024, and data will be available by September 2024.

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SYNTHESIS OF NOVEL QUINONES WITH ANTIVIRAL ACTIVITY AGAINST IMPORTANT HUMAN FLAVIVIRUSES

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Flaviviruses such as the dengue serotypes (DENV 1 to 4), and Zika (ZIKV) viruses pose a significant global burden to human public health worldwide. Despite advances in drug development, there are no effective antivirals or vaccines available for the treatment of these rapidly spreading viruses. Natural products (e.g. flowers, leaves, herbal plants) are a potential source of chemical compounds from which it has been documented antiviral activities with good tolerability and minimal side effects. Quinones are abundant natural substances, mainly characterized by intramolecular unsaturated cyclic diketone structures, and includes benzoquinones, naphthoquinones, and anthraquinones. Quinones are known to contribute to various biological activities, including pharmacological effects such as anticancer, anti-inflammatory and antiviral properties. As quinones have different biological activities for different receptors, it is considered a privileged structure. Here, we enhanced the structural complexity of quinones by alkylation and/or acylation reactions increasing their Fsp^3, and evaluate their antiviral activity against DENV (1 to 4) and ZIKV *in vitro*. A library of 21 natural compounds were initially tested for their ability to cause cytotoxicity (μM) on mammalian cells *in vitro*. Then, concentrations that maintained a cell viability higher than 90% were used to inhibit the infection with DENV (1 to 4) and ZIKV using a cell-based neutralization assay. Preliminary results indicate that carminic acid, together with aloemodin and their derivatives A2, A3, A4, A8 and A9 were able to reduce the infection of mammalian cells with all DENV serotypes and ZIKV. Further experiments will help to elucidate the magnitude of their antiviral activity (EC_{50}) as well as the antiviral mechanisms by which viral inhibition occurs in mammalian cells. These results are promising as natural products must play an important role in contributing to antiviral drug development as alternatives to combat the increasing burden of mosquito-borne diseases worldwide.

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BIASES IN ATTRIBUTION METHODS FOR NOROVIRUS ACUTE GASTROENTERITIS

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The estimated global burden of acute gastroenteritis (AGE) attributable to norovirus varies by the method used to estimate the pathogen-specific burden of disease. One method ("detection-as-etiology" [DE]) considers any norovirus detection to be etiologic, such that the population attributable fraction (PAF) of AGE is norovirus prevalence; but many coinfections are often observed among AGE cases, so not all detection is etiologic, causing overestimation. Another method ("odds-ratio" [OR]) considers the PAF to be function of the odds ratio comparing detection of norovirus among AGE cases and healthy controls, but this method may be confounded by natural immunity acquired from prior norovirus infection, causing underestimation. To assess the biases in these attribution methods and develop an alternative method, we developed a norovirus transmission model accounting for repeated infection and natural immunity to estimate the incidence of symptomatic norovirus infection, from which a model-based (MB) PAF was calculated. We fit the model to the country-specific norovirus prevalence in AGE cases and controls in the multinational MAL-ED cohort study, understanding relationships between enteric infections and a variety of health outcomes, to estimate the transmission rates of

norovirus and other pathogens and solve for the endemic equilibrium. We used the equilibrium states to calculate country-specific PAFs for the DE and OR methods. We characterized the bias as the difference between the MB PAF and the other PAFs. The MB norovirus prevalence in the AGE cases and controls was generally consistent with the observed. The PAF of the DE method expectedly exceeded the others, while the OR PAF was unexpectedly larger than the MB. The biases in the DE and OR methods are similar across most countries, with average relative differences of +290% and +92%, respectively, compared to the MB. Modifications of the model to reflect the variations in natural history by country that were observed in MAL-ED may further refine the attribution bias estimates.

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TOSCANA VIRUS - FINDING THE NEW VECTORS

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Arbovirus *Phlebovirus toscanaense* (TOSV) is an emerging but still neglected human pathogen that circulates in countries around the Mediterranean Sea. The manifestation of the disease varies from non-symptomatic forms through febrile illness to central nervous system disease. Although, it is one of the leading causes of meningitis and encephalitis, information about TOSV biology and epidemiology is limited. Based on the nucleotide sequences, TOSV is currently divided into 3 genetic lineages A, B and C; but the latter was only described based on partial sequences and virus isolate has never been obtained. Currently, there are only two species of sand flies (Diptera: Phlebotominae), *Phlebotomus perniciosus* and *P. perfiliewi*, considered as a proven TOSV vectors. However, the spread of TOSV to the new areas as well as the TOSV detection in several sand fly species suggested that the vector spectrum could be much broader. Here we aim to study in detail the vector competence of four sand fly species (*P. tobbi*, *P. sergenti*, *P. papatasi,* and *Sergentomyia schwetzi*) to two TOSV strains: 1500590 (TOSV A) and MRS20104319501 (TOSV B). Sand flies were infected by artificial feeding system with blood containing virus and fed females were collected and dissected at days 4, 8 and 14 after infection for virus quantification by infectious viral particles titration and RT-qPCR assay. First, we show that TOSV B appears to be more successful in development in sand flies than TOSV A. Moreover, *P. tobbi* with an infection rate of 66% and 53% at D4 and D8, respectively, seems to be the most susceptible species with a weak gut barrier to infection. In contrary, *P. sergenti* seems to be less susceptible to TOSV B with an infection rate of 5.5%, even though the virus disseminated in the head of all infected females. Additionally, *P. papatasi* and *S. schwetzi* appear to be refractory to TOSV B strain infection. In conclusion, our data suggest that two more sand fly species (*P. tobbi* and *P. sergenti*) are potential vectors of TOSV. In the context of climate changes and human activities, this information is crucial as sand flies are expected to expand to new areas, together with pathogens they carry.

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THE IMPACT OF CHRONIC SCHISTOSOMIASIS ON CO-INFECTIONS WITH DENGUE VIRUS IN MADAGASCAR

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Chronic schistosomiasis is highly prevalent in the tropics and can cause high morbidity. Research on the impact of this disease on morbidity caused by viruses circulating in the same areas, such as dengue virus (DENV), is scarce. Madagascar is a country highly endemic for schistosomiasis with only sporadic outbreaks of DENV. Our hypothesis is that chronic schistosomiasis might confer protection against DENV infections or dengue fever progression. A total of 990 serum samples, collected through a cross sectional study in schistosomiasis and DENV endemic regions of Madagascar have been collected and analyzed for Schistosome infection (59,5 %) and DENV/*Flaviviridae* seroprevalence (3,3 %/16,9 %) through an in-house PCR and pan-DENV IgG ELISA, respectively. Among them, 822 samples were used in a plaque reduction neutralization test (PRNT) to assess their potential to alter DENV infectivity. A significant reduction of the median plaque number in Schistosome-infected participants was observed and this effect remained significant when adjusting for other biological variables such as age and sex. In our Malagasy study population, we observed a low seroprevalence of DENV in a highly endemic schistosomiasis area. Our preliminary results corroborate our initial hypothesis of schistosomiasis interfering with DENV infections with the underlying molecular mechanisms remaining to be further investigated.

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MONITORING SURFACE CONTAMINATION WITH SARS-COV-2 AND INFLUENZA IN AN ADVANCED RESEARCH LABORATORY SETTING IN GHANA: A PROPOSAL FOR EFFECTIVE PREVENTIVE MEASURES

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The emergence of respiratory viruses such as SARS-CoV-2 and influenza presents significant challenges to public health. Understanding surface contamination and transmission dynamics within laboratory settings is crucial for implementing effective preventive measures. The aim of this study was to monitor laboratory surfaces contamination with SARS-CoV-2 and influenza viruses in an advanced research laboratory. We pre-moistened swabs with Virus Transport Medium and swabbed common shared surface areas in the laboratory environment, and its surroundings. Swabs were tested for the presence of SARS-CoV-2 and influenza viruses using real time RT-PCR with primers/probes and assays described by the CDC,USA . A total of 674 samples were collected from these surfaces between June 2023-April 2024 and tested. Out of this, 52% (352/674) were collected before commencement of work day and 48% (322/674) close of work. The distribution of swabbed surfaces were as follows: 16% (106/674) from lab benches, 8% (53/674) from biosafety cabinet used for RNA extraction, 8% (53/674) from biosafety cabinets used to prepare master mix only, 8% (53/674) from biosafety cabinets for template and positive controls addition only, 16% (106/674) from freezer door handles, 8% (53/674) from centrifuges and vortexes, 16% (108/674) from lab door handles and 5% (36/674) from a shared table used by all staff. Of the samples tested, 0.30% (2/674) SARS-CoV-2 RNA was detected from lab door handles before start of work day. The rest of the samples tested negative for SARS-CoV-2 and influenza. SARS-CoV-2 RNA was detected in the samples. Though not significant (p value = 0.397), the resultsshows the importance of such an attempt as it has implications for contamination and health of staff. Again, the fact that all other surfaces were negative for SARS-COV-2 shows strict adherence to decontamination procedures and good laboratory practices. This proactive approach will not only safeguard the health of research staff and limit contamination, but also provide valuable insights for similar settings globally. It is recommended that staff wash their hands prior to exiting laboratories.

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MULTIFACTORIAL CHARACTERIZATION OF DENGUE TRANSMISSION DYNAMICS IN THE FRENCH CARIBBEAN ISLANDS TO BETTER PREPARE FOR FUTURE EPIDEMICS

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Dengue is now the most widespread arboviral disease with incidence increasing more than 10-fold over the past 20 years, reaching a peak of 5.2 million cases in 2019, according to World Health Organization (WHO). The Americas are currently facing an unprecedented crisis, with more than 4 million cases of dengue recorded since the outbreak began in 2023, according to the Pan American Health Organization (PAHO). While it is endemic in all tropical and subtropical areas of the world, the Caribbean is one of the most affected regions, especially since the reintroduction of the *Aedes aegypti* vector in the 1970s. Since 2006, all four serotypes of dengue virus (DENV) have been detected during differents epidemics, with heterogeneous circulation in the French Caribbean islands (Guadeloupe and Martinique). During the recent outbreak in 2019-2021, three DENV serotypes were detected (DENV-1, DENV-2 and DENV-3), but curiously, their circulation was not homogeneous, with DENV-2 predominating in Guadeloupe, while DENV-3 was the main serotype circulating in Martinique. To investigate if genomic features of serotypes circulating in both islands were different, full genome sequencing was carried out on strains collected during the recent 2019-2021 outbreak in Guadeloupe and Martinique. Phylogenetic data revealed the homogeneous presence of genotype V for DENV-1, cosmopolitan genotype for DENV-2 and genotype III for DENV-3 in both French departments. To determine whether these differences in circulation of these viral strains are linked to a difference in vector transmission capacity, recent evaluations of vector competence of the 3 serotypes circulated during the 2019-2021 outbreak, as well as the current epidemic (DENV-2 only), were carried out on 6 populations (3 in Guadeloupe and 3 in Martinique) of *Aedes aegypti*, the local mosquito vector. Overall, these results confirm the active circulation of DENV in these regions, will help identify the factors inducing the epidemiological differences observed between the two islands and contribute to a better preparedness to cope with DENV emergences in the French Caribbean islands.

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A COMPREHENSIVE ANALYSIS OF COINFECTION DYNAMICS MODULATING MOSQUITO VECTOR COMPETENCE

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Arboviruses constitute a significant global health burden in part due to their complex ecologies and transmission dynamics. A growing area of interest towards controlling such pathogens are insect-specific-viruses (ISVs), as arbovirus-ISV coinfection has been shown to modulate vector competence, decrease viral titer, and block dissemination of medically important viruses. The biological mechanisms through which ISVs can impact arboviruses are poorly understood, but may include superinfection exclusion, sequestration of host factors, or effects on mosquito physiology. Studying these interactions can shed light on virus-virus interactions and vector competence within mosquitoes. However, such experimental approaches can be complex, and lack of standardization in data reporting makes comparison of outcomes across studies difficult to interpret. Through a comprehensive literature search we will collect and standardize coinfection experimental outcomes highlighting infection, dissemination, and transmission of arboviruses into a database. This database will support modeling networks for known ISV-arbovirus interactions in mosquitoes, which will be applied towards predicting ISVs that can suppress arboviral transmission. We will then test these predictions using *Aedes* sp. cell lines that have either competent or dysfunctional RNAi responses. Further testing will include additional *in-vitro* and mosquito colony experiments to validate modeling predictions and better understand ISV-arbovirus-vector interactions.

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MIDGUT ESCAPE OF YELLOW FEVER 17D VACCINE IN *AEDES AEGYPTI* AT AUGMENTED TEMPERATURES

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Yellow fever virus (YFV) is spread to humans by *Aedes* mosquitoes and is endemic in tropical regions of Latin America and Africa. Climate change projections predict a range expansion of *Aedes aegypti* and an increased risk of transmission to humans. In endemic regions, YFV outbreaks are mitigated using the highly safe and efficacious live attenuated vaccine, YFV-17D. Previous studies have addressed the competence of *Ae. aegypti* for YFV-17D. While this vaccine replicates in the mosquito midgut, it does not disseminate efficiently compared to wild-type YFV strains. For many *Aedes*-arbovirus pairings, increased temperatures alter vector competence. However, the impact of temperature on *Ae aegypti* vector competence for YFV-17D is poorly understood. Therefore, we exposed *Ae. aegypti* to YFV-17D and held them at varying temperatures (29°C, 32°C, and 34°C). On days 7 and 14 post-infection, we collected midguts, and legs and wings, then measured viral RNA using qRT-PCR to determine midgut infection and escape. We found a temperature-dependent increase in YFV-17D midgut dissemination; 54% of mosquitoes at 34°C had YFV-17D in their legs and wings compared to 8% of mosquitoes at 29°C. While mosquitoes had increased rates of dissemination at 34°C, they also displayed increased levels of virus in their legs and wings at both time points. This suggests that higher temperatures lead to both increased midgut escape and YFV-17D replication in *Ae. aegypti*. Ongoing research will characterize mechanisms of enhanced midgut escape at increased temperatures and determine whether YFV-17D can infect and escape the salivary glands, allowing for transmission. Additionally, we will sequence the virus to determine whether YFV-17D attenuating mutations are maintained through midgut escape.

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A SPATIALLY RESOLVED AND ENVIRONMENTALLY INFORMED FORECAST MODEL OF WEST NILE VIRUS AND ST. LOUIS ENCEPHALITIS VIRUS IN COACHELLA VALLEY, CALIFORNIA

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St. Louis encephalitis virus (SLE) is endemic to California and was detected annually until 2003 when West Nile virus (WNV) was identified in California. SLE was not detected again in California until 2015, and has been endemic since the recent introduction.. WNV and SLE exist in a complex transmission cycle that uses the same amplifying host, i.e., birds, and mosquito vectors. WNV is known to be a faster replicating virus, achieving higher viremias in both birds and mosquitoes. SLE, while slower, appears to be able to reach detectable transmission levels during periods when WNV transmission is low in the system, but it is still unclear how infection with one disrupts the transmission of the other. Preliminary analyses suggest that since the reintroduction of SLE to California in 2015, WNV and SLE transmission have occurred simultaneously. Like the dominance of WNV after its introduction in 2003, SLE outcompeted WNV from late 2015 when introduced and in 2016, possibly due to bird naïveté. In-season dynamics between WNV and SLE in mosquitoes may be dependent on when each

virus emerges, as both have the potential to outcompete the other and spillover to humans. Thus, a better understanding of how interactions of SLE and WNV impact the transmission cycle may improve our ability to predict arboviral risk and spillover events. This study builds on our previously developed multi-model inference system of WNV in Coachella Valley, California, and aims to incorporate and mathematically explain the interplay between WNV and SLE. We developed and tested a spatially resolved ensemble model to understand how fluctuations in environmental conditions influence WNV mosquito infection rates in the Coachella Valley. Using 17 years of mosquito surveillance data, we will compare how environmental conditions associated with WNV amplification change related to the SLE observed infection rates. Accurate early season predictions of arboviral risk have the potential to allow local abatement districts and public health entities to implement early season interventions such as targeted adulticiding and public health messaging before human transmission occurs.

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A DOUBLE THREAT TO ARTEMISININ-BASED COMBINATION THERAPY (ACT). EFFICACY IN AFRICA: REDUCED SUSCEPTIBILITY OF *PLASMODIUM FALCIPARUM* TO BOTH ARTEMISININ AND LUMEFANTRINE

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Clinical management of uncomplicated malaria caused by Plasmodium falciparum is reliant on the effectiveness of artemisinin-based combination therapy (ACT). New parasite genotypes encoding variants of the pfk13 gene are now emerging in Africa, and these are less susceptible to the artemisinin component drugs of ACT. This then poses a risk of resistance-selection against ACT partner drugs. Parasites of Ugandan origin isolated from two ACT-treated UK travellers with documented treatment failure, adapted to long-term culture in 2022, were less susceptible to lumefantrine in vitro than parasites from successfully treated individuals. This suggests that changes in parasite susceptibility to lumefantrine may contribute to treatment failure in these patients. Thus, the major African ACT, artemether-lumefantrine (AL), may now be at risk. We present a comprehensive assessment of in vivo treatment outcomes, in vitro parasite susceptibility to artemisinin and lumefantrine, and genomic and genotyping data from UK travellers with imported P. falciparum infections presenting from 2022 to 2024. This series includes 16 cases that suffered a relapse of symptomatic parasitaemia within weeks of initial treatment with AL. Future drug strategies for more effective malaria chemotherapy in Africa will be proposed in the light of these findings. Finally, we will consider the wider public health implications of a potential emergence of reduced lumefantrine susceptibility among African populations of P. falciparum.

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COMBINATION OF REDOX MODIFIERS WITH ARTEMISININ RESULTS IN INCREASED PARASITE SUSCEPTIBILITY TO ARTEMISININS

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Resistance has been recorded for every class of antimalarial, including artemisinin combination therapies (ACTs), the current first line. Drug resistant parasites have been reported to have an increased ability to manage oxidative stress and maintain redox homeostasis following drug treatment, possibly due to an enhanced antioxidant system. We hypothesised that disrupting this redox balance by targeting the parasites' glutathione pathway will make parasites more susceptible to oxidative stress, and therefore re-sensitise them to existing antimalarials. This work aims to tackle resistance by identifying redox-modifying drugs that can be combined with artemisinin derivatives. Growth inhibitory studies and ring-stage survival assays were used to determine the antimalarial activity of different redox compounds and to identify compounds that could be synergistic with artemisinin in vitro. Real time analysis of parasite intracellular glutathione was observed using *P. falciparum* NF54*attB*$^{[hGrx1\text{-}\ roGFP2]}$ parasite line and a plate reader based redox assay. Untargeted and targeted thiol metabolomic were carried out to identify metabolic changes in drug treated parasites. We identified sulforaphane (SFN) to be a promising candidate, which alters parasite redox status and potentiates the activity of artemisinin. The combination of 15μM SFN with 700nM dihydroartemisin (DHA) in early ring-stage parasites resulted in a decrease in parasite survival compared to DHA alone (41% ± 7.3).15μM SFN resulted in an increased oxidative burden within parasites after 1 h incubation. Untargeted and targeted thiol metabolomics confirmed that SFN's antimalarial activity is entirely redox mediated and not as a result of major metabolic changes within the parasite The addition of SFN to existing antimalarial therapies would re-sensitise resistant parasites to existing antimalarials thereby extending their life span. Ongoing studies will elucidate the mechanism responsible for this synergistic activity and determine the safety and efficacy of this approach in drug-resistant in vivo models of malaria.

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VARIABILITY IN ANTIMALARIAL DRUG SUSCEPTIBILITY PATTERNS IN KISUMU AND MARIGAT DURING THE PERIOD OF INCREASING FREQUENCY OF ARTEMISININ RESISTANCE GENOTYPES

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Malaria remains a major public health threat globally affecting 241 million people annually. Persistent malaria burden has been attributed to rapid emergence and spread of parasite resistance to policy recommended drugs. Consequently, timeliness of detecting drug resistance in diverse transmission regions is critical. This established susceptibility of *Plasmodium falciparum* parasites from Kisumu and Marigat between 2018 and 2023 using in vitro testing, genomic analyses and passive monitoring of treatment outcomes. A total of 637 consenting individuals aged 6 months and over, presenting with uncomplicated malaria were treated with Coartem® according to weight band and monitored on Day 7 to assess treatment outcomes. Up to 5mL whole blood samples collected from each individual prior to start of medication were latter tested for in vitro susceptibility to 14 antimalarial drugs. Each sample was tested for species composition, single nucleotide polymorphisms (SNPs)in drug resistance genes, and presence of residual parasitemia on day seven using genomic analyses techniques. 475/ 637 individuals comprising 385 from Kombewa and 90 from Marigat tested positive for malaria by polymerase chain reaction (PCR) assay. In vitro susceptibility showed mean ±standard deviation values of 25.1±32.5ng/ml for chloroquine, 32.7±22.3 ng/ml for quinine, 2.9±2.3 ng/ml for artemether and 40.0±38.3 ng/ml for lumefantrine. 70% of the infections contained P. falciparum single species infection while 30 % were contained P. falciparum species alongside other nonfalciparum species as multiple species infections. SNPs analyses showed three nonsynonymous mutation Pfk13 gene V568G, T508N and N554S in two samples and 36% mutation in PfMDR1-Y184F. PfMDR1 N86Y and Pfcrt K76T were wild-type for the entire study period. None of the day 7 visit samples tested positive for malaria by molecular diagnosis suggesting that all infections resolved after treatment with coartem®. Continuous monitoring of changing parasite susceptibility by in vitro and molecular methods is essential for early detection of resistance.

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MALARIA DIAGNOSIS AND DRUG RESISTANCE IN A MILITARY HOSPITAL IN YAOUNDE, CAMEROON

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The burden of malaria remains high in Cameroon, with almost 35% overall mortality. We studied diagnosis and drug resistance genes (DRG) for malaria in Yaounde military hospital, Yaounde, Cameroon. Microscopy, HRP2 Rapid Diagnostic Test (RDT), qPCR, and sequencing for DRG were used in this study. From March 2021 to December 2023, we enrolled 3,000 acute febrile illness cases (median age 35 years, 49% males). Microscopy identified 1,267 (42.2%) cases and had a higher positive detection rate than RDT (762 cases, 25.4%). qPCR identified 557(32.4%) cases out of 1,698 tested. HRP2 RDT negative cases had a mean of 43.9% in microscopy and in qPCR positive cases, suggesting a high prevalence of *pfhrp2* gene deletion and evidence for shifting from RDTs based only on HRP2. Sequencing for *Pfcrt*, *Pfcytb*, *Pfk13*, *Pfdhfr*, *Pfdhps*, *Pfmdr1*, and *Pfatp6* antimalarial DRG was done on a random set of 250 microscopy positive samples. For *Pfk13*, no mutations were observed in the propeller region, however, multiple mutations including G112E (4%), L116I (1%), K189T (58%), K189N (4%), L258M (1%) and R225K (1%) were noticed outside this region. *Pfatp6* mutant alleles H243Y (9%), L402V (14%), E431K (18%) and D436Y (1%) were detected. Wild type allele *cytB* was present in all samples. *Pfdhfr* haplotype N51I/C59R/S108N was detected in 95% of the samples, whereas C59R/S108N was observed in an additional 3%. *Pfdhps* mutant alleles were I431V (14%), S436A (37%), A437G (79%), K540E (2%), A581G (11%) and A613S (12%). *Pfcrt* new mutation C44F was noticed in all samples, K49Q in 0.8%, the triple resistant genotype (M74I/N75E/K76T) in 1.6% and M74I/N75D/K76T in 0.8%. *Pfmrd1* resistant genotype (N86Y) was found in 11% and the mutant allele Y184F in 75% of the isolates. Mutations associated with artemisinin and atovaquone resistance were not detected, suggesting efficacy of these drugs in Yaounde, whereas mutations conferring sulfadoxine-pyrimethamine resistance predominate. Finally, we noticed a decline in the prevalence of mutant chloroquine resistance alleles compared to previous decade. This study indicates a high prevalence of antimalarial DRG polymorphisms.

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INVESTIGATING *PLASMODIUM FALCIPARUM EX-VIVO* DRUG RESPONSES TO ARTEMISININ-BASED COMBINATION THERAPIES (ACTS) PARTNER DRUGS IN GHANA

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Antimalarial drug resistance poses a threat to malaria control. While artemisinin-based combination therapies (ACTs) are presently the most effective frontline antimalarials, signs of resistance are emerging in Africa. This includes resistance to artemisinin driven by mutations in *Plasmodium falciparum kelch13* gene and reduced efficacy of ACT partner drugs, but the extent of resistance to partner drugs such as AQ and LUM is not well understood. We assessed the *ex-vivo* sensitivity of clinical isolates cultured from individuals attending LEKMA or University of Ghana hospitals with confirmed malarial fever. We also determined the prevalence of known antimalarial drug resistance markers in these isolates using ONT-based amplicon sequencing. Mean 50% inhibitory concentrations (IC_{50}) results were below standard thresholds for resistance to CQ, DHA and AS, except one isolate that had mean IC_{50} values of 26.20 nM and 38.30 nM, above cutoffs for DHA and AS respectively. This isolate did not carry any validated *kelch13* mutations. Two isolates (4.08 %) and seven isolates (14.29 %) showed reduced susceptibilities to LUM and PPQ, respectively. About 29.50 % and 45.50 % isolates carried the combined *dhfr:dhps* quintuple mutant (IRNI-AGKAA) and quadruple mutant (IRNI-SGKAA) respectively. These combined mutant haplotypes are known to confer increased resistance to SP. In conclusion, we demonstrated that parasites are still sensitive to CQ, DHA and AS. However, there is emerging tolerance to LUM and PPQ that needs further investigation.

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AMPLICON DEEP SEQUENCING OF *PFKELCH13* GENE IN PATIENTS WITH *PLASMODIUM FALCIPARUM* MALARIA DURING THE THERAPEUTIC EFFICACY STUDY TRIALS FROM 2020 TO 2022 IN SENEGAL

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Senegal has used artemisinin-based combination therapy (ACT) to treat uncomplicated *Plasmodium falciparum* infection since 2006. Artemisinin (ART) resistance is mediated by mutations in the *Pfkelch13* (*PfK13*) gene and parasite genomic background modulates this resistance. Therapeutic Efficacy Studies (TES) demonstrate that ACTs including artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ) remain efficacious in Senegal. The appearance of ART resistance in Africa increases the urgency for ART resistance surveillance in Senegal. We used TES samples from Senegal to identify *PfK13* mutations among *P. falciparum* infections detected after day 0 (D0) of ACT treatment. We used amplicon sequencing of 400 TES samples from Kédougou, Kolda, and Kaolack (2020 - 2022). Participants were treated with AL or ASAQ on D0 with 28 (AL) or 42 (ASAQ) day follow up. Samples came from individuals that were parasite positive after D0, with priority given to pairs of samples (D0 and day of failure or DF). The 400 samples include 34 from 2020 (17 D0 + 17 DF); 22 from 2021 (11 D0 + 11 DF); and 56 from 2022 (28 D0 + 28 DF). We included an additional 288 DF samples from 2022. Samples were subjected to targeted amplicon sequencing of pooled and indexed samples. Sequencing data were aligned to the reference (PF3D7_1343700) sequence and four mutations in the propeller domain were identified from among the 400 samples. These variants and their frequencies included: V566L (0.25%), A578S (0.74%), V589I (0.25%), V637I (0.5%). An additional four mutations were found outside the propeller domain: T149S (0.25%), K189T (15%), K189N (1%), R255 (0.25%). None of these mutations are validated as associated with ART resistance. While new *PfK13* mutations need to be phenotypically tested for partial ART resistance, the appearance of DF infections may also result from partner drug resistance. Ongoing molecular surveillance for known and emerging malaria drug resistance mutations is important for detection of emerging risk and to identify novel mutations that may contribute to ART resistance in different genomic backgrounds.

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DISSECTING THE ROLE OF *PLASMEPSIN II AND III* IN PIPERAQUINE RESISTANT *PLASMODIUM FALCIPARUM* LINES

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Artemisinin (ART) combination therapies (ATC) are the current first line anitimalarials used world-wide. Resistance to both ART and the partner drugs like piperaquine (PPQ) are occurring and spreading in South East Asia. Major genetic determinants associated with recrudescence attributed to the partner drug PPQ are increased copy numbers of *plasmepsin II* and *III* and as well as mutations in the *chloroquine resistance transporter* (*pfcrt*). While mutations in *crt* were shown to be protective in vitro, experimental data on the role of plasmepsins in PPQ resistance is sparse. We have previously presented a bimodal growth response to increasing PPQ concentrations in PPQ resistant *Plasmodium falciparum* isolates from Cambodia in the absence of *crt* mutations. We chose the area under the curve (AUC) instead of the conventional half-maximal effective concentration (EC_{50}) used in drug assays to quantify the bimodal response. To specifically determine the role of plasmepsins in the response to PPQ, we used a relevant Cambodian isolate with a duplication in *plasmepsin II* and *III* but no mutation in *pfcrt*. Using this clonal isolate, we generated *plasmepsin II*, *plasmepsin III* and *plasmepsin II/III* combination KO lines with the CRISPR/Cas9 system. Our data demonstrate that a reduction in in *plasmepsin II* or *III* decreases the AUC three or six fold, respectively, compared to the parental line indicating direct involvement of *plasmepsin II* and *III* in the PPQ response at high concentrations. We detected a three to six fold increase in free heme in parasites treated with PPQ but no major differences between hemoglobin catabolism in parasite lines with different *plasmepsin* copy numbers. In contrast, changing the homeostasis of the food vacuole with pH modulators (CCCP or concanamycin A) did reduce survival under high PPQ exposure up to 50%. We demonstrated that increased *plasmepsin* copy number enhances survival under high PPQ pressure in Cambodian parasites and likely contributes to the emergence of resistance.

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POPULATION PHARMACOKINETICS OF ARTEMETHER-LUMEFANTRINE PLUS AMODIAQUINE IN PATIENTS WITH UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

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Uncomplicated falciparum malaria is commonly treated with an artemisinin-based combination therapy (ACT), which has contributed to the reduction of the worldwide burden of malaria. Resistance to the artemisinin component and to the partner drug in ACTs has been observed in Southeast Asia, and artemisinin resistance has recently also emerged in eastern Africa. 'Triple' ACTs, consisting of two partner drugs with different mechanisms of action and similar pharmacokinetic profiles, could help to counter the effects of artemisinin resistance and prolong the efficacy of partner drugs. When adding a new compound to a combination, assessments of potential drug-drug interactions are needed to verify that all components attain therapeutic levels while remaining safe. The analyses presented here used data from two randomized, controlled interventional trials conducted in 7 Asian and 1 African countries, in which artemether-lumefantrine was given with or without amodiaquine to patients with malaria. Both studies included a cohort with dense pharmacokinetic sampling, combined with sparse data from the rest of the patients. Concentration-time data of artemether, dihydroartemisinin, lumefantrine, desbutyl-lumefantrine, amodiaquine, and desethylamodiaquine were analysed using nonlinear mixed effect modelling, implemented in NONMEM. Pharmacokinetic models developed for all drugs showed that amodiaquine does not impact the pharmacokinetics of lumefantrine. The model demonstrated showed good predictive performance and goodness-of-fit. No clinically relevant drug-drug interactions were identified, indicating that dose adjustment is not necessary for the triple combination. Also, three different models describing the pharmacokinetics of artemether, lumefantrine, amodiaquine, and their respective metabolites were successfully developed. These models could be used to simulate the effects of altered dosing of this triple combination.

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MODEL-GUIDED STRATEGIES FOR MITIGATING ANTIMALARIAL DRUG RESISTANCE: BENEFITS OF EARLY ADOPTION OF TRIPLE ARTEMISININ-BASED COMBINATION THERAPIES IN UGANDA AND TANZANIA

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The emergence and spread of drug-resistance mutations in Plasmodium falciparum pose a significant threat to malaria control efforts worldwide. As resistance to artemisinin-based combination therapies (ACTs) continues to evolve, there is an urgent need to evaluate alternative treatment strategies to mitigate the impact of drug resistance. We used a mathematical model to simulate the spread of drug-resistant mutations, particularly the 561H, 469Y, and 675V mutations, associated with resistance to artemisinin, under different treatment scenarios. We compared the outcomes of continuing with artemether-lumefantrine (AL) as the first-line therapy, switching to the triple ACT artemether-lumefantrine-amodiaquine (ALAQ) at different timepoints, temporarily adopting artesunate-amodiaquine (ASAQ) as an interim measure, and other available drugs (e.g. DHAPPQ, extended doses for AL to 5 days) deployments in Uganda and Tanzania. Our model predicts that an immediate switch from AL to ALAQ would result in the lowest number of treatment failures over the next five years (2024-2029). Delaying the transition to ALAQ by four years could double or even triple the number of treatment failures. Furthermore, the earlier the adoption of ALAQ, the more effective it would be in delaying the spread of the kelch13 variants, with predicted frequencies of 0.35 (immediate deployment) and 0.5 to 0.65 (4-year delay) in Tanzania for 2029. For countries where ALAQ will not be available soon, temporarily switching to ASAQ (3-day treatment) emerged as a viable second-best option.

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INCREASING VALIDATED ARTEMISININ PARTIAL RESISTANCE MARKERS CONFIRMED IN ETHIOPIA DURING NATIONAL SENTINEL-BASED *PLASMODIUM FALCIPARUM* MOLECULAR SURVEILLANCE

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Ethiopia aims to overcome a recent resurgence of malaria cases and eliminate local malaria transmission by 2030. With the emergence of artemisinin partial resistance (ArtR) in Africa, molecular surveillance is critical to monitor the relevant drug resistance markers. This study reports the results of sentinel site-based molecular surveillance for antimalarial drug resistance mutations. Between 2020 and 2022, dried blood spots (DBS) were collected from febrile outpatients ≥6 months old with microscopically confirmed falciparum malaria at 12 sentinel sites across a range of transmission settings. Molecular inversion probe (MIP) sequencing was used to target mutations associated with artemisinin and partner drug resistance: *kelch13, pfmdr1, pfcrt, pfdhfr,* pfdhps genes, target genome-wide markers to assess complexity of infection (COI) and parasite relatedness. A total of 1,200 patients positive for *P. falciparum* was assessed. Median age was 20 years (IQR: 14-30), and 489 (40.8%) were female. In the Kelch 13 propeller, the R622I mutation is reported mutation reported at high prevalence (>16%, range (0-58.8%) with variability across regions. A 675V mutation (WHO-validated) was were reported for the first time in Ethiopia (<5%) in Gambella region. Additional validated (441L, 574L) and candidate markers (527H, 537A) were detected in low frequency. Moreover, several partner drug resistance markers were identified; mutations in *mdr1* (184F), *dhps*, *dhpr* and *crt* were nearly fixed across the country. Majority (87.2%) of genotyped samples carried monogenomic infections (COI=1) and were highly-related to evidence of genetic clustering at the health facility level. Principal component analysis showed evidence of parasite clustering at the regional clustering regional level with district clustering of Gambella parasites. These analyses confirm the high prevalence and expansion of 622I mutation and identify other validated markers (675V and 441L) that require further investigation. Detection of multiple ArtR suggest intensive monitoring of ACT efficacy in vivo for early identification of partner drug resistance and ACT failure.

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UNDERSTANDING THE BIPHASIC DOSE-RESPONSE CURVE ASSOCIATED WITH PIPERAQUINE RESISTANCE IN *PLASMODIUM FALCIPARUM*

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The recent failure of dihydroartemisinin plus piperaquine (DHA+PPQ) antimalarial combination therapy in Southeast Asia poses a significant threat to malaria control efforts. A unique *in vitro* characteristic of PPQ-resistant *P. falciparum* is a bimodal dose-response curve indicating increased parasite survival under high drug concentrations. Due to the unique shape of the dose- response curve, area under the curve (AUC) has replaced the traditional IC_{50} when assessing susceptibility to PPQ. Previous work identified that a combination of novel substitutions in the chloroquine transporter (PfCRT) paired with multiple copies *plasmepsin II/III* (*pm2/3*) are required to generate this bimodal curve, with additional copies of *pm2/3* associating with an increased AUC. To further investigate factors driving this novel phenotype, we modified the standard 72h drug exposure to adjust the stage at which parasites were initially exposed to PPQ (early ring, late ring, trophozoite, or schizont) as well as duration of drug exposure. We performed these experiments using the parents of a previously conducted genetic cross as well as several PPQ-resistant isolates which are unique both in PfCRT genotype as well as *pm2/3* copy number. Our results reveal that exposing late-stage parasites to PPQ eliminates the bimodal nature of the dose-response curve (AUC: $p < 0.001$) without any significant change in PPQ susceptibility (limited point IC_{50}: 22.4nM vs 23.5nM; $p = 0.235$). Furthermore, we paired additional phenotypes and measurements with the disappearance of the biphasic portion of the dose-response curve to further understand the biological factors which contribute to this novel phenotype.

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EX VIVO SUSCEPTIBILITY OF UGANDAN *PLASMODIUM FALCIPARUM* ISOLATES TO DIHYDROARTEMISININ AND THE NOVEL TRIOXOLANE LEAD RLA-4735

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Artemisinin partial resistance (ART-R) has emerged in eastern Africa and threatens the efficacy of artemisinin combination therapies. In an attempt to identify novel antimalarials with improved properties, we studied synthetic endoperoxides inspired by artemisinins, but potentially not subject to ART-R. We compared susceptibilities of *Plasmodium falciparum* isolates to dihydroartemisinin (DHA), the active metabolite of clinically relevant artemisinins, the synthetic trioxolane artefenomel, which has potent activity but formulation and PK challenges and RLA-4735, a trioxolane designed to address ART-R and solubility/formulation challenges. We collected 39 isolates from eastern Uganda in 2019 and 166 isolates from northern and eastern Uganda in 2023-24, all from subjects with symptomatic *P. falciparum* infection. Susceptibilities were determined using the *ex vivo* ring-stage survival assay (RSA: % survival, relative to controls, 66 h after a 6-hour 700 nM pulse of compound), and a 72 h growth inhibition assay (IC_{50}), with SYBR Green detection. For 2019, RSA median survival was 0% for DHA, artefenomel, and RLA-4735. Median IC_{50}s were 1.5 nM (range 0.5 - 3.3 nM) for DHA, 0.5 nM (0.04 - 3.3 nM) for artefenomel, and 2.6 nM (1.1- 7.4 nM) for RLA-4735. For 2023-24, RSA median survival was 5.3% (range 0.0%-39.1%) for DHA, 0.0% (0.0%-1.9%) for artefenomel, and 0.0% (0.0%-3.23%) for RLA-4735, and median IC_{50}s were 3.8 nM (0.4 - 12.8 nM) for DHA, 3.0 nM (0.01 - 31.7 nM) for artefenomel, and 3.6 nM (0.05 - 23.4 nM) for RLA-4735. RSA median survival was higher in 2023-24 than 2019 for DHA, consistent with spreading ART-R, but not for artefenomel or RLA-4735. Also, median IC_{50}s were higher in 2023-24 than in 2019 for DHA and artefenomel, but not for RLA-4735. In summary, RLA-4735 demonstrated potent activity with both the RSA and IC_{50} assays against Ugandan *P. falciparum* isolates over time, including against isolates with reduced DHA susceptibility. We speculate that reduced iron reactivity and prolonged parasite residence time due to exceptionally high protein binding explain the potent antimalarial activity and lack of susceptibility to ART-R of RLA-4735

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HIGH EFFICACY OF ARTEMETHER LUMEFANTRINE AND ARTESUNATE PYRONARIDINE WITH SINGLE LOW DOSE PRIMAQUINE IN ADULT PATIENTS WITH *PLASMODIUM FALCIPARUM* IN A SETTING WITH HIGH PREVALENCE OF MARKERS OF PARTIAL ARTEMISININ RESISTANCE AND *PFHRP2 OR 3* GENE DELETION IN ETHIOPIA: A SINGLE BLIND RANDOMIZED CONTROLLED TRIAL

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The emergence and expansion of *Plasmodium falciparum* (*Pf*) parasites with reduced sensitivity to artemisinins in East Africa threatens progress in malaria control. *Pf* parasites with *pfkelch13* 622I variant are uniquely reported in the Horn of Africa and may co-occur with deletions in *hrp2* and *hrp3* gene that allow parasites evade diagnosis by rapid diagnostic tests (RDT). In this study, *Pf* infected adult patients were followed for 42 days following the WHO therapeutic efficacy surveillance protocol, between December 2021 and July 2022, in a randomized two-arm prospective efficacy trial (Artemether-Lumefantrine [AL, n=101] or Pyronaridine-Artesunate [PA, n=98] plus primaquine [PQ]). Recurrent infections and paired samples were genotyped by targeting *Pfmsp2* and *Poly-α*, digital PCR was used to genotype *pfhrp2/3* gene deletion, and *pfkelch13* and *pfmdr1* genes were sequenced on Illumina iSeq100. No early treatment failures were observed in both arms. All but one patient in the AL arm cleared their microscopy detectable parasites by day 3 whilst late parasitological failure (LPF) was observed in 11 patients (day 21-42) of which 8 were confirmed recrudescences. PCR-adjusted treatment success were 97.8% (AL) and 98.9% (PA) on day 28 and 94.2% (PA) on day 42. The *pfkelch13* 622I variant was detected in 62.5% (5/8) of the paired recrudescent infections but not in confirmed reinfections. The *pfmdr1* NFD haplotype (86, 184, 1246) linked with lumefantrine failure was detected in all LPF samples. At recruitment, 41.6% (82/197) of infections were HRP2-based RDT negative of which 68.3% (56/82) were *pfhrp2* gene deleted. Although numbers were small, the *pfkelch13* 622I variant was detected more in *hrp2/3* gene deleted (71.4%, 5/7) than wild type (50%, 7/14) infections. Both AL and PA with PQ were efficacious for the treatment of uncomplicated *Pf* malaria in adults in a setting with rapid expansion and co-occurrence of parasites with *pfkelch13* 622I mutation and *hrp2/3* gene deletions. The findings in this study call for further detailed investigation to include children, assessing efficacy without adding PQ, and preparing for action such as multi-first line treatments.

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EXPLORING THE *IN VITRO* PHARMACOLOGY OF 8-AMINOQUINOLINE ANTIMALARIAL COMPOUNDS.

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The 8-aminoquinolines are the only licenced drug class for the treatment of relapsing malaria. Key members of the class include currently licenced primaquine and tafenoquine; as well as legacy compounds: pamaquine and pentaquine. The hypothesised mode of action for primaquine comprises a 2-step biochemical relay: (1) Cytochrome P450 (CYP)-mediated (predominantly CYP 2D6) metabolism into reactive intermediates; and (2) redox cycling of metabolites with CYP reductase (CPR) to form anti-parasitic levels of Reactive Oxygen Species (ROS). This work investigated whether this mechanism is class-wide; scrutinising CYP-mediated metabolism of, and subsequent ROS production from the 8-aminoquinolines. This study provides a thorough exploration into the physicochemical and pharmacological properties of 8-aminoquinolines and clinically relevant combination partners. Key DMPK analyses include hepatic metabolism with HμREL® co-culture clearance assay and investigations into CYP-specific metabolism, inhibition, and induction. Preliminary data into the pharmacodynamic mechanisms of 8-aminoquinoline action includes the measurement of CYP-mediated ROS using Pan-CYP and CYP-specific inhibitors and measures of cellular oxidative stress including Haem Oxygenase-1, as well as interrogation of *in vitro* efficacy using a *Plasmodium cynomolgi* liver stage assay. Evidence is presented in support of a divergent bioactivation step (1), and convergent ROS-mediated step (2) in the mechanism of action across the 8-aminoquinoline class, with tafenoquine not showing hepatic metabolism or CYP-mediated ROS production. Tafenoquine licencing now requires compulsory co-administration with chloroquine due to treatment failure with alternative regimen, piperaquine-dihydroartemisinin. This study suggests that these drug-drug interactions are unlikely to be CYP-mediated for both primaquine and tafenoquine. Ongoing research is underway to confirm the potentiating effect of chloroquine, and inhibitory effect of dihydroartemisinin on the redox-related efficacy of 8-aminoquinolines.

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THERAPEUTIC EFFICACY AND SAFETY OF ARTEMETHER LUMEFANTRINE (AL) AND ARTESUNATE AMODIAQUINE (ASAQ) FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN KAGERA REGION, TANZANIA 2023

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The World Health Organization (WHO) recommends pre-emptive antimalarial diversification to limit drug pressure and, when drug efficacy falls below 90%, a change in national policy. Artemisinin partial resistance (APR) and low uncorrected artemether-lumefantrine (AL) efficacy, are each indicative of increased pressure on lumefantrine. In 2022, Tanzania confirmed APR in Kagera region, and <90% AL efficacy in Pwani region. Low uncorrected efficacies have also been reported in Kagera, Pwani, Tanga (2022); and Tabora (2023) regions. We conducted this TES to

assess APR in Kyerwa district, neighboring Karagwe district and Kayonza district, Rwanda, which reported APR in 2015 and 2018. Children aged 6 months to 10 years were recruited in Kyerwa, treated with AL or artesunate-amodiaquine (ASAQ), and followed for 28 days to assess drug efficacy as per the 2009 WHO protocol. The primary outcome measure was polymerase chain reaction (PCR)-corrected efficacy using a 3/3 *msp1/ msp2/glurp* approach with gel electrophoresis. Parasite clearance rate and day 7 lumefantrine concentration levels were assessed. From June 2023 to January 2024, 176 participants (88 AL, 88 ASAQ) were enrolled; 87 (98.8%) AL and 88 (100%) ASAQ reached an endpoint. Respective uncorrected and corrected Kaplan-Meier efficacies for AL were 73.6% and 96.6% and 100.0% and 100.0% for ASAQ. Day 3 parasitemia was observed in 27 (15%): 8 (9.2%) AL, 19 (21.6%) ASAQ. The median parasite clearance half-life was 3.19 hours for AL and 3.04 hours for ASAQ. There was no association between day 7 lumefantrine concentration and malaria reinfection risk (hazard ratio=1.25, p=0.614). Genotyping for *k13* is ongoing to confirm APR. With high day 3 parasitemia, low uncorrected efficacy, and regional findings of APR in neighboring Rwanda and Uganda, which both use AL as first-line, a switch from AL to an alternate first-line ACT (ASAQ, Dihydroartemisinin Piperaquine) in Tanzania treatment guidelines should be considered as per WHO guidance. ASAQ's 100% efficacy and antagonistic selective resistance mechanism make it a strong replacement candidate for AL.

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THE UTILITY OF QPCR ESTIMATION OF PARASITE DENSITY IN EVALUATING THE EFFECT OF SULFADOXINE-PYRIMETHAMINE AS PERENNIAL MALARIA CHEMOPREVENTION

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Perennial malaria chemoprevention (PMC) is a strategy recently updated by the World Health Organization to protect infants from malaria infections contributing to the overall reduction of disease burden. To evaluate these guidelines, the Plus Project investigates the effect of PMC with sulfadoxine-pyrimethamine (SP) in countries such as Cameroon and Côte d'Ivoire. qPCR is a more sensitive diagnostic method than point of care rapid diagnostic tests (RDT) and microscopy despite not readily operationalized for use in national programs. Thus, those can lead to false or missed diagnosis and underestimating the number of malaria cases. Therefore, this study aims to assess the sensitivity of qPCR and how programmatic tools compare with this molecular diagnostic method in measuring the impact of PMC. This study is nested within a larger study conducted in Côte d'Ivoire (regions Seguela and Cani) and Cameroon (regions Mbankomo and Soa) between July and August of 2023. A subset of samples from children aged aged between 10 weeks and 6 months (Côte d'Ivoire) or 6 and 9 months (Cameroon) were selected from 'cases' (children having the opportunity to take the expanded PMC-SP dosing) and controls (children who received standard of care). All children were tested for malaria using RDTs and microscopy, followed by blood spots collected on filterpaper. A highly sensitive qPCR method targeting *Plasmodium falciparum cytochrome ß* gene was employed to confirm and estimate parasite density. Additionally, conducted *Plasmodium* speciation to further explore the presence of non-Pf malaria cases. A total of 230 and 59 patients were positive by both RDT and microscopy in Côte d'Ivoire and Cameroon, respectively. Among those samples, 67.8% and 64.4% were positive by qPCR, with an estimated median parasite density of 401 (range: 6 - 110,256) and 501 parasites per microlitre (range 5 - 29,338), respectively. Further analysis will be conducted to evaluate the correlation between microscopy density and Ct values. The study will provide data on the diagnostic capacity of RDT and microscopy, and the utility of qPCR as an additional tool to evaluate the impact of interventions.

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COMPARATIVE EVALUATION OF ANTIMALARIAL DRUG EFFICACY IN THREE STUDY SITES IN MALI

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Malaria remains a significant public health threat in Africa. The increasingresistance of *Plasmodium falciparum* parasites to available antimalarial treatmentsunderscores the urgent need for new therapeutic strategies. Some drugs previouslywithdrawn due to observed resistance are now being reconsidered for their potential utilityin certain regions due to the dynamic landscape of parasite resistance. This study aims toassess the efficacy of 15 antimalarials, categorized into three groups: drugs withdrawn due toresistance, currently used drugs, and new drugs under investigation. The goal is to explore theevolving efficacy of these treatments in the face of changing resistance patterns andpotentially reintegrate withdrawn drugs into effective treatment regimens. *P. falciparum* parasites were collected from three sites in Mali (Kolle, Bougoula-Hameau, and Faladje) and analyzed in a laboratory in Bamako. Each drug was tested on freshlycollected parasites, followed by a staining process using SYBR Green and Mitotracker. Thedrugs' efficacy was assessed by measuring parasite viability with flow cytometry, whichprovided data to estimate each drug's 50% inhibitory concentrations (IC50). We anticipate significant variability in the efficacy of antimalarial drugsacross the study sites, reflecting the genetic diversity of *P. falciparum* strains and their levelsof resistance. New-generation medications are expected to show higher efficacy againstresistant strains, offering promising prospects for malaria treatment. This study will provide critical insights into the efficacy of antimalarial drugs indifferent study sites. It has the potential to inform on the current status of used antimalarialsand support the development of tailored strategies with new ones.

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MINIMUM INOCULUM OF RESISTANCE STUDIES TO SUPPORT ANTIMALARIAL DRUG DISCOVERY

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Malaria remains a significant global health burden with an estimated 249 million cases and 608,000 deaths as of 2022. The emergence and spread of *Plasmodium falciparum* parasites resistant to multiple first-line drugs makes it imperative to develop new therapeutics with novel modes of action. Minimum inoculum of resistance (MIR) studies applied to candidate drugs provide a powerful tool to quantitatively assess the risk of resistance and measure its phenotypic impact in vitro. These experiments often extend to the identification of resistance mediators, a subset of which are drug targets. Here, we present our MIR studies on five different targets: dihydroorotate dehydrogenase (PfDHODH), ATPase4 (PfATP4), translation elongation factor 2 (PfeEF2), acetyl CoA synthetase (PfACS),

and phosphatidylinositol-4 kinase (PfPI4K), targeted by the compounds DSM265, KAE609, M5717, MMV019721 and MMV390048, respectively. Data from these results can be used to predict whether resistance would be quickly selected in the field. Compounds with robust MIR data can be used as a positive control for studies to assess the resistance liabilities of candidate therapeutics.

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RISK OF SELECTION AND TIMELINES FOR THE CONTINUED SPREAD OF ARTEMISININ AND PARTNER DRUG RESISTANCE IN AFRICA

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The introduction of artemisinin combination therapies (ACTs) has significantly reduced the burden of *Plasmodium falciparum* malaria, yet the emergence of artemisinin resistance (ART-R) as well as partner drug resistance threatens these gains. Recent confirmations of *de novo* ART-R markers in Africa, in particular in Rwanda, Uganda and Ethiopia, underscore the urgency of addressing this issue in Africa. Our objective is to characterise this evolving resistance landscape and understand the speed with which ART-R will continue to spread in Africa. We use a mathematical modelling approach to evaluate the risk posed by ART-R and explore scenarios for how ART-R will continue to spread in Africa. We incorporate current best estimates of both ART-R and partner drug resistance by bringing together WHO, WWARN and MalariaGen Pf7k data on antimalarial resistance in combination with a literature review to estimate model parameters known to impact the selection of ART-R for each malaria-endemic country. We identify 12 malaria endemic countries in Africa to prioritise for surveillance and future deployment of alternative antimalarial strategies, based on quickly selecting for ART-R once established. In scenarios designed to explore the continued spread of deletions in Africa, we identify 9 high-threat countries (Djibouti, Ethiopia, Kenya, Malawi, Rwanda, Sudan, Tanzania, Uganda, Zambia) that are most at risk of ART-R both spreading to and subsequently being rapidly selected for. In these 9 countries, under a range of scenarios, we predict that ART-R will spread out from the current hotspot in Central Africa, and within 30 years will replace the majority of parasites (>50% frequency). Our results provide a refined and updated prediction model for the emergence of ART-R in an effort to help guide antimalarial policy and prioritise future surveillance efforts and innovation. These put into stark context the speed with which antimalarial resistance may spread in Africa if left unchecked, confirming the need for swift and decisive action in formulating antimalarial policies focused on containing ART-R in Africa.

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GENOMIC SURVEILLANCE OF *PLASMODIUM FALCIPARUM* IN GOLD MINING AREAS IN THE BRAZILIAN AMAZON BASIN

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There is an association between gold mining activities, deforestation and increase in the number of malaria cases, as observed in the Brazilian Amazon. In Brazil, about 140,000 cases of malaria were reported in 2023, and the state of Pará contributed 17% of this burden. In this state there was a 21% increase in gold mining areas and a concerning 132% increase in the number of *Plasmodium falciparum* cases. Difficulties in accessing diagnosis and low adherence to treatment increase vulnerability to malaria, contributing to resistance of parasites to antimalarials. Deletions in the *pfhrp2/3* genes can impact the performance of rapid diagnostic tests. These factors pose challenges to malaria control and elimination. We analyzed 49 blood samples from patients infected with *P. falciparum* in gold mines located in Pará, Brazil. After DNA extraction, the samples were analyzed through semi-nested PCR and the fragments obtained were resolved by gel electrophoresis. The prevalence of deletions in *pfhrp2/3* genes was 6.12%. We assessed the prevalence of drug resistance markers in *P. falciparum* by carrying out a targeted amplicon sequencing protocol using the MinION platform from Oxford Nanopore Technologies. Multiplex PCR with specific primers for each gene was followed by sequencing. Mutations associated with *P. falciparum* resistance were detected in all isolates, with mutations for chloroquine (*pfcrt* K76T, C72S, and *pfmdr1* Y184F), for pyrimethamine (*pfdhfr* N51I and S108N), and for sulfadoxine (79% with double mutations - *pfdhps* A437G and A581G and 21% with triple mutations - A437G, A581G and K540E). No mutations associated with artemisinin resistance (*pfkelch13*) were found. Although no mutations associated with resistance to artemisinin have been detected, the misuse of antimalarials or illegal medicines poses a threat to the emergence of resistance to this antimalarial or partner drugs. Furthermore, deletions in the *pfhrp2/3* genes significantly impact the use of rapid diagnostic tests, which are crucial for diagnosis, especially in remote areas. These findings highlight the importance of ongoing genomic surveillance in malaria-endemic regions.

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LEVERAGING A *PLASMODIUM FALCIPARUM* GENETIC CROSS TO IDENTIFY CANDIDATE DETERMINANTS OF MULTIGENIC RESISTANCE TO QUININE AND CHLOROQUINE

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The emergence of *Plasmodium falciparum* strains showing partial resistance to artemisinin (ART) in multiple countries in east Africa poses a substantial threat to malaria treatment. ART derivatives constitute the core component of first-line combination therapies to treat uncomplicated malaria and are used to treat severe disease. Should ART resistance spread, alternative drugs will be required, yet the options are limited. The WHO recommends quinine (QN) as an option for treating severe malaria when artesunate or artemether are not available or are contraindicated. Moderate *P. falciparum* resistance to QN has been reported, but its genetic basis has remained elusive. We conducted a genetic cross between the QN-resistant Cam3.II parasite and the drug-sensitive NF54 parasite, using human liver-chimeric FRG-NOD mice. This cross yielded 120 independent recombinant progeny. Phenotypic analysis of progeny, combined with whole-genome sequence data, enabled us to apply quantitative trait loci mapping to identify regions associated with QN resistance. Our results identified a segment on chromosome 7, which for both IC_{50} and IC_{90} analyses included *dmt1* that encodes a putative drug/metabolite transporter. IC_{50} (but not IC_{90}) analyses also associated the QN response with mutant *pfcrt*, located 200 kb upstream of *dmt1*. Genetic disruption of *dmt1* sensitized Cam3.II parasites to QN, and transport studies with proteoliposomes reconstituted with recombinant mutant DMT1 showed evidence of QN transport. These data implicate *dmt1* as a component of a multigenic basis of QN resistance. We also identified a peak on chromosome 12, whose genes include mutant *ftsh1* that is a potential resistance mediator. This chromosome 12 peak was also associated with CQ resistance in addition to the dominant *pfcrt* peak on chromosome 7. Our data reveal a multigenic basis of QN resistance and identify a potential new modulator of mutant *pfcrt*-mediated CQ resistance.

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THE GULART STUDY: A CROSS-SECTIONAL SURVEY OF ARTEMISININ PARTIAL RESISTANCE AND SPECIES DIVERSITY IN FIVE NORTHERN UGANDAN DISTRICTS

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Partial resistance to artemisinin derivatives, vital drugs in the treatment of malaria, has emerged in multiple East African countries and is linked to mutations in the *Plasmodium falciparum* (*Pf*) Kelch 13 protein (*Pfk13*). Published studies in Uganda have relied on convenience sampling, which are unable to provide an estimation of community-level prevalence. We employed a GIS-based two-stage cluster randomized cross-sectional survey of n=598 asymptomatic children <5 years in five districts of Northern Uganda: Gulu (n=180), Amuru (n=113), Lamwo (n=101), Pader (n=90), and Omoro (n=114) from Aug 2022 to Jan 2023. In addition, we sampled n=102 patients presenting with uncomplicated malaria at the Gulu Regional Referral Hospital (GRRH). In the asymptomatic community cohort, 54.2% were male, and the mean age was 1.9 yrs (SD=1.4). 44.1% (n=263) were positive for *Pf* by PfHRP2-based RDT and 54.3% (n=325) were positive for any *Plasmodium spp.* infection by real-time PCR. While the majority (66.8%; n=217/325) were positive for *Pf*, we found a strikingly high burden of *P. ovale* species (*Po*): 31.4% (n=102) were *Po* mono-infections and 22.2% (n=72) were *Pf-Po* co-infections. An additional 4.0% were *Pm* (n=13) and 0.6% (n=2) were *Pv* infections. Of the n=102 diagnosed as uncomplicated malaria cases at GRRH, a surprising n=32 were *Po* mixed or mono-infections by RT-PCR. Apart from *Pf* and *Po*, no other species were detected among symptomatic patients. Our study reveals a striking community-based prevalence of *Po* in children sampled in all districts, including in individuals presenting for care with symptomatic disease at GRRH. In addition, *PfK13* was successfully amplified by PCR for n=158/217 of *Pf*+ community samples. Thus far, C469Y has been identified by high-resolution melting (HRM) in our community samples. Further work, namely HRM and NGS, is underway to complete characterization of circulating *PfK13* haplotypes in the community. Together, these data present a complex scenario in Northern Uganda which necessitate urgent changes in malaria diagnostic and treatment policies in the region.

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DIAGNOSIS OF *PLASMODIUM* SPECIES USING A.I. TECHNIQUES VERSUS STANDARD MICROSCOPY

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Malaria diagnosis using standard techniques is challenging and time-consuming, leading to discrepancies and delays. Innovative technologies utilizing advanced technologies are changing the diagnostic landscape. The miLab™MAL, an automated malaria diagnostic solution, was compared with standard microscopy at Labcorp® reference laboratories. 409 samples submitted for parasitic examination were prepared with thick and thin smears and Noul's malaria diagnostic solution, miLab™MAL, and evaluated for positivity, negativity, and speciation. 399/409 samples were manually negative, while 397/409 were negative by miLab™MAL. Two samples initially classified as negative manually were found positive by miLab™MAL. Upon re-examination of the peripheral smear, very rare trophozoites, constituting less than 0.1% of the erythrocytes, were identified in both samples. In nine out of ten cases, *Plasmodium falciparum* was identified by both methods. In one case, *Babesia sp.* was identified by microscopy, but miLab™MAL identified *Plasmodium falciparum*. Our studies show that miLab™MAL was accurate in identifying the presence or absence of *Plasmodium*. All positive samples detected by microscopy were also identified with miLab™MAL. The miLab™MAL also showed greater sensitivity than the manual method. All cases negative for *Plasmodium* by microscopy were also negative by the miLab™MAL method (100% specificity), indicating that intraerythrocytic inclusions were not confused with malarial parasites. The miLab™MAL correctly identified *Plasmodium falciparum* species in 11/12 cases compared to the 10/12 cases by standard microscopy. Because machine learning tools for Babesia were not programmed into the miLab™MAL, this led to the discrepancy. Based upon the study's findings, miLab™MAL can be used to screen out negative *Plasmodium* samples. Since the positivity rate for malaria in reference laboratory specimens is low, resources can be saved using this technology. Due to the limited number of positive samples (n=12), further studies in malaria-endemic areas are necessary to assess the reliability of *Plasmodium* speciation.

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GENOTYPING OF PLASMODIUM FALCIPARUM MEROZOITE SURFACE PROTEIN 2 (PFMASP-2) REVEALED DIFFERENT ALLELIC PROFILES IN BLOOD AND SALIVA SAMPLES FROM MFOU HEALTH DISTRICT IN CAMEROON

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Monitoring Genetic diversity of malaria parasites might help address constant emergence of resistance of *Plasmodium falciparum* to antimalarials. the usefulness of Pf*MSP2* to monitor *P. falciparum* polymorphism is hampered by the lack of non-invasive sample collection method. In the current study we sought to assess the suitability of saliva as a biological material to assess the diversity of *P. falciparum*. To this end, we collected total of 27 saliva and 50 blood specimens from malaria positive patients at Mfou health district, Cameroon. Genomic *Plasmodium* spp. DNA was extracted from blood and saliva samples, and used in nested-PCR to detect the presence of *P. falciparum* and the different alleles of *Pfmsp-2*. The presence of *P. falciparum* was confirmed by nested PCR with a positivity rate of 94% (47/50) and 88.88% (24/27) in blood and saliva samples respectively. Altogether, 14 different alleles of the *Pfmsp-2* gene with bands ranging between 279-1178bp were detected in blood. The genetic diversity and multiplicity of Infection (MOI) of *Pfmsp-2* was 10.61% and 2.81 respectively in blood samples. In contrast, only 6 alleles of the *Pfmsp-2* gene with bands ranging between 450-708pb were detected in saliva samples. Here, the genetic diversity of *Pfmsp-2* gene and the multiplicity of infection were 35.29% and 1.33 respectively. Quadruple allelic infections (4 types of alleles) were predominant (29,78%) in blood, while single allelic infections (1 allele) were predominant in saliva (86,67%). These results demonstrated the use of saliva as specimen for investigating genetic diversity endemic area. Furthermore, our findings depict an extensive genetic diversity of Pfmsp-2 observed in Mfou and it could herald the rise and spread of drug resistant strains of *P. falciparum* which could have implication in MSP2-based vaccines efficacy in this locality.

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POINT-OF-CARE TEST OF BLOOD *PLASMODIUM* RNA WITHIN A PASTEUR PIPETTE USING A NOVEL ISOTHERMAL AMPLIFICATION WITHOUT NUCLEIC ACID PURIFICATION

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We present Pasteur Pipette-assisted Isothermal Probe Amplification (pp-IPA), a novel molecular point-of-care test (POCT) for malaria detection in resource-limited settings. In this approach, specific, tailed probes capture released 18S rRNA of *Plasmodium* onto the inner wall of an oligo-conjugated Pasteur pipette through sandwich hybridization. After

washing off impurities and unbound probes, the bound tailed probes are ligated to form complete dumbbell-shaped templates for subsequent isothermal amplification using a pair of primers, bypassing nucleic acid extraction and reverse transcription. The entire assay takes 60 - 80 min to complete requiring only a Pasteur pipette and a water bath. Experimental results confirm pp-IPA's analytical sensitivity to be $1.28*10^{-4}$ parasites/µl, a sensitivity 3 - 4 orders of magnitude higher than existing molecular POCT methods for malaria, with 100% specificity against various blood-borne pathogens causing malaria-like symptoms. Additionally, pp-IPA needs only liquid-transfer skill for operation and the cost for per test is around $0.25. pp-IPA's simplicity, affordability, high sensitivity/specificity, and minimal equipment requirement make it a promising point-of-care pathogen identification tool in resource-constrained regions.

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MOLECULAR AND SEROLOGICAL ANALYSIS OF AFEBRILE *PLASMODIUM FALCIPARUM* INFECTION IN SOUTHERN MOZAMBIQUE: A PROSPECTIVE COHORT

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Afebrile *Plasmodium falciparum* (*Pf*) infections have a debilitating impact on health and represent a hidden source of transmission that can compromise malaria elimination efforts. Understanding the dynamics and biological factors that maintain parasite-host interactions at the subclinical level would contribute to the ongoing debate on the relevance of afebrile infections as a barrier to malaria elimination, and guide the use of interventions to reduce this silent reservoir. In this study, healthy Mozambican individuals were screened at household level using a rapid diagnostic test (RDT) to detect Pf infection. Positive cases were confirmed microscopically and followed up for 28 days (daily visits for the first 4 days and weekly visits until the 28th day) during the 2020-23 rainy season. Antimalarial treatment was administered either upon reaching the end of the follow-up period or in response to clinical symptoms occurred before day 28. Blood samples and basic clinical-demographic information were collected at every visit. Samples were analysed using a combination of genetic and serological tools. The longitudinal analysis used data from 146 of the 177 enrolled individuals, excluding individuals with less than 3 observations on days 7, 14, 21 and 28. Seventeen of the 146 participants (11.6%) spontaneously cleared the infection and 11 (7.5%) developed fever during the follow-up. In 34 participants (23.3%), parasite densities and HRP2/LDH levels decreased dramatically and stabilized at low levels (i.e. below the geometric mean of the clearance samples), whereas in 28 participants (19.2%) they increased and stabilized at high density levels (i.e. above the geometric mean of the fever samples). In 56 participants (38.4%), parasite densities and HRP2/LDH levels were maintained at intermediate levels. Thus, approximately half (57.6%) of the afebrile RDT-detected infections maintained densities with high transmission potential. Ongoing molecular and serological characterization will provide further insight into the parasitological and immunological factors linked to disease progression in areas of low malaria transmission.

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MALARIA PREVALENCE AMONG PATIENTS ATTENDING TWO HEALTH CENTRES IN IKWUANO L.G.A, ABIA STATE, NIGERIA USING BLOOD AND URINE SAMPLES

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Malaria, a life threatening disease caused by the protozoa of the genus Plasmodium is transmitted to man through the bites of infected female Anopheles mosquitoes. The study was done between July and December, 2023 to determine the prevalence of malaria among patients attending Amawom and Umudike health centres using the conventional microscopy and RDT kit methods. Two mls of venous blood and 200 ul of urine were collected from 200 patients who gave their consent using sterile syringes for blood and sterilized dry mouthed cork screwed plastic containers for urine. Blood was dispensed into EDTA bottles and gently mixed. Blood samples were examined using conventional microscopy for thin and thick blood smears and Carestart TM strip for blood while urine test was done with SD Bioline strip. The overall prevalence of malaria with microscopy was 24.0% while RDT for blood and urine were 12.0% and 10.5% prevalences respectively. More males (27.3%) than females (20.8%) were infected. The age group 20-30 years recorded more infection (32.6%). The need for development of new, simple, quick, accurate non invasive and cost-effective diagnostic tests for malaria can be complemented by the use of RDTs, especially RDT for urine for non-invasive approach, since the results of RDTs used in the study have shown their usefulness as a rapid and simple tool for malaria diagnosis. This also promises to be a useful diagnostic tool that can be deployed for use in poor resource settings where regular supply of electricity and absence of an expert microscopist can be challenges to the use of microscopy

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STRENGTHENING THE QUALITY OF MALARIA MICROSCOPY THROUGH A CASCADE TRAINING MODEL IN TANZANIA

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In 2023, >1 million malaria microscopy tests were conducted in high-burden Mainland Tanzania and 35,550 were conducted in Zanzibar, an elimination-targeted area. However, there were no certified expert microscopists, and only 70.1% of health facilities (HFs) performed satisfactorily on malaria microscopy during Malaria Service Delivery and Quality Improvement (MSDQI) evaluations. We assessed the impact of a cascade model to expand the cohort of certified microscopists at HFs. A cohort of 12 microscopists underwent WHO-External Competency Assessment of Malaria Microscopy (ECAMM) expert certification. This expert cohort was further expanded with those passing advanced malaria diagnostic refresher training (MDRT) and ultimately served as MSDQI supervisors, quality improvement mentors, and administrators of laboratory external quality assurance (EQA) proficiency testing (PT), and basic MDRT. We used EQA PT and MSDQI evaluations to assess microscopy performance improvement of those trained with the cascade model. The 12 expert microscopists conducted 9 MDRT trainings, resulting in a total of 177 trained microscopists, and expanding the expert cohort by 25. In Zanzibar, 85 PT rounds conducted by this expert cohort demonstrated significantly improved scores from 84% to 92% in parasite identification (PID), 18% to 54% in species identification (SID), and 32% to 45% in parasite counting (PC) ($p<0.001$ for all PT). In mainland, 11 PT rounds demonstrated improved scores from 93% to 100% in PID, 64% to 77% in SID, and 43% to 50% in PC, but did not reach significance. In the same period, microscopy performance in 14 Mainland HFs receiving supervision and mentorship from the expanded cohort significantly improved MSDQI scores from 40% to 92% in smear preparation and staining ($p<0.001$); 60%

to 100% in slide examination; 33% to 71% in PT enrollment ($p<0.001$); and 33% to 57% in internal quality control performance. This cascade training model rapidly established a cohort of expert microscopists who, in turn, significantly expanded the cohort of trained microscopists and contributed to significant improvements in HF PT nationwide.

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MALARIA MICROSCOPY EVALUATION AND QUALITY ASSURANCE IN RURAL CLINICS IN WESTERN KENYA

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While rapid diagnostic tests are widely used, they have several limitations, and blood smear (BS) examination by microscopy remains the gold standard for malaria diagnosis. However, poor quality reagents, limited technical capacity, and turnaround times all threaten the ability to reliably provide accurate results in public health facilities (HF) in malaria endemic areas of Kenya. To assess the quality of malaria microscopy, we evaluated the concordance of BS results at 28 HF with expert microscopy in Siaya County, western Kenya. At each HF, the quality of reagents, slide preparation, standard operating procedures availability, and infrastructure (electricity and microscope) were documented. Approximately 20 patients per HF assessed for malaria by microscopy between January and March 2024 were randomly selected to have their BS re-examined by an expert microscopist. Two expert examinations were conducted for each patient, one on-site re-examination of the routine HF-prepared slide using the HF microscope (slide 1), and the second off-site at the Kenya Medical Research Institute (KEMRI) malaria laboratory, where a second dried but unstained slide was stained and examined (slide 2) as the gold standard. Concordance between the routine HF results and expert re-examined HF slide at the HF (slide 1) and expert stained HF slide at KEMRI (slide 2) were evaluated, and sensitivity and specificity calculated. Overall BS positivity was 35% (166/480). There was 85% (405/480) concordance between the routine HF results and slide 1 expert re-reading, with a range of 50% (10/20) to 100% (20/20), by HF. There was 81% (336/411) concordance between the HF results and slide 2, with a range from 65% (7/13) to 100% (10/10). Compared to slide 2, the routine HF results had sensitivity and specificity of 72% and 87%, respectively. HF with the lowest concordance had poor BS quality 21% (6/28), contaminated reagents 7% (2/28), and low-quality microscopes with intermittent electricity 4% (1/28). While overall concordance was high, the variability in results and moderate sensitivity highlight the need for ongoing monitoring of malaria microscopy quality at public HF.

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AN EFFECTIVE CASCADING CLASSIFIER FOR PATIENT-LEVEL MALARIA DIAGNOSIS ON THE MILAB™ PLATFORM WITH FOCUS-STACKING TINY VISION TRANSFORMER

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Determining a proper diagnosis can take varying lengths of time and effort. In the case of malaria, inspecting a smeared blood slide through a microscope is the most common method of diagnosis. AI solutions, such as those conducted with the miLab™ platform, have been proposed to inspect the blood cells digitally, and cascading classifiers have shown great performance. However, clumped or blurry cells are still difficult for the AI to classify correctly. These hard samples require review by an expert to provide an accurate diagnosis; however, this comes at the cost of increased time and monetary cost to provide a diagnosis. This study introduces a new deep-learning model based on a pre-trained vision transformer; fine-tuned on hard samples. Reducing the workload of a human expert, TinyViT, a state-of-the-art but small model, can augment the workflow of the miLab™ platform and decrease the number of cells required to be reviewed. To circumvent the shallow depth of field limitations, focal stacking using multiple auto-focused images was used to generate the input image. Experts have extensive experience examining images prepared using different staining qualities. To mimic this experience, we apply realistic microscopy image augmentations to improve generalization when fine-tuning the pre-trained model. Adding additional steps to the existing pipeline introduces unnecessary overhead; therefore, this method is used only when there are few equivocal cells to review. We have internally validated that extending cascading classifiers improved malaria readout performance. The number of cells designated for user review decreased, reducing the time experts need to confirm cells, even if using a more accurate AI model takes extra operation time. Appending TinyViT to the end of the miLab™ process improved the overall performance to 97% and reduced the number of false positives and negatives while not significantly increasing processing time. As a result, 80% less resources can be spent confirming cells, and it can instead be spent by on-site experts helping more people, improving accessibility, and maintaining a good patient-provider experience.

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DETECTION OF *PLASMODIUM VIVAX* IN NORTHERN KENYA VIA MICROSCOPY CONFIRMED BY MOLECULAR SPECIATION

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In Kenya, *Plasmodium falciparum* is the predominant parasite responsible for malaria infections, mainly in western Kenya. Presence of *P. vivax* can complicate both diagnosis and treatment, posing a challenge for malaria control in endemic counties. We describe confirmed detection of *P. vivax* cases in northern Kenya in the aftermath of heavy rains, Sept-Dec 2023. We conducted a retrospective review of data from the Kenya Health Information Systems between December 2023-February 2024 in the five northern counties of Isiolo, Marsabit, Mandera, Samburu and Wajir to ascertain increase in malaria cases. In the peripheral clinics, blood smears with morphological features inconsistent with *P. falciparum* at time of diagnosis were encouraged to be sent for confirmation by expert microscopy and PCR at the National Malaria Reference Laboratory (NMRL). In the five northern counties, 7,860 confirmed cases of malaria were reported between Dec 2023-Feb 2024, up from 2881 cases—a 173% increase from the same period in the previous year. So far, NMRL has processed 9 samples sent for species confirmation—six were confirmed as *P. vivax*, and three as *P. falciparum.* Additional samples remain but NMRL has not processed them due to limited reagents. Detection of *P. vivax* in the northern counties that border Ethiopia is of great concern, suggestive of potential cross-border transmission. Strengthening diagnostic and speciation capacity by microscopy is critical, especially because rapid diagnostic tests used in Kenya do not detect *P. vivax*. Complementing microscopy with molecular diagnostics can also improve speciation in a timely manner. Recent malaria outbreak investigations in Wajir and Marsabit counties also found >40 cases of *P.* vivax. Ongoing malaria surveillance, particularly on *P. vivax*, through strengthened microscopy and molecular confirmation in the northern counties is critical to inform national malaria program decisions and improve response, especially as weather patterns change to become more conducive to malaria transmission.

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EVALUATION OF THE PERFORMANCES OF RAPID DIAGNOSTIC TESTS TO DETERMINE THE PREVALENCE OF *PLASMODIUM FALCIPARUM PFHRP2* GENE DELETIONS IN THE HEALTH DISTRICT OF NANORO, BUKINA FASO

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Malaria diagnostic methods rely essentially on rapid diagnostic tests (RDTs) based on histidine-rich protein 2 in peripheral health centers and microscopy only performed in reference centers. Nowadays, the reliability of RDT results would be threatened by the appearance of strains that do not secrete *pfhrp2* antigen, making these parasites undetectable by RDTs. The objective of this study was to evaluate the performances of RDTs and to determine the prevalence of *Plasmodium falciparum pfhrp2* gene deletions in the health district of Nanoro. The study population consisted of children under Seasonal Malaria Chemo Prevention (SMC) coverage and aged 6-59 months. At each visit for chemo-prevention, blood samples were taken for the preparation of thick drops and blood smears. A rapid diagnostic test was also done to assess malaria infection on site. Blood was spotted on a filter paper for the detection of *pfhrp2* gene deletions using PCR.A total of 1059 children with a mean age of 34 months (range 6-59) participated in this study. The analysis of RDT performance indicators allowed us to obtain a specificity of 84.00% and a sensitivity of 77.06%. False positives were estimated at 15.99% compared to 22.94% false negatives. On a total of two hundred (200) samples analyzed by PCR, we obtained a prevalence of 2.58% of *pfhrp2* gene deletion. This study is one of the first to reveal the presence of *pfhrp2* gene deletions in Burkina Faso. With approximately 2.6% prevalence, this value is below the threshold of 5% set by the WHO to consider a change in the type of RDT. Therefore, HRP2 RDTs are still indicated for the diagnosis of malaria in Burkina Faso. However, a large-scale study to monitor the temporal dynamics of these *Plasmodium falciparum* strains that do not produce the *pfhrp2* antigen is necessary in Burkina Faso.

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STRENGTHENING THE LABORATORY DIAGNOSIS OF MALARIA IN GUINEA: THE KEY ROLE PLAYED BY WHO-CERTIFIED LOCAL EXPERTS

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Malaria continues to represent a substantial health burden in Guinea. In 2021, USAID | Guinea StopPalu+ facilitated the WHO certification of 10 local malaria microscopists from referral hospitals supported by the project. Since then these experts have been used to oversee and lead malaria diagnosis training workshops for laboratory technicians, as well as conduct regular supportive supervisions to monitor the quality of malaria diagnosis at health facilities. Here we describe how the quality of malaria diagnosis in Guinea has been strengthened, including elaborating on best known practices and lessons learned. We describe observations and findings from two cycles of quarterly supportive supervision visits to 22 specialized microscopy laboratories in 19 of the country's 39 districts. Visits included direct observations by the supportive supervision team of technicians performing laboratory malaria diagnosis, key informant interviews, a review of laboratory registers, and an assessment of laboratory competence against WHO-provided reference microscopy slides. Substantial improvements were seen across various domains following two cycles of supportive supervision. In terms of the External Quality Assessment, the correct diagnosis of malaria improved from 89% to 98%, correct species identification improved from 65% to 83%, and correct parasite quantification improved from 49% to 55%. Microscope maintenance improved from 86% to 91%, and the specialized technical interventions improved from 0% to 27%; similarly, the availability of key commodities improved substantially (e.g., the availability of Giemsa and immersion oil improved from 77% to 100% and 91% to 100%, respectively). Facilities that conducted internal quality control efforts increased from 27% to 36%. Two cycles of supportive supervision by 10 WHO-certified local malaria microscopists led to substantial improvements in the malaria diagnostic capacity of laboratory technicians in 22 laboratories. Additionally, key improvements in quality service provision were made, including with regards to the availability of commodities and functional equipment.

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ECONOMIC EVALUATION OF MALARIA DIAGNOSTIC STRATEGIES FOR MALARIA CAMPS IN REMOTE VILLAGES OF ODISHA STATE, INDIA

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In India, malaria predominantly affects tribal populations in remote areas of Odisha state. The deployment of 'malaria camps' (MCs) with a mass screening-and-treatment (MSAT) intervention was shown to be effective in reducing PCR-positive Plasmodium infection prevalence. *Plasmodium falciparum* histidine-rich protein-2 (*pfhrp2*) gene deletions may, however, lead to false-negative RDT results, posing a challenge to MSAT's sensitivity to detect true malaria cases. We evaluated the incremental cost-effectiveness (ICER) of two alternative malaria detection strategies in the context of MSAT, following standard guidelines for cost-effectiveness analysis. A decision tree model was developed with three arms with arm 1 representing the comparator screening strategy which is the existing HRP-2-based RDT and arms 2 and 3 being the alternative screening strategies with an LDH-based RDT and an isothermal (LAMP-based) molecular diagnostic strategy, respectively. The number of DALYs averted and the associated incremental costs were estimated to calculate ICER from both a healthcare provider and a societal perspective. Deterministic and probabilistic sensitivity analyses were both conducted to ensure the robustness of the findings. The ICER of Arm 2 was estimated at $0.98/DALY averted (95% CrI=[$0.64/DALY averted, $2.04/DALY averted]) from the healthcare provider perspective, and at $0.40/DALY averted (95% CrI=[cost-saving, $3.00/DALY averted]) from the societal perspective. The ICER of Arm 3 was $114.05/DALY averted (95% CrI=[$65.03/DALY averted, $352.04/DALY averted]) from the healthcare provider perspective and was $113.43/DALY averted (95% CrI=[$64.37/DALY averted, $351.25/DALY averted]) from the societal perspective. Transitioning to either an LDH-based RDT or a LAMP-based molecular diagnostic represents a cost-effective alternative to the current HRP-2-based RDT utilized in the MSAT component of the MCs. Notably, the LDH-based RDT exhibited a significantly less incremental cost while averting more disease burden compared to the LAMP-based method.

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EFFICACY AND SAFETY OF ARTEMETHER + LUMEFANTRINE AND ARTESUNATE + AMODIAQUINE FOR UNCOMPLICATED MALARIA IN EQUATORIAL GUINEA

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Malaria remains a significant public health challenge in Equatorial Guinea, particularly among children and pregnant women. With the country's national malaria control program, endorsing Artemether + Lumefantrine (AL) as the first-line treatment since 2017, continuous surveillance is essential to monitor ongoing efficacy and detect early signs of drug resistance. This study aims to evaluate the therapeutic efficacy and safety of the national first-line (AL) and second-line (Artesunate + Amodiaquine, ASAQ) malaria treatments in young malaria patients in Equatorial Guinea. This prospective cohort study will be conducted from March 2024 to July 2024 in three sentinel sites: Malabo (Bioko Island), Bata, and Ebibeyin Districts (located on the mainland of Equatorial Guinea). After obtaining informed consent from parents and guardians, we will consecutively enroll febrile children aged 6 months to 10 years diagnosed with uncomplicated *Plasmodium falciparum* malaria. Each site will parallel-test AL and ASAQ[CD1] [PJBD2] , given orally for a complete 3-day treatment course. The study aims to recruit treatment cohorts of 88 patients each for AL and ASAQ, summing to a total of 528 participants across all sites. Treatment efficacy will be assessed through close monitoring of clinical and parasitological outcomes for a 28-day follow-up period. The study will employ thick and thin blood smear malaria microscopy, PCR and sequencing to understand successful treatment rates, and to distinguish recrudescence from newly acquired infections. Drug safety evaluations will focus on the incidence and nature of adverse events associated with these treatments. Results will provide an evidence base for malaria drug policy in EG, hopefully supporting AL as the first line treatment and evaluating the role of ASAQ as a second-line therapy, ensuring optimal care for malaria patients in Equatorial Guinea.

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EVALUATION OF FOR EFFICACY OF ARTEMISININ-BASED COMBINATION THERAPIES ON *PLASMODIUM FALCIPARUM*, PLASMODIUM MALARIAE AND PLASMODIUM OVALE INFECTIONS IN MALI

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Most cases of malaria are caused by *Plasmodium falciparum*. Non-falciparum species (*P. vivax*, *P. ovale*, *P. malariae…)* can cause malaria infections as well. Little work exists on the efficacy and clearance of non-falciparum species; andall strategies are oriented on the P. *falciparum* species. The purpose of this study was to clearance and efficacy of ACT on *P. malariae*, *P. ovale* and *P. falciparum* on data from the WANECAM1 network in Mali.The database of the WANECAM1 study was used to perform the analysis for this thesis. The 28-day WHO *in vivo* protocol was used for estimation of therapeutic responses. The WWARNParasite Clearance Estimator Software was used for the estimation of the parasite clearance half-life. The classic parasite clearance time was estimated by taking the median of the parasitaemianegativation time.Out of a total of 4172 volunteers. The median parasite clearance half-life times were 2.9 h, 4.79 hand 4.74 h respectively for *P. falciparum*, *P. malariae* and *P. ovale*. There was a significantdifference between the half-life times of *P. falciparum* compared to those of *P. malariae* and *P.ovale* ($p<0.001$) while there was no significant difference between the half-life times of non-falciparum species. The classical parasite clearance time was 24h and 36h. Adequate clinical andparasitological response (ACPR) was 79.81% for *P. falciparum*, while ACPR were 99.32% and98.18% for *P. malariae* and *P. ovale*, respectively, with a significant difference statistically ($p <0.05$).We conclude that the parasite clearance half-life of *P. falciparum* species was faster compared to*P. malariae* and *P. ovale* species.The ACTs used in the study were more effective on *non-falciparum* species than on *P. falciparum*.

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OPTIMIZATION OF MULTIPLE-STAGE ACTIVE ANTIMALARIAL PRODIGININES

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Over the past several decades, natural products have an extensive history as pioneering agents for drug development. In particular, many of the promising antimalarials know to date are the natural products and/or their derivatives. Recently, we have discovered and developed prodiginine chemotype as novel class of orally efficacious antimalarial agents. Our work has shown that a number of the prodiginine derivatives were equally effective against a panel of *Plasmodium falciparum* pan-sensitive and multi-drug resistance strains at low nanomolar concentrations, suggesting potential to discover a new drug target to combat malaria parasites. In addition, these compounds inhibited formation of hypnozoites and schizonts in both radical cure and prophylactic modes at low concentrations. Herein, we present the detailed optimization and structure-activity relationships of prodiginine chemotype with enhanced antiplasmodial activities against both the asexual blood and liver stage malaria parasites and improved metabolic and pharmacokinetic profiles. This material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. Research was conducted under an IACUC-approved animal use protocol in an AAALAC International-accredited facility with a Public Health Services Animal Welfare Assurance and in compliance with the Animal Welfare Act and other federal statutes and regulations relating to laboratory animals.

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PRECLINICAL DEVELOPMENT OF NOVEL DUAL-STAGE ACTIVE ANTIMALARIALS

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The global impact of malaria remains staggering despite extensive efforts to eradicate the disease. The challenges for a sustainable elimination include the failing effectiveness of front-line artemisinin-based combination therapy (ACT) due to emerging resistance and safety concerns associated with limited radical cure options for relapsing *Plasmodium vivax*. There is an urgent need for novel, effective, affordable and safe antimalarial drugs to overcome drug resistance, and ideally, such agents would be efficacious against both blood stage and liver stage malaria infections. We have developed a novel antimalarial acridone chemotype with dual stage efficacy against both liver stage and blood stage malaria, as well as single-dose cure ability and potential to prevent relapsing infection. Our novel acridone chemotype represents a broad-spectrum approach with potential to vanquish many challenges. Extensive and comprehensive preclinical evaluations of our late lead acridone candidate will be presented.

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DRUG INTERACTION BETWEEN DIHYDROARTEMISININ-PIPERAQUINE AND SULFADOXINE-PYRIMETHAMINE IN PREGNANT WOMEN RECEIVING MALARIA CHEMOPREVENTION

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Comparative trials of intermittent preventive treatment in pregnancy (IPTp) have shown that dihydroartemisinin-piperaquine (DP) is a more efficacious antimalarial, but sulfadoxine-pyrimethamine (SP) is associated with better fetal growth. We hypothesize that DP+SP for IPTp may be superior to either therapy alone. However, potential drug-drug interaction between DP and SP requires investigation. We completed pharmacokinetic (PK) studies nested in a placebo-controlled, double-blinded randomized trial of pregnant women living in Busia District, Uganda who were randomized to IPTp with SP, DP, or DP+SP every 4 weeks starting at 16- or 20- weeks gestation. For intensive PK, serial sampling from day 0-23 was performed after the 28th gestational week IPTp course in 87 participants (27 DP, 36 SP, 24 DP+SP). For sparse PK, paired day 28 (trough) samples were analyzed in 198 participants (98 SP, 98 DP+SP) after the 20th and 28th gestational week IPTp course. Sulfadoxine (SDX), pyrimethamine (PYR), and piperaquine (PPQ) levels were determined using liquid chromatography tandem mass spectrometry. Non-compartmental analyses were used to determine PK parameters. Intensive PK analyses demonstrated that coadministration of DP+SP significantly reduced geometric mean C_{max} and $AUC_{day0-23}$ of SDX (by 25% [90% CI: 13%–33%] and 25% [11%–33%]) and PYR (by 26% [17%–34%] and 34% [26%–42%]) (all $p<0.05$). Sparse PK analyses indicated that co-administration of DP+SP significantly reduced trough SDX levels after the 28th, but not the 20th gestational week IPTp course (31% [10%–47%] versus 6% [-19%–26%] reduction; p-interaction=0.025). PYR levels were reduced with coadministration of DP+SP at both the 20th and 28th gestational week IPTp course (reductions of 18% [5%–30%] and 33% [22%–43%]; p-interaction=0.027). Co-administration of DP+SP moderately reduced PPQ C_{max} and $AUC_{day0-23}$ by 13% [-11%–32%] (p=0.34) and 19% [4%-32%] (p=0.046). Thus, coadministration of DP+SP significantly reduced SP exposure with a greater magnitude during the 3rd vs. 2nd trimester. Further investigation is needed to define optimal dosing strategies for IPTp with DP+SP.

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MICROVOLUME ANALYSIS OF ANTIMALARIAL DRUGS FOR PEDIATRIC PHARMACOKINETIC-PHARMACODYNAMIC STUDIES

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It is desirable to quantify antimalarial drugs in microvolume samples to support pharmacokinetic studies in pediatric populations, due to the limited volume of blood. We used capillary tube sampling to obtain plasma or dried blood spots (DBS), which were processed with protein precipitation, liquid-liquid extraction, or solid phase extraction, and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). We have developed plasma methods to determine concentrations of artemether and dihydroartemisinin (50 µL), piperaquine (25 µL), hydroxychloroquine and its metabolites (20 µL), amodiaquine (AQ) and desethylamodiaquine (DEAQ, 10 µL), lumefantrine and desbutyl lumefantrine (5 µL), sulfadoxine (SDX), and pyrimethamine (PYR, 5 µL). We also explored methods to determine piperaquine, lumefantrine, AQ and DEAQ concentrations from DBS. Here we present a method for determination of AQ, DEAQ, SDX, and PYR concentrations from 10 µL plasma. The method was developed on a Waters Acquity UPLC system (I class) coupled with Sciex TripleQuad 6500^{+} tandem mass spectrometry (MS/MS) managed with the software Analyst® 1.6.3. Plasma samples (10 µL) were processed by solid-phase extraction with an HLB micro-elution plate. Chromatographic separation was achieved on an ACE® Excel C_{18} analytical column (50 x 2.1 mm, 1.7 µm) eluted with water (A) and acetonitrile (B), both containing 0.1% formic acid at a flow rate of 0.8mL/min in gradient mode. The injection volume was 5 µL for AQ and DEAQ and 1 µL for SDX and PYR. The instrument time per sample was ~2 min. The calibration ranges were 0.1 – 100 ng/mL for AQ, 0.2 – 200 ng/mL for DEAQ. 0.2 – 200 ng/mL for PYR, and 20 – 20,000 ng/mL for SDX. Precision and accuracy were within 15%. The recoveries were 93.4±0.5 %, 87.8±2.2 %, 97.9±4.8 %, and 95.1±3.2 %, respectively. Matrix effect was negligible. DEAQ was unstable in plasma, with ~50% degradation overnight. The method was used to analyze 366 clinical samples, among which 82% have quantifiable AQ/DEAQ and 83% have quantifiable SDX/PYR. In summary, LC-MS/MS enables microvolume sampling and subsequent drug analysis to support clinical studies in pediatric populations.

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PRIMAQUINE PHARMACOKINETICS AND RADICAL CURE EFFICACY IN *PLASMODIUM VIVAX*-INFECTED ADULTS IN THAILAND

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Clearing dormant *Plasmodium vivax* hypnozoites with the anti-malarial drug, primaquine (PQ), may be hampered by ineffective metabolism of the drug into its active metabolites, particularly in individuals with polymorphisms in the cytochrome P450 2D6 enzyme. We conducted a clinical trial in Thailand designed to both assess efficacy of radical cure PQ (15 mg/day for 2 weeks) and to identify biomarkers of *P. vivax* hypnozoites. *P. vivax*-infected adults were randomized to one of two arms: EARLY group receiving PQ with concomitant oral artesunate (AS) for five days and the DELAYED group receiving PQ alone, six weeks after AS treatment. Both arms stayed in study housing for the first 28 days both to minimize risk of re-infection and obtain samples for retrospective analyses of hypnozoite biomarkers.

Recurrences of *P. vivax* over the 6-month study period were diagnosed by blood smear, both at study-specific time points and if clinical symptoms developed, and then confirmed with 6-species polymerase chain reaction (PCR) testing. Relapses were treated with PQ and chloroquine (CQ). For all volunteers, urine PK samples were collected for 24 hours after the first dose of PQ and at scheduled timepoints throughout the 2-week course. Thirty *P. vivax* patients were enrolled, with 28 receiving radical cure PQ: 12 with AS+PQ, 10 with PQ alone and 6 who received only AS, relapsed before six weeks, then received CQ+PQ. One volunteer in PQ+AS group, none in PQ alone, and three in the PQ+CQ had *P. vivax* recurrences, giving efficacy of 92% (1 of 12), 100% (0 of 10) and 50% (3 of 6), respectively. Urine PQ PK parameters for each volunteer and per drug regimen will be presented. Methemoglobin (metHgb), generated during PQ administration and a suggested signal of efficacy, was highest in the PQ+AS group (peak 4.6%, range 0-11%) versus PQ alone (3.6%, range 0-8.3%) or PQ+CQ group (2.8%, range 0-4.9%). These results will contribute to our knowledge of PQ metabolism parameters as predictors of radical cure efficacy, particularly when able to be combined with future hypnozoite biomarker data.

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DISCOVERY OF NOVEL ANTIPLASMODIAL COMPOUNDS USING RING FUSION OF INDOLE ALKALOIDS

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To mitigate the threat of emerging resistance to available antimalarials, new screening libraries are needed to discover novel chemotypes. Compound collections of commercial or "in-house" origin are often limited in diversity and stereochemical complexity. To address the lack of chemical diversity in current drug discovery efforts, we have developed an innovative "Complexity to Diversity" ring distortion approach to rapidly generate a diverse and unique library of complex small molecules from stereochemically complex indole alkaloids. Through the process of ring distortion, the complex ring systems of natural products are re-engineered utilizing ring fusion, cleavage, and expansion using various chemical reactions. Previous work in our lab has shown success in generating antiplasmodial compounds through ring distortion of vincamine and yohimbine - taking inactive starting compounds to products with submicromolar EC_{50}s against the multidrug resistant Dd2 parasite line with excellent selectivity. Using the ring-distortion approach of reserpine, a library of 83 compounds were synthesized and tested for antiplasmodial activity and selectivity. From these efforts, a reserpine derivative, AB-2-81 with potent antiplasmodial activity (EC_{50} 131 ± 21 nM) with high selectivity (SI >191) was identified. This work validates the value of ring distortion in re-engineering of natural products to develop new class of antiplasmodials.

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IN SILICO, IN VIVO AND *IN VITRO* TOXICITY ASSESSMENT OF NOVEL HETEROCYCLICS WITH ANTIMALARIAL ACTIVITY

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The emergence of resistance against most frontline antimalarials underpins the need for novel drugs. However, toxicity is a bottleneck for the further development of many inhibitory molecules. Although many *in silico* and *in vitro* approaches are available, *in vivo* models tend to simulate the real conditions more closely. Combined strategies may improve the detection and selection of molecules worth of further testing lowering time and costs. The aim of this study was to test the potential of *Galleria mellonella* (Insecta: Lepidoptera) as a low-cost *in vivo* model combined with *in silico* and *in vitro* assays to assess the toxicity of compounds with potential antimalarial activity. A total of 20 heterocyclics from an in-house library, showing inhibitory effects on *Plasmodium falciparum* parasite cultures (IC_{50} <1 μM) were selected for toxicity testing. *In silico* analysis was performed using SwissADME (Brent alerts) and ProTox-II. *In vitro* toxicity for cell membranes was assessed by hemolytic activity in human red blood cells (RBC) and the half-lethal doses (LD_{50}) were determined using six-instar larvae of *G. mellonella*. The larvae were initially injected with 500mg/kg and if >60% survived after five days, the assay was performed using higher doses up to 2000 mg/kg. Ten compounds showed no Brent alerts, Protox analysis revealed that 8 (out of 10) compounds showed predicted hepatotoxicity, 3 immunotoxicity, 6 carcinogenicity and 4 mutagenesis. None of the compounds was cytotoxic. In most cases the predicted likelihood of toxicity was low (consensus score:< 0.7), 3 compounds with higher predicted immunotoxicity and predicted toxicity level 4 (1000mg/kg) showed to be less toxic in the *Galleria* model. Most active compounds showed not induction of RBC damage at >200 μM, however two diphenyl-pyrazolines induced RBC hemolysis at lower concentrations (>50 μM). LD_{50} in *G. mellonella* classified most compounds as low or no toxic whereas *in silico* predicted toxicity was higher. *Galleria* model provides a more accurate representation of *in vivo* toxicity as *in silico* accuracy relies on the structural similarity of the novel compounds with those in the database.

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PARASITE CLEARANCE AND PROTECTION FROM *PLASMODIUM FALCIPARUM* INFECTION: CLINICAL RESULTS FROM A THREE-ARM, PARALLEL, DOUBLE-BLINDED, PLACEBO-CONTROLLED, RANDOMIZED TRIAL OF PRESUMPTIVE SULFADOXINE-PYRIMETHAMINE VERSUS SULFADOXINE-PYRIMETHAMINE PLUS AMODIAQUINE VERSUS ARTESUNATE MONOTHERAPY AMONG ASYMPTOMATIC CHILDREN 3-5 YEARS OF AGE IN CAMEROON

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The World Health Organization's (WHO) 2022 malaria chemoprevention guidelines recommend providing sulfadoxine-pyrimethamine (SP) to asymptomatic children living in high-transmission malaria areas as a perennial malaria chemoprevention (PMC). We will present results from a three-arm, parallel, double-blind, placebo-controlled, randomized trial in Cameroon designed to measure the effect of parasite genotypes associated with SP resistance on the efficacy of SP and SPAQ among asymptomatic children between 3-5 years of age (NCT06173206). Our sample size has 80% power to detect a significant difference in duration of protection in the presence or absence of the I431V mutation, derived from 1000 simulations and these assumptions: 6 infections per person per year, 40% microscopy prevalence, 10% loss-to-follow up, 30% *Pfdhps* I431V frequency, 28-day protection against *Pfdhps* I431 parasites, 15-day protection against *Pfdhps* 431V parasites, 85% genotyping success at *Pfdhps* codon 431. Children are randomly assigned to one of three directly-observed treatment groups: (i) SP group (n=450) receive daily artesunate (AS) placebo on days -7 to -1, then active SP plus placebo amodiaquine (AQ) on day 0, and placebo AQ on days 1 and 2; (ii) SPAQ group (n=250) receive placebo AS on days -7 to -1, then active SPAQ on day 0, and active AQ on days 1 and 2; and (iii) AS group (n=200) receive active AS on days -7 to -1, then placebo SP on

day 0 and placebo AQ on days 0 to 2. On days 0, 2, 5, 7, and thereafter weekly until day 28, children provide blood for thick smear slides. For future qPCR, dried blood spots are collected on the same days and weekly thereafter to day 63. We will report unblinded results including: (i) time-to-parasite clearance among SP and SPAQ recipients who were positive on day 0 by qPCR and followed to day 63; (ii) mean duration of SP and SPAQ protection against infection, and (iii) mean duration of symptom-free status among SP and SPAQ recipients who were parasite free on day 0 by qPCR. Our conclusions will reflect on the utility of the new WHO malaria chemoprevention efficacy study protocol follow-up to day 28 versus day 63.

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PARASITE CLEARANCE AND PROTECTION FROM *PLASMODIUM FALCIPARUM* INFECTION: CLINICAL RESULTS FROM A TWO-ARM, PARALLEL, DOUBLE-BLINDED, PLACEBO-CONTROLLED, RANDOMIZED TRIAL OF PRESUMPTIVE SULFADOXINE-PYRIMETHAMINE VERSUS ARTESUNATE MONOTHERAPY AMONG ASYMPTOMATIC CHILDREN 3-5 YEARS OF AGE IN ZAMBIA

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The World Health Organization's (WHO) 2022 malaria chemoprevention guidelines recommend the provision of sulfadoxine-pyrimethamine (SP) to asymptomatic children who reside in areas of high malaria transmission as perennial malaria chemoprevention (PMC). We will present results from a two-arm, parallel, double-blind, placebo-controlled, randomized trial in Zambia that is designed to evaluate the effect of parasite genotypes on the efficacy of single-dose SP among asymptomatic children between 3-5 years of age (NCT06166498). Our sample size has 77.4% power to detect a significant difference in duration of protection in the presence or absence of *Pfdhps* K540E, derived from 1000 simulations with the following assumptions: 10 infections per person per year, 37.8% prevalence by microscopy, 10% loss to follow up, 80% frequency of *Pfdhps* K540E, 30-day protection against *Pfdhps* 540K parasites, 18-day protection against *Pfdhps* 540E parasites and 85% genotyping success at *Pfdhps* codon 540. Children are randomly allocated to one of two groups for directly-observed treatment. Over seven consecutive days (days -7 to -1), children in the SP group (n=400) receive placebo artesunate (AS), then active SP (day 0). In contrast, children in the AS group (n=200) receive active artesunate for seven consecutive days, followed by placebo SP (day 0). Then, on days 0, 2, 5, 7, and weekly thereafter until day 28, children provide finger-prick blood for thick smear slides. Dried blood spots are collected on these same days for future qPCR analysis, and collected weekly thereafter until day 63. Children who become symptomatic are treated with artemether-lumefantrine if positive by malaria rapid diagnostic test. We will report unblinded results including: (i) time-to-parasite clearance among SP recipients who were positive on day 0 by qPCR and measured to day 63; (ii) mean duration of SP protection against infection, and (iii) mean duration of symptom-free status among SP recipients who were parasite free on day 0 by qPCR. Our conclusions will reflect on the utility of WHO's new malaria chemoprevention efficacy study protocol with its follow-up to day 28 versus day 63.

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PACRALIMA NITIDA FRUIT-RIND AND LEAF EXTRACTS EXHIBITED ANTIPLASMODIAL AND IMMUNO-MODULATORY EFFECTS AGAINST *PLASMODIUM BERGHEI*-INFECTION IN SWISSMICE

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Malaria has continued to remain a public health challenge, especially in some tropical and sub-tropical regions of the world. Although, a significant reduction in mortality and morbidity was recorded between 2005 and 2015, decreased susceptibility of *Plasmodium falciparum* to the current first-line antimalarial drug, artemisinin-based combination therapy (ACT), has been reported in Southeast Asia and other continents which further complicate the severity of the disease, especially in low-income countries like Nigeria. Numerous strategies have been employed to combat artemisinin resistance and one of them is the intensified efforts toward the discovery of novel drugs from plant sources that may be alien to the parasite. This study therefore evaluated the antiplasmodial and immuno-modulatory effects of chloroform-methanol extracts of *Pacralima nitida* fruit-rind and leaf in *P. berghei-infected* mice. The bioactive constituents of the plant were extracted using standard protocol. Extracts obtained were assessed for antiplasmodial activity by the standard four-day suppressive test on *P. berghei* (*ANKA*) infected mice (Swiss strain). The absorption spectra from the HPLC chemical finger-prints of the extracts revealed several peaks representing bioactive phytochemicals while the results from the animal study showed that the extracts were dose-dependently ($p < 0.05$) active against *P. berghei* parasite in comparison with the untreated infected mice (negative control). Dose-dependent decreases ($p < 0.05$) in some oxidative stress indices of the extracts-treated groups as against the infected control were observed. The pro-inflammatory cytokines levels were assessed and were found to be significantly low in the extracts-treated groups relative to the infected control. Results from the study suggest that methanol extracts of *P. nitida* fruit rind and leaf possess appreciable antiplasmodial properties with some immuno-modulatory effect against the *P. berghei* parasite.

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EFFECT OF SEASONAL MALARIA CHEMOPREVENTION IN STUNTING CHILDREN IN KOULIKORO, MALI

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Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine plus amodiaquine (SP+AQ) is an effective and promising strategy for controlling malaria morbidity and mortality in areas of intense seasonal transmission. Despite its effectiveness several controversies regarding the occurrence of clinical malaria among eligible children and challenges of the strategy in the context of high prevalence of malnutrition in area where it is implemented make questionable the benefit of SMC in malnourished children compared to those with normal nutritional status. This study investigated the risk of clinical malaria among stunting versus normal children eligible for SMC in Koulikoro, an area where the frequencies of the two diseases are high during the rainy season. A total of 2613 children eligible for SMC were enrolled just before the first round of SMC in July 2020. At baseline *Plasmodium falciparum (P.f)* infection and nutritional status was assessed for study participants and children were classified in

two comparison groups: normal and stunted. All participants were followed from the start to the end of SMC through passive case detection to determine the incidence of clinical malaria define as fever and malaria RDT or blood smear positive. The risk of malaria in both groups was estimated using the Wald test. The overall prevalence of asymptomatic malaria and stunting were 11.2% and 62% respectively. Ended, 847 children as normal and 89 as stunted. During the SMC season the overall incidence was 25.6%. Comparing the first occurrence of *P.f* parasitemia during the SMC season, the cumulative incidence of malaria was 20.6% in the normal group (n=336) vs. 33.7% in the stunted group (n=332). Stunted children had significantly more first malaria episodes RR= 1.97 (95% CI, 1.73-2.25). These results suggest a reduction of the effect of SMC treatment in preventing clinical malaria among stunted children compared to normal children. Thus, a combined intervention targeting the two diseases could increase the effectiveness of SMC in area where the two diseases are highly seasonal.

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EXPERIENCES FROM DIGITALIZING INSECTICIDE-TREATED NETS (ITNS) MASS DISTRIBUTION CAMPAIGNS IN ZAMBIA

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The Zambia National Malaria Elimination Programme conducts universal mass distribution of insecticide-treated nets (ITNs) every three years. In 2023/2024, Zambia used an Electronic Data Management Information System (EDMIS) to implement the ITN campaign for the first time. Prior to this, paper-based data collection was used, resulting in numerous challenges. Here we describe the development of EDMIS and lessons learned during its use to support deployment of ITNs targeting an estimated 20 million Zambians. A two-month consultation process was used that involved an assessment of the data infrastructure architecture. A data collection form was developed to collect information on household members, sleeping spaces, GPS coordinates, ITNs allocated and distributed, and data quality and validation checks. Over 10,000 phones and a HPE ProLiant DL380 Gen10 Plus server were procured to manage data entry, storage, and analyses. To address possible upload challenges and loss of data, paper-based registers were used as backup. A total of 20,664,899 persons in 3,883,195 households were registered, 17.45% less than the 4,560,912 projected households. As at March 27, 2024, 10,178,609 ITNs (one net per two people) were distributed and captured on EDMIS countrywide, translating to 89.4% of the enumerated population protected. During the process, bottlenecks were identified and support for about 10,000 data users was provided at full operating capacity. However, about 20% of data failed to upload to DHIS2 while in the field during registration and distribution, which was attributed to internet challenges in rural areas. This delayed the campaign by three months. The lessons learned and best practices established during the implementation of the EDMIS will contribute to the success of future campaigns, particularly by building staff capacity at district level in IT skills. However, with unpredictable outcomes in the digital space, the paper registers remain important in the execution of ITN campaigns.

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IMPROVING INTEGRATED COMMUNITY CASE MANAGEMENT (ICCM) BY COMMUNITY HEALTH WORKERS - AN EXAMPLE OF MALARIA MANAGEMENT IN NCHELENGE DISTRICT, ZAMBIA

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In Zambia, the 2021 national malaria prevalence was estimated to be 23%, according to data from the malaria indicator survey. Luapula Province, which includes Nchelenge District, had the highest prevalence at 63%. The Ministry of Health (MOH) plans to train 40,000 Community Health Workers (CHWs) nationwide by 2025 in integrated community case management (iCCM) including malaria. Between 2021 and 2023, trained CHWs increased from 382 to 405 in Nchelenge District. Although CHWs were being trained, many were not sufficiently equipped with malaria commodities, as it was reported in May 2021 that the availability of rapid diagnostic tests (RDTs) and the first-line antimalarials were at 0% and 5% respectively (56.7% reporting rate). During the regional supply chain review meeting with the MOH and partners in 2021, contributing factors to the commodity availability at CHW level, such as health facilities (HFs) not including CHWs' needs, low reporting rates, and low data quality, were identified. Following the findings, the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project partnered with the MOH to establish a consistent supply of commodities by working with provincial and district MOH staff to ensure that approved order quantities for HFs include CHWs' needs for iCCM and introduced a commodity ordering and tracking tool (COTT) for community level reporting for stock levels, consumption, losses, and adjustments. The tool provides an efficient way for CHWs to manage and track essential commodities with limited oversight and has now been integrated into the MOH-led iCCM trainings. These initiatives enhanced the availability of RDTs to 85%, and first-line antimalarials to 75% (80.6% reporting rate) in May 2023, at CHW level, and contributed to an increase in malaria case detection by CHWs from 79 cases in May 2021 to 5,366 cases for timely treatment in May 2023. These results indicate the importance of considering CHW expansion in commodity management. Strengthening CHW supply chain management skills may have helped the monitoring and maintenance of adequate commodities.

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QUANTIFYING FOR ROLE OF IMPORTATION ON SUSTAINED MALARIA TRANSMISSION IN SOUTHEAST UGANDA

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Importation of malaria parasites through human movement poses a threat to control. However, understanding the role of importation is challenging because it is difficult to differentiate between local and imported infections in areas with some level of transmission. We aim to quantify the role of importation on malaria in Kamwezi, Uganda, a region characterized by spatial variation in burden. We enrolled 400 households in a 2-year longitudinal study in summer 2023, collecting travel and movement histories, data on malaria episodes, and blood samples during bimonthly visits. Passive surveillance captured symptomatic infections at a local health facility alongside the cohort. Our outcomes included parasite positivity (asymptomatic infections) and symptomatic malaria cases. Regression models analyzed the association between travel and outcomes, stratifying by village-level transmission intensity. After four survey rounds involving

5,821 visits of 1,872 individuals, 3.8% (224) had recent malaria illness, and 16.6% (264) tested positive for asymptomatic infection at baseline. 8.3% (488) of individuals reported overnight travel and 6.9% (404) reported evening movement. We did not find evidence for an association between travel and asymptomatic infection, nor did we find an association between travel and symptomatic malaria in higher transmission villages. We found evidence supporting an association between travel and symptomatic malaria (incidence rate ratio = 2.45, 95% confidence interval 1.45-4.08) in lower transmission villages, such that travel accounted for 10% of malaria cases, with travel to higher transmission areas elevating risk. Furthermore, we found that movements during evening to higher transmission villages were associated with malaria illness. By the conference, 18 months of follow-up will be complete, allowing a probabilistic model estimating importation probability for all cases. We will also generate genotype data to differentiate between local and imported infections. Understanding these factors is crucial for developing interventions to reduce the impact of importation on sustained transmission.

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MALARIA ELIMINATION IN CABO VERDE: AN OVERVIEW ABOUT FOR HISTORY, CASE DATA FROM FOR LAST 35 YEARS (1985-2023) AND CHALLENGES AHEAD

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On January 12th, 2024, Cabo Verde was officially certified by the WHO as a malaria-free country after six consecutive years without local cases. This study analyses the malaria history of Cabo Verde, from 1953 to certification in 2024, brings some lessons learned and discusses challenges for the future as a malaria-free country. A literature review was conducted; descriptive analyses were done with the last 35 years' data (1988-2022), and cases were mapped using the Quantum GIS Software. Six reference stages and three periods of malaria interruption can be highlighted. The first interruption was for five years (1968-1972), the second for three years (1983-1985), followed by outbreaks, and finally, certification in 2024. From 1988 to 2022, 3,089 malaria cases were reported, being 2,381 (77.1%) local and 708 (22.9%) imported. To achieve elimination, after the last malaria outbreak in Cabo Verde in 2017, the NMCP reviewed the strategies and developed the new NSP for Malaria Elimination 2020-2024. It included implementing active and reactive foci investigations and effecting the vector control. The vector control strategies, included larval source management, indoor residual spraying (IRS) and environmental modification. Concerted efforts focusing on behavioural change and social mobilization were also crucial aspects in achieving elimination, associated with the robust epidemiological surveillance system in place, capable to detect timely, treat correctly and the follow-up of all cases. With the certification, Cabo Verde became an African country reference in the health sector organization, multisectoral and partnership in malaria control. Maintaining the certification imposes several challenges to the country's sustainability and perennially. The lessons learned and experiences about malaria control and elimination in Cabo Verde is an opportunity and hope to the others African countries that can benefit to save more lives and improve the quality of life of populations.

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ARE THERE GENDER DIFFERENCES IN FOR GAPS IN MALARIA TREATMENT CASCADE IN GHANA? IMPLICATIONS FOR MALARIA ELIMINATION

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Effective case management is critical to Ghana's malaria elimination agenda. Identifying gender differences in the malaria treatment cascade will help tailor interventions to address specific needs that will maximize benefits from scarce resources. We set out to explore gender differences in the malaria treatment cascade in Ghana. This was a nationally representative community-based survey among participants 18 years and older, in six randomly selected regions. The outcomes included gender differences in malaria treatment cascade of one-month and six-month prevalence of self-reported malaria. Overall, 3022 participants were engaged, including 1547 females, with a median age of 32(25-43) among males vs. 31(24-41) among females. The one-month self-reported malaria prevalence was 20.8% (19.4 - 22.3), 20.3% among males vs. 21.3% among females. A higher prevalence was observed among females in the Greater Accra region (17.5% vs. 10.5%) and the Central region (28.8% vs. 19.3%), $p<0.05$. Of the 628 malaria cases, 60% were tested, and 95.5% tested positive. Among the positive cases, 72,2% were prescribed orthodox medication, predominantly ACTs, 15.3% took complementary and alternative medicine (CAM), and 11.9% took both orthodox and CAM treatments. Stratified by sex, significant differences were not observed in the malaria treatment cascade except that, more females with negative tests took orthodox treatments, (38.5% vs. 0%, $p<0.05$), as well as CAM products (61.5% vs. 50.0%, $p <0.05$). Self-reported malaria in the past 6 months was 57.4% (55.6 - 59.1), and of 1733, 59.4% were tested, (males: 58.1% vs. females: 60.7%). Malaria RDT testing was significantly higher among females than males, 66.2% vs. 58.9%, ($p<0.05$). Fewer females tested positive (94.6% vs. 97.3%). Of the 695/1,733 cases, (40.1%) positive malaria cases treated with orthodox medicines, significantly more females (42.3%) were treated with orthodox medicines compared to males (37.8%), $p<0.05$. Exploring the factors that account for the relative gender differences in the treatment cascade gaps can potentially enhance malaria elimination efforts in Ghana.

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ONE HEALTH BY USING GREEN SYNTHESIS OF NANOPARTICLES TO IMPROVE COMMUNITY ENVIRONMENT

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Mosquitoes are main vectors of parasitic diseases such as dengue, malaria,filariasis,Japanese encephalitis, chikungunya and so on . These diseases cause death in humans and animals.The constant use of chemical insecticides against mosquitoes has led to a physiological resistance . Nanotechnology is a rapidly growing field due to its unique functionality and a wide range of applications. The aqueous extract of fresh leaves of *Ocimum basilicum* have been used to synthetize nanoparticles. The synthesized nanoparticles was characterized by using ultraviolet spectrophotometry, X-Ray diffraction, and Fourier transform infrared spectroscopy methods.The wavelengths between 400-600nm confirmed experimentally the formation of silver nanoparticles. They were crystalline in nature and constituted by the following chemical groups: Alcohols, amines,

alkyls, aldehydes and ketones. The larvicidal effect against *Anopheles gambiae* has been tested. The LC50 determinated after 24 h and 48 h. The results showed an increase in potency with time. The mortality of AgNPs *O. basilicum* having concentration of 2.0 to 2.5 ppm after 24 h. The LC_{50} for AgNPs *O. basilicum* were 1.54 ppm after 24 h, while after 48 h the LC_{50} reached 0. 95ppm.The green synthesis of silver nanoparticles using *O. basilicum* water extract were effective against *Anopheles gambiae* larvae. Their insecticide properties that do not require the presence of any harmful material. This method is eco-friendly, low-cost, and safe for human health and his environment Biocontrol agents derived from this methodology could be considered as a suitable alternative to control vector-borne diseases in developing countries.

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PREVALENCE OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN A MALARIA-ENDEMIC REGION OF COLOMBIA: IMPLICATIONS FOR RADICAL CURE OF *PLASMODIUM VIVAX*.

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Glucose-6-phosphate dehydrogenase deficiency (G6PDd) is a common genetic condition with important implications for radical cure of *Plasmodium vivax* (*Pv*), the most common malaria species in Colombia and Latin America (LA). G6PDd is associated with a higher risk of hemolytic events when using 8-aminoquinoline drugs. The prevalence of G6PDd and its relation to *Plasmodium sp*ecies infection is poorly known in this region. A cross-sectional study was conducted in Quibdó, Colombia. Participants were randomly selected among the general population (GP) (n=1267), indigenous communities (IC) (n=194), and outpatients with suspected malaria (OSM) (n=542). Participants were screened for G6PD levels using a quantitative finger-prick blood test and were classified as deficient, intermediate, or normal phenotype. *Plasmodium sp.* infections were determined by polymerase chain reaction (PCR). G6PDd and *Plasmodium* infection prevalence were calculated for each population and risk factors for G6PDd were explored. The study was conducted between July and November 2023. The prevalence of G6PDd was 10.4%, 0%, and 7.0% in the GP, IC and OSM, respectively. The prevalence of *Plasmodium sp.* infection was 17.8%, 40.7%, and 47.8% in GP, IC, and OSM, respectively. Among GP and IC, *Pv* was more frequent than *Pf* (GP Pv=11.2% & Pf=0.1%; IC Pv=26.2% & Pf=0.1%), and most *Pv* infections were asymptomatic. Being Afro Colombian (Prevalence ratio (PR) 6.81; 95% CI [3.21 - 18.08]) and male (PR 1.71; 95% CI [1.29 - 2.29]) were risk factors to be G6PDd, while being G6PDd resulted in lower *Plasmodium* infection (PR 0.41; 95% CI [0.25 - 0.63]). Afro-Colombian populations in Quibdó have a high G6PDd and thus, a higher potential risk of hemolysis, suggesting that a G6PD test must be implemented before the use of a high dosage of primaquine or tafenoquine. Effective malaria control is a big challenge in the study area due to the high burden of asymptomatic infections, caused by *Pv*. G6PDd was not found among the studied IC, which harbors the highest burden of *Pv* suggesting an opportunity for the adoption of new interventions for radical cure in this population.

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MASS DRUG ADMINISTRATION FOR MALARIA IN LOS CHILES, COSTA RICA: ITS IMPLICATIONS FOR ELIMINATION

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Despite the significant achievements, malaria is still a public health problem in Costa Rica (CR). Malaria cases are concentrated in a few regions from which, Los Chiles foci have been responsible for the 81% of the CR cases in 2022. To contribute to the elimination of malaria in the main active foci (Los Chiles) in Costa Rica, a MDA was proposed by the MOH and partners. Three localities were selected San Gerardo, Coquital, and Medio Queso; and two farms that overall reported 64% of the cases in Los Chiles canton (97% Plasmodium falciparum, Pf)). We reported the results of a non-interventional, observational study conducted between January and June 2023. Two MDAs cycles were implemented among people who provided verbal consent and without any contraindications. A preparatory phase (Jan-Mar 2023) included an updated census, protocol design, planning, and door-to-door sensitization of the selected communities. Chloroquine (CQ) full treatment was given supervised for 3 days to the selected population in 861 households, and 2 farms. Overall, the average CQ completeness (full CQ 3d course) in the MDA1 (Apr 1-7) and MDA2 (Jun 5-9) among the selected 3 localities was 82% and 59.2%, respectively. In contrast, the average CQ completeness among participants in the farms was 33.4% in MDA1 and 47.7% in MDA2. Among all groups, the CQ refusal rate was increased 5x times - from 3.1% in MDA1 to 15.8% in MDA2. Adherence to more than two CQ doses was 88% and 89% in MDA1 and MDA2, respectively. Malaria cases dropped to zero after the end of MDA1 for 12 months; surveillance activities (passive/active case detection) have been maintained. The addition of a MDA in Los Chiles was successful in eliminating malaria transmission in the target areas for 12 consecutive months. To our knowledge, this is the first MDA for malaria conducted in Latin America after the updated WHO recommendations for chemoprevention strategies in June 2022. MDA (and other chemoprevention strategies) should be considered, assessed its feasibility, and incorporated more frequently at NMCPs to accelerate elimination targets.

7201

TARGETED TREATMENT WITH PRIMAQUINE FOR THE ELIMINATION OF *PLASMODIUM VIVAX IN A BORDER AREA OF THE GREATER MAEKONG SUB REGION*

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Plasmodium vivax malaria's high incidence hampers the Greater Mekong Sub-region's (GMS) 2030 malaria elimination goals. Thailand's adoption of the 1-3-7 surveillance framework for rapid case detection and containment

is commendable, yet insufficient due to challenges like hypnozoite-induced relapses and poor adherence to the 14-day primaquine (PQ) regimen. Hence, additional control measures are imperative to meet elimination targets. This study integrated the 14-day PQ treatment with reactive case detection activities as part of the 1-3-7 surveillance approach, termed Targeted Primaquine Treatment (TPT). Three districts with the highest reported *P. vivax* incidence along the Thailand-Myanmar border were selected as study sites. Within each district, two villages with similar geographical and malaria prevalence profiles were assigned as treatment or control groups. While individuals in the control group received standard malaria prevention and control measures (SMPC), eligible individuals in the treatment group received TPT (PQ 0.25mg/kg/day for 14 days) under directly observed treatment, in addition to SMPC, with the target of 150 index cases per group. The impact of TPT will be assessed by comparing two indicators (incidence and prevalence) before and after TPT in both groups. From October 2023 to March 2024, 55 index cases were identified across the two groups, with over 300 individuals receiving the 14-day PQ regimen. The TPT will continue until July 2024 to cover the peak malaria transmission in these areas. Preliminary analysis with available results detected an impact of TPT on the infection rate in the treatment group but minimal change in the control group. Notably, no severe adverse effects related to PQ were reported. In conclusion, early results of TPT shows potential in reducing the burden of vivax malaria. Its integration into existing malaria elimination efforts, such as the 1-3-7 strategy, requires minimal additional resources. Thus, TPT offers a viable strategy to enhance *P. vivax* malaria elimination, not only in Thailand but also in the broader GMS and Southeast Asia regions where *P. vivax* remains prevalent.

7202

ADVANCING MALARIA DIAGNOSTIC AND TREATMENT ACCESSIBILITY: A COLLABORATIVE APPROACH TOWARDS ACHIEVING NATIONAL TARGETS IN BENIN

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In Benin, significant improvements have been made in combating malaria, evidenced by a notable decrease in incidence rates by over 20% in 2023. However, this positive development is counteracted by a 17% rise in malaria lethality, escalating from 1.2 to 1.4 per 1000 cases. Nonetheless, hospital lethality has remained steady at 1.6%. These statistics underscore a pressing issue in malaria-related fatalities and emphasizes the urgent necessity for enhanced commodity access, especially for severe malaria cases. To address the challenges related to commodity access, the National Malaria Control Program has undertaken various initiatives, including supply chain activities focused on supervision, healthcare facility training, central-level quantification activities and supply data reviews. While these efforts have led to a continuous decrease in stock outs across the country since 2021, the availability of testing and treatment remains moderate, fluctuating between 70% and 80%. This level falls below the national target of 95%. Availability of testing and treatment commodities were addressed with comprehensive data reviews aiming at strengthening malaria surveillance activities and leveraging data insights to strengthen commodities access. Since 2023, one annual coaching session has been conducted, empowering healthcare providers to deliver accurate and timely malaria diagnosis and treatment. Building upon the successes of the previous year's efforts, which were primarily centered around healthcare facility training, this coaching approach has evolved this year to include 40 hospitals. By broadening the scope of the coaching to include hospitals, the National Malaria Control Program aims to extend its reach and impact, especially regarding severe malaria, and ensuring that diagnostic and treatment accessibility is optimized across all levels of the healthcare system. To further strengthen this initiative, results from the collaborative efforts of the data reviews will be used to directly inform the content and focus of coaching sessions, ensuring alignment with evolving challenges and priorities.

7203

IMPROVING DATA QUALITY AND SUPPLY CHAIN SERVICE DELIVERY THROUGH TARGETED CAPACITY BUILDING IN RESOURCE-CONSTRAINED SETTINGS: A CASE STUDY OF TWO SELECTED LOCAL GOVERNMENT AREAS IN KANO STATE, NORTHERN NIGERIA

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Variances between dispensed-to-user data from the pharmacy and the number of patients accessing malaria prevention and treatment services have remained a source of concern in Kano State Nigeria. This mismatch can result in inaccurate quantification leading to overstocking or understocking of health facilities resulting in wastage which affects commodity security. For improved supply chain data management and accountability, formal refresher training is needed to retain institutional capacity amidst high attrition of personnel because of transfers, retirements, and migration. The Targeted capacity building (TCB) model was introduced to bridge the attrition gap of trained personnel without adequate resources for robust refresher training in all facilities. Twenty-four health facilities and 30 staff were selected in two local government areas (LGAs) with data triangulation variance greater than 10% and less than -10% indicating weak performance. A TCB session was planned to focus on the root causes and how to reduce the variance between the data sources. To ensure knowledge is retained after the training, a performance monitoring plan was developed with health facility workers and LGA personnel for follow-up. Before TCB, the cumulative average variance between dispensed to user data and the number of clients accessing malaria services recorded on the facility register and other registers collating malaria services between January and June 2023 was -44% and 25% respectively. These values improved to -22% and 8% for the respective LGAs following TCB from July to December 2023. The findings support the approach of using targeted capacity building in resource-limited areas, focusing on facilities and LGAs with performance issues. Continued analysis should be done to ascertain if the TCB approach can be sustained and continuously used.

7204

UTILIZATION OF MALARIA CORE TEAM STRATEGY ENHANCES STATE GOVERNMENT STAFF CAPACITY AND IMPROVES EFFICIENCY. A CASE STUDY OF OGUN STATE, SOUTHWEST NIGERIA

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Management Sciences for Health (MSH), a sub-recipient of Catholic Relief Services, implemented the Global Fund Malaria Grant, New Funding Model (NFM3) in 11 states in Nigeria from 2021-2023. One perennial challenge which the MSH project team sought to address during this period was that the State Malaria Elimination Programs (SMEP) staff lacked the capacity

to coordinate project activities and provide technical assistance to health workers, leading to a lack of ownership of grant interventions and making sustainability nearly impossible. MSH project team introduced the Malaria Core Team (MCT) strategy to enhance the capacity of SMEP personnel to address identified gaps. The MCT consists of SMEP technical staff and MSH state-based technical staff. MSH staff coached and mentored the government personnel in providing on-the-job training to service providers, through joint site visits. SMEPs now take ownership of grant interventions and ensure accountability for malaria health products, promoting sustainability. MCT members monitor project activities without MSH staff support and provide training to health workers using MSH-designed and national tools. Four SMEP personnel participated in a 2021-2023 MCT visit to Ogun State, visiting 180 health facilities, mentoring 450 workers, and advocating for smooth implementation, ensuring 40% of project-supported facilities were visited. The strategy of MSH, which involves working closely with governments, has significantly improved service delivery and reporting at the facility level. The Malaria Core Team's monitoring and supervisory visits have improved service providers' compliance with National Malaria Treatment guidelines, particularly in secondary health facilities. These visits have helped providers become more familiar with the guidelines and current treatment practices, especially for severe malaria. The MCT has resolved issues such as non-reporting, poor documentation, and poor data quality, reducing the risk of serious problems.

7205

INTEGRATING ACTIVE SURVEILLANCE AND ENTOMOLOGY FELLOWSHIP FOR SUSTAINABLE MALARIA CONTROL AND ELIMINATION IN SOUTHERN ANGOLA

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Synergy initiatives aimed at enhancing malaria surveillance for elimination in border regions of Southern Angola started in 2017. The Ministry of Health is strengthening efforts for a sustainable path for a malaria elimination together with its regional partners. Under the Elimination 8 funded program, a strategy for active surveillance, including malaria case-based notification tracker system, was rolled out. Recently, a training program was conducted in Cunene and Cuando Cubango Provinces focusing on building capacity and sustainability of interventions for active surveillance. Fifty-three health workers of selected health facilities and focal points of 5 districts were trained on DHIS2 tracker, data driven decision making, vector control and entomology as path to scale up interventions. In addition, a fellowship program was set up to implement an entomological surveillance programme building local capacity. The intensification of capacity building interventions and integration with fellowship activities will allow to increase the scope of sentinel sites and enhance foci classification, investigation and response. This collaborative effort, led by the Ministry of Health, aimed to strengthen malaria information systems and case-based reporting to identify local transmission foci. This integrated approach not only enhances intervention effectiveness but also strengthens overall health system capacity, ensuring long-term sustainability and resilience against disease resurgence in the region. This abstract highlights the significance of interlinking active surveillance programs with entomology fellowships to achieve sustainable malaria control and elimination goals.

7206

THE IMPACT OF 1-3-7 FOCUS INVESTIGATION SURVEILLANCE IN A PRE-ELIMINATION SETTING IN SOUTHERN ZAMBIA: A ZONAL-RANDOMIZED TRIAL

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Since 2016, eleven countries have been certified as malaria free, but none of these are in continental Africa, where elimination challenges are unique. Recommended elimination strategies, like 1-3-7 focus investigation, feature heightened case-based surveillance and focal community response to index cases. A passively detected malaria "index" case, be reported within one day, classified within three days, and followed up in its community with focal response within seven days. To date, no study has measured the effect of 1-3-7. Choma District, located in Southern Province, Zambia is a very low transmission setting (under-5 RDT prevalence is 3.3%). The MUSEMO study was a 24-month zonal-randomized study in two health center catchments areas in Choma District to measure the impact of 1-3-7 on the prevalence and incidence of malaria. 1-3-7 was deployed in a randomly-selected half of the zones in the study area. Surveys measured malaria prevalence in index-case communities 7 and 35 days after index case diagnosis to compare 1-3-7, "intervention", and non-1-3-7, "control" zones through multi-level logistic regression. Health facility data reported weekly zonal incidence and Poisson regression estimated changes in incidence rate across intervention and control areas. Community qPCR prevalence increased between the 7 and 35-day visits from 1.9% to 2.8%, but there was no significant difference across arms. The weekly zonal incidence as reported through surveillance was 81% lower in the zones using 1-3-7 surveillance (ratio of IRR: 0.19, 95% CI: [0.08,0.43], p-value <0.01). The increase in community-level prevalence suggests there is ongoing local transmission in the weeks after an index case, and that current focal 1-3-7 response does not interrupt this. The decrease in catchment-wide incidence provides evidence that the surveillance component of 1-3-7 may drive improved awareness of localized malaria risk and planning and response to mitigate it. These findings support the use of the 1-3-7 surveillance approach to focus investigation and to add additional focal response strategies to day-7 activities.

7207

VILLAGE HEALTH TEAMS IMPROVING THE MANAGEMENT OF MALARIA IN CHILDREN UNDER 5 YEARS IN UGANDA'S WEST NILE REGION: A CASE OF MOYO DISTRICT

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Malaria remains a significant health challenge in low- and middle-income countries, particularly affecting children under 5 years and pregnant women. In Uganda's West Nile Region, malaria prevalence is 22%. Moyo District in West Nile has been grappling with high malaria test positivity rates, ranging from 62% (January 2023) to 91% (December 2023). To address the problem, in September 2023, all 466/466 village health team members (VHTs) in Moyo were trained on case identification and fever management through integrated community case management (iCCM) of malaria, pneumonia, and diarrhea in children under five years of age. A cascaded training approach was used through the levels of service delivery in the district, starting from the district to the VHT. Training focused on case management and reporting of data and was followed by quarterly VHT meetings and mentorships to ensure compliance and accountability for commodity refills. At the start of the intervention, the

National Medical Stores (NMS) supplied 11,691 malaria commodities to 30 health facilities in Moyo, of which 70% (8,133) went to the VHTs. The availability of commodities for iCCM in Moyo ensured that malaria test and treatment ratios remained above the 95% national target. Following the iCCM training, VHT knowledge scores increased to an average of 75% from 39% at baseline. The number of children under five years attended to by VHTs within the community increased to 2,872 from 1,694 before the intervention. Fever cases attended to by VHTs also increased to 2,595 from 1,552. The success of this approach underscores the potential of VHT-led iCCM to significantly improve access to malaria case management services, particularly in hard-to-reach communities.

7208

MODELING THE IMPACTS OF SEVERE STORMS ON MALARIA INCIDENCE IN MOZAMBIQUE FROM 2016-2023

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Increases in frequency and severity of extreme weather events (e.g. cyclones, tropical storms, and severe storms) are a hallmark of climate change, and impact established programs to control and eliminate malaria. Mozambique is already experiencing these, with increases in tropical storms, tropical cyclones, and floods over the past 10 years impacting the entire population and currently does not have the capacity to respond to all of the infectious disease challenges that result. The National Malaria Control Program (PNCM) is charged with implementing and maintaining the infrastructure to support P. falciparum prevention, control, and elimination programs throughout the country. In this resource poor setting, the progress of these programs is under constant threat when infrastructure is damaged due to severe weather events because emergency response is limited to the highest impacted areas. Areas outside of direct impact, have not received support in the aftermath, and not specifically for malaria. We integrated malaria surveillance data and climate data for both named and unnamed storms to determine geographic areas in Mozambique that are at an increased risk of malaria due to infrastructure damage following severe weather events. We used databases from the World Meteorologic Organization database of named tropical storms and cyclones to identify the locations and tracts of the eyes of the storms. We quantified the areas impacted by these storms using NASA satellite precipitation data matched to the time and locations of the eyes of the storms. We integrated temperature data from NASA satellites also. We used daily precipitation data, monthly temperature data, and daily wind data (from NASA weather stations) to detect storms that don't reach the classification to be a named storm. We used these data with the malaria incidence data aggregated to the District level to quantify the population at risk in these areas following severe storms using a Bayesian time-series model. This study will present preliminary findings of our models for at the national level in Mozambique.

7209

EFFECTS OF COMMUNITY MALARIA CASE MANAGEMENT TO THE OVERALL MALARIA INCIDENCE IN BUSIA COUNTY KENYA 2022

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The objective of the study was to determine whether Case Management of Malaria (CCMm) by Community Health Volunteers (CHVs) affect the trends of malaria incidence in Busia Kenya from 2018 to 2023. The study determined the annual proportion and trends for malaria cases tested and treated at health facilities and Community Units and correlated the trends with annual malaria incidence out-patient malaria cases, weather patterns, climate change, and commodity availability at the community level. This was a retrospective cross-sectional involving the analysis of routinely collected malaria data as reported on the Kenya Health Information Systems. The proportion of Suspected Malaria Cases being tested by Community Health Volunteers compared to those tested at Health facilities increased from 11% in 2019 to 45% in 2022. The rate of malaria infections per month remained almost constant, with peak infections occurring in May annually, except in May 2020. Over time the contribution of CCMm in overall malaria case management and incidence has increased, with more malaria cases being treated in the Community as of mid 2022. The incidence of Malaria has remained high over the years. The study concluded that CCMm improves access to Malaria treatment services but does not reduce the Annual Malaria Incidence in Busia County.

7210

MALARIA AND ANAEMIA PREVALENCE AND ASSOCIATED FACTORS AMONG PREGNANT WOMEN INITIATING ANTENATAL CARE IN GHANA

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Malaria infection in pregnancy is associated maternal anemia and low birth weight. Although there are improving levels of implementation of recommended malaria and anemia control interventions in Ghana, there is no commensurate reduction in maternal anemia prevalence and low birth weight. A health facility-based cohort study was conducted between 2018 and 2020 to identify current risk factors of low birth weight and maternal anemia in 2 regions of Ghana. The baseline malaria infection and anemia prevalence and associated factors is reported here. Five thousand, one hundred and ninety-six pregnant women of all parities, ages and gestational ages were enrolled at first antenatal care visit in Ashanti and Volta regions of Ghana. Descriptive and inferential statistics were conducted on data collected on socio-economic and demographic characteristics, obstetric history, ITN ownership and use, presenting complaints and laboratory results of full blood count, G6PD and sickling status, malaria parasite, HIV, syphilis, Hepatitis B, schistosoma and helminth infections using STATA version 16. The mean (SD) age and gestational age were 27.3 (6.5) years and 15.5 (8.37) weeks respectively. ITN use was 59.8% compared to 80.8% ownership. Overall malaria parasite prevalence was 5.7%; higher in Ashanti (10.24% [95% CI: 8.92 - 11.68]; mean parasite density = 982/µl) compared to Volta (2.63% [CI: 2.07 - 3.29]; mean parasite density = 18226/µl). Overall anemia prevalence was 55.2%; higher in Volta region (65.6% [95% CI: 63.78 - 67.31]) than in Ashanti (42.6% [95% CI: 40.53 - 44.60]). Women with malaria infection were more likely to be resident in Ashanti, primipara, of lower wealth status and reported at least a clinical symptom. Women were more likely to be anemic if resident in Volta region, had malaria infection, were younger than 25years, booked ANC later and of lower wealth index (P<0.001). Although malaria infection prevalence is relatively low it still poses a risk to maternal anemia. Maternal anemia is high and of serious public health importance appearing to be related more to geographic location and wealth index.

7211

THE RELATIONSHIP BETWEEN PLACENTAL MALARIA AND PREECLAMPSIA

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Pre-eclampsia (PreE) and malaria are leading causes of perinatal morbidity and mortality in sub-Saharan Africa. Placental malaria (PM) has overlapping pathophysiology with PreE, causing abnormal angiogenesis in the placenta. Placental damage from PM may predispose patients to PreE. Previous studies have demonstrated an association between hypertensive disorders of pregnancy and PM but are limited by a failure to characterize the PM (acute v. earlier in pregnancy) and type of hypertensive disorder (PreE, eclampsia, all hypertensive disorders of pregnancy). Utilizing placental specimens and clinical data collected during a randomized

controlled clinical trial of intermittent preventive therapy during pregnancy in Malawi, we aimed to examine the association between PM and PreE. All individuals from the parent study with singleton pregnancies and placental histopathology and PCR available were included in this analysis. All patients were HIV-uninfected and primi- or secundigravid. No patients had chronic hypertension or advanced maternal age. Chi-squared tests were performed. Among the 751 individuals meeting inclusion criteria, 125 (16.7%) had evidence of PM. Of those, 105 had hemozoin pigment present, indicative of an infection earlier in pregnancy. Out of the 751 participants, 31 (5.0%) had PreE, 6 had eclampsia (1.0%) and 82 (13.1%) had any type of hypertensive disorder of pregnancy. There was no statistically significant difference in rates of PreE, eclampsia or hypertensive disorders of pregnancy based on the presence of PM or hemozoin pigment. Although, individuals with hemozoin pigment had nearly twice the rate of preeclampsia as those without (6.7% v. 3.7%, p=0.16). We suspect that placental infection in the 1st or 2nd trimester, rather than acute infection at the time of delivery may increase the risk of PreE. This study is limited by its sample size, and is likely underpowered to detect a difference in PreE rates based on PM. Further studies characterizing the relationship between PM and hypertensive disorders of pregnancy are warranted, with particular focus on the role of antimalarial treatments in reducing the risk of PreE.

7212

MALARIA-GUT MICROBIOTA INTERACTIONS WITHIN THE CONTEXT OF GEOGRAPHIC REGIONS, NUTRITION, PARASITIC CO-INFECTION & AGE IN RWANDA

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Malaria, caused by *Plasmodium* species, is a major health problem affecting the global south disproportionately. The gut microbiota (GM) play a critical role in health and disease including infections such as malaria. Evidence shows a significant interplay between the host GM and both the transmission and severity of malaria. Malaria-GM interactions may be shaped by several factors including, but not limited to, geographic location, nutrition, co-infections such as soil-transmitted helminths (STH) and age. Therefore, we used a multidimensional approach to explore interactions between malaria and the GM in Rwanda. Between 11/2021 and 09/2022, we conducted a study in three malaria-endemic provinces of Rwanda: East, South and West. We recruited 169 participants (85 females and 84 males) aged between 2-78 years. In addition to questionnaire-derived data, malaria diagnosis by rapid diagnostic test (RDT) and blood smear was followed by STH screening in stool by formalin-ether technique to make comparison groups. Fecal microbiota was analyzed using 16S rRNA gene sequencing. We discovered a significantly differential beta-diversity ($p < .002$, PERMANOVA) which may be explained by a 20-30% lower fiber intake ($p<.001$, ANOVA) observed in the West compared to both the other provinces. Relative abundance of *Faecalibacterium* and *Succinivibrio* was significantly higher in the West than in the East/South ($p<.001/p<.02$, Kruskal-Wallis) and lower in the West than in the South ($p<.01$, Kruskal-Wallis) respectively. Unlike age, infection status was not linked to GM composition differences. Moving forward, we are collecting samples with a better representation of asymptomatic and severes cases to perform metagenomic and micronutrional analyses.

7213

A REVIEW OF 15 YEARS OF CRYPTIC MALARIA IN THE UNITED KINGDOM

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Autochthonous malaria transmission has not been observed in the United Kingdom since 1953. Nearly all malaria cases diagnosed in the UK are imported, in individuals who acquire their infection during travel to a malaria-endemic region. Cryptic malaria cases where there is no history of recent travel of that nature and for which initial epidemiologic investigations cannot identify a plausible mode of acquisition are rare in the UK, making up less than 1% of cases since 2000. All cryptic malaria cases in the UK are investigated according to published national guidance. We reviewed 15 years of cryptic malaria in the UK between 2009 and 2023, to identify trends, compare investigation outcomes and inform updates to national cryptic malaria guidance. Nine cases of cryptic malaria, 8 *Plasmodium falciparum* and one *P. malariae*, were reported in the UK between 2010 and 2023, with the highest annual total of 3 cases in 2023. All cases were reported in Southern England, with the majority reported in London. Additional investigations were undertaken by the UK Health Security Agency's national Travel Health team, Malaria Reference Laboratory, local health protection teams and the national Medical Entomology team, to identify the potential source of infection for each case. Other stakeholders were included where appropriate. Five cases were classified as possible 'baggage' or 'airport' malaria, one as recrudescence in a semi-immune person due to pregnancy, one as a probable case of transfusion-transmitted malaria due to *P. malariae* and no clear sources were identified for the remaining two cases. Autochthonous transmission was excluded in all cases. Although it is considered unlikely that malaria will become endemic again in the UK, climate change could facilitate a re-emergence of natural transmission of malaria. Thorough investigation of cryptic malaria cases is essential in identifying potential sources of infection, and to ensure accurate and timely surveillance, which is vital to detect and prevent autochthonous malaria in the UK.

7214

KNOWLEDGE, ATTITUDES, AND PRACTICES OF MALARIA TREATMENT IN RWANDA: A CROSS-SECTIONAL STUDY

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Malaria remains a significant public health threat. Prompt diagnosis with effective treatment is a key malaria intervention and its success depends on communities having knowledge of and adhering to malaria treatment guidelines. Rwanda, the first African country to confirm partial artemisinin resistance, must promptly address this threat by ensuring optimal malaria treatment practices in the community. This study measured the malaria knowledge, attitudes, and practices (KAP) among febrile patients seeking treatment at government clinics, aiming to identify factors influencing malaria treatment practices across Rwanda. A cross-sectional study was

conducted in six health centers in areas of high malaria transmission in Rwanda. Patients or caregivers of children seeking treatment for fever were enrolled and interviewed using semi-structured questionnaires. The frequency and proportions of the KAP indicators were determined using descriptive statistics. From December 2023 to February 2024, 406 participants were enrolled, and 56% were female, most lived rurally (80%), and 50.2% attended primary school. Malaria knowledge was high: symptoms (86.7%), transmission (82.7%), and control (73.7%). Only 71.2% owned insecticide-treated nets (ITNs), 50.5% received indoor residual spraying (IRS). 44.3% (180/406) sought malaria treatment in the last 6 months; of those, 46.1% completed medication in 3 days, 36.7% stopped in 2 days, 10.6% over 3 days, 2.8% unsure. Furthermore, 26.8% (109/406) took antimalarials for fever without diagnosis; 54.1% got them from drug outlets/pharmacies. Malaria knowledge and positive attitudes towards treatment and prevention strategies among participants were high across all health centers. However, these positive attributes did not translate into malaria prevention and treatment behaviors. Specifically, poor adherence to malaria treatment was observed, which is likely potentiating the emergence of resistance. In an era of developing drug resistance, there is an urgent need to identify and implement effective interventions to boost malaria treatment and adherence practices in Sub-Saharan Africa.

7215

QUANTIFYING THE RELATIONSHIP BETWEEN MALARIA IN PREGNANCY AND MATERNAL ANEMIA USING ROUTINE ANTENATAL CARE-BASED SURVEILLANCE DATA IN TANZANIA

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Whilst malaria is associated with an increased risk of severe anemia, especially in first-time mothers, the relationship is not well characterized. To address this gap, we used routine antenatal care (ANC) surveillance data from mainland Tanzania (January 2016-September 2023) from pregnant women attending their first ANC visit. We evaluated trends in maternal malaria and severe anemia (hemoglobin (Hb) <85g/L) prevalence using descriptive statistics and used binomial mixed-effects logistic regression to estimate adjusted severe anemia prevalence, accounting for variation in Hb testing coverage. National malaria prevalence was 6.8% and severe anemia prevalence was 1.7%. Of the 17.2 million women attending first ANC, 91.8% were tested for malaria, but only 63.4% were Hb tested. Health facilities Hb testing <75% of attendees (compared to ≥ 75%) had higher malaria prevalence (8.37% vs 5.87%) and a higher percentage of women visiting after the first trimester (34.0% vs 25.2%), suggesting those who were not tested for severe anemia were likely those most at risk of severe anemia. After adjusting for variation in Hb testing coverage, our estimate of severe anemia cases increased 46.5% (unadjusted n = 184994, adjusted n = 271089). We found a weak positive correlation between malaria and adjusted severe anemia prevalence in different regions over time (Spearman's $\rho = 0.371$, $p<0.05$). From age-disaggregated data, we found that as malaria prevalence increased, the relative risk of severe anemia increased in younger women. When malaria prevalence in under 20s was 0, the risk of severe anemia in pregnant women under 20 compared to women over 25 was 0.98 (95% Confidence Interval (CI): 0.92, 1.04), and as malaria prevalence reached 30%, the relative risk increased to 1.44 (95% CI: 1.31, 1.58). Our work shows the value of routine ANC data in providing temporal and spatial granularity on ANC coverage and prevalence of malaria and severe anemia in pregnancy. This analysis will be used to inform Tanzanian maternal health policy on resource allocation and intervention coverage to reduce maternal malaria- and severe anemia-related morbidity and mortality.

7216

MALARIA HIGH RISK POPULATION ASSESSMENT IN ZANZIBAR, MAY-AUGUST 2023

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In malaria elimination settings, cases tend to cluster geographically and occur among certain subpopulations. Clustering is often related to certain factors such as occupation or mobility, which increase an individual's risk for malaria infection. The U.S. President's Malaria Initiative supported a case-control study to identify malaria high-risk populations (HRPs) in Zanzibar. Patients presenting with symptoms of malaria at selected facilities were recruited from historically high burden shehias in two urban districts (Mjini and Magharibi B) and two rural districts (Kati and Micheweni). Between May and August 2023, the study recruited 197 cases and 557 controls matched by age group and sex. Logistic regression was used to explore associations between risk factors and the epidemiological outcome of local malaria infection, classified as no travel outside Zanzibar in the prior three weeks. In urban districts, night watchmen/police (odds ratio [OR] 5.3, 95% confidence interval [CI]: 2.7-10.6, $p<0.001$), construction workers (OR 3.0, 95% CI: 1.8-5.0 $p=0.007$), and farmers (OR 1.6, 95% CI: 1.1-2.2, $p=0.01$) were found to be at risk for malaria infection. Other high-risk behaviours in urban districts included night-time activities (OR 2.8, 95% CI: 1.8-4.3, $p<0.001$), meals taken outside (OR 2.0, 95% CI: 1.1-3.4, $p=0.01$), and recent travel within Zanzibar (OR 3.3, 95% CI 1.5-7.1, $p=0.002$). In rural districts, night-time activities (OR 3.8, 95% CI: 1.5-9.9, $p=0.006$) and taking meals outside (OR 2.7, 95% CI 1.1-6.6, $p=0.03$) were risk factors for malaria; however, there were no significant associations between occupational group and infection. There was no statistical association between malaria infection and net use in urban districts, but in rural districts, prior night net use was protective (OR 0.38; 95% CI: 0.2-0.8 $p=0.015$). In urban populations, some occupations were associated with increased risk of malaria infection, while only behaviors were associated with increased risk of malaria infection in rural populations. These findings suggest intervention targeting occupational groups could reduce malaria risk among HRPs in urban areas.

7217

ASYMPTOMATIC MALARIA RESERVOIRS IN HONDURAS: A CHALLENGE FOR ELIMINATION

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Malaria elimination efforts have resulted in substantial progress during the last 25 years. In central America, Honduras has decreased the incidence of malaria to less than 2,408 cases in 2023 and aspires to reach elimination by 2030. However, reaching the elimination goal requires an evaluation of existing strategies, understanding the prevalence of asymptomatic and submicroscopic infections, and the incorporation of novel intervention tools tailored toward decreasing transmission in the country.
We conducted an active surveillance study during November 2023 in the community of Kaukira (Gracias a Dios Department), which is a major focus

of malaria transmission in Honduras. Households were randomly selected, and all eligible individuals were invited to participate. Participants provided sociodemographic and epidemiological data, and a finger prick sample for a rapid diagnosis test (RDT), photoinduced electron transfer PCR (PET-PCR), and conventional PCR testing.
A total of 138 participants were enrolled from 81 households. Most subjects were female (n=91, 65.9%) with a mean age of 42 years and all tested negative by RDT. Molecular testing detected 17 malaria positive samples (12.3%) with 15 of these typed, resulting in eight cases of *P. falciparum*, six cases of *P. vivax* and one mixed infection. Parasitemia levels were low, ranging from 100 parasites/µL to less than 0.25 p/µL. None of the positive cases were symptomatic during enrollment. Statistical analysis revealed that individuals who had previously lived with someone diagnosed with malaria were three times more likely to test positive for malaria (Fisher exact test p<0.05, OR 3.3, 95%CI:0.9-11.4).
Our study highlights ongoing transmission of malaria in Kaukira due to the presence of human asymptomatic malaria reservoirs which can hamper malaria elimination efforts. Furthermore, the association between previous malaria exposure in the household and current infection underscores the need for targeted interventions. Finally, our results highlight the need for highly sensitive detection methods as part of the surveillance strategy to achieve the goal of malaria elimination.

7218

EVIDENCE OF DECLINING MALARIA TRANSMISSION IN ZIMBABWE, 2014-2023

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While global malaria progress has stalled in recent years, Zimbabwe has reported declines in annual incidence. We sought to examine the malaria epidemiological trend and assess if changes were a result of decreased outpatient attendance, testing, or reporting. We used R to extract and analyze malaria data reported in the national health management information system from 2014-2023. Between 2014-2023, a mean of 95% of health facilities submitted monthly data reports on time, but only 44% of reports had all malaria variables completed. Confirmed malaria cases reported by health facilities and community health workers (CHWs) decreased from 552,305 in 2014 to 244,247 in 2023 (56% decrease), resulting in a 59% decrease in reported annual malaria incidence, from 39 to 16 cases per 1,000 individuals. On average, 44% of cases were diagnosed by CHWs, increasing from 23% in 2015, when CHW coverage increased, to 57% in 2023. Over 70% of cases were reported between February and June, aligning with the rainy season. Three of the 10 provinces, Manicaland, Mashonaland Central, and Mashonaland East reported 75% of total annual malaria cases. The malaria case fatality rate decreased from 0.156% to 0.124% (21% decrease). The number of all-cause outpatient visits decreased 34%, from 12.6 million visits in 2014 to 8.3 million in 2023; however, the increased proportion of cases diagnosed by CHWs did not account for decreased outpatient attendance. Test positivity decreased 43%, from 37% in 2014 to 21% by 2023. When adjusted for potentially decreased testing (provider discretion and rapid diagnostic testing stockout) and reporting completeness, the overall trend of testing decreased by 23%. Even when corrected for missing data and testing rates, reported malaria cases have decreased in Zimbabwe.

7219

IMPACT OF THE INTERRUPTION OF SEASONAL MALARIA CHEMOPREVENTION IMPLEMENTATION ON MALARIA INCIDENCE IN BANDIAGARA, MALI

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Malaria remains a major public health threat, with 249 million cases and 608,000 deaths in 2022. Most deaths were in the African region in children under five (WHO, 2023).Seasonal malaria chemoprevention (SMC) is an effective control strategy that has led to a significant reduction in morbidity. A decline in malaria incidence in Bandiagara, Mali, a vaccine testing site, following the combined implementation of control strategies that included SMC was observed in 2017-2018 compared to the previous decade. Since 2016, SMC has been a nationwide measure in Mali. This study aimed to assess the impact of a 2021 interruption of SMC in Bandiagara on malaria incidence. SMC resumed in 2022.A cohort of 240 children in three age strata (3 months-5 years, 6-10 years and 11-18 years) was followed from July 2021-December 2022 in Bandiagara, an area with intense seasonal malaria transmission. We measured malaria incidence in number of episode person-years for 2021 and 2022. Overall, malaria incidence was higher in 2021 compared to 2022 with, respectively, 2.04 and 0.96 episodes, IRR=2.12 (95% CI: 1.75- 2.55; p<0.001). The incidence in the 3 months-5 years age strata was, respectively, 1.7 and 0.5 episodes in 2021 and 2022, IRR=3.5 (95% CI: 2.3-5.7; p<0.001). For the 6-10 years strata, the incidence was higher in 2021, with 1.8 episodes vs 1.1 episodes in 2022, IRR=1.56 (95% CI: 1.13- 2.15; p=0.0025). For children 11-18 years, the incidence was also higher in 2021, with 2.5 episodes vs 1.1 episodes in 2022, IRR=2.31 (95% CI: 1.73- 3.08; p<0.001). In 2021, the malaria incidence for children aged 6-10 years was similar to children 3 months-5 years, IRR=0.96 (95% CI: 0.68- 1.37; p=0.42). That year, children under 10 years old had a lower malaria incidence than children above 10 years, IRR=0.68 (95% CI: 0.49- 0.94; p=0.0084).The high malaria incidence in 2021 is likely a consequence of the SMC interruption and indicates the need for further support for SMC efforts. Interestingly, SMC interruption also impacted malaria incidence in children outside the targeted age group, suggesting the need for further investigation of malaria spread and vulnerability in pediatric populations.

7220

CONDUCTING AND OVERCOMING PEDIATRIC CLINICAL TRIALS CHALLENGES IN LOW AND MIDDLE INCOME COUNTRY SETTINGS: EXPERIENCE IN THE DEMOCRATIC REPUBLIC OF CONGO

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Africa carries the major burden of malaria worldwide with children being the most affected. Despite increased efforts in pediatric drug development, a notable lack of approved pediatric formulations for anti-malarial drugs in young infants remains. Products intended for older children are often administered to young infants increasing the risk of misdosing and adverse reactions. Clinical trial conduct in children in low and middle-income countries (LMIC) poses challenges due to restricted funding, specific clinical needs, ethical and regulatory protections and lack of infrastructure. In 2020, we initiated the CALINA study in a regional, regulatory clinical trial naïve, Congolese hospital. The study evaluated a new dosage of arthemether-lumefantrine (5mg/60mg) in the treatment of uncomplicated malaria in neonates and infants < 5 kilograms of body weight. To enable this, a decentralized trial approach was set-up. This included training

and weekly communication with the referral health centers, enabling a community network, obtaining participant feedback and getting buy-in from local authorities. Between 2020 to 2023, 14'350 infants presented with suspected malaria at the peripheral centers for consultation (10km radius from the study site); 284 infants were pre-screened out of which 50 were transferred to the main hospital and screened at site. This lead to 21 infants being included in the study, with no loss to follow-up, the highest recruiting study site. Through understanding of the patient pathway and efficient site set-up and management, the study demonstrated the complexity and success in recruiting a highly vulnerable population in LMIC settings. Although, the return on investment for such intensive set-up is disputable, a conventional trial configuration does not necessarily work when reaching vulnerable patients. A decentralized approach set-up to the endemic sites with a focus on patient pathway is key to successful recruitment. The need for expertise, capacity strengthening and constant site support to ensure operational efficiency is paramount for successful completion of such trials.

7221

SCOPING REVIEW OF NEUROLOGICAL SEQUELAE DUE TO *PLASMODIUM FALCIPARUM* AND *VIVAX* CEREBRAL MALARIA, 1980-2023

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Malaria is a deadly vector-borne disease transmitted by Anopheline mosquitos with the majority of disease burden being caused by the parasites Plasmodium falciparum and vivax (*P.f.* and *P.v.*). Cerebral malaria (CM) is considered the most severe complication due to its high mortality rate and potential to leave survivors with residual neurological sequelae. We aim to describe the current data landscape of *P.f.* and *P.v.* CM neurological sequelae prevalence and duration by conducting a scoping review. Three databases (Pubmed, SciELO, Web of Science) were searched from 1980-2023 as were reference lists. Representative populations in locations endemic for *P.f.* or *P.v.* at the time of the study were included. We pre-registered the review protocol (PROSPERO ID CRD42023431162). We found 2,589 sources, 2,008 of which were excluded during title/abstract screening. After full text screening, 76 of the remaining 169 papers were excluded due to study overlap. 11 studies identified from the references of other malaria systematic reviews were also included. A total of 104 articles were extracted and analyzed, covering 26 countries. Most studies (76; 71.0%) were conducted in Sub-Saharan Africa, 17 in South Asia (15.9%), 10 in Southeast Asia, East Asia, and Oceania (9.35%), and 4 in North Africa and Middle East (3.74%). Across time, 18 (16.8%) studies took place in the 1980s, 49 (45.8%) in the 1990s, 33 (30.8%) in the 2000s, and 7 (6.54%) in the 2010s. There were no studies conducted in Latin America, the Caribbean, or in 2020-23. Although 47.7% (51) of studies provided information on the sequelae acquired, only 29.0% (31) included sequelae duration. 5 (4.67%) studies included data on *P.v.* CM, of which only 2 focused solely on *P.v.* The lack of studies in *P.v.*-prominent areas combined with the absence of more recent data indicate significant gaps in the current research. This work will be updated through 2024 and serve as the basis for a further systematic review and quantitative synthesis. As some countries approach elimination, studies on prevalence and duration of CM neurological outcomes are needed to accurately quantify malaria burden and track elimination progress.

7222

PLASMODIUM OVALE CURTISI AND P.O WALLIKERI CO-CIRCULATION AMONG MALARIA INFECTED PATIENTS IN THREE HEALTH FACILITIES IN DSCHANG, WEST REGION OF CAMEROON.

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Malaria is a vector-borne parasitic disease that continues to be a global public health threat to humans. Four different species of Plasmodium have been identified to cause malaria in African settings: *P. falciparum*, *P. malariae, P. ovale sp., and P. vivax*. Previous cross-sectional surveys in 2013 and 2017 have indicated the circulation of *P. vivax* in Cameroon prompting further investigation into the circulation of falciparum and non-falciparum species among patients presenting with symptoms consistent with acute uncomplicated malaria. This study evaluated the presence of malaria infection among these individuals using molecular methods in the West region of Cameroon. A cross-sectional facility-based study was carried out among 431 clinically suspected cases of malaria in 2020 from three health facilities in Dschang. Socio-demographic and clinical data were collected from all consenting patients. In addition, blood spots on Whatman chromatographic paper (number 03) were collected from the patients. These blood samples were subjected to DNA extraction and a real time PCR-based assay which detects the Plasmodium 18s rRNA gene. Samples positive for *P. ovale* were further characterised as *P.o curtisi* or *P.o wallikeri* using realtime PCR assay and custom primers. Among 431 samples, 215(49.9%) were positive for *P. falciparum*, 12(2.8%) for *P. ovale* in mixed infections with *P falciparum*, and 5(1.2%) mono infections. 1 for *P. malariae*(0.2%) mono infection and 3 for *P. falciparum* and *P. malariae* mixed infection (0.7%). 195(45.2%) samples were negative for any Plasmodium species. Speciation real time PCR detected 9 *P.o curtisi* and 5 *P.o wallikeri* infections. 3 samples identified as mixed, indicating co-circulation of *P. ovale* species in Dschang. Risk factors for infection will be assessed by bivariate analysis. Non-falciparum infection was present, but relatively uncommon in acutely febrile patients in 2020. No *P. vivax* infections were detected different from previous reports in the same region from 2017. The variation in non-falciparum prevalence needs to be further evaluated to determine the impact these species will have on malaria control.

7223

NOSOCOMIAL MALARIA: RISK OF MALARIA AFTER HOSPITALIZATION AT JINJA REGIONAL REFERRAL HOSPITAL, UGANDA: A COHORT STUDY

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In endemic settings, public hospitals may provide ideal grounds for malaria transmission, infection and disease. We determined risk of malaria among patients hospitalized with non-malaria illness at Jinja Regional Referral Hospital (JRRH), Uganda. This is an ongoing prospective cohort study. Eligible patients (negative malaria test at admission, requiring prolonged hospitalization, and provision of consent) are consecutively screened and enrolled at the Accident and Emergency Unit of JRRH. Upon enrollment, study participants undergo clinical assessment and a blood sample is collected for malaria testing (blood smear, RDT, and PCR). This assessment is repeated on days 7, 14, 21, 28, 35, and 42 after hospitalization, on the discharge day, and on non-scheduled days if fever is reported. Risk of malaria infection is reported as incidence. Associated factors are to

be determined using regression models. From July 2023 to March 2024, 301 patients have been screened; 133 excluded and 168 enrolled. Of 168 participants who have completed follow-up, 18 (11%) tested positive for malaria infection. Of the 18 positive patients, 15 (83%) were male, 14 were RDT and microscopy positive and four were RDT positive only. The median age and time to infection was 33 years (IQR 20-40) and 19 days (IQR 14, 24), respectively. Two patients turned positive on day 7, two on day 13, and rest after day 14. The geometric mean parasite density was 1086 (95% CI 290, 4058) parasites/ul of blood. One patient was symptomatic and *P. falciparum* accounted for all infections. Only one patient had a medical condition (tetanus), the rest had different fracture types. The cumulative incidence of malaria infection among patients hospitalized with non-malaria illness is high. Protective measures need to be considered among hospitalized patients in endemic regions. The magnitude of the problem, including possibility of transmission of non-malarial mosquito-borne diseases among hospitalized patients, needs to be further studied. Complete results will be presented at the conference.

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AN EXPERIMENTAL HUMAN BLOOD-STAGE MALARIA MODEL FOR STUDYING *PLASMODIUM KNOWLESI* INFECTION

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The zoonotic parasite *Plasmodium knowlesi* has emerged as a major threat to malaria control in Southeast Asia. *P. knowlesi* is now the only cause of indigenous human malaria in Malaysia and is increasingly reported in neighbouring countries. Human experimental induced blood stage malaria (IBSM) models of *P. falciparum*, *P. vivax*, and *P. malariae* have provided insights into parasite biology and disease pathogenesis, and enabled evaluation of diagnostics and therapeutic interventions for these species. The aim of this study was to develop an IBSM model for *P. knowlesi*. First, the laboratory-adapted YH1 *P. knowlesi* strain, previously adapted to grow in human erythrocytes, was further adapted to grow in human serum and expanded *in vitro* to produce a new malaria cell bank (MCB) designated YH1-HS. We are now undertaking a volunteer infection study to evaluate the safety and infectivity of this new *P. knowlesi* MCB, and to characterise replication rates, host response to disease, and pharmacodynamic response to artemether-lumefantrine. We will enrol up to 4 malaria-naïve healthy adults in cohorts of 1 participant each. Participants will be intravenously inoculated with *P. knowlesi*-infected erythrocytes. The first participant will receive ~2,800 viable parasites, with participants in subsequent cohorts receiving a higher dose of parasites depending on results from preceding cohorts. Definitive antimalarial treatment with artemether-lumefantrine will be initiated when parasitemia, as measured by qPCR, reaches ≥10,000 parasites/mL, or on day 21 if qPCR remains negative. This study will provide insights into *P. knowlesi* biology and host response to disease, in addition to establishing a model to evaluate therapeutic interventions against this emerging parasite. Data will be presented.

7225

MOLECULAR EPIDEMIOLOGY OF RESIDUAL PLASMODIUM SPP. TRANSMISSION IN A PERUVIAN AMAZON BASIN COMMUNITY

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Plasmodium vivax remains a health threat in the Peruvian Amazon. Malaria caused by P. vivax often manifests as submicroscopic infections, serving as reservoirs that could hinder elimination efforts and contribute to persistent transmission. Active disease surveillance is essential for detecting asymptomatic cases, estimating risk for military populations, and informing public health interventions.We conducted a prospective malaria cohort study in Santa Rita, a rural community in the Peruvian Amazon basin, from March 2021 to January 2022. The study included a baseline screening and eleven follow-ups among individuals aged three months and older. We collected socio-demographic, clinical, and epidemiological information, along with whole blood for malaria microscopy and molecular testing, and serum samples for serology. We enrolled 351 subjects with a mean age of 27.2 ± 20.5 years and a female to male ratio of 1:1. The mean number of follow-ups per subject was 7.5 with 77.8% (273/351) completing their first follow-up to 51.6% (181/351) by the twelfth follow up.Five subjects tested positive by microscopy for P. vivax (1.4% prevalence) and one for P. falciparum (0.28% prevalence). A subset of 153 participants (1,597 samples) that were visit at least nine times and/or had a positive microscopy result underwent RT-qPCR. A prevalence of 30.06% (46/153) for P. vivax and 0.65% (1/153) for P. falciparum was found. Among the 153, 47 tested positive for malaria by TaqMan real-time PCR at least once during the follow-up period and 10 participants tested positive by the same detection method more than five times during their follow-up visits, with the highest recording positivity in 10 out of 12 follow-up visits. Our study showed a high submicroscopic/microscopic malaria ratio of 24.8 in Santa Rita and a group of persistently positive asymptomatic individuals. This may hinder malaria elimination efforts and contribute to malaria transmission in the community. Furthermore, our results emphasize the need of diagnostic methods with higher sensitivity to detect infections on a submicroscopic level to strive toward successful elimination strategies.

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A NATIONAL MOLECULAR SURVEILLANCE PROGRAM FOR THE DETECTION OF *PLASMODIUM SPP.* AND *P. FALCIPARUM* MARKERS OF ARTEMISININ RESISTANCE IN PAPUA NEW GUINEA - 2019-2023.

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Background: Papua New Guinea (PNG) has the highest burden of malaria in the Western Pacific Region and is committed to regional malaria elimination targets. Strengthening surveillance and laboratory capacity is therefore a high priority in PNG to enable the National Malaria Control Program (NMCP) and Provincial Health Authorities (PHA) to make evidence-based decisions within their local context. STRIVE is a partnership-based implementation research and surveillance strengthening project that has established a molecular-informed sentinel surveillance system integrating real-time data dashboards and mapping tools that can be readily accessed and

utilised by the NMCP and provincial partners in a user-friendly manner to support planning, stratification and containment. Method: Eight sentinel health facilities capture febrile illness case data and collect dried blood spot on filter paper from a subset of patients. Samples are sent to a central laboratory and screened using polymerase chain reaction (PCR) that amplifies a conserved region of the 18S rRNA gene. Species-specific quantitative PCRs (qPCR) are then performed on positive samples and a qPCR specific for the kelch-13 C580Y gene is performed on *P. falciparum* positive samples. Result: Between 2019-2023, molecular surveillance confirmed the presence of Plasmodium spp. infections in 53.4% of febrile illness cases observed at the 8 sentinel sites. *P. falciparum* and *P. vivax* predominated, detected in 31.6% and 15.5% of cases respectively, with *P. malariae* and *P. ovale* rarely observed in 0.3% and 0.1% of cases respectively. Kelch13 C580Y mutations were detected in *P. falciparum* cases in at all sites, with the highest proportion in Buimo catchment in Lae, Morobe Province. In late 2022, an outbreak of *P. falciparum* was detected in the highlands fringe site, informing and guiding local response measures. Discussion: Establishing a molecular surveillance program to guide national and local decision-making in PNG has been feasible and is providing the priority evidence the NMCP requires for targeted therapeutic efficacy monitoring and responding to outbreaks in non-endemic settings.

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EXPLAINING TRENDS IN PLASMODIUM FALCIPARUM TRANSMISSION IN AFRICA SINCE 2000

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Concern has grown in recent years about the slowing rate of progress against malaria in Africa, with population growth in many places outpacing reductions in per capita incidence. The reasons for this are much speculated upon, but ultimately poorly quantified. In this analysis, spatio-temporal trends in key drivers of African malaria since 2000 - donor-funded intervention coverage, but also urbanisation, health-system strengthening, and an increasingly changing climate - are reconstructed using mathematical and statistical models. A geostatistical model then links these drivers to the Malaria Atlas Project's database of infection prevalence observations (>55k geolocated points), to estimate their individual and cumulative impact on trends in malaria prevalence and incidence since 2000. We find that within established transmission boundaries malaria control is responsible for the majority of change in burden this century, but that the impact of vector control has waned in recent years as coverage has failed to reach targets. Our results suggest improvements in horizontal interventions - strong health-systems offering accessible and efficacious treatment to those in need - have played a critical role in reducing malaria prevalence in children under five, but more needs to be done to target remote populations with low access to healthcare. Counterfactual analysis removing the impact of direct malaria control (ITNs, ACTs, IRS, SMC) reveals a changing baseline - socioeconomic development in Africa has fundamental altered inherent environmental and personal receptivity. Changes in receptivity attributable to the climate, meanwhile, are highly stochastic, highlighting vulnerabilities both at transmission fringes (where intervention coverage is low), and within high-burden settings (where intervention coverage levels are most threatened by indirect effects of climate change).

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CASE STUDY: ROYAL THAI ARMY SOLDIERS DEPLOYED FOR UN PEACEKEEPING OPERATIONS IN SOUTH SUDAN IN 2023 EXPERIENCE HIGH RATES OF *P. FALCIPARUM* AND *P. OVALE* MALARIA UP TO NINE MONTHS POST-DEPLOYMENT

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Peacekeeping operations in sub-Saharan Africa continue to be impacted by malaria both in-country and among returning service members. The Royal Thai Army (RTA) deploys an Engineering Company to Juba and Rumbek, South Sudan to conduct peacekeeping operations as part of the UN Peacekeeping Mission in South Sudan. Each deployment is approximately 12 months long and units are rotated yearly. The unit is provided doxycycline one week before travel and mefloquine via direct observation therapy during deployment and for four weeks after returning. Malaria diagnosis is conducted using rapid diagnostic tests and treatment is provided according to WHO guidelines. In 2023, the 273-person RTA unit experienced a high rate of prophylaxis failure with 27 Soldiers (9.9%) diagnosed and treated for malaria while deployed and another 37 Soldiers (13.6%) testing positive for malaria following return from deployment, including 18 cases of *P. ovale* (Po), 14 cases of Pf, 4 cases of mixed Pf/Pv, and 1 case of Pv; this constituted the largest single apparent Po cluster observed in a military unit in recent history. Eight malaria cases (all Pf) were identified within one week of returning from deployment during a unit-wide microscopy screening. The remaining 29 cases (6 Pf, 4 Pf/Pv, 18 Po, and 1 Pv) were identified 1-9 months following return from deployment and when Soldiers became symptomatic and sought medical care. Given that both Pf and Po are relatively rare in Thailand it is likely such infections were originally acquired in South Sudan. This case study highlights two significant areas of concern. First, there was a high rate of sub-clinical (18 of 273) and sub-microscopic (10 of 273) Pf malaria in returning Soldiers who were given mefloquine prophylaxis. Second, there was a high rate of latent Po infection among deployed Soldiers (18 of 273) that was only detected weeks to months after returning from deployment. These findings highlight shortcomings to existing malaria prophylaxis and screening strategies for military units deploying to endemic areas and underscore the importance of active surveillance and/or presumptive treatment when these units return.

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SPATIO-TEMPORAL EPIDEMIOLOGY OF URBAN MALARIA OVER DIFFERENT TRANSMISSION SEASONS IN ACCRA, GHANA.

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Urban malaria has largely been ignored, but evidence is emerging that urban areas in Africa are receptive to malaria transmission. In Ghana, despite urban communities of greater Accra being considered low malaria risk and some areas earmarked for a push for elimination, pockets of moderate malaria transmission remain. This study aims to use three surveys spanning different transmission cycles to better understand the spatiotemporal malaria epidemiology in the Greater Accra Region of Ghana to support appropriate interventions towards malaria elimination. For each cross-sectional survey, 13 health facilities, stratified by malaria risk, and 100 households per catchment area were randomly selected. This was repeated at 3 time points throughout the transmission season.

All consenting household members were tested for malaria and anaemia and completed a questionnaire. QGIS™ and R/Rstudio software were used to map malaria cases and the number of malaria episodes. Spatio-temporal analysis with Anselin local Moran's I and Getis-Ord Gi* statistics were conducted. Preliminary results from the dry season survey include 2930 individuals sampled from 1313 households (average household size of 3.6). Of these, the average age was 29.8 (SD 18.7), with 42.9% males and 52.1% females. The overall malaria prevalence was 2.2% (95% CI: 1.7 - 2.8) but ranged from 0.8 to 5.9 per facility catchment area. The prevalence of anaemia was 7.1%% (95% CI 6.2-8.1) but ranged from 1.8 to 18.2% per facility catchment area. Low utilisation of insecticide-treated bednets (10%) the night before the survey was reported. The predominant forms of vector control employed in households were fumigation (15.9%) and mosquito repellents (5.1%). Our preliminary data confirms a low but heterogeneous prevalence of malaria infections during the dry season in Accra and a low-reported use of vector control methods typically employed in rural settings. Combined with the seasonal patterns observed, these results will fill an important gap in understanding urban malaria risk in Accra and other similar settings and help inform intervention strategies appropriate for this context.

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DESCRIPTION OF INPATIENT MALARIA CASE MANAGEMENT AT HEALTH FACILITIES IN SOUTHEASTERN TANZANIA, 2023

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In Tanzania, malaria service quality is assessed through Malaria Services and Data Quality Improvement (MSDQI) supportive supervision (SS). In 2023, PMI supported the National Malaria Control Program in Tanzania to investigate factors associated with malaria hospitalization and mortality rates using facility registers and SS data in Lindi, Mtwara, Pwani, and Ruvuma regions. A descriptive analysis of inpatient MSDQI data from 36 (28%) health facilities was conducted. Selection prioritized facilities with high malaria case counts and/or poor performance during previous MSDQI rounds. Stock availability of emergency medicines used to treat severe malaria complications, diagnostic accuracy, and health worker competence managing severe malaria cases were assessed. Scores from record review and MSDQI assessments were categorized as poor (below 50%), moderate (50- to 75%), and good (75% and above). From January to December 2023, the facilities reported 109,132 admissions, of which 10,834 (9.9%) were for severe malaria (31% of all [34,948] malaria cases) and 134 malaria deaths (1.2% case fatality rate [CFR] among severe admissions). Among the 10/36 (29%) facilities reporting severe malaria cases and malaria deaths, "good" scores were obtained by 97% for injectable artesunate preparation and administration; 70% for severe malaria treatment dose per patient weight; 54% for adequate emergency medicine stock, such as anticonvulsants and oxygen; 64% for management of associated emergency conditions; and 64% for adherence to national guidelines for treating complications associated with severe malaria. Despite an overall low CFR, serious remaining gaps in the inpatient management of severe malaria highlight the need for a comprehensive assessment of emergency commodity availability and ongoing support to improve service delivery. Improving healthcare providers' skills in managing severe malaria at the primary level could lower mortality rates and enable prompt treatment of complications.

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MAPPING MALARIA SEASONALITY IN SUB-SAHARAN AFRICA: METHODOLOGY AND INSIGHTS

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Seasonality is an important aspect of the epidemiology of malaria, and seasonal signals are evident in many metrics that measure transmission intensity and burden of disease. Understanding intra-annual variation, especially when attributable to epidemiologically-sensible environmental signals, can provide insight vital for accurate burden estimation, near-term predictions of outbreaks, evaluating the efficacy of seasonally-timed interventions, and the strategic planning of intervention campaigns and of clinical trials. Furthermore, understanding and combating malaria in highly seasonal areas will be critical for reducing global burden of this disease, as some of the highest burden areas are highly seasonal.

We have developed a geostatistical modelling framework to describe the intra-annual variation in the monthly proportion of P.*falciparum* incidence for sub-Saharan Africa between 2000 and 2020. Our model is trained using a comprehensive new data base of publicly available malaria time-series observations and incorporates a range of temporally dynamic environmental covariates. We derive key seasonal characteristics from the predictions of this model including season timing (onset, peak, and duration), seasonal intensity, and the number of seasons. We use inter-year variation of these characteristics to gauge temporal variation.

We present a range of products including maps of the derived characteristics: season timing, seasonal intensity, and inter-year variance. We discuss the apparent spatial structure in the arrangement of these characteristics, and the demarcation of seasonal and non-seasonal locations. Additionally, we provide insight into the influence of environmental factors; including maps illustrating the spatially heterogeneous relationship between the observed signals and the underlying climatic drivers. These findings provide useful insight into malaria seasonality and have the potential to improve the cost-efficacy of seasonally timed campaigns, which is critical those individuals currently living in areas with seasonal malaria.

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LONG-ACTING FORMULATION OF IVERMECTIN FOR EFFECTIVE MALARIA CONTROL: INSIGHTS FROM AN AGE-STRUCTURED MODELLING STUDY.

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Despite a great decrease of malaria cases and deaths starting from the twenties, a stagnation, and even an increase in the last years, highlight the limits of available tools for controlling the disease. A novel approach, complementary to existing ones, is to render Anopheles blood meals toxic by treating hosts using systemic insecticides like ivermectin. Efficacy of this strategy is hampered by the short remanence of approved oral dose, and thus, the requirement of repeated dosing to achieve full coverage. Hence, long-Acting Ivermectin Formulations (LAIFs) would increase efficacy with costs and logistical reliefs. In the frame of the IMPACT project, a LAIF candidate from the BEPO® technology has been selected using cattle model. Pharmacokinetics and pharmacodynamics (PK/PD) data showed sustained entomocidal efficacy for at least 3 months after a single injection. Here, we developed a mathematical model to predict associated

transmission blocking effects. Unlike other mathematical models in this context, we incorporated continuous structural variables, including humans age, and time post-LAIF injection (for both humans and vectors). Hence, we captured the longitudinal dynamics of (i) ivermectin systemic concentrations in the human bloodstream, and (ii) ivermectin associated effects on mosquitoes' life span after a blood meal on treated human.
Using our experimental PK/PD data, the model was run in a context of perennial transmission with a baseline of 30% clinical case prevalence and 80% Plasmodium prevalence in the population. Different scenariii were tested where efficacy duration, formulation dose and proportion of the population treated were adjusted. A 70% coverage of the 6-60 years old with LAIF at a dose of 1mg/kg (three months efficacy) would decrease malaria case prevalence from 30 to 19% (36% decrease) for 89 days. Translated to entomological parameters, this corresponds to a 65% decrease of infectious Anopheles' population. Using our model, we therefore demonstrated that MDA using our candidate LAIF would meet the WHO requirements of more than 20% decrease of clinical case prevalence for novel malaria vector control tools.

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BACTERIAL VAGINOSIS IS ASSOCIATED WITH INCREASED RISK OF PLACENTAL MALARIA

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Bacterial vaginosis (BV) is a common cause of vaginal discharge characterized by a shift in the microbiota from a *Lactobacillus*-dominant community towards a diverse set of anaerobic and facultative species. BV is associated with increased risk of adverse birth outcomes (low birth weight, preterm birth, chorioamnionitis) and reproductive tract infections (STI acquisition, HIV transmission). Although malaria and BV are considered independent risk factors for adverse birth outcomes, there are no published studies examining the vaginal microbiota within the context of malaria in pregnancy. Here, we demonstrate a novel association between BV and/or decreased vaginal lactobacilli during pregnancy and increased risk of placental malaria (PM). We analyzed data from an ongoing double-blinded randomized trial of intermittent preventive treatment during pregnancy (IPTp) in Uganda. In multigravida with evidence of malaria parasitemia during pregnancy, we found that BV at delivery was associated with increased odds of moderate-to-severe past-chronic PM, defined as histopathology with ≥ 10% HPF with hemozoin pigment deposited in fibrin (aOR=2.3 [95% CI: 1.4-3.8]). In a subset of participants, we used 16S rRNA amplicon sequencing to characterize the vaginal microbiota during pregnancy (at 12-20 and 32 weeks gestation). Among multigravida, we found a positive correlation between microbial diversity (suggestive of BV) and PM severity. BV-associated taxa—*Atopobium* and *Gardnerella*--were significantly more abundant with increasing PM severity. To test whether the vaginal microbiota was correlated with PM in an independent cohort, we analyzed data from an IPTp trial in Malawi and Tanzania (IMPROVE). In participants assessed for BV at 16-28 and 32-35 weeks gestation, vaginal fluid Gram stain with decreased *Lactobacillus* morphotypes was associated with increased risk of PM (OR=1.6, 95% CI: [1.0-2.4]). Overall, our data support a previously undescribed link between vaginal microbiota and PM. Further studies are needed to determine whether interventions targeting the vaginal microbiota impact severity of PM and related birth outcomes.

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ASSESSMENT OF THE INFECTIVITY OF MALARIA PARASITES FROM ASYMPTOMATIC SCHOOL CHILDREN TO *ANOPHELES* MOSQUITOES IN A HIGH TRANSMISSION AREA IN GHANA

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Asymptomatic malaria is prevalent in Ghana. Majority of these infections are sub-microscopic, and carriers would normally not seek treatment. They would therefore serve as infectious reservoirs for malaria transmission. This study assessed the infectivity of parasites from asymptomatic children to *Anopheles* mosquitoes in a high transmission area in Ghana. Ninety-eight healthy children were screened for malaria by microscopy and nested polymerase chain reaction using sequence specific primers targeting the 18rna of the *Plasmodium* gene. Presence of sub-microscopic gametocyte was determined by amplification of the *Pf*g377 gene by reverse transcriptase polymerase chain reaction. Whole blood samples from the asymptomatic children were used in a direct membrane assay using laboratory raised colonies of *Anopheles gambiae.* Infectivity was determined by the presence of oocysts in mercurochrome-stained dissected midguts viewed under the light microscope. Mosquito infection rate as well as oocyst density were recorded. Out of the 98 children who were screened, 73 (74.49%) were asymptomatic for malaria. Out of these, 13.70% (10/73) carried microscopic densities of parasites. Parasite density (geometric mean (95% CI)) amongst these participants was 2,560(1,383.29-6,903.39(parasites/µl). Molecular analysis indicated that 82.46% (57/73) had malaria parasites. Amongst these, 64.38% (47/57) were classified as having sub-microscopic infections. None of the participants carried gametocytes by microscopy, however *Pf*g377 gene amplification was observed in 33.33% (19/57) participants. Blood samples from 4 out of these 19 individuals (21.05%) were infectious to mosquitoes. These infections were observed in 9 midguts out of a total of 862(1.04%) midguts dissected for all feeding experiments. The total oocyst density observed was 28. Prevalence of asymptomatic malaria infections was high, and were associated with carriage of sub-microscopic densities of gametocytes which were infectious to mosquitoes. The asymptomatic children would therefore serve as a reservoir for onward transmission of malaria within the community.

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G6PD DEFICIENCY VARIANTS AND MALARIA: INSIGHTS FROM A HOSPITAL BASED STUDY IN AWKA, SOUTHEAST NIGERIA

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Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is prevalent in malaria-endemic regions, has been linked to a reduced risk of severe malaria due to impaired parasite growth in deficient erythrocytes. Conversely, it poses a high risk of hemolytic anemia in patients treated with the antimalarial drug primaquine. This study aims to investigate the prevalence of G6PD deficiency variants, their impact on hemoglobin levels, malaria parasite density, and their implications for malaria treatment policy in Awka, Anambra State, Nigeria. **Methods**: A subset of 100 malaria patients at Chukwuemeka Odimegwu Ojukwu Teaching Hospital in Awka, Nigeria, underwent screening for common G6PD mutations (A376G and G202A), which are particularly prevalent among individuals of West African descent. Malaria infection was confirmed using Rapid Diagnostic Test kits. The G6PD gene region was amplified using PCR, and Sanger sequencing techniques were employed to study the polymorphisms associated with G6PD variants.
Results: Molecular analysis revealed that the B variant (normal) was predominant, with 83% of the participants possessing this variant, while

17% had the mutant A+ (A376G) variant associated with mild G6PD deficiency. None of the participants tested positive for the A- (A376G/G202A) variant associated with severe G6PD deficiency. Both the B variant and the A+ variant (moderate) showed no significant impact on the hemoglobin and parasitemia levels of the study participants.
Conclusion: This study found only a low prevalence of the G6PD A+ (moderate variant) mutation among the participants, with no significant impact on their hemoglobin and parasitemia levels. This suggests that the observed G6PD deficiency variants may not have substantial implications for the management of malaria in this population.

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DECLINE IN THE INCIDENCE OF MALARIA IN BENIN IN 2023: INVESTIGATION OF ASSOCIATED FACTORS AND HOW TO MAINTAIN THE TREND

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Consecutively over past 4 years, Benin has observed a steady upward trend in incidence of malaria, despite the various interventions implemented to control the disease. For the first time in 2023, a drop in incidence was observed. The poor quality of routine epidemiological surveillance data and the low care seeking behavior were the main hypotheses put forward for this decline.Routine malaria data collected monthly and hosted on DHIS2, the repository for all health system data in Benin were analyzed. We analyzed indicators related to confirmed malaria cases with assessment of the temporal and spatial trend from 2020 to 2023 in relation the specificities in some interventions scaled-up nationwide for the first time in 2023.The number of confirmed malaria cases rose by 10.3% from 2020 to 2021(that is from 2.19 million cases to 2.42 million cases), then an upward trend was maintained between 2021 and 2022, with the number of cases rising from 2.42 million to 2.67 million (this is an increase of 10.2%). Between 2022 and 2023, an opposite trend was observed, with a 22.1% drop in the number of confirmed cases, from 2.67 million to 2.08 million. Compared to 2022, the number of tested cases increased by 1.5% and the positivity rate fell by 16%. This drop maybe attributable to the combined effect of several interventions: i) a new monthly data quality assessment method with the used rapid diagnostic test (RDT) cassettes verification as proof, which improves indicators relating to data quality; both campaigns of ii)the seasonal malaria chemoprevention (SMC) implemented in eligible areas in the northern side of the country; and the mass mosquito net distribution campaign, achieved good coverage of targets nationwide; and iii) the intensification of community-based interventions with the commitment of civil society organizations through the Zero Malaria Alliance. Malaria incidence in Benin declined in 2023, probably due to the synergistic effect of three majors' interventions put in place to control the disease. These interventions need to be reinforced in 2024 to maintain the improvement trend in malaria epidemiological surveillance indicators in Benin

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MODELING THE TEMPORAL INCIDENCE OF FEVER AND CLINICAL MALARIA IN DANGASSA, DISTRICT OF KATI, MALI FROM 2014 TO 2016

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Malaria remains one of the leading causes of morbidity and mortality in much of sub-Saharan Africa. Our objective was to study the temporal variations of the incidence of malaria and fever in Dangassa from October 2014 to December 2016 and to make an analytical comparison of these incidences.
Our study was conducted in Dangassa on the right bank of the Niger River with year-round access to the river water. This was a longitudinal study consisted of following healthy participants between cross passages: - 526 participants from October 2014 to June 2015 - 825 participants from June 2015 to November 2015 - 1234 participants from November 2015 to June 2016 - 987 participants from June 2016 to December 2016.
The Poisson regression model with the number of person months offset was used to estimate the person-month incidence of fever and malaria as a function of age class, season and sex parameters.
Results: The incidence rate of fever in the 5 to 9 year age group was 1.81 times that of children under 5 with a significant p ($p = 0.001$). Malaria during the high transmission season was 2.3 higher than the low transmission season with a significant p ($p < 0.001$).
Conclusion: This study has a significant variation in the variation of the incidence of fever and malaria in particular according to the age group of the season with a strong tendency during the period from June to November corresponding to the period of strong transmission in Mali.

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UNDERSTANDING RELATIONSHIPS BETWEEN ENVIRONMENTAL TEMPERATURE, RAINFALL, AND MALARIA IN CHILDREN UNDER 5 YEARS OF AGE IN SENEGAL

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Malaria transmission is greatly affected by weather conditions; thus, climate change is one of the main factors that could affect future trend of malaria cases in endemic countries. This research aimed to investigate the effect of temperature and precipitation on malaria in children under 5 years of age (U5) in five regions of Senegal (Diourbel, Kédougou, Kolda, Sédhiou, and Tambacounda). Monthly, district-level data on population and reported U5 children with malaria were gathered from the Senegal's national health management information system (HMIS) between 2018 and 2022. Monthly temperature and precipitation were estimated using remote sensing data from MODIS and from the Global Precipitation Climatology Centre. Time series analyses were performed to describe the trend of malaria incidence and weather indicators. The relationship between malaria incidence and weather indicators was investigated using generalized additive random effect models. From January 2018 to December 2022, 121,030 malaria cases in CU5 were reported in the HMIS for the study area. Malaria incidence declined from 68.2 cases per 1,000 CU5 to 18.6 cases per 1,000 CU5 (-72.1%) from 2018 to 2022, with a substantial decrease in 2020 and 2021. From 2018 to 2021 average temperatures decreased (MD: -4.2%; IQR: -2.7%; -5.7%) linked with increased precipitation (MD: 10.8%, IQR: 1.1%; 16.7%). In 2022, precipitation diminished (MD: -24.8%, IQR: -16.9%; -30.3%) and temperature increased (MD: 5.2%, IQR: 3.4%; 7.6%). Malaria incidence was significantly associated with weather conditions occurring in the previous 5 months. The association between malaria incidence and rainfall was larger than with temperature. Understanding climate-malaria links could help health systems to adapt their surveillance and intervention systems to address malaria vulnerability and adapt to a changing climate.

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TOWARDS ELUCIDATING THE IMPACT OF TRANSMISSION HETEROGENEITY ON THE RELATIONSHIP BETWEEN MALARIA PARASITE GENETICS AND CLINICAL INCIDENCE

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Molecular surveillance is emerging as a critical tool for malaria genomic epidemiology, and the integration of genetic metrics could synergize with and improve malaria transmission studies. In Senegal, we showed that clinical incidence and genetic metrics such as the frequency of multiple strain infections or complexity of infection (COI, the number of strains per infection) have a complex relationship. Specifically, relations between genetic metrics and clinical incidence differ sharply in regions with an annualized incidence greater than 10 cases per thousand year (‰) versus regions with less than 10‰. We hypothesize that changes in parasite genetics in higher transmission areas (>10‰) largely reflect differences in bulk transmission intensity, while those in lower transmission areas (<10‰) are more sensitive to differences in transmission heterogeneity (variation in transmission structure among populations, individuals, and vectors). To explore this hypothesis, we use GenEpi, a model which layers parasite genetics over a detailed, agent-based malaria transmission model (EMOD) to identify the parameter regimes where parasite genetics is more sensitive to changes in bulk transmission intensity or transmission heterogeneity. Here, we describe the model design and calibration strategy that will be used to address these questions. This involves: 1) fitting the model to the observed incidence and genetic metrics of three moderate-to-high transmission (>100‰) sites in Senegal, 2) comparing model predictions to genetic data collected from three low transmission settings (≲ 10‰), and 3) modeling different forms of transmission heterogeneity to determine whether they could be responsible for any deviations between modeled and observed values. Distinguishing genetic signals associated with transmission heterogeneity from those with bulk transmission intensity could inform tailored intervention campaigns designed to disrupt the transmission structure of a target population and, hence, be of great value to national malaria control programs.

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PLASMODIUM FALCIPARUM GENE SIGNATURES OF MALARIA DISEASE SEVERITY IN KENYAN CHILDREN

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We present signatures of disease severity from our analysis of *Plasmodium falciparum* (*Pf*) transcriptomes (n=60) obtained from pediatric patients with malarial anemia in a holoendemic transmission region: Siaya, Kenya. The statistical signal was enriched with several strategies including the exclusion of patients coinfected with HIV and/or bacteremia, to reduce alternative sources of variance. LASSO model selection identified 13 genes associated with low hemoglobin (Hb) levels and five associated with high Hb levels with a univariate *P*-value (by Welch two-sample t-test) less than 0.1. The majority of the 13 genes associated with poor outcomes (*i.e.*, low Hb) are central to known virulence mechanisms in blood-stage malaria and several have been investigated as potential malaria drug targets, *i.e.*, histone H3, mitochondrial ATP synthase, type I signal peptidase, plasmepsin X, STPP-2B (calcineurin), *Pf*EMP1 and RIFIN. LASSO model selection applied to particular subsets of the genes, such as kinases, metabolic genes, secretion systems, and those interacting with erythrocytes identified additional genes that may be linked with disease severity. Sequedex, a metagenomic analysis technique based on signature peptides, identified redox-related functional groups in the human host transcriptome that were elevated in severe disease (Hb<6.0 g/dL) but had no functional categories for *Plasmodium*. To better understand how genetic variation and gene expression patterns of highly divergent genes such as *Pf*EMP1 in the dataset were associated with low Hb levels, *Pf* transcriptomes were mapped onto the 14 *Plasmodium* chromosomes of the Kenya reference isolate (pfKE01) derived from plasmoDB. Our methodology included using peptide 10-mer analysis to address low complexity regions and genome duplications, read mapping with Bowtie2, and gene assignment using HTSeq. Using this approach, we aim to gain an enhanced understanding of the relationship between gene expression patterns and malaria severity.

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PLASMODIUM FALCIPARUM GENETIC DIVERSITY IN THE BLOOD STAGE VACCINE CANDIDATE ANTIGEN PFCYRPA IN SENEGAL

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Malaria represents a public health burden. Current estimates revealed a plateaued curve of the disease-associated morbidity and mortality, while approved vaccines are yet to show strain-transcendent protection. Our present study evaluates the breadth of genetic diversity of one of the malaria vaccine candidates in early phase I clinical trials, *P. falciparum* Cysteine-Rich Protective Antigen (PfCyRPA) and also predicts the functional impact. Samples used in this study were collected from informed consents patients diagnosed with symptomatic malaria infections in Kédougou, Senegal. *P. falciparum* gDNA was extracted prior to *PfCyRPA* amplification. *PfCyRPA* genomic sequencing were obtained through targeted deep amplicon sequencing using the NovaSeq 6000 platform and sequence reads analyzed using the Geneious Prime Software. Non-synonymous single nucleotide polymorphisms were called relative to the 3D7 reference sequence using a minimum variant frequency of 0.02 and minimum coverage of 1000 reads. To predict the functional impact, PfRh5-CyRPA complex was constructed using Pymol (PDB ID: 4U0Q and 6MPV) and structural predictions with mAb binding was performed. A total of 93 *Pf* clinical isolates were included in this experiment. Overall, we identified 15 distinct SNPs, of which only four (F41L, V165I, N270T and V292F) have previously been reported. The majority of the novel SNPs were rare and only identified in a single isolate, except for R236N (N=4), R50C (N=2), I196F (N=2) and K211Q (N=2). Furthermore, our structural threading analysis revealed 3 novel SNPs occurring near epitopes bound by inhibitory monoclonal antibodies, potentially impacting immune evasion, while other SNPs were predicted to impact *PfCyRPA* structure or interactions with its binding partner PfRH5. Our data demonstrate that *PfCyRPA* exhibits a relatively greater genetic diversity than previously described. The structural

studies reveal that novel SNPs could have functional implications on *PfCyRPA* recognition by inhibitory antibodies, complex formation, or structural modelling, all hypotheses that we are exploring functionally.

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EFFECTS OF RECOMBINATION ON LINKAGE DISEQUILIBRIUM IN THE EPIDEMIOLOGY OF PLASMODIUM FALCIPARUM MALARIA

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When multiple beneficial alleles are present in a population, there is no general evolutionary result guaranteeing that recombination will speed up or slow down the emergence and evolution of genotypes carrying multiple beneficial alleles. Translated to infectious disease control, this evolutionary ambiguity means that when multiple types of drug resistance are present, we cannot be sure whether recombination will act more strongly (1) to bring together single-resistant genotypes into multi-drug resistant (MDR) genotypes, or (2) to break apart MDR genotypes into single-resistant genotypes. We introduce a new version of an established and validated individual-based malaria transmission model where we have added individual mosquito bites, interrupted feeding by mosquitoes, and individual recombination events of different Plasmodium falciparum genotypes inside the mosquito's salivary glands. Recombination among P. falciparum genotypes occurs from two sources of variation: multi-clonal infections and interrupted feeding by mosquitoes, and the results from our modeling analysis show that 80% to 95% of recombinant falciparum genotypes are created from single uninterrupted bites on hosts with multi-clonal infections. However, higher rates of interrupted feeding accelerate the emergence of double-resistant genotypes from single-resistant genotypes through recombination. A comparison of drug-resistance management strategies with this new model shows that, over a 15-year timeframe, triple ACT strategies show the largest reductions in treatment failures, multiple first-line therapy approaches show the second-largest reductions, and ACT cycling approaches show the smallest reductions in future treatment failures.

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ASSESSING CHANGES IN *PLASMODIUM FALCIPARUM* GENETIC DIVERSITY IN NIGERIA POST-ACTS IMPLEMENTATION

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Understanding parasite genetic diversity over time and across regions can help gauge the impact of ACTs on parasite populations. We utilized a high-resolution method that employs targeted sequencing of microhaplotypes to evaluate changes in Plasmodium falciparum transmission intensity in Nigeria, 15 years post-ACTs introduction. We utilized 593 DBS samples from children aged 12-60 months collected from therapeutic efficacy studies performed across six States at four time points between 2010 and 2020. We extracted genomic DNA and performed amplicon sequencing of 100 highly diverse microhaplotypes. The median expected heterozygosity (He) of the microhaplotypes was 0.56 (interquartile range: 0.43-0.73) across all States and not significantly different across time. A majority (61%) of the microhaplotypes had He>0.5 indicating sustained genetic diversity over time and across States, comparable to findings in Mozambique. Notably, 85% of infections were polyclonal, with mean complexity of infection (COI) of 3.4, suggesting high within-host diversity. The mean intra-host relatedness among parasite clones was 0.63, suggesting significant inbreeding and a major role of cotransmission in maintaining polyclonal infections within all populations; this however, resulted in an effective COI of 1.95. Spatio-temporal pairwise comparison using identity by descent showed low proportion (<3%) of significantly related parasites across all States, consistent with the high genetic diversity observed across all States regardless of the Year. This is in line with previous studies from Nigeria. Our study indicates no genetic evidence of reduction in malaria transmission intensity over the study period, aligning with national survey reports from 2010 and 2018. The persistent high genetic diversity and lack of decline in transmission underscore the need for ongoing surveillance of the malaria parasite's genetic landscape. This analysis suggests that merely increasing the coverage of existing interventions may not suffice. Instead, exploring new strategies or enhancing existing ones to effectively combat malaria in Nigeria is imperative.

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MALKINID (MALARIA KINSHIP IDENTIFIER): A LIKELIHOOD MODEL FOR IDENTIFYING PARASITE GENEALOGY RELATIONSHIPS BASED ON GENETIC RELATEDNESS

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Pathogen genomics is a potent tool for tracking infectious disease transmission. In malaria, sexual reproduction and recombination in mosquitoes can generate genetically related progeny whose genomes contain identical-by-descent (IBD) segments. In theory, IBD can be used to distinguish genealogical relationships (parent-child [PC], full-sibling [FS], etc) to reconstruct transmission history or identify parasites for genotype-to-phenotype quantitative-trait-locus (QTL) experiments. We developed a new likelihood model, *MalKinID* (Malaria Kinship Identifier), based on genomic data from three laboratory-based genetic crosses (yielding 440 PC and 9060 FS comparisons). *MalKinID* uses the genome-wide IBD proportion and the per-chromosome max IBD segment block and IBD segment count distributions to identify parasite genealogical relationships. *MalKinID's* performance was assessed using empirical lab-cross data and simulated, point importations. *MalKinID* accurately identified lab-generated F_1 progeny with >80% sensitivity and showed that 0.39 (95% CI: 0.28, 0.49) of the second-generation progeny of an NF54 and NHP4026 cross were F_1s and 0.56 (0.45, 0.67) were backcrosses of an F_1 with the parental NF54 strain. For simulated, outcrossed point importations, *MalKinID* accurately reconstructs genealogy history with high precision and sensitivity. The F1-scores for PC, FS, second-degree, and third-degree relatives were 0.95 (0.84, 1.0), 0.94 (0.72, 1.0), 0.84 (0.60, 1.0) and 0.84 (0.64, 0.94), respectively. However, when importation involves inbreeding, such as during serial cotransmission, the precision and sensitivity of *MalKinID* declined, with F1-scores of 0.76 (0.56, 0.92) and 0.23 (0.0, 0.4) for PC and FS and <0.05 for second-degree and third-degree relatives. *MalKinID* lays the foundations for identifying different parasite genealogical relationships, which can be used to reconstruct transmission lineages in outcrossed parasite populations or used to separate progeny for QTL experiments.

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PLASMODIUM FALCIPARUM ADAPTS TO FRONTLINE DRUG CHANGES THROUGH NEW HAPLOTYPES AT OLD TARGETS

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Populations of *Plasmodium falciparum* regularly confront orchestrated changes in frontline drug treatment that drastically alter the parasite's selection landscape. When this has occurred, the parasite has successfully adapted to the new drugs through novel resistance mutations. These novel

mutations, however, may emerge in a genetic background already shaped by prior drug selection. In some instances, selection imposed by distinct drugs has targeted the same loci in either synergistic or antagonistic ways, resulting in genomic signatures that can be hard to attribute to a specific agent. Here, we use two approaches for detecting sequential bouts of drug adaptation: haplotype-based selection testing and temporal changes in allele frequencies. Using a set of longitudinally acquired samples from French Guiana, we determine that since the introduction of the new drug artemether-lumefantrine (AL) there have been rapid hard selective sweeps at both known and novel loci. We additionally identify genomic regions where selection acted in opposing directions before and after widespread AL introduction. At four high-profile genes with demonstrated involvement in drug resistance (*crt*, *mdr1*, *aat1*, and *gch1*), we saw strong selection before and after drug regime change, however, selection favored different haplotypes in the two time periods. Similarly, the allele frequency analysis identified numerous coding variants whose frequency trajectory changed sign under the new drug pressure. These selected alleles were enriched for genes implicated in artemisinin and/or partner drug resistance in other global populations. Overall, this suggests that subtle changes throughout the genome impact drug resistance, and this may explain the observation that some *P. falciparum* populations experience novel evolutionary trajectories—rather than a return to "wildtype"—after drug removal.

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HMMIBD-RS, AN ENHANCED IMPLEMENTATION OF *HMMIBD* FOR PARALLELIZABLE IDENTITY-BY-DESCENT DETECTION FROM HAPLOID GENOMES

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Identity-by-descent (IBD) is a key tool in malaria parasite population genomics to infer genetic relatedness, selection signals, and population demography. The hidden Markov Model-based probabilistic method *hmmIBD* has been widely used to infer IBD in species with high recombination rates and low marker density, such as *Plasmodium falciparum* (*Pf*). In previous work, we found that *hmmIBD* had higher accuracy in detection of IBD segments compared to identity-by-state-based methods. However, the power of the *hmmIBD* algorithm is currently limited by its non-parallelizable implementation, and the assumption of uniform recombination rate across the genome, limiting its application to large data sets or to genomes with variable recombination. Here, we present a new tool, *hmmibd-rs,* that reimplements the original *hmmIBD* algorithm in a memory-safe language, Rust. The tool allows the direct input of a common genotype data format (BCF), the specification of a non-uniform recombination rate map, and the utilization of multi-core CPU for parallelization, with performance increasing almost linearly with the number of threads. Using simulation, we showed that *hmmibd-rs,* can detect IBD segments from 30,000 simulated *Pf*-like 100-centimorgan (cM) chromosomes in 9 hours using 64 threads, compared to 3-4 weeks when using single-threaded *hmmIBD*, demonstrating scalability for large data sets such as MalariaGEN Pf7 (n > 20,000 isolates). We also found that the incorporation of a recombination rate map into *hmmibd-rs* largely reduced detection of false positive IBD segments (≥ 2 cM) in low recombining regions and moderately decreased false negative rates in high-recombining regions in genomes simulated with non-uniform recombination rates, compared to *hmmIBD*, which uses an average rate. Ongoing work will apply this new tool to the MalariaGEN Pf7 data set to measure the computation time used for IBD detection and determine the extent to which the incorporation of variable recombination rates (estimated from population samples or existing genetic cross data) impacts downstream inferences of parasite demography in different malaria transmission settings.

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GENETIC SURVEILLANCE REVEALS THE CLONAL REPLACEMENT DYNAMICS AND SPATIAL STRUCTURE OF *PLASMODIUM FALCIPARUM* IN SÃO TOMÉ AND PRÍNCIPE

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Despite ongoing efforts to eliminate malaria in São Tomé and Príncipe (STP), there has been an increase in case numbers in recent years. Understanding the composition of the remaining transmission is crucial for tailoring effective elimination strategies. In this study, we collected amplicon sequencing data from 980 samples and integrated it with longitudinal surveillance data from 2010 to 2016 to examine the genetic composition of the parasite population. The mean multiplicity of infection (MOI) was 1.3, and the proportion of polyclonal infections was 11%, indicating that transmission intensity was low. Notably, the temporal trends of these genetic metrics did not align with incidence rates. In low transmission settings, where parasite population size is small, genetic metrics are expected to be highly influenced by stochastic fluctuations in the composition of circulating infections. Our results suggest that temporal changes in genetic metrics may not necessarily reflect changes in transmission intensity. Furthermore, while the majority of samples (87%) were genetically linked to other samples, suggesting limited genetic diversity, we observed continuous turnover in genetic clusters accompanied by changes in drug-resistance haplotypes during the study period. Principal component analysis suggests that the STP samples were genetically similar to those from Central and West Africa, pointing to the possibility of importation. The parasite diversity was lowest at the end of the study period, which is indicative of successful malaria control efforts. In summary, our study reveals dynamic changes in the parasite population in STP, highlighting the need to not only prioritize targeted interventions against hotspots of transmission but also to implement reactive case detection and collect travel histories to prevent the introduction of new parasites into this island nation as it approaches elimination. This study also serves as a case study for implementing genetic surveillance in a low transmission setting.

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APPLICATION OF HIGHLY MULTIPLEXED AMPLISEQ TARGETED NGS ASSAYS FOR GENOMIC SURVEILLANCE USE CASES FOR *P. FALCIPARUM* AND *P. VIVAX* IN ASIA, AFRICA AND LATIN AMERICA

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Malaria remains a major global health problem. Research has advanced our knowledge of malaria epidemiology and ecology, but emerging drug and diagnostic resistance highlight the urgency of continuous surveillance. Genomic surveillance, a field of study using genetics to track diseases, aids in decision-making and policy for malaria control and elimination. While genomic surveillance of viral and bacterial pathogens is becoming mainstream, genomic tools are not routinely used in malaria surveillance, partly due to the size and complexity of the parasite genome. Here we

present a set highly-multiplexed sequencing assay (AmpliSeq) which have been developed for cost-effective targeted deep sequencing of *P. falciparum* or *P. vivax* of specific genomic regions of interest. These assays combine phenotypic and population genetic markers to study parasite dynamics, which has been successfully piloted in several countries, including Burkina Faso, Democratic Republic of Congo, Peru, Vietnam, and in travelers and migrants in Belgium.We demonstrate genetic surveillance use cases, such as drug-resistance of *P. falciparum* in Vietnam, Burkina Faso and DRC, the increasing rate of *hrp2/3* deletions in Peru, and the origin of imported *P. vivax cases* in Belgium. High-resolution identity-by-descent relatedness analysis in Vietnam indicated a high level of *P. vivax* parasite connectivity in coastal provinces, and a distinct highly-related population in a remote highland province. An imported clonal *P. vivax* outbreak in a Peruvian Amazon border community was detected. In addition, we are investigating *Pfcsp* diversity in a vaccine trial site in Burkina Faso. This approach can effectively differentiate and characterize parasite isolates over time and space, and is easily adaptable to diverse epidemiological contexts. It can guide, surveillance and implementation of core control interventions such as vector control, chemotherapy and prophylaxis, and vaccine deployment strategies, among others. The priority is to make this tool available to key actors in endemic countries to increase ownership and ensure data usage for decision-making and policy.

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TEMPORAL GENOMIC ANALYSIS REVEALED MAINTAINED GENETIC DIVERSITY AND COMPLEXITY OF INFECTION AMONG PLASMODIUM FALCIPARUM INFECTIONS IN MAINLAND TANZANIA:2021-2022

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Plasmodium falciparum infections in endemic countries exhibit high genetic diversity, posing challenges to malaria control efforts. Recent studies have reported the heterogeneous genetic diversity of P. falciparum in mainland Tanzania, highlighting the need for integrated approaches in malaria surveillance. Understanding the temporal dynamics of genetic diversity and the complexity of infection (COI) is crucial for effective malaria control and elimination strategies. Here we present the preliminary analysis for countrywide temporal dynamics of P. falciparum genetic diversity and COI of malaria parasites in 13 regions of Mainland Tanzania from 2021 to 2022. About 34,550 individuals were screened by malaria rapid diagnostic tests (RDTs) through cross-sectional surveys conducted between February and July 2021-2022, of which 14,871 were malaria positive. DNA extraction was done using the Chelex 100+Tween20 method and sequenced by molecular inversion probes (MIPs). The data was analyzed using MIPtools and R software. The mean COI was 1.53 (ranging from 1.55 in 2021 to 1.51 in 2022) and did vary across years (p-value =0.02), indicating the persistence of heterogeneous genetic diversity within the country. The proportion of polyclonal infections was 40.4% in 2021 and 46.1% in 2022. The mean COI was heterogeneous across the studied regions, with the lowest mean COI of 1.27 in Dodoma and the highest being 2.01 in Kagera. The COI correlated with regional transmission intensities (correlation ratio = 1). The expected heterozygosity was 0.28 in 2021 and 0.36 in 2022, indicating little genetic diversity. The principal component analysis did not detect parasite population structure over time. The results reveal a striking persistence of moderate genetic diversity and complexity of infection over time, indicative of ongoing supper infection/co-transmission within individual hosts. Further analysis will be performed to fully assess temporal parasite genetic diversity to support effective malaria management and elimination in the country.

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DIVERSITY AND MULTIPLICITY OF *PLASMODIUM FALCIPARUM* INFECTIONS AMONG ASYMPTOMATIC SCHOOL CHILDREN IN ANKAZOABO, SOUTHEN MADAGASCAR

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< Malaria remains a major public health problem in Madagascar. Understanding *Plasmodium falciparum* population diversity and transmission dynamics provides information on the intensity of malaria transmission, which is needed for assessing malaria control interventions. This study aimed to determine P. *falciparum* allelic diversity and multiplicity of infection (MOI) among asymptomatic school-age children between five to fifteen year-old in Ankazoabo district, South of Madagascar in December 2023.From 360 asymptomatic study participants, a total of 99 samples positive for *P. falciparum* were included for molecular analysis. Samples were characterized by nested PCR and genotyping the polymorphic regions of *msp-1* and *msp-2*. For *msp-1*, 86.87 %(86/99), and *95.95*% (95/99) for *msp-2* were detected. In *msp-1* ,K1 was the predominant allelic family detected in 80.23% (69/86) of the isolates followed by MAD20 and RO33. For *msp-2,* the frequency of IC/3D7 and FC27 were 82.11%(78/95) and 70.53%(67/95) respectively. Fifty three percent of isolates had multiple genotypes and the overall mean of multiplicity of infection (MOI) was 2.3. Correspondingly, the excepted Heterozigosity(He) value for *msp-1*(He=0.54) and *msp-2*(He=0.51).The findings of this study revealed higher genetic diversity of the *msp-1* and *msp-2* allele families in *P.falciparum* isolates in this malaria endemic area. However continued monitoring of status of the local genetic diversity profile in *P.falciparum* population is required to support malaria control and elimination strategies. >

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REVEALING NOVEL GENETIC VARIANTS IN THE MALARIA TRANSMISSION BLOCKING VACCINE CANDIDATE PFS25

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Malaria remains a significant global health challenge, causing nearly a quarter of a billion cases worldwide in 2022. The approval of 2 new liver-

stage vaccines is a major advance, but there remains an urgent need for more effective vaccines that target other stages of the parasite's life cycle. Transmission-blocking vaccines (TBVs) offer promise for malaria elimination by reducing transmission within communities through targeting the sexual stages. However, the genetic diversity of the parasite antigens presents a significant obstacle to vaccine development. We employed next-generation amplicon deep sequencing to identify Pfs25-associated non-synonymous SNPs in 209 *Plasmodium falciparum* samples from four African countries: Senegal, Tanzania, Ghana, and Burkina Faso. Using a very sensitive threshold of 1% variant frequency, we identified 24 SNPs including 25 novel variants, and assessed their population prevalence and variant frequency in complex infections. Five variants were detected in multiple samples (L63V, V143I, S39G, L63P, and E59G), while the remaining 21 were rare variants found in individual samples. Analysis of country-specific prevalence revealed varying proportions of mutant alleles, with Ghana exhibiting the highest prevalence (55.3%), followed by Senegal (27.6%), Tanzania (6.9%), and Burkina Faso (6.9%). We further categorized SNPs based on their frequency, identifying dominant variants with frequencies exceeding 25% and rare variants with frequencies below 2%. Threading analysis of the Pfs25 protein structure revealed SNPs in two categories: 1) SNPs that have the potential to influence the binding between Pfs25 and antibodies and can lead to immune evasion, and 2) SNPs that can potentially modify the structure of Pfs25 protein. Our results show that while Pfs25 remains a relatively highly conserved gene, we identified additional SNPs beyond the 9 previously reported. Most of these newly discovered SNPs display low variant frequency and population prevalence. Further research exploring the functional implications of these variations will be important to elucidate their role in malaria transmission.

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AMPLICON AND SNP GENOTYPING OF *P. FALCIPARUM* AND *P. VIVAX* CASES IDENTIFIES HIGHLY RELATED SAMPLE CLUSTERS AS BHUTAN APPROACHES ELIMINATION

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Bhutan is slated for malaria elimination by 2025, and cases have declined sharply over the last 20 years. Approaching elimination, malaria cases are often imported and occur in border regions. Understanding genetic relatedness between parasites can help distinguish imported from local cases. DNA was extracted from dried blood spots for 114 *Plasmodium vivax* and 30 *Plasmodium falciparum* isolates collected from individuals with clinical infection in Bhutan from 2016 to 2021. *P. falciparum* genotyping was conducted using the 129-amplicon AMPLseq panel, and *P. vivax* genotyping using a SNP barcode comprised of 130 variable sites. The resulting amplicon and SNP genotypes were compared to the same sites extracted from publicly available whole genome sequence data (MalariaGEN Pf7 and Pv4 for *P. falciparum* and *P. vivax*, respectively) from isolates collected in India, Bangladesh, and Myanmar. Isolates with poor genotyping coverage and polyclonal isolates without a clear predominant clone were excluded, resulting in 64 genotyped *P. vivax* isolates and 12 *P. falciparum* isolates for analysis. Dcifer was used to estimate genetic relatedness, and InfoMap community network detection was performed to identify clusters of highly related parasites. We identified two clusters of identical *P. falciparum* isolates, each with 100% identity at the 104 genotyped amplicons, and 7 clusters of identical *P. vivax* isolates, with 100% identity at the 130 variable sites. One *P. vivax* and one *P. falciparum* cluster contained isolates from non-consecutive collection years, suggesting persistence of parasite clones over time in this very low transmission area. Neither *P. vivax* nor *P. falciparum* isolates from Bhutan clustered with isolates from neighboring countries, likely due to limited representation of sequences from border regions in the MalariaGEN database. This lack of data from immediately adjacent districts limits our ability to infer whether cases were imported or locally-acquired based on genotyping data alone; such inferences will require integration with additional epidemiologic data on the timing of diagnosis, travel history, and patient proximity.

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PULSED MICROWAVE IRRADIATION INDUCES APOPTOSIS LIKE CELL DEATH IN *PLASMODIUM FALCIPARUM* VIA FAS/FASL DEATH RECEPTOR PATHWAY

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Pulsed Microwave Irradiation Induces Apoptosis-Like Cell Death in *Plasmodium falciparum* via FAS/FASL Death Receptor PathwayMost of the signaling pathway events involved in the apoptotic process of protozoa remain unknown, and *P. falciparum* is no exception. A previous study by our research group demonstrated that the parasite *P. falciparum* exhibits regulated cell death markers when exposed to microwaves (MW). In this study, we investigated the presence of proteins in *P. falciparum in vitro* following exposure to pulsed MW irradiation at 2.45 GHz frequency. After MW exposure, we used a commercial human dot-blot array to identify 43 target proteins associated with programmed cell death (PCD). We compared protein expression levels between control and treated samples using ImageJ, a digital image analysis software. Notably, MW-treated samples showed significantly higher signal intensity for the death receptor Fas and its ligand FasL, which are known to activate the caspase cascade in multicellular organisms and in some eukaryotic single-celled microorganisms. We also observed increased expression of HSP70, HSP60, BID, and BAX, proteins that participate in the Fas/FasL mediated apoptosis pathway leading to mitochondrial outer membrane permeabilization (MOMP) and cell death. Interestingly, *P. falciparum* possesses metacaspases encoded by the PfMCA1, 2, and 3 genes. Our results suggest that the activation of death receptor FAS/FASL like in *P. falciparum* triggers the activation *of P. falciparum* metacaspases. We propose that FAS/FASL like proteins are present *in P. falciparum* and play a significant role in the parasite's apoptosis-like cell death.

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SETTING A MRDT-BASED STRATEGY FOR MONITORING THE OCCURRENCE OF *PLASMODIUM FALCIPARUM HRP2* AND *HRP3* DELETIONS IN MADAGASCAR

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In the island of Madagascar – where *Plasmodium falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* coexist, the malaria rapid diagnostic test (mRDT) has become an essential tool for improving malaria case management since 2006. The most used mRDT in the Malagasy health system detects both the pan-specific LDH and the *P. falciparum* HRP2. However, the deletion of the *pfhrp2* gene threatens the accuracy of the HRP2-based test. There therefore is a need to set a robust method for monitoring the occurrence of *pfhrp2* and *pfhrp3* gene deletions. During malaria detection in August 2023 in 373 children aged from 5 to 14 years in Ankililoaka in the dry southwestern part of the island, blood samples were collected by finger-prick for mRDT and molecular analysis using dried blood spots. Of the 194 (52%) mRDT positive samples, 105 were mRDT pan LDH and HRP2 positive, 76 mRDT HRP2 positive but pan LDH negative, and 13 mRDT pan LDH positive but HRP2 negative. These 13 HRP2 negative samples

were PCR analyzed. Five samples contained *P. falciparum* and one case of *pfhrp2* and *pfhrp3* double deletions (0.5%), and two cases of *pfhrp3* single deletions (1.1%) were confirmed. Our results demonstrated the occurrence of *pfhrp2/3* deletions among *P. falciparum* isolates from the southern part of Madagascar at a low level. Above all, the standard operating procedures for detecting *P. falciparum hrp2/3* deletions were successfully established for developing a national survey to guide the national malaria control program on the mRDT choice.

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GUT MICROBIOTA-INDUCED IMMUNE TOLERANCE IMPAIRS SYSTEMIC IMMUNITY AGAINST SEVERE MALARIA

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Severe malaria caused by *Plasmodium* spp. infection leads to hundreds of thousands of deaths annually. Our lab uses *P. yoelii* and C57BL/6 mice from diverse vendors to study the influence of gut microbiota on malaria severity. Recently, we showed microbiota-dependent germinal center contraction and reduced antibody quality post-infection, leading to hyperparasitemia. This phenotype is replicated by introducing cecal material from hyper-parasitemic mice into regular and germ-free mice. While the causality is established, the intricate mechanisms remain unclear. Here, we found that susceptible mice had increased T regulatory cells in their Peyer's Patches and spleens after infection, correlated with reduced IFN-γ production. When exposed to sub-colitis doses of DSS, malaria-resistant mice developed colitis, while susceptible mice were resistant to weight loss, confirming the tolerogenic nature of their microbiota. Both groups showed similar levels of intestinal damage and bacterial translocation post-infection, suggesting malaria-dependent microbiota-independent gut injury. Moreover, modulation of splenic adenosine immunosuppressive pathways involving A2AR and CD39 is enhanced by tolerogenic microbiota in different leukocytes during malaria infection. Treatments to repair the gut barrier or to antagonize A2AR after intestinal damage post-infection significantly mitigate parasitemia, weight loss, and mortality while enhancing immunity. These findings highlight the vital role of the gut microbiota in shaping systemic immunity during infections, underscoring the potential of therapeutic interventions targeting the gut barrier to mitigate malaria severity and enhance outcomes.

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AGEING OF *PLASMODIUM FALCIPARUM* MALARIA SPOROZOITES ALTERS THEIR MOTILITY, INFECTIVITY AND REDUCES IMMUNE ACTIVATION *IN VITRO*

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Sporozoites (SPZ), the infective form of *Plasmodium falciparum* (Pf), can be inoculated into the human host skin by Anopheline mosquitoes. These SPZ migrate at ± 1µm/s to find a blood vessel and travel to the liver where they infect hepatocytes. At the skin they are still low in number and vulnerable to immune attack by antibodies and macrophages. This is why whole SPZ and SPZ proteins are used as the basis for most malaria vaccines. Mosquitoes inoculate SPZ into a human host between 14 and 25 days after infectious blood meal. However, it is unknown whether residing time within the mosquito affects the SPZ. We aimed to unravel how the age of *Pf* SPZ in salivary glands (14, 17, or 20 days post blood meal) affects their infectivity and the ensuing immune responses. We investigated SPZ numbers, viability, motility using dedicated sporozoite motility orienting and organizing tool software (SMOOT) and infectivity of HC-04.j7 liver cells. *In vitro* co-culture assays with SPZ stimulated monocyte-derived macrophages (MoMϕ) and $CD8^+$ T-cells, analyzed by flow cytometry, were used to investigate immune responses. We found that SPZ age did not result in different SPZ numbers or viability. However, we observed a markedly different motility pattern, whereby motility decreases from 89% at day 14 to 80% at day 17 and 71% at day 20 (p=<0.0001). Similarly, infectivity of day 20 SPZ dropped to 50% as compared with day 14 SPZ (p=0.004). MoMϕ were better able to take up day 14 SPZ (7.6%) than day 20 SPZ (4.1% p=0.03) and displayed an increased expression of pro-inflammatory CD80, IL-6 (p=0.005) and regulatory markers PDL1 (p=0.02), IL-10 (p=0.009) upon phagocytosis of younger SPZ. Interestingly, co-culture of these cells with $CD8^+$ T-cells revealed a decreased expression of activation markers CD137 and IFNγ as compared to their day 20 counterparts. These findings suggest that older (day 17-20) *Pf* SPZ are less infectious and have decreased immune regulatory potential. Our data shows a first step in enhancing our understanding of how mosquito residing time affects *Pf* SPZ and could impact our understanding of the *Pf* infectious reservoir and the potency of whole SPZ vaccines.

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LEVERAGING BIRTH COHORTS TO TRACE COMPLICATED MALARIA RISK AND ITS IMMUNOLOGICAL CORRELATES AT EACH INFECTION IN INFANCY

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Infections with *P. falciparum* range from asymptomatic to life-threatening. Protection from severe disease is usually acquired in the first few years of life, though it is unknown how this protection is encoded immunologically. Uncovering this mystery holds promise for developing and evaluating interventions that prevent severe disease and death. We leveraged three birth cohorts from high-transmission settings in Uganda for a detailed view of malaria risk and associated immunological changes in infancy. Monthly, active case finding allowed the faithful capture of each infection in more than 900 children aged 8 weeks to 2 years. Across thousands of *P.falciparum* infections, we find that the risk of complicated malaria is highly dynamic in early life. First infections tended to have lower parasitemias and were mostly uncomplicated. Median parasitemia increased in subsequent infections but reached a plateau after about three infections. The probability of symptoms, given a parasitemic episode remained constant in early life. In contrast, complicated disease risk peaked around malaria episode 5 and then quickly, exponentially declined thereafter,while median parasitemia remained unchanged. In multivariate analyses, the order of infection, more than age or parasitemia, significantly predicted complicated malaria risk in our cohort. Single-cell analysis of *P.falciparum*-specific T cells revealed changes in activation and differentiation associated with high and low-risk infections. Our data suggest that protection from severe disease is acquired after just a few malaria episodes. This occurs even when median parasitemias remain unchanged, and thus represents a mechanism of disease tolerance. This tolerance mechanism is likely distinct from clinical immunity, as the probability of developing symptoms remained constant in this cohort.

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REACTIVITY OF ANTIBODIES AGAINST MALARIA AND OTHER PARASITIC DISEASES TO THE ANTIGENS N, S AND S1 SUBUNIT RDB951 USED IN COVID-19 SEROLOGY

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In response to the SARS-CoV2 (COVID) pandemic, several antibody (Ab) sero-surveillance assays were developed. However, studies suggesting that samples from malaria endemic areas have Ab that cross react with

COVID serology assays may limit their utility in these settings. We used a multiplex bead assay (MBA) to assess if Ab from parasite positive samples from United States (US) patients reacted against three COVID antigens: nucleocapsid (N), the spike protein (S) or its subunit RDB951 (R). The study tested 816 pre-COVID samples: 704 from the US with Ab positive results (Ab+) for malaria or 13 other parasitic diseases, 91 from Africa with Ab+ for filariasis, and 21 from US individuals with no reactivity for parasitic diseases. Controls were 33 samples collected during the COVID pandemic. Resulting data were assembled in contingency tables and analyzed by Chi-square/ Fisher's exact tests. Among pre-COVID samples, Ab+ against the COVID antigens were found in 14 (1.7%) samples for N, 26 (3.2%) for S, and none for R. No sample was Ab+ for N and S. Among the 33 samples from the COVID period, 10 (30.3%) had Ab+ for N, 20 (60.6%) for S and 19 (57.6%) for R, and 18 (54.5%) had simultaneous Ab+ for S and R. Among pre-COVID US samples positive for a parasitic disease, significant associations were found between filariasis positive samples (6/72, 8.3%) and Ab+ to S ($p=0.015$). Among 35 malaria Ab+ samples, one sample had Ab+ for N, and another had Ab+ for S. Among the 91 African pre-COVID samples, only 6 had Ab+ for N and 2 for S. Meanwhile, the COVID pandemic control group had Ab+ against the N, S and R antigens that were significantly associated with the COVID period ($p<0.001$). The MBA data showed that US malaria positive sera were not associated with Ab+ for COVID antigens N, S or R, and that Ab developed against other etiologies, as determined by MBA in pre-COVID samples, could contribute to some cross reactivity against either the N or S antigens but not likely against the R antigen.

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A NOVEL MURINE MODEL FOR INVESTIGATING THE PATHOGENIC ROLE OF COAGULATION IN MALARIA-ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME

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Malaria-associated acute respiratory distress syndrome (MA-ARDS) is a complication of severe malaria, characterized by pulmonary complications such as edema, inflammation, hemorrhages, and alveolar damage. The role of coagulation in the pathogenesis of MA-ARDS is poorly understood. Aiming to understand the pathogenic pathways that lead to lung malaria, including dysregulated coagulation, we developed an experimental murine model that lacks endothelial tissue factor (TF), the primary initiator of the extrinsic coagulation cascade. We hypothesized that altered TF expression would suppress the inflammatory response, oxidative stress, and endothelial disruption, resulting in reduced vascular leakage in the lung. We further hypothesized that sexual dimorphism would influence disease severity, with males being more susceptible. We assessed disease progression in P. berghei NK65 infected (IV, 105) endothelial tissue factor-deficient ($F3^{flox/flox}$ Tie-2^{Cre}) mice. Parasitemia, anemia, and body condition were measured longitudinally over 16 days. At 16 days post-infection, lung tissues were weighed and processed for histology and molecular analysis. Body condition score as measured by activity and behavior was significantly reduced in males relative to females regardless of TF expression. Females lacking endothelial TF had significantly lower parasite burden in comparison to males, while tissue factor intact female and male mice had similar parasitemia. Lung index, anemia, and body weight in all experimental groups were similar. Ongoing studies are examining lung histology and the expression of inflammatory, anti-oxidant, pro- and anti-coagulant associated genes to further assess the extent to which TF expression and sex influence lung pathology in this model.

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COMPARING MIXTURE MODELING APPROACHES FOR CLASSIFYING LONG-TERM MALARIA SEROLOGICAL MARKERS IN NORTHERN LAOS

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In Lao People's democratic (Lao PDR), malaria is hypo-endemic and *Plasmodium vivax* is a common cause of malaria infection; current diagnostic tools are insufficient for detection of malaria infection. Serological assays can be a valuable tool for elucidating infection timelines and estimating the likelihood of *P. vivax* hypnozoite presence. Challenges in serology include defining antigenic targets, and classification of individuals based on semi-quantitative assays. This study presents a comparison of two statistical models to classify parasite exposure based on Luminex assays. We also apply regression models to quantify factors associated with historical exposure. A cross-sectional study in Lao PDR was conducted in four providences. Participants provided biological samples and demographic information. The prevalence of four putative long-term markers was classified using two mixture models: (1) deterministic finite mixture model (dFMM), and (2) novel probabilistic finite mixture model (pFMM) using a Weibull distribution in a Bayesian framework. Thirty-eight individuals (0.8%) were PCR-positive for current parasitemia. The seronegative proportion of the population by model is as follows for each marker: PvAMA1 (59.3% by dFMM, 11.9% [80% CrI: 3.5, 31.8] by pFMM); PvMSP119 (18.0% by dFMM, 17.4% [80% CrI: 1.0, 42.9] by pFMM); PfAMA1 (57.5% by dFMM, 23.6% [80% CrI: 21.6, 25.5] by pFMM); PfMSP119 (58.2% by dFMM, 26.9% [80% CrI: 24.7, 29.2] by pFMM). Seroprevalences based on the pFMM model are consistent with expectations in this region which is approaching elimination. Factors including age, geography, sex, and occupation were associated with individual-level seropositivity (cumulative exposures). This was consistent with expectations of long-term markers. While serology is a useful tool, the lack of validated classification methods leads to arbitrary cut-points under strong assumptions. This pFMM provides a complimentary and nuanced framework to interpreting serological data. A probabilistic approach can better capture the uncertainty found in this inherently complex data.

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TARGETS OF CSP-BASED MALARIA VACCINES: WHAT WE MISSED IN 1987 AND WHAT IS MISSING NOW

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The current circumsporozoite protein (CSP) based licensed malaria vaccines can be improved by the inclusion of novel CSP targets. In the wake of increasing relevance of non-*falciparum* species, a cross-species vaccine is desirable. In this study, we profiled the CSPs of *Plasmodium falciparum, Plasmodium malariae,* and *Plasmodium ovale* in terms of protein sequence and structure, and naturally-acquired CSP-specific IgG in malaria-exposed individuals. We sought to uncover cross-species conserved domains to prioritize in the design of a cross-species vaccine. Also, we probed potentially protective CSP motifs by comparing immune responses between malaria "protected" and "at-risk" cohorts. Sequence alignments were done using Clustal Omega. Protein structures were predicted using

ColabFold and compared using TM-align. Total IgG, IgG avidity, and IgG subclass measurements against full-length proteins (PfCSP, PmCSP, PoCSP) and peptides (20mer with 10aa overlap) were done by indirect ELISA. Western/dot blotting was done to confirm ELISA results and identify immunodominant CSP peptides. Sequence and structural similarities were low across full-length proteins; highest in the C-terminus. We observed the conservation of essential sequences cross-species; the PEXEL motif, the protease cleavage site, and region II+. There was similar anti-PfCSP and PoCSP and a lower anti-PmCSP total IgG levels. We uncovered 16/27(PfCSP), 16/26(PmCSP), and 13/26(PoCSP) seropositive peptides by dot-blot. IgG profiles of the PEXEL (N-terminus), minor repeat (junctional), major repeat (central repeat), and region II+ (C-terminus) peptides reveal high and diverse peptide recognition in the malaria "protected" cohort; IgG was polarized to peptides of the central repeat and the C-terminus in the at-risk cohort. Our study reaffirms CSP-specific antibody feedback inhibition in naturally malaria-exposed individuals. We propose cross-species targets; the PEXEL, protease cleavage site, and region II+. Our data suggests that a potent anti-CSP response is high and diversified across CSP domains. This study contributes to the design of effective vaccines.

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INVESTIGATING THE ASSOCIATION BETWEEN MALARIA INFECTION AND AUTOANTIBODY PRODUCTION IN MURINE AND HUMAN STUDIES.

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The relationship between malaria and autoimmunity remains controversial, with previous studies showing that infection promotes or inhibits inflammatory conditions. We, therefore, set out to investigate the link between *Plasmodium* infection and autoimmunity using murine models and studies in patient cohorts. The development of rheumatoid arthritis associated anti-citrullinated protein autoantibodies (ACPA) responses were assessed in *Plasmodium chabaudi* infected mice. Subsequently, we evaluated the impact of these heightened ACPA responses on the development of a model of experimental arthritis in mice following infection with *P. chabaudi* infection. We demonstrate that infection with *P. chabaud*i leads to increased ACPA peaking at two weeks post infection; and remaining high even after parasite clearance compared to naïve mice. Under the conditions used in our study these autoantibodies did not appear to influence the outcome of experimental autoimmune arthritis. Extending our findings to humans, we measured the levels of ACPA in individuals residing in areas of either low or moderate malaria transmission. Using microarray, we assessed the range of autoimmune markers exhibited by ACPA high individuals and flow cytometry was also used to assess T cell phenotypes associated with an autoimmune profile. As in the murine studies, individuals living in higher malaria transmission areas had elevated levels of ACPA. Individuals with higher ACPA exhibited diverse autoantibody profiles, suggesting a general increase in autoreactivity. We also noted lower FOXP3 regulatory T cell levels in individuals with higher ACPA levels compared to those with lower responses. These data suggest that malaria infection induces a range of autoantibody responses in both mice and humans. In our murine model, the pre-existing ACPA response following a single infection did not influence the development of experimental autoimmune arthritis. However, the impact of multiple malaria infections on the risk of developing autoimmune disease warrants further investigation.

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PROTEIN SEQUENCE AND STRUCTURE, AND ANTIBODY PROFILE OF THE AMA1 FROM THREE *PLASMODIUM* SPECIES.

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The need for an effective malaria vaccine is imperative. The prevalence of non-*falciparum* species in the clinical setting calls for the design of broad-spectrum intervention tools. To achieve this in vaccine design, it is necessary to establish species-specific immune mechanisms. The Apical membrane antigen (AMA1) is an advanced vaccine candidate with its potential evidenced by neutralizing antibodies. In this study, we investigated sequence and structural conservation between AMA1 proteins of *P. falciparum, P. malariae,* and *P. ovale* using *in silico* techniques and characterized IgG responses in six different populations in Ghana. Protein sequence comparison was done using Clustal Omega (significant at similarity >30%). Protein structures were predicted by homology modeling using Swiss-Model. Monoclonal antibody cross-reactivity was determined by Western blot. Our study cohorts include community, hospital (follow-up days 0,7,21), and a malaria "protected" and "at-risk" cohort sampled in the same geographic area. Total IgG, IgG subclasses, and IgG avidity were measured by indirect ELISA , and data was analyzed in R. There was high sequence similarity(>50%) and structural concordance(TM>0.9) between all antigens. All antigens were recognized by malaria-hyperimmune IgG in Western blot with intensities of PfAMA1>PmAMA1>PoAMA1. Using PfAMA1-generated monoclonals, we observed cross-reactivity between PfAMA1 and PmAMA1 for MAb N3-1D7. Comparing immune response against the three antigens, PfAMA1 recorded the highest IgG levels and seropositivity in all sample groups corresponding with species transmission intensity. Across the three antigens, anti-PfAMA1 IgG avidity was highest only in our clinical follow-up cohort on day zero. Dominating IgG subclasses were IgG1 and IgG2. This study affirms species transmission intensity in Ghana and the conservation of AMA1 in terms of sequence and structure. This is the first study that profiles and compares cross-species immune responses against AMA1 in naturally immune individuals. This study contributes to anti-AMA1 immunology towards vaccine design.

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MALARIA EXPOSURE RISK AND NATURALLY ACQUIRED IMMUNITY AMONG STUDENTS FROM SOUTHERN AND NORTHERN GHANA

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In Ghana, malaria remains a significant public health issue, with different regions experiencing varying levels of transmission intensity. This study examined the differences in malaria exposure and the development of naturally acquired immunity between students from Ghana's northern and southern regions. A cross-sectional study was conducted on a group of 189 healthy students from the Nyankpala Campus of the University for Development Studies (UDS) using a structured questionnaire to assess their malaria exposure history, risk, and prevention-seeking behavior. In addition, the study measured their IgG levels against *P. falciparum* 3D7 crude antigens, HB3VAR06, and IT4VAR60 using an indirect ELISA. This study uncovered that though individuals from the northern regions showed

a nearly significant difference in malaria susceptibility (p=0.054), there were no notable differences in malaria prevention-seeking behaviors compared to those from the southern region. Furthermore, no significant differences were observed in the levels of IgG antibodies against crude antigens, however, variations were found in the levels of IgG antibodies against HB3VAR06 antigens. The HB3VAR06-specific IgG levels were relatively higher among individuals from the north (p=0.027), whereas those from the south had higher levels of IT4VAR60-specific IgG but not significant (p=0.155), suggesting that individuals from the two regions may have been exposed to different VAR clones of the parasite. In general, the levels of naturally acquired IgG antibodies showed no correlation with the risk of malaria exposure. The result of this study provides valuable insights into the prevalence and risk factors associated with malaria in the study population and a potential geographical selection of parasites between southern and northern Ghana.

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UNVEILING IMMUNODOMINANT REGIONS OF PFCERLI1: INSIGHTS FOR MALARIA VACCINE DEVELOPMENT

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Malaria is a disease of major global health concern. *Plasmodium falciparum* is the deadliest human *Plasmodium* parasite. An effective malaria vaccine would be an important additional tool in the fight against malaria. Merozoite proteins of Plasmodium falciparum have been studied for malaria vaccine development. One of such antigens is the Plasmodium falciparum Cytosolically Exposed Rhoptry Leaflet Interacting protein 1 (*Pf*CERLI1). *Pf*CERLI1 is essential for red blood cell invasion by merozoites; antibodies against *Pf*CERLI1 are inhibitory to red blood cell invasion. In this study, we determined the immunodominant regions of PfCERLI1 to prioritize as targets for vaccine development. Five overlapping peptides were designed and synthesized to cover three-quarters of the full-length protein. Full-length protein structure was predicted using ColabFold. The predicted structure was visualized and edited in PyMol. Initial peptide seroreactivity using hyperimmune IgG purified from Ghanaian adults was determined by dot blot. Total IgG was measured using indirect ELISA. Sera samples were obtained from Madina (community samples and malaria-diagnosed hospital samples) and Lekma (clinical follow-up with days 0,7,21). All *Pf*CERLI1 peptides are reactive to naturally-acquired IgG. Our findings reveal varying levels of recognition among *Pf*CERLI1 peptides. Notably, peptides 5 and 7 exhibited immunodominance in the Madina cohort in both community and clinical samples. All anti-peptide IgG increased with age moderately in the clinical cohort. Adjusted for age, we observed higher total IgG levels in the community cohort compared to the hospital cohort except for peptide 3. In the clinical cohort, peptides 3, 4, and 5 were immunodominant at all time points. We observed significant IgG decay at day 7 for all peptides except 3 and 7. Our results show a correlation of peptide IgG with the development of anti-malaria immunity in naturally-exposed individuals. We are inclined to conclude that *Pf*CERLI1 is an essential target for vaccine design. Understanding the immunodominant regions of *Pf*CERLI1 brings us closer to a targeted and effective malaria vaccine.

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EARLY MALARIA IMMUNE SIGNATURES IN NAÏVE ADULTS EXPERIMENTALLY INFECTED WITH *PLASMODIUM FALCIPARUM* REVEAL HIGH AND LOW RESPONDERS

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The immune response to *Plasmodium falciparum* (Pf) is complex, involving innate responses that induce regulatory mechanisms, which determine infection outcomes and acquired immunity. In malaria-naive adults inoculated with Pf sporozoites via needle injection in Barcelona, we conducted analyses including genome-wide gene expression, cytokine and antibody profiling, and dendritic cell (DC) phenotyping. There were minimal responses on days 1 and 7. However, low density infections at day of parasite detection by thick blood smear (TBS) elicited robust innate responses, with 1251 differentially expressed genes compared to baseline (|log2FC|>0.6 & FDR<0.01), increased plasma cytokines and frequencies of activated DC ($CD86^+$, $PDL1^+$ & $CD40L^+$). Top upregulated genes included CXCL10, CXCL9, and CCL2, correlating with their elevated plasma concentrations. Upregulated blood transcriptional modules (BTMs) were related to interferon, DC activation, and cell cycle regulation, while downregulated BTMs were linked to NK, T and B cells, which correlated with lymphocyte cell counts (rho>0.7, p<0.01). Interestingly, transcriptional analysis revealed 'high' and'low' responders, with larger gene expression changes in high responders. BTMs associated with innate responses (DC, monocytes, platelets, interferons, inflammation, and chemokines) were upregulated in high responders. This coincided with higher cytokine concentrations and increased frequencies of activated DC. Consistently, cell deconvolution showed more activated DC and M1 macrophages. Instead, BTMs linked to adaptive responses (B & T cells, plasma cells) and NK cells were more downregulated. No significant differences were observed in pre-patent period (12.17 *vs* 12.27 days) and TBS parasite density at patency between the two groups. However, time to positive qPCR was longer in low responders (9.33 *vs* 7.73 days, p=0.02). Furthermore, high responders exhibited significantly more neutropenia and fever at patency. Innate responses to a first Pf infection in adults are highly variable and may impact parasite kinetics, clinical outcome, and whole parasite vaccine responses.

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ANTI-CIRCUMSPOROZOITE PROTEIN ANTIBODIES AS MARKERS FOR MALARIA TRANSMISSION MONITORING

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Malaria, remains a global burden, despite progress towards elimination in some endemic areas. Researchers are renewing efforts to track transmission to assess anti-malarial interventions. This correlation underscores the need for robust methods for monitoring malaria exposure and transmission. Antibodies to the *Plasmodium* antigen, circumsporozoite protein (CSP), is a promising alternative to the existing methods used for transmission intensity estimation. However, this may vary within populations and could be compromised by CSP antigen polymorphism. This study aimed to assess the use of anti-CSP antibodies as markers of recent exposure to malaria, taking antigen polymorphism into consideration. Sixty children and 120 adults from 2 regions of Ghana were sampled monthly for a year. Malaria infection status and parasite density were assessed by PCR. Enzyme-linked immunosorbent assays were used to determine anti-CSP antibody seroprevalence against the recombinant PfCSP (3D7 strain) and two conserved 24-mer peptides (NANPNANP repeats and NVDPNANP repeats) from the central repeat region of PfCSP. The *csp* genes were

amplified using Sanger sequencing and analyzed using MEGA 11 software. Parasite prevalence was 65% and 1% among children and adults respectively. Seropositivity varied significantly by month among children for anti-CSP (p-value<0.001), Anti-24 mer peptide 1 (p-value=0.001) and anti-24 mer peptide 2 (p-value=0.004). Seropositivity however did not significantly vary amongst adults. Parasite prevalence was significantly higher in children than in adults over the period, but antibody seropositivity was high in both children and adults. This study supported previous works on anti-CSP antibody method for monitoring malaria transmission. Further, these results showed that anti-CSP antibody measurement could be more useful in adults in low malaria transmission areas with undetectable levels of *Plasmodium* parasites even by PCR. Although *csp* gene is polymorphic, this did not significantly affect the levels of antibodies as measured with a standard strain for estimating malaria exposure among our study participants.

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PLASMABLAST IG REPERTOIRE DYNAMICS THROUGH REPEAT *PLASMODIUM FALCIPARUM* CHALLENGES REVEAL SIGNATURES OF NEGATIVE SELECTION

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To understand the development of immunity against malaria, a controlled human malaria challenge (CHMI) model was used to expose malaria-naïve individuals to the same *P. falciparum* (*Pf*) strain (NF54) four times over two years. Consistent with the gradual immunity observed naturally, the time to parasite detection increased significantly (delayed patency (DP)) by the 3rd CHMI. Plasmablast Ig repertoire maturation was tracked 7 days after peak parasitemia at each CHMI. Clone copy numbers and CDR3 counts for the major clones (CDR3 >200 or clone copy >20 000) increased significantly after exposure to Pf in all participants with DP and peaked at CHMI-2 in most DP. In contrast, the participants without DP had no significant increase in clone copy number or CDR3 count until CHMI-4. In these major clones, the ratio of replacement to silent mutations (R/S) declined from baseline through the 4 CHMIs and there was a significant decrease in R/S for the 12 Ig heavy chain variable genes associated with anti-Pf immunity in DP only. Phylogenetic analysis indicated that clones with longer tree lengths (more divergence) correlated with increasing negative selection (omega). These patterns suggest that a certain level of B cell activation is needed to reduce parasite replication and DP. However, there is a limit to the maturation of specific clones, possibly because most additional replacement mutations do not improve affinity and are selected against. Disclaimer: The opinions and assertions expressed herein are those of the authors and do not reflect the official policy or position of all the affiliated Institutions. The authors do not have a financial interest in any commercial product, service, or organization providing financial support for this research.

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VENOUS BLOOD GAS ANALYSIS IN UGANDAN CHILDREN WITH SEVERE MALARIA

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Acidosis, defined as base deficit (BD) >8mmol/L, is a criterion of severe malaria (WHO guidelines 2023). If the BD is not available, a plasma bicarbonate concentration [HCO_3^-] of <15mmol/L or venous plasma lactate ≥5mmol/L can be used to define acidosis. Kussmaul respirations may also suggest acidosis. We examined the agreement between markers of acidosis and their predictive value for mortality among children with severe malaria. Venous blood gas measurements (i-STAT biochemistry analyzer, Abbott Point of Care) from children <5 with severe falciparum malaria enrolled in a past clinical trial (July 2011 to June 2013) were examined retrospectively. Inclusion criteria were: (1) <5yr of age; (2) *P. falciparum* detected by both microscopy and rapid diagnostic test; (3) met criteria for severe malaria; and (4) venous blood gas measurement recorded at admission. 124 children (median age 2yr, 44% female) were included. Acidosis (BD > 8 mmol/L) was present in 59/124 (48%), hypobicarbonatemia in 51/124 (41%), hyperlactatemia in 42/121 (35%), and Kussmaul respirations in 58/124 (47%). Base deficit was inversely correlated with [HCO_3^-] (ρ= -0.93, p<0.0001), directly correlated with lactate level (ρ=0.38, p<0.0001), and was significantly higher in patients with Kussmaul respirations (9.7 mmol/L (IQR 4.5-14) versus 5.7 mmol/L (IQR 2.9-11), p=0.0064). Using BD>8mmol/L as a reference standard, hypobicarbonatemia, hyperlactatemia, and Kussmaul respirations were 85%, 53%, and 59% sensitive, and 98%, 83%, and 65% specific for detection of acidosis, respectively. There were 11 deaths (8.9%). All 11 deaths occurred in children with acidosis (OR >3.1, p=0.00018). Hypobicarbonatemia, hyperlactatemia, and Kussmaul respirations increased the odds of death by 17-fold (95%CI 2.3 - 760, p=0.00063), 3.1-fold (95%CI 0.68 - 16, p=0.094), and 13-fold (95%CI 1.8 - 590, p=0.0029), respectively. Our findings support the current WHO definition of acidosis: BD>8mmol/L is a strong predictor of mortality in children with malaria. Other markers of metabolic acidosis (hypobicarbonatemia and Kussmaul respirations) also have prognostic value.

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DYSREGULATION OF NETOSIS IN PEDIATRIC PATIENTS WITH SEVERE MALARIAL ANEMIA

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Human malaria remains among the leading global causes of childhood morbidity and mortality, accounting for 249 million cases and 608,000 deaths annually. The World Health Organization African Region accounts for the majority (95%) of fatalities of which 80% occur in children <5 years. In western Kenya, a holoendemic *Plasmodium falciparum* area, severe malarial anemia (SMA, Hb<6.0 g/dL) is the primary manifestation of severe childhood malaria. Although antimalarials are pivotal for malaria control, rising drug resistance underscores the importance of defining novel molecular targets to support drug discovery efforts. As such, we explored the entire expressed transcriptome (Illumina® NovaSeq 6000) in the peripheral blood of Kenyan children with either SMA (n=18) or non-SMA (Hb≥6.0 g/dL, n=39), excluding cases of sickle cell disease. There were 1,682 differentially expressed genes (DEGs, *padj*<0.05) in SMA relative to non-SMA: 1,403 up-regulated and 279 down-regulated. Pathway analysis using MetaCore™ (threshold: $\log_2$foldchange=0.585, *padj*<0.05) revealed that NETosis in Systemic Lupus Erythematosus (SLE) was the top disrupted pathway (*padj*=8.134E-5) in children with SMA. NETosis is a cellular process initiated by pathogen products, antibodies, immune complexes, and cytokines for the formation and release of neutrophil extracellular traps

(NETs), composed of decondensed chromatin DNA and neutrophil granule peptides/proteins (e.g., PERM, alpha-defensin, leukocyte elastase, and histones). Consistent with chromatin decondensation and formation of NETs,
children with SMA had up-regulation of PERM (+1.77), alpha-defensin (+2.20), leukocyte elastase (+1.68), histone H1 (H1-0:+1.1 and H1-2:+0.71) and H2 (H2AC6:+1.04). In addition, NETs activate the classical complement pathway by interacting with C1q which was also upregulated in children with SMA (C1QA:+1.34, C1QB:+1.33, and C1QC:+1.52). Collectively, these results identify molecular mechanisms associated with enhanced chromatin decondensation and formation of NETs as potential therapeutic targets to reduce tissue hypoxia and organ dysfunction.

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ASYMPTOMATIC *P. FALCIPARUM* INFECTION IS NOT ASSOCIATED WITH EXPOSURE TO SOIL TRANSMITTED HELMINTHS IN CHILDREN FROM A MULTI SCHOOL-BASED STUDY IN ESSE, CAMEROON

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Asymptomatic *Plasmodium* carriage is a major public health threat affecting both children and adults and hindering malaria eradication, yet the mechanisms that allow for asymptomatic malaria are unclear. Many LMICs are endemic for both malaria and soil-transmitted helminths (STH). Studies have confirmed that helminths secrete various proteins during infection to regulate host immune responses as a survival strategy meanwhile reducing host immune responses to other inflammatory processes. We conducted a two-part study to evaluate if STH infection drives the phenotype of asymptomatic *Plasmodium* infection. First, a one-month longitudinal study of 134 primary school children across 3 school-based study sites in Esse, Cameroon (where both malaria and STH are endemic) was performed to identify the prevalence of asymptomatic *P. falciparum* infection, factors associated with subsequent development of symptomatic malaria, and the prevalence of STH co-infection. Blood samples determined malaria status and anemia, daily temperature checks were used to monitor for symptomatic disease development, and stool samples screened for STH infection using the Kato Katz method. Due to presumed falsely low Kato Katz results, a secondary retrospective study was conducted to establish STH IgG positivity. Overall, 85.8% of children had asymptomatic *P. falciparum* infection by microscopy, 88.8% had serologic positivity for at least one STH antigen, and 76.1% had asymptomatic *P. falciparum* plus STH exposure. We found no significant difference in the proportion of children with STH exposure and asymptomatic vs. symptomatic *P. falciparum* carriage (88.7% vs 83.3%, p >0.05), or in the proportion of asymptomatic *P. falciparum* carriers who were STH-exposed vs. STH-unexposed (85.7% vs. 86.7%, p > 0.05). The quantity of reactive antibody to STH was no different in asymptomatic vs. symptomatic *P. falciparum* carriers (p>0.05), and, for asymptomatic children, there was no correlation between anti-STH antibody level and *P. falciparum* load (p > 0.05). While limitations exist, we observed no association between STH exposure and asymptomatic *P. falciparum* infection.

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UPREGULATION OF GENE TRANSCRIPTS FOR SEVEN CRITICAL *PLASMODIUM FALCIPARUM* GLYCOLYTIC ENZYMES IN PEDIATRIC SEVERE MALARIAL ANEMIA

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The potential of novel therapeutic targets for severe malaria infections caused by *Plasmodium falciparum* is essential. This can be achieved by harnessing components of the parasite's metabolic pathways vital for its viability and infectivity in human hosts. One such target is the glycolytic pathway responsible for energy generation for the parasite's activities. This pathway is catalyzed by enzymes that control the flow of glycolytic metabolites. Enzymes in the pathway also influence non-glycolytic processes essential for the infectivity of the parasite such as: (i) the motility of sporozoites towards the liver cells and the subsequent attachment and entry into the hepatocytes, (ii) the egress of merozoites, (iii) infection of red blood cells, and (iv) the adherence of the parasites to the endothelial vessels. To explore if genes encoding key enzymes in the glycolytic pathway of *P. falciparum* contribute to the pathogenesis of severe malaria anemia [SMA, hemoglobin (Hb)<6.0 g/dL], a major manifestation of severe malaria, we performed *P. falciparum* transcriptome profiling on the peripheral blood of pediatric malaria patients in Siaya County Referral Hospital, Kenya, stratified into two clinical groups: SMA (n=20) and non-SMA (Hb≥6.0 g/dL, n=40). Our results revealed significant upregulation (FDR-adjusted $P<0.05$) of genes encoding seven key parasitic enzymes in the glycolytic pathway in children with SMA: pyruvate kinase 2 (*PykII*, $\log_2$FoldChange=1.262), phosphoglycerate mutase (*PGM*, $\log_2$FoldChange=0.710),phosphoglycerate kinase (*PGK*, $\log_2$FoldChange=0.645), enolase (*ENO*, $\log_2$FoldChange=0.609), triosephosphate isomerase (*TIM*, $\log_2$FoldChange=0.608), phosphoglycerate mutase (no gene symbol, $\log_2$FoldChange=0.533), and 6-phosphofructokinase (*PFK9*, $\log_2$FoldChange=0.519). Harnessing key enzymes in the glycolytic pathway of *P. falciparum* presents a promising avenue for targeting severe malaria infections, as evidenced by significant upregulation of these enzymes in pediatric patients with SMA, suggesting their potential role in disease pathogenesis.

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HEME AND HEMOGLOBIN SCAVENGING DEFICIENCIES IN PEDIATRIC SEVERE MALARIAL ANEMIA-- INSIGHTS FROM PLASMA PROTEOMICS

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Severe malarial anemia (SMA: Hb<6.0 g/dL, with any density parasitemia) is the primary clinical manifestation of severe malaria and among the

leading causes of morbidity and mortality in children under five years in holoendemic *Plasmodium falciparum* transmission regions, such as Siaya County, western Kenya. *P. falciparum* infection causes hemolysis of infected and uninfected human erythrocytes, resulting in the release of heme and free hemoglobin (Hb) into peripheral circulation. These molecules act as blood toxins to exposed cells and can promote organ failure when not promptly scavenged. To define molecular signatures associated with severe disease, we utilized an aptamer-based technology (SomaScan) to quantify 6,612 circulating human proteins in plasma samples collected from children (3-36 months) with non-SMA (Hb≥6.0 g/dL, n=20) and SMA (n=20) upon enrollment (pre-treatment: day 0). The proteomics revealed that levels of 670 plasma proteins were significantly higher in SMA relative to non-SMA (P<0.05, FDR<0.25), whilst the circulating levels of 665 proteins were significantly lower in SMA vs. non-SMA (P<0.05, FDR<0.25). Of the 1,335 differentially expressed proteins (DEPs), two critical heme scavengers, hemopexin and alpha-1-microglobulin, as well as the sole Hb scavengers, haptoglobin isoforms, were all down-regulated in the SMA group: hemopexin (log_2FoldChange= -0.842, P=3.753E-4); alpha-1-microglobulin (log_2FoldChange=-0.385, P=3.660E-3); haptoglobin, mixed type (log_2FoldChange=-3.961, P=8.089E-3); and haptoglobin isoform 2 (log_2FoldChange=-3.944, P=4.372E-3). Collectively, these proteomic results demonstrate that SMA is characterized by a deficiency of scavenging capability for heme and free hemoglobin during severe malaria infections.

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TRANSCRIPTOMIC INSIGHTS INTO COMPLEMENT-ASSOCIATED GENE DYSREGULATION IN CHILDHOOD SEVERE MALARIAL ANEMIA

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Severe malarial anemia (SMA: Hb<6.0 g/dL) is among the leading causes of global childhood morbidity and mortality. In holoendemic *Plasmodium falciparum* transmission regions, such as western Kenya, severe malaria primarily manifests as SMA. We have previously demonstrated that genetic variations in complement components alter the longitudinal risk of SMA and mortality. To extend these findings, we examined the entire expressed transcriptome in peripheral blood samples collected from children (1-59 mos.) with non-SMA (Hb≥6.0 g/dL, n=41) and SMA (n=25). Of the 585 human complement-associated genes identified in NCBI, 566 of the genes were contained within the RNA-Seq data with 189 genes differentially expressed in children with SMA relative to non-SMA at FDR≤0.050. Of the 189 genes, 79 were up-regulated and 110 were down-regulated. Gene ontology (GO) enrichment analysis using clusterProfiler in R revealed complement activation (FDR=$8.49x10^{-22}$), humoral immune response (FDR=$1.09x10^{-21}$), and complement activation (classical pathway, FDR=$6.60x10^{-15}$) as the top-enriched biological processes. Collagen-containing extracellular matrix (FDR=$5.25x10^{-15}$), blood microparticle (FDR=$1.61x10^{-13}$), and secretory granule lumen (FDR=$1.46x10^{-12}$) were the most enriched cellular processes. Glycosaminoglycan binding (FDR=$8.02x10^{-09}$), cytokine binding (FDR=$1.62x10^{-06}$), and extracellular matrix structural constituent (FDR=$2.97x10^{-06}$) as the top associated molecular functions. Functional pathway enrichment analyses using MetaCore™ (threshold: log_2foldchange=0.585 and FDR<0.05) showed that SMA was characterized by dysregulation in Plasmin Signaling (FDR=$2.93x10^{-8}$), Classical Complement Pathway (FDR=$4.32x10^{-8}$), and C3a Signaling (FDR=$6.32x10^{-6}$) related to the immune response. Collectively, these findings illustrate that acute malaria, and particularly SMA is associated with dysregulation in several complement signaling cascades.

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PLASMODIUM KNOWLESI INFECTION IS ASSOCIATED WITH ELEVATED CIRCULATING BIOMARKERS OF BRAIN INJURY AND ENDOTHELIAL ACTIVATION

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Introduction: Malaria remains a major public health concern with substantial morbidity and mortality worldwide. In Malaysia, the emergence of *Plasmodium knowlesi* has led to a surge in zoonotic malaria cases and deaths in recent years. Signs of cerebral involvement have been observed in a non-comatose, fatal case of severe *knowlesi* infection, but the potential impact of this malaria species on the brain remains underexplored.
To address this gap, we investigated circulating levels of brain injury, inflammation, and vascular biomarkers in a cohort of *knowlesi*-infected patients and controls.
Methods: Archived plasma samples from 19 patients with confirmed symptomatic *knowlesi* infection and 19 healthy, age-matched controls from Peninsular Malaysia were analysed. A total of 52 plasma biomarkers of brain injury, inflammation, and vascular activation were measured using Luminex and SIMOA assays. Wilcoxon tests were used to examine group differences, and biomarker profiles were explored through hierarchical clustering heatmap analysis.
Results: Bonferroni-corrected analyses revealed significantly elevated brain injury biomarker levels in *knowlesi*-infected patients, including S100B (p<0.0001), Tau (p=0.0007), UCH-L1 (p<0.0001), αSyn (p<0.0001), Park7 (p=0.0006), NRGN (p=0.0022), and TDP-43 (p=0.005). Compared to controls, levels were lower in the infected group for BDNF (p<0.0001), CaBD (p<0.0001), CNTN1 (p<0.0001), NCAM-1 (p<0.0001), GFAP (p=0.0013), and KLK6 (p=0.0126). Hierarchical clustering revealed distinct group profiles for circulating levels of brain injury and vascular activation biomarkers.
Conclusions: Our findings highlight for the first time the impact of *Plasmodium knowlesi* infection on the brain, with distinct alterations in cerebral injury and endothelial activation biomarker profiles compared to healthy controls. Further studies are warranted to investigate the pathophysiology and clinical significance of these altered surrogate markers, through both neuroimaging and long-term neurocognitive assessments.

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TRANSCRIPTOME PROFILE OF BLOODSTAGE *PLASMODIUM FALCIPARUM* IN CHILDREN WITH SEVERE MALARIAL ANEMIA

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About 80% of malaria-related deaths in the World Health Organization African region occur in children <5 years, who develop severe malarial anemia [SMA, hemoglobin (Hb)<6.0 g/dL] as the primary clinical manifestation of severe malaria. However, differential expression of *Plasmodium falciparum* genes in SMA vs. non-SMA remains largely unexplored. As such, we characterized the entire *P. falciparum* transcriptome in peripheral blood obtained from children (3-36 months) with non-SMA (Hb≥6.0 g/dL, n=40) and SMA (n=20) at enrollment. Next-generation sequencing was performed at a depth of >20 million high-quality mappable reads. Reads were mapped to a Kenyan isolate (*pf*KE01) reference genome using the HTSeq platform, revealing 3,155 *P. falciparum* mRNA transcripts. Expression levels of 566 genes were significantly ($p \leq 0.05$) altered in SMA (499 up- and 67 down-regulated). Principle component analysis revealed that the first two principal components explained 72.9% of the variance. Gene expression deconvolution analysis showed a higher proportion of trophozoites ($p=0.028$) and a lower proportion of ring stages ($p=0.008$) in SMA, but comparable proportions of schizont and gametocyte stages between SMA and non-SMA. Notably, the male gametocyte proportion was higher than the female gametocyte proportion across all malaria patients ($p=1.000E-6$). Weighted gene co-expression network analysis of the 566 differentially expressed genes identified five modules enriched in the following functional terms: molecular function-threonine-type endopeptidase activity ($p=3.780E-5$); biological process- proteasomal ubiquitin-independent protein catabolic process ($p=4.780E-6$); cellular component- proteosome complex ($p=1.710E-12$), and KEGG-proteasome ($p=6.060E-8$). This study provides the first transcriptional profile of blood-stage *P. falciparum* in children with SMA, highlighting the parasite's reliance on proteasome-mediated protein degradation pathways for survival within the host and suggesting potential targets for therapeutics.

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PROBING THE RELATIONSHIPS BETWEEN COAGULATION, INFLAMMATION, AND OXIDATIVE STRESS IN PLACENTAL MALARIA PATHOGENESIS

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Plasmodium falciparum infection in pregnancy contributes to poor birth outcomes via adherence of infected erythrocytes in the placenta, precipitating maternal responses that induce placental damage and dysfunction. This syndrome, termed placental malaria (PM), is characterized by placental oxidative stress and dysregulated inflammatory and coagulation responses, though the extent to which these responses are molecularly linked is unclear. Preliminary data in human PM identifies correlations between key markers of these processes, but do not prove causation. To pursue this question, a mouse model was utilized. *P. chabaudi* infection in *Tnf*$^{-/-}$ and endothelial tissue factor-deficient (*F3*$^{flox/flox}$ Tie-2^{Cre}) mice and ablation of tumor necrosis factor (Tnf) and anticoagulant treatment in mice infected with the rodent-infective parasite improved pregnancy outcomes. Relative to infected C57BL/6J (B6) controls, infected *Tnf*$^{-/-}$ mouse embryos showed two to four-fold reduced expression of protease activated receptor 2 (*F2rl1*), which links activated coagulation with inflammatory responses. Tissue factor (*F3*) expression was 50% reduced, while endothelial protein C receptor (*Procr*) transcripts increased three to five-fold, supporting the notion that coagulation and inflammation are co-regulated in PM, with reduced inflammation promoting natural anticoagulant function. With anti-coagulant drug treatment of the dam, transcripts for cytokines and chemokines (*Ifng, Tnf, Il10, Il1b,* and *Ccl2*), antioxidants (*Sod1*, *Sod2*, and *Nfe2l2*) and *F3* were significantly downregulated relative to sham-treated, infected B6 mice, whereas *Procr* transcripts were elevated. These results support the assertion that inflammation, coagulation and oxidative stress are functionally linked in PM pathogenesis, and suggest that targeting of one or more of these responses therapeutically may be broadly protective by disrupting all three pathogenic processes.

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REGULATED CELL DEATH IN PLACENTAL MALARIA: NECROPTOSIS ASSOCIATES WITH INFECTION AND INFANT BIRTH WEIGHT

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Placental damage and dysfunction are key features of malaria infection during pregnancy and associate with poor birth outcomes. Necrotic shedding of villous trophoblast is a key feature of placental malaria (PM), but the molecular basis for this outcome has not been explored. Toward this end, primary human trophoblast (PHT), villus explants and placenta from malaria-infected women and mice were used to assess markers of necroptosis by RT-qPCR, western blot, bead-based protein complex detection, and immunostaining. Receptor interacting protein kinase 3 (RIP3) and phosphorylated mixed lineage kinase domain-like protein (pMLKL), as well as RIP1/RIP3 necrosomal complexes, all indicators of activation and execution of necroptosis, were significantly higher in human placenta with PM. RIP3 levels in infected placenta inversely correlated with infant birth weight and positively correlated with placental hemozoin load. In contrast, while *in vitro* exposure of syncytialized PHT to hemozoin induced elevated transcripts for *RIPK1* and *RIPK3*, no RIP3 or pMLKL was detected in isolated cells. Furthermore, *in vitro* treatment of PHT with activators of necroptosis (tumor necrosis factor, cycloheximide and carbobenzoxy-valyl-alanyl-aspartyl-[O-methyl]-fluoromethylketone (Z-VAD)) failed to induce this cell death pathway, instead driving trophoblast apoptosis. Only treatment conditions that included the caspase inhibitor Z-VAD, which suppresses apoptosis, were able to restore PHT viability to control levels. Thus, under the *in vitro* conditions used in this study, PHT was resistant to necroptosis, yet, *in vivo*, this cell death pathway appears to play an important role in PM pathogenesis and associated poor birth outcome. Regulation of cell death pathways in the syncytiotrophoblast requires further investigation to establish critical triggers that can precipitate placental loss of function and pregnancy compromise in PM. Current work is assessing this cell death pathway in placental tissue explants which more accurately model the native physiological and architectural context of the syncytiotrophoblast.

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THE RELATIONSHIP BETWEEN PLACENTAL MALARIA INFECTION, HIV, INTESTINAL PERMEABILITY, AND INFLAMMATION IN POST-PARTUM KENYAN WOMEN

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Placental malaria, which compromises maternal health and causes poor infant health outcomes in association with *Plasmodium falciparum* infection, has long been associated with intense and damaging inflammatory responses in the maternal peripheral and placental blood. HIV infection further exacerbates these outcomes. Maternal responses to these infections lead to significant placental dysfunction, but how they impact other organ systems in pregnant women has been less well studied. The aim of this study was to determine the relationships between placental malaria (PM), HIV serostatus, markers for intestinal permeability (lipopolysaccharide (LPS), LPS-binding protein (LBP), and zonulin), and markers of inflammation (interleukin-6 (IL-6), IL-8, IL-10, Tumor Necrosis Factor (TNF), TNF receptor II (TNFRII), and interferon γ-induced protein 10 (IP-10)) in post-partum women exposed to malaria and HIV in Kenya. Clinical and diagnostic parameters (i.e., infection status, self-reported maternal health pre-partum, and infant outcomes), as well as levels of these biomarkers in the peripheral venous blood (measured by ELISA), were analyzed. LPS and zonulin levels weakly to moderately positively correlated with placental parasite load, and

zonulin was significantly elevated with PM and PM/HIV co-infection as well as self-reported recent malaria infection. LPS was elevated in women with low birth weight infants relative to normal birth weight infants, and positively correlated with markers of inflammation (TNF, IL-6, IL-8, IL-10, and IP-10). These data suggest that infection-associated inflammatory cytokine and chemokine responses coincide with induction of gut permeability in pregnant women, and may synergize to exacerbate poor maternal and infant outcomes. Future investigations to establish the causal relationships between these responses in malaria and HIV infected women could reveal potential new targets for diagnostics and therapeutic intervention.

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BIOCHEMICAL AND BIOINFORMATIC CHARACTERISATION OF UNDERSTUDIED ERYTHROCYTE SURFACE EXPRESSED HYPERVARIABLE PROTEIN FAMILIES IN PLASMODIUM FALCIPARUM

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Title: BIOCHEMICAL AND BIOINFORMATIC CHARACTERISATION OF UNDERSTUDIED ERYTHROCYTE SURFACE EXPRESSED HYPERVARIABLE PROTEIN FAMILIES IN *PLASMODIUM FALCIPARUM.* **Abstract:**Malaria, is a vector borne disease, caused by infection with Plasmodium species, responsible for approximately 608 thousand deaths and 249 million cases worldwide in 2022, with 94% cases in sub-Saharan Africa, the majority caused by infection with Plasmodium falciparum (Pf). Parasite virulence is partly caused by evasion of the human host immune system during the blood stage of infection. Sequestration and cytoadherence are characteristic Pf virulence factors, enabled by parasite-derived proteins expressed on the surface of infected erythrocytes (IEs). These proteins are associated with acquired immunity to Pf and with antigenic variability also called Variant Surface Antigens (VSAs). VSAs are translocated from blood stage Pf to be expressed on the surface of the IE membrane. STEVOR is a VSA protein family encoded 40 stevor gene copies per parasite, expressing single variant per parasite. Members of the family differ mostly in their hypervariable region, which is exposed to the circulation and possesses antigenic epitopes. The variable domain is associated with P. falciparum exposure and potentially clinical outcome. Seroreactivity and recognition to the variants are age and exposure dependent, with higher reactivity in adults and higher domain recognition in individuals with clinical disease. This study demonstrates successful expression of isolated domains of STEVOR proteins as recombinant proteins, characterizes their antigenicity and expands understanding of the Pf proteome. By developing specific in-silico model, this study characterizes STEVOR variants into clusters for the selection and subsequent development of a library of variants to explore the breath of antibody responses to the library in various Sub-Saharan African populations, characterized with different malaria endemicity levels.

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PRECARIOUS SECURITY CONTEXT AND ADAPTATIVE METHODS TO IMPLEMENT SEASONAL MALARIA CHEMOPREVENTION (SMC) IN BURKINA FASO

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Burkina Faso's Permanent Secretariat for Malaria Elimination, SP/Palu, has been organizing Seasonal Malaria Chemoprevention (SMC) campaigns since 2014 to prevent malaria illness and deaths in children under five years during the rainy season. SMC treatments are administered by community distributors (CDs) through door-to-door visits and at fixed distribution points at health facilities. The USAID-funded Integrated Health Services (IHS) project supports SMC distribution in 19 districts in 3 regions. Since 2015, the country has been contending with insecurity, leading to a surge of internally displaced persons (IDPs), many of them children. This has implemented SMC a challenge in many areas, including 16 out of 19 IHS-supported districts. In addition, during the 2023 SMC campaign, 37 of 598 health facilities in these districts were closed, and affected health and community workers relocated. To ensure that all eligible children receive treatments, the IHS project adapted its SMC interventions to facilitate the reach of eligible targets. This included introducing a "tick card" for children at IDP sites, training additional CDs, increasing the number of CD trainers, selecting an IDP to raise awareness with the public crier jointly, and verifying insecticide-treated net availability in affected districts. 16 IDP sites were encountered in IHS-supported districts during the 2023 SMC campaign. 5,957 internally displaced children were treated during cycle 0 (7 districts) and 26,944 during cycle 4 (19 districts). IDPs reached with SMC in IHS-supported districts represented 9% of IDP children who benefitted from SMC nationwide; children benefiting from SMC in HIS area represent 21% of all children treated in the country. In IDP sites, challenges encountered included difficult access to some IDP sites, inadequate communication between CDs and households, and a lack of data to estimate the number of children at IDP sites for planning and drug quantification. Coverage isn't ensured, but substantial efforts are being made to reach vulnerable and displaced populations.

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PERFORMANCE OF A NEW COMMUNITY HEALTH POLICY IN BENIN FOR DISTRIBUTING INSECTICIDE-TREATED NETS: EXPERIENCE OF 2023 MASS CAMPAIGN

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The national insecticide-treated bed net (ITN) policy in Benin is universal coverage of 1 ITN for 2 people per household. Benin recently adopted a community health policy in which paid community health workers (*Relais Communautaire*, [RC]) deliver a package of non-clinical interventions to their communities. For the 2023 campaign, RCs conducted door-to-door ITN distribution (Community-based approach [CBA]) to about 200 households (HH) as part of their routine work. We compared CBA distribution with traditional distribution (Employee-based approach [EBA]), in which employees are hired to distribute ITNs at fixed points in villages. Both approaches included training for HH enumeration, and ITN distribution using the RedRose digital platform (RCs had work smartphones, hired staff were lent smartphones). The data collected included HH location and the number of residents by age while the RedRose application generated HH ITN targets. The ITN coverage (ITNs delivered/HH ITN targets) from the six CBA and eight EBA districts was compared using a Chi-square test in R Studio. ITN coverage was significantly higher in CBA compared with EBA districts (98% [373,706/381,247] vs. 92% [436,548/473,884]; $p<0.05$) though the CBA required more distribution days than EBA (8-15 vs. 4 days, respectively). CBA HHs benefited from individual messages regarding ITN use and maintenance rather than group messaging at EBA delivery sites. CBA did not require additional labor costs for distribution as these were incorporated into RC salaries. ITN distribution coverage was higher using door-to-door CBA delivery vs traditional fixed-point EBA delivery. Additional evaluations of the two systems will help to determine future delivery modes.

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EVALUATION OF SEASONAL MALARIA CHEMOPREVENTION IMPLEMENTATION IN THE UPPER EAST REGION OF NORTHERN GHANA

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AbstractGhana adopted the WHO-recommended Seasonal Malaria Chemoprevention (SMC) in 2016 following a pilot study as a vital strategy for malaria control. This study monitored the implementation of SMC to ensure the intervention is achieving its target.We conducted a prospective longitudinal study in four administrative districts of the Upper East Region of Ghana. Children aged between 3 and 59 months were sampled and followed up one week after each cycle of SMC dosing to complete a questionnaire. SMC status was determined through the caregiver's report and child welfare cards, if available. Caregivers were asked if the participant had been treated for malaria since the last cycle. Simple and multiple logistic regressions were employed to determine associations between SMC adherence and the independent variables, with all results interpreted at a 95 % confidence level (CI).A total of 2099 participants were enrolled in this study. This study reported an average SMC coverage of 87% (CI: 86.7-89.5) per cycle with a 2% dropout after the first cycle. SMC adherence rate remained above 82% (CI: 1.4-2.5), with malaria incidence decreasing in those who received all four doses of SMC compared to partial recipients. The main reasons reported for non-adherence were the participant not available/in school (74%), caregiver refusal (14%), and forgetfulness (5%). Significant predictors of adherence were household size (aOR=1.04, 95% CI: 1.01-1.08), sleeping under bednets (aOR=1.88, 95% CI: 1.44-2.48), and indoor residual spraying (IRS) presence (aOR= 0.83, 95% CI: 0.69-1.99). Despite achieving an average coverage of 87% per cycle, it falls short of the national target of 90%. Notable reasons for drop-outs and non-adherence were, the caregiver being unavailable
during the distribution, highlighting the need for diversified approaches in SMC campaigns to enhance coverage and adherence, and maximize intervention benefits.

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LOCALIZATION IN ACTION: TRANSITIONING INDOOR RESIDUAL SPRAYING MANAGEMENT TO HOST COUNTRY GOVERNMENT IN ANKAZOABO DISTRICT, ATSIMO ANDREFANA REGION, MADAGASCAR, 2023

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Localization in action: Transitioning indoor residual spraying management to host country government in Ankazoabo District, Atsimo Andrefana Region, Madagascar, 2023

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ABSTRACT

As part of PMI's approach to promoting shifting power to local actors, PMI Evolve is committed to strengthening capacity of the national malaria program (NMP) to manage indoor residual spraying (IRS) operations while promoting gender equality, social inclusion and climate change mitigation. For the 2023 spray campaign, after a memorandum of understanding was signed between NMP and PMI Evolve to delineate the roles and responsibilities of both parties and ensure standardized procedures across different phases of IRS operations, the NMP led all stages of IRS implementation in Ankazoabo Sud district. NMP and district health services coordinated and monitored IRS implementation, trained actors, handled logistics and environmental compliance and provided trainings. PMI Evolve provided technical guidance to NMP, procured spray materials, funded expenses and supported NMP in national results dissemination. The intervention covered 20,613 structures (93.8% of structures found), and 85,385 people. With support from local, district and regional health systems, NMP successfully coordinated and planned activities, managed staffing, and social mobilizations through community meetings. Along with the district health team, NMP and PMI Evolve will prioritize IRS implementation sustainability plan and preparation for 2024.

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SEASONAL MALARIA CHEMOPREVENTION IN NORTHERN MOZAMBIQUE: A COST-EFFECTIVENESS ANALYSIS

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Malaria is endemic in Mozambique and one of the leading causes of death in children under five years old. In 2020 the country adopted the WHO-recommended Seasonal Malaria Chemoprevention (SMC) strategy, and started delivering the intervention in 2, 4 and then all 23 districts of Nampula province by 2023. The aim of this study was to estimate the cost-effectiveness of SMC in Nampula, Mozambique. Costs were analyzed from a health care provider perspective and reported in 2023 US$. Data on resource use were collected from intervention records by the Malaria Consortium, data on the beneficiaries were collected from surveys after Cycle 4, and malaria cases and deaths averted by SMC were estimated based on prevalence data obtained from available data sources, e.g., Global Burden of Disease 2019 and the Malaria Incidence Survey 2018. Incremental cost-effectiveness ratios (ICERs) were estimated by round, for the three rounds conducted between 2020 and 2023, and sensitivity analyses were conducted to test the robustness of the ICERs. We found that the total financial cost of SMC in Mozambique was US$ 8,994,226.90 (2023) for three rounds implemented between 2020 and 2023. We estimated a cost per targeted child of $5.99; a cost per household with eligible children visited by a community distributor at $7.00; a cost per child who received day 1 SPAQ at $7.37; a cost per child who received day 1 SPAQ by community distributor adhering to DOT at $7.73; and a cost per child who received 3 full-day course SPAQ at $7.49. In addition, we estimated a cost per malaria case averted at $27.20, and a cost per malaria death averted at $3,107.97. Cost-effectiveness was higher in round three, suggesting substantial economies of scale. The ICERs were robust to a variety of alternative assumptions on benefit estimates as well as discounting rate. Finally, we found that $1,670,827.55 could have been saved if the program did not include ineligible children (60-119 months old). In line with existing evidence from other African countries, SMC is cost-effective in Mozambique: SMC is a beneficial prevention strategy to improve under-five health in the country, at a relatively low-cost.

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ACCEPTABILITY OF A SCREENING AND TREATMENT STRATEGY TO THE POPULATION AS PART OF STRENGTHENING THE IMPACT OF SEASONAL MALARIA CHEMOPREVENTION IN BURKINA FASO

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Population screening and treatment strategies are now making considerable headway in the fight against malaria. In order to improve the effectiveness of seasonal malaria chemoprevention **(**SMC), which has been recommended since 2014 for the prevention of malaria in children, the SMC-RST project has been implemented in Burkina Faso. This project consists of screening and simultaneous treatment of roommates of children under SMC coverage. This study aims at determine the social, cultural and behavioural factors that facilitate or hinder adoption and adherence to the newly added antimalarial treatment. We conducted a qualitative study of 41 roommates, 5 health care workers, 5 field workers between October 2022 to January 2023 using purposive sampling in 5 rural villages in the Health District of Nanoro. Data collection combined in-depth interviews and observations of interactions between housemates and data collectors. Interviews were conduct in local language audio recorded and transcribed. Data were coded and a thematic analysis was carried out using QSR N'vivo 12 software. Our findings reveal good acceptability of this new screening and simultaneous treatment intervention for roommates of children with SMC coverage. Indeed, participants perceive an improvement in the health of children under 5 years of age under SMC coverage through the intervention. They appreciate the fact that they can be screened and treated at home, free of charge, and that they can prevent illness or treat themselves before it gets worse. Health care workers mentioned that they received fewer consultations from children under 5 since the start of the intervention, despite the fact that this is a time of high malaria rates. Overall, the study had a positive impact on the health of children under 5 and their housemates. It demonstrated a positive perception of simultaneous screening and treatment of roommates of children under SMC coverage.

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LEVERAGING PERENNIAL MALARIA CHEMOPREVENTION (PMC) PILOT IMPLEMENTATION TO PAVE THE WAY FOR PMC AND MALARIA VACCINE CO-IMPLEMENTATION IN THE DEMOCRATIC REPUBLIC OF CONGO

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The World Health Organization recommends both PMC and malaria vaccine for the prevention of Plasmodium falciparum malaria in children in areas of moderate to high malaria transmission. Although the funding sources are currently different (i.e. through the malaria program and immunization program), these two interventions are recommended to be delivered through the same EPI platform and target the same age group. Furthermore, the rollout phase involves similar steps, including the establishment of coordination mechanisms between the malaria program and EPI, the development of an optimal delivery schedule, the modification of national Health Information Management System (HIMS) tools, and the development of a community engagement plan to ensure uptake. The DRC recently introduced PMC with rollout starting in December 2023. The country has opted for a six-contact model administering Sulfadoxine-Pyrimethamine (SP) at 10 and 14 weeks of age, 6, 9, 12 and 15 months. The country has also been approved by Gavi to receive support for initial subnational malaria vaccine introduction, with a four-dose schedule at 6,7,9 and 24 months. As the service provision is integrated at the point of delivery (i.e. health facility), meaning the same healthcare provider will deliver both PMC and malaria vaccine, an approach leveraging PMC introduction to prepare for malaria vaccine rollout was taken. Hence, the coordination mechanism created to co-develop the PMC schedule was leveraged for vaccine introduction. The coordination platform includes the Malaria Program, EPI, Nutrition Program (NNP), Health Promotion and Communication Program, HMIS department, National Program to fight Cholera and Diarrheal Diseases, the National Supply Chain for Essential Drugs, and implementing partners. During PMC introduction, through an inclusive and consensual decision-making process, all normative documents and HMIS data collection and reporting tools updated to capture PMC data incorporated aspects related to malaria vaccine. These include the vaccination register, the tally sheet, the child vaccination card as well as the national DHIS2 platform.

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ACCEPTABILITY OF INTEGRATING NOVEL MALARIA PREVENTION TOOLS INTO ROUTINE IMMUNIZATION VISITS IN CAMEROON

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Cameroon is among the 11 countries with the highest malaria burden worldwide. In the past year, Cameroon began implementing the RTS,S/AS01 malaria vaccine and perennial malaria chemoprevention (PMC) for children <24 months of age. We conducted a 2-phase health facility cross-sectional study (Nov-Dec 2023 dry season and April-June 2024 rainy season) to examine vaccine acceptability and PMC uptake through routine immunization services at Cameroon Baptist Convention Health Services (CBCHS). We selected 7 CBCHS clinics in 5 regions in Cameroon with varying malaria prevalence. Caregivers of children presenting for immunizations were randomly selected for a brief survey. In the dry season phase, we surveyed 353 caregivers: median age 29 years (IQR 25-32), 96.6% female, 64% with at least secondary education; 84% reported the child slept under a mosquito net the night before, and 11% reported that the child had fever/malaria in the prior 2 weeks. Only 47% of caregivers knew of the malaria vaccine, and 91% said they would accept it for their child at CBCHS. However, 33% expressed concerns about the vaccine: fear of side effects (23%), uncertain about safety (9%), possible interaction with other vaccines (7%), uncertain of efficacy (7%), other (13%). 23% said ≥1 neighbor would not accept the vaccine. A higher proportion (76%) had heard of PMC ("Fansidar for infants"), and 50% reported that their child had received ≥1 dose. Few caregivers expressed concerns about PMC. In multivariable logistic regression, caregivers in the highest vs lowest wealth quartile were less likely to be willing to accept malaria vaccine (OR 0.08 [95% CI: 0.01-0.78]). Having fever/malaria in the prior 2 weeks was associated with not expressing concerns about the vaccine (OR 2.89 [1.10-7.57]). The rainy season survey and dried blood spot analyses are ongoing. Integration of malaria vaccine and PMC into routine immunization visits is acceptable to caregivers of young children attending CBCHS, although

continued efforts are needed to increase confidence in these interventions. Alternative strategies are needed to reach those who do not regularly attend routine immunization visits.

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IMPACT ON PREGNANCY OUTCOMES OF INTERMITTENT PREVENTIVE TREATMENT WITH SULPHADOXINE-PYRIMETHAMINE IN URBAN AND PERI-URBAN PAPUA NEW GUINEA - A RETROSPECTIVE COHORT STUDY.

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Background Intermittent preventive treatment in pregnancy with sulphadoxine-pyrimethamine (IPTp-SP) prevents low birth weight (<2,500 g) and other adverse pregnancy outcomes through malaria and non-malarial mechanisms. Malaria transmission in Papua New Guinea (PNG) is highly heterogeneous. The impact of IPTp-SP in settings with little or no malaria transmission, such as the capital Port Moresby, is unknown.
Methods A retrospective cohort study was conducted amongst HIV-negative women with a singleton pregnancy who delivered at Port Moresby General Hospital between 18 July and 21 August 2022. The impact of IPTp-SP doses on adverse birth outcomes and anaemia was assessed using logistic and linear regression models, as appropriate.
Results Of 1,140 eligible women amongst 1,228 consecutive births, 1,110 had a live birth with a documented birth weight. A total of 156 women (13.7%) did not receive any IPTp-SP, 347 women (30.4%) received one, 333 (29.2%) received two, and 304 (26.7%) received the recommended ≥3 doses of IPTp-SP. A total of 65 of 1,110 liveborn babies (5.9%) had low birth weight and there were 34 perinatal deaths (3.0%). Anaemia (haemoglobin <100 g/L) was observed in 30.6% (243/793) of women, and 14 (1.2%) had clinical malaria in pregnancy. Compared to women receiving 0-1 dose of IPTp-SP, women receiving ≥2 doses had lower odds of LBW (adjusted odds ratio [aOR] 0.50; 95% confidence interval [CI] 0.26, 0.96), preterm birth (aOR 0.58; 95%CI 0.32, 1.04), perinatal death (aOR 0.49; 95%CI 0.18, 1.38), LBW/perinatal death (aOR 0.55; 95%CI 0.27, 1.12), and anaemia (OR 0.50; 95%CI 0.36, 0.69). Women who received 2 doses versus 0-1 had 45% lower odds of LBW (aOR 0.55, 95%CI 0.27, 1.10), and a 16% further (total 61%) reduction with ≥3 doses (aOR 0.39, 95%CI 0.14, 1.05). Birth weights for women who received 2 or ≥3 doses versus 0-1 were 81 g (95%CI -3, 166) higher, and 151 g (58, 246) higher, respectively.
Conclusions Provision of IPTp-SP in a low malaria-transmission setting in PNG appears to translate into substantial health benefits, in a dose-response manner, supporting the strengthening IPTp-SP uptake across all transmission settings in PNG.

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A RANDOMIZED CONTROLLED TRIAL OF DIHYDROARTEMISININE PIPERAQUINE FOR SEASONAL MALARIA CHEMOPREVENTION IN CHILDREN UNDER 10 YEARS OLD IN KOULIKORO, MALI

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Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine-amodiaquine (SP-AQ) was recommended by the Word Health Organization (WHO) in 2012 for children under five year-old living in highly seasonal malaria transmission areas. Efficient SMC implementation has been met with challenges with treatment compliance and adverse drug effects. Also, increasing resistance markers among *Plasmodium falciparum (P.f)* to both SP and AQ in these countries require more attention when scaling up SMC for malaria elimination initiatives. This study aimed to assess the effectiveness of Dihydroartemisinine-piperaquine (DHA-PQ) as an alternative to the standard regimen for SMC while extending the age limit to up to 9 years. In 2019 and 2020, six villages within the health district of Koulikoro, Mali were cluster-randomized to receive either SP-AQ or DHA-PQ. The primary outcome was malaria incidence, defined as the presence of fever plus a positive malaria rapid diagnostic test. Cross-sectional surveys were used to determine the effect of each treatment regimen on asymptomatic malaria and anemia at the start and the end of the SMC campaign in each cohort. Adverse side effects, and compliance to treatment were assessed through monthly household survey. Over 95% of children received the first dose of SMC treatment under direct observation in both study arms, and about 71.5% (SP-AQ arm) and 82.0% (DHA-PQ arm) received 3 to 4 rounds of SMC yearly. Nausea (OR: 0.37, 95% CI: 0.29–0.47]) was the most frequent SAE reported and more frequent in the SP-AQ arm. Asymptomatic *P.f* prevalence decreased by 18% (95% CI: 0.66–1.97) in the SP-AQ arm versus 26% (95% CI: 0.57–0.94) in the DHA-PQ arm. DHA-PQ was associated with reduced the risk of malaria disease over SP-AQ by 49% (incidence risk ratio [IRR]: 0.51, 95% CI: 0.46–0.55). Our findings show that both treatment regimens are highly effective among children between under 10 years-old with more advantages for DHA-PQ such as fewer side effects, and significant reduction in both asymptomatic infection carriage and incidence. The findings are relevant to countries were SMC with SP-AQ has shown high impact on malaria burden.

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EVALUATION OF CLOTHIANIDIN INDOOR RESIDUAL SPRAYING (IRS) AND PIPERONYL BUTOXIDE (PBO) INSECTICIDE-TREATED NET (ITN) CO-DEPLOYMENT COMPARED TO PBO ITNS ONLY USING HEALTH MANAGEMENT INFORMATION SYSTEM DATA IN SIERRA LEONE, 2017-2023

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Indoor residual spraying (IRS) and pyrethroid/piperonyl-butoxide (PBO) insecticide-treated nets (ITNs) are proven malaria vector control tools; however, the impact of their combined use is not well studied. To combat increasing insecticide resistance and high malaria burden, the Sierra Leone National Malaria Control Program conducted a mass distribution of PBO ITNs between May-June 2020. Clothianidin-based (CTD) IRS was co-deployed in Bo and Bombali districts between May-June 2021 and 2022. Using an observational study design, six years of routinely reported Health Information System data (May 2017-April 2023) and 20 months of vector density data (July-April from 2020-2022) were evaluated to estimate the epidemiological and entomological impact of IRS and PBO ITN co-deployment in Bo and Bombali compared to PBO ITNs alone in two control districts, Karene and Port Loko. Negative binomial mixed effects modeling frameworks were used to independently estimate confirmed malaria case

incidence, human biting rate (HBR), and indoor resting density (IRD) over time. In both intervention groups, there were significant post-intervention declines in confirmed case incidence compared to baseline (IRS + PBO ITNs: -43.4% [95% credible interval (CI): -44.5%, -42.4%]; PBO ITNs only: -41.9% [95% CI: -43.0%, -40.8%]). However, there was no significant difference in confirmed case incidence overall between areas that received co-deployment or PBO ITNs alone (-1.5% [95% CI: -3.6%, 0.5%]). Only during the third year post-PBO ITN distribution did the co-deployment areas observe greater reductions in confirmed case incidence (2.7% [95% CI: 0.2%, 5.2%]). Co-deployment was also associated with a 10% greater reduction in HBR (IRR: 0.90, 95% CI: 0.82-0.99, p-value: 0.04) but no significant difference in IRD (IRR: 0.95, 95% CI: 0.75-1.21, p-value: 0.68). These results leveraging routine data sources could suggest that PBO ITNs may not be providing sufficient protection for their intended duration, but IRS may provide some protection.

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SUB-NATIONAL AND SUB-ANNUAL COVERAGE OF SEASONAL MALARIA CHEMOPREVENTION IN AFRICA 2012-2023

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The use of seasonal malaria chemoprevention (SMC) to prevent malaria in children has expanded rapidly since it was recommended for use by the WHO in 2012. SMC has been shown to be highly effective at reducing malaria incidence in control trials, suggesting that the rapid scale up of SMC will have important implications for the burden of malaria. To quantify this impact and adequately incorporate SMC when mapping and predicting burden, detailed information on the spatiotemporal intervention coverage of SMC will be required. SMC coverage is measured either during campaigns, where data is collected on the number of children receiving SMC drugs per distribution cycle, or in surveys where the proportion of children receiving SMC drugs is recorded. Campaign data is available for most country-years, however, coverage estimates often exceed 100%, which may indicate inaccurate estimates of target populations or that drugs were going towards non-target populations (e.g., older children). While surveys are perhaps a more robust measure of coverage, they were only conducted in a subset of administrative units and years and thus cannot provide complete Africa-wide coverage estimates. Here, we use the geographically complete campaign estimates to provide a binary (yes/no) coverage layer of where and when SMC was deployed and then estimate proportional SMC coverage from the survey results and an infilling methodology. Our results provide sub-annual and sub-national estimates and maps of SMC coverage for sub-Saharan Africa for years 2012-2023. By producing monthly results, we standardise for shifts in the timings of SMC campaigns and changes in the number of cycles distributed. Key findings of this research include (a) affirming the well documented geographical expansion of SMC and quantifying this expansion in terms of population coverage; and (b) enumerating the considerable heterogeneity in coverage levels achieved in early SMC campaigns, which became more consistent and higher by 2021.

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DEVELOPMENT OF AN ELQ-331 LOADED IMPLANT FOR LONG-TERM PROTECTION AGAINST MALARIA

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Protection of US military personnel in regions around the world endemic with malaria currently rely on the prophylactic use of oral medications that must be taken on a daily basis. This situation is not ideal and introduces the challenge of compliance under the stress of warfare and active combat. Development in other fields (HIV, contraception, and psychiatry) suggest that long-acting injectables and implantables could be developed as a long-acting preventative, providing 3 months or longer of broad protection from malaria infection and transmission. With support from the PRMRP program of the US Department of Defense, we have designed and developed a subdermal implant, loaded with the prodrug ELQ-331, using the patented Proneura® implant technology. After iterative rounds of testing, our most advanced implant design provided steady release of the active antimalarial agent, ELQ-300, in low bloodstream concentrations that were sufficient to protect mice from multiple sporozoite challenges (10,000 sporozoites/challenge) for at least 16 weeks, which was the duration for this efficacy evaluation. Full details of our successful findings, together with long-term strategies to advance this technology for the prevention of malaria infection and transmission in humans, in soldiers and civilians alike, will be presented. Note: Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s), and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. Research was conducted under an IACUC-approved animal use protocol in an AAALAC International-accredited facility with a Public Health Services Animal Welfare Assurance and in compliance with the Animal Welfare Act and other federal statutes and regulations relating to laboratory animals.

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THREE YEARS OF MONITORING AND EVALUATING SEASONAL MALARIA CHEMOPREVENTION DELIVERY IN NEW LOCATIONS IN EAST AND SOUTHERN AFRICA: RESULTS AND LESSONS FROM THREE COUNTRIES

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The scale-up of seasonal malaria chemoprevention (SMC) in West and Central Africa has been widely considered a success story. Updated World Health Organization guidelines for malaria no longer restrict SMC to specific geographies. This provides greater flexibility which enables malaria-endemic countries to adapt chemoprevention strategies to suit local epidemiology. Since 2021, SMC has been introduced and delivered in new geographies in East and southern Africa (ESA). We present results and lessons from three years of implementing, monitoring and evaluating SMC programs using sulfadoxine-pyrimethamine plus amodiaquine(SPAQ) targeting children under five in Mozambique, South Sudan and Uganda. End-of-cycle household surveys using lot quality assurance sampling (LQAS) methods

and end-of-round surveys were conducted in the 2021-2023 rounds. Surveys were used to monitor program performance against coverage, quality, safety and community awareness, knowledge and acceptability standards. Data were analyzed to compute estimates for each performance indicator by monthly cycle and location, expressed as percentages with 95% confidence intervals (CI). SMC programs targeted a population of around 200,000 eligible children in Mozambique and Uganda in 2021, increasing to 1.6 million children in the three countries in 2023. Coverage in terms of receipt of Day 1 SPAQ by eligible children exceeded 90% in most cycles and locations, ranging from 77.2% (95% CI: 70.8-82.5) to 100.0%. Similar levels of administration of Day 1 SPAQ as directly observed therapy and receipt of the full three-day course of SPAQ were maintained. Results also indicate that SMC was generally delivered to high safety, community awareness, knowledge and acceptability standards. There were however notable within-country variations in coverage and other indicators between locations and over time. Overall, results demonstrate the feasibility and sustainability of SMC when delivered at scale in new geographies in ESA. Observed sub-national disparities in program performance have implications for instituting program improvement efforts in future SMC campaigns.

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FACTORS ASSOCIATED WITH MALARIA INCIDENCE AMONG CHILDREN RECEIVING SEASONAL MALARIA CHEMOPREVENTION IN NINE STATES IN NIGERIA.

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Seasonal malaria chemoprevention (SMC) is an intervention used to prevent malaria among vulnerable populations, particularly children under five years of age. Understanding the factors associated with malaria incidence among SMC-eligible children is essential to optimize the impact of this intervention. This study aimed to understand the relationship between caregiver's characteristics, such as gender, education, occupation, adherence to dosing schedule, reporting of adverse reactions to SMC drugs and belief in SMC effectiveness and delivery factors; community drug distributors (CD) visit to household, are associated with malaria incidence. We extracted data from 11,880 caregivers of SMC-eligible children randomly sampled during SMC end-of-round surveys conducted in November and December 2023 across nine SMC implementing states in Nigeria. A Pearson chi-square test was used to determine the association between each independent variable and children reported with malaria. Mixed-effects logistic regression was used to identify adjusted association between the independent and outcome variables. A total of 2,365 (19.91%) caregivers reported their child had a fever in the past month, of which 1,539 (53.6%) received a diagnostic test and 1,266 (21.6%) tested positive for malaria. The odds of testing positive for malaria were lower in caregivers who adhered to dosing schedule (aOR = 0.667, 95% CI = 0.53 - 0.85 p<0.001), believed SMC is effective (aOR = 0.484, 95% CI = 0.36-0.64 p<0.001) and were employed in skilled manual work (aOR = 0.602, 95% CI =0.45-0.79 p<0.001) and sales (aOR = 0.535, 95% CI = 0.44-0.64 p<0.001). Individuals who experienced adverse reactions related to SMC drugs were almost three times more likely to be malaria positive than those who did not (aOR = 2.606, 95% CI =2.066-3.286 p<0.001). The study concludes that adherence to dosing schedule of SMC drug and caregiver's belief in SMC effectiveness are associated with reduced malaria incidence in SMC eligible children. Further research is required to better understand the causal pathway of increased malaria incidence among children reporting adverse reaction to SMC drugs.

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CLUSTER RANDOMIZED CONTROLLED TRIAL TO ASSESS THE SAFETY AND TOLERABILITY OF FIVE MONTHS' REPEATED DOSES OF DIHYDROARTEMISININ PIPERAQUINE AND SULFADOXINE PYRIMETHAMINE PLUS AMODIAQUINE WHEN USED FOR SEASONAL MALARIA CHEMOPREVENTION IN CHILDREN UNDER FIVE IN UGANDA.

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Seasonal malaria chemoprevention (SMC) with sulfadoxine pyrimethamine plus amodiaquine (SPAQ) is recommended for children at risk of severe malaria living in areas of seasonal transmission. Previous studies have demonstrated the safety of monthly SPAQ courses for up to four SMC cycles annually. However, the safety of additional cycles remains unexplored. A potential alternative SMC drug regimen is dihydroartemisinin piperaquine (DP) but there is a paucity of data on its safety when administered monthly for SMC. This study evaluated the safety and tolerability of five monthly cycles of SMC with SPAQ versus DP in children under five in Karamoja, Uganda. A three-arm open-label superiority and non-inferiority cluster-randomized controlled trial (cRCT) was conducted in 2022 as part of a hybrid effectiveness-implementation study. A total of 3,749 children were randomized to receive SMC with either SPAQ (1,698) or DP (1,667), while 384 acted as control and relied on standard malaria care over the five-month high-transmission period. Adverse events following SPAQ or DP administration were collected from caregivers during end-of-cycle surveys. A total of 115 (7.0%) children in the SPAQ arm and 168 (10.3%) in the DP arm experienced at least one adverse event following administration of the medicines over the five monthly cycles (p=0.001). Across both arms, the most reported adverse events were fever (33.1% of reported events in the SPAQ arm and 31.5% in the DP arm), vomiting (26.9% in the SPAQ arm and 23.8% in the DP arm) and headache (15.7% in the SPAQ arm and 17.9% in the DP arm). However, reports of nausea (p<0.001), vomiting (p<0.001) and skin rashes (p=0.02) were significantly higher in the DP arm than in the SPAQ arm. Adverse events occurred more frequently in the earlier cycles across both arms. Less commonly reported adverse events across both arms included abdominal pain, cough and dizziness. No serious or fatal adverse events were reported in either arm. The administration of DP and SPAQ for SMC over five cycles were found to be safe and well-tolerated among children in Karamoja, Uganda.

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DIRECT EVIDENCE OF FACTORS ASSOCIATED WITH SEASONAL VARIATIONS IN THE USE OF INSECTICIDE-TREATED NETS IN NIGERIA

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Despite the substantial contribution of insecticide-treated nets (ITNs) to malaria reduction in Africa, encouraging their consistent use remains challenging. Understanding underlying factors is important for developing strategies to improve ITN use. Several studies have shown perceptions related to heat and mosquito abundance are important determinants of ITN use in populations with access, but there has been limited direct evidence linking seasonal climatic variations with ITN use. We conducted repeated household surveys, in different seasons in Ondo State of Nigeria, to investigate seasonal changes in ITN use rates and the potential determinant factors.Five household surveys were conducted, using similar study design and sample sizes, before an ITN distribution campaign in December 2021 and post-campaign in April 2022, and June, August and October 2023.

A multi-stage stratified cluster sampling design was used to select 832 households in 52 wards during each survey. Household interviews were conducted using a digital questionnaire. Satellite-driven data on rainfall estimates and temperature were analysed in relation to ITN use rates overall and among populations with access. Data on household characteristics, types of available nets, and age and gender of household members were also collected and used in the analysis. The study showed significant seasonal variations in ITN use among populations with access. Reasons for non-use of available nets included feeling hot, perception of mosquito abundance, climate, urban-rural residence, age and condition of nets, and availability of extra nets in the households. The study confirmed the crucial effects of seasonality and climatic factors, especially rainfall and temperature patterns in determining ITN use rates, with increases in the rainy season and reductions in the hot, dry season. ITN use among populations with access is determined by interactions of multiple factors that should be considered when designing behavioral change communication strategies, as well as timing of distribution campaigns, promotional messages, and surveys to evaluate outcomes of the intervention.

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PROMOTING THE USE OF THE INTERCEPTOR DUAL AI G2 INSECTICIDE TREATED NETS TO REDUCE MALARIA INFECTIONS THROUGH FOCUSED SOCIAL BEHAVIOR CHANGE CAMPAIGNS IN NAMAYINGO DISTRICT, UGANDA.

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PACE, with support from BASF, is running the hang-up, keep-up campaign to promote Interceptor G2 dual Active Ingredient Insecticide Treated Nets (ITNs) against malaria in Namayingo district, Uganda. This follows the Ministry of Health's distribution of IG2 ITNs to 9.4 million households across 18 districts, via a universal net coverage campaign. A post-distribution Social and Behavioral Change (SBC) campaign in Namayingo Town Council and Buswale sub-counties aims to enhance net use to reduce malaria infections in district. A baseline assessment was conducted in to provide benchmarks against which changes in knowledge, attitude and practices (KABs) regarding net use would be measured. A cross-sectional study design employed quantitative methods of data collection. 8,238 household were targeted to participate in the baseline whether they received nets or not. We administered questionnaires to 8,195 household in 63 villages to identify KABs that impact the utilization of nets. Analysis conducted using STATA version 14. Findings revealed that 94% of households, confirmed that they had received IG2 Dual AI ITNs; while 6,158 (80%) did not hang or use the newly distributed nets one month post ITN distribution. Among those who did not use/hang up the nets, cited reasons that included concerns about the smell or irritation caused by the net 497 (32%), the perception that it was too hot 399 (26%), and the intention to hang it later (24%) among others. 85.3% were aware of the correct net hanging and usage practices and believed that ITNs were effective in protecting them against mosquito bites. SBC and monitoring of net use should be implemented during, and post universal ITN distribution campaign foster to positive knowledge, attitude and practices regarding net use for malaria prevention.

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CLOSING THE ACCESS-USE GAP: INVESTIGATING INFLUENCERS OF BEHAVIOR AROUND INSECTICIDE-TREATED NET USE IN NIGERIA AND UGANDA

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Over the last two decades insecticide-treated nets (ITNs) have been distributed as a method to prevent malaria and were responsible for 68% of the cases averted between 2000 and 2015. However, the consistent use of ITNs among communities is low, even in areas where access is high, which limits the impact of this intervention and poses a barrier to the control of the disease. To date information on barriers to net use have been collected as part of routine surveys which provide limited insights into the motivations that influence human behaviour. This formative phase - conducted between April and August 2024 - uses a mixed-method approach to explore factors that influence ITN use in areas of Nigeria and Uganda where access to ITNs is high and use rates are low. The findings from this formative research will be used to inform co-created interventions with communities that encourage ITN use. A pilot study will also be conducted to test the feasibility and acceptability of these interventions. This research will guide the design and deployment of appropriate behavioural change intervention strategies to improve ITN use in similar contexts across Africa. We are conducting a desk review of published literature and analysis of existing survey data to inform tools for primary data collection. Qualitive research, using purposive sampling, will then be carried out to investigate the factors identified in more depth. We will conduct focus group discussions with target communities, and local and national stakeholders are invited to participate in in-depth interviews. Direct observations will also be carried out in communities to observe the user experience with ITNs. Results will be analysed using a behavioural science lens to identify which factors can be targeted with behaviour change interventions. We present key findings on the barriers and enablers to ITN use in communities where access rates are already high. Our results provide a comparison across two countries, and offer evidence-based recommendations to enhance ITN uptake.

7300

PREDICTORS OF COHORT RETENTION AMONG ELIGIBLE CHILDREN RECEIVING SEASONAL MALARIA CHEMOPREVENTION IN NINE STATES IN NIGERIA

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Seasonal malaria chemoprevention (SMC) with sulfadoxine/pyrimethamine plus amodiaquine (SPAQ) has shown high protective efficacy against malaria in children under five during the high transmission season. Adherence to a full three-day course of SPAQ over four or five cycles (cohort retention) is required to confer adequate protection. This study measured cohort retention and identified child, caregiver and health systems-related predictors of retention among eligible children. Data were extracted from SMC end-of-round (EoR) survey conducted between November and December 2023 in nine states in Nigeria. The EoR survey randomly sampled 11,880 primary caregivers of eligible children aged 3-59 months. Mixed effects multivariable logistic regression models were fitted to explore the child, caregiver and health systems factors associated with cohort retention. The results indicate that 82.9% (95% CI: 82.2-83.6) of children received full three-day course of SPAQ in all cycles. We observed lower odds of retention among children with history of fever (aOR: 0.82, 95% CI:0.70-0.95) or adverse drug reactions (aOR: 0.76, 95% CI: 0.64-0.92), children whose primary caregivers were not responsible for

child medical decisions (aOR:0.78, 95% CI:0.64-0.94), children whose caregiver had post-secondary education (aOR: 0.71, 95% CI:0.57-0.88). Conversely, higher odds were observed as child age increased (p<0.01), where caregivers were knowledgeable about SMC eligibility (aOR: 1.59, 95% CI:1.21-1.89), in households that were visited by lead mothers (aOR: 2.39, 95% CI:2.09-2.73), when SPAQ was administered under direction supervision by drug distributors (aOR: 1.47, 95% CI:1.21-1.80), and when drug distributors were known to caregivers (aOR: 1.59, 95% CI:1.41-1.80). Understanding the factors that influence SMC cohort retention can help programmes design appropriate interventions to improve cohort retention throughout the SMC round. Further research may be required to understand the negative association between retention and caregivers' education status.

7301

A REVISED TOOLKIT TO SUPPORT PLANNING, IMPLEMENTATION AND MONITORING OF CONTINUOUS DISTRIBUTION OF INSECTICIDE TREATED NETS

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Despite the deployment of more than 1.3 billion insecticide-treated nets (ITNs) in the past five years, ITN access and use remains below the levels observed in 2017. Approximately half of countries that distribute ITNs expect no more than an average of two years of useful life from their nets and some national malaria programmes (NMPs) have considered shifting their ITN mass campaign cycle from every three to every two years. However, recent modelling for ITN distribution strategies has shown that full scale deployment of continuous distribution (CD) can provide better ITN access for 20% fewer ITNs compared to 3-year mass campaigns, assuming ITNs have a median useful life of at least 2.5 years. Implementation experience from Ghana, Madagascar, Senegal and Tanzania at different subnational scales shows that ITN CD maintains access and is operationally feasible and cost-effective. However, widespread uptake of CD strategies (like community- and school-based distribution) has not occurred, and best practice guidance has not been systematically updated since 2017. The CD working group of the Alliance for Malaria Prevention has revised the CD Toolkit (available at www.continousdistribution.org) in 2024 to provide new step-by-step guidance, tools and editable resources necessary to support planning, implementation and monitoring of CD. New guidance on ITN quantification for CD channels is presented alongside country success stories and lessons learned. The online toolkit has been developed with NMPs and technical partners implementing and supporting CD and is designed to remove barriers to initiating CD as part of a national vector control strategy. Website and material use will be monitored during 2025, with elements adapted based on user feedback. Expanding CD offers opportunities to improve and maintain ITN access. NMPs are encouraged to align with WHO Malaria Guidelines and donor recommendations, review operational and financial data, and consider increasing CD to complement or replace ITN mass campaign distribution, using resources available through the CD Toolkit to support planning and implementation.

7302

IMPACT OF SEASONAL MALARIA CHEMOPREVENTION ON THE INCIDENCE OF MALARIA AMONG CHILDREN UNDER THE AGE OF FIVE YEARS IN LAU LOCAL GOVERNMENT AREA OF TARABA STATE, NIGERIA

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Malaria continues to pose a significant threat to public health, particularly among children under the age of five, in many parts of sub-Saharan Africa, including Nigeria. Lau Local Government Area (LGA), situated at the bank of river Benue in Taraba State, Nigeria, faces significant challenges in combating malaria due to factors such as high transmission rates, limited access to healthcare services, and socio-economic disparities. With financial support from The Global Fund to fight AIDS, TB and Malaria, Management Sciences for Health implemented Seasonal Malaria Chemoprevention (SMC) across nine LGAs within Taraba State, including Lau. This paper explores the impact of the SMC campaign on the incidence of malaria among children under the age of five in Lau LGA of Taraba State. To examine the impact of the SMC campaign on malaria incidence among children under five years old, we analyzed the malaria test positivity rates (TPR) among this age group before the initiation of SMC (January 2020 to June 2021) and during the period of SMC implementation (July 2021 to November 2023) across all supported public health facilities in the LGA. The data used for this assessment was obtained from DHIS2, and data analysis was conducted using Statistical Package for Social Sciences (SPSS). The TPR ranges from 64.82% to 83.84% prior to SMC and from 34.98% to 62.78% two months after the start of SMC. The average TPR before SMC initiation stood at 74.74%, whereas it decreased to 51.25% two months after the commencement of SMC. Analysis of variance revealed a significant difference ($p < 0.05$) in the mean TPRs before the initiation of SMC and two months thereafter. These results suggest that the SMC campaign has significantly reduced malaria incidence among children under five in Lau LGA from an average of 74.74% to 51.25%. The decrease in malaria TPR observed among children at health facilities indicates the effectiveness of SMC in preventing and controlling malaria within the target population.

7303

THE IMPACT OF THREE ADDITIONAL DOSES OF PMC ADMINISTERED THROUGH EPI SCHEDULES ON VITAMIN A SUPPLEMENT UPTAKE IN CAMEROON

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Vitamin A is crucial for child development and deficiency is associated with increased morbidity and mortality, particularly from infectious diseases. In Cameroon, four vitamin A doses (6-11 months: 100000 IU, 12-59 months: 200000 IU) are recommended as part of the expanded program on immunization (EPI) but attendance is typically poor, especially for the three doses in the second year of life. As part of one visit, Cameroon's national malaria programme (NMP) recommends administering sulfadoxine-pyrimethamine (SP) for perennial malaria chemoprevention (PMC) which may provide additional attendance incentive. This study evaluates the

impact on vitamin A coverage of three additional doses of SP to the PMC schedule, during EPI visits that coincide with vitamin A. Data come from a prospective cohort of children under 2 years of age in Cameroon beginning July 2023. The study took place at two sites, Soa, the intervention area with up to eight PMC doses co-implemented with four vitamin A contacts, and Mbankomo, the control with up to five PMC doses co-implemented with one vitamin A contact. Beginning May 2023, all children residing in the study areas with parental consent were enumerated, and any EPI visits recorded using their EPI book. All subsequent PMC and/or EPI visits for participants were recorded by field workers based in health facilities using an assigned ID in the EPI book or through a name look-up form. Generalized estimating equations (GEE) were used to estimate a marginal model for the effect of intervention area and time on the proportion of children who received at least one dose of vitamin A supplementation. Preliminary results from the recruitment cross-sectional survey found 10.1% (397/3921) of children under 2 years received initial vitamin A supplements as indicated by their EPI books. In terms of the first vitamin A visit only, the contact point consistent between the two sites, coverage was 10.3% and 9.6% (p>0.05) in Soa and Mbankomo, respectively. Findings from this study will provide valuable insights for policymakers and NMPs into the impact of integrating additional doses of SP into the EPI schedule on improved vitamin A uptake.

7304

DOES MOSQUITO NET USE CONTRIBUTE TO MALARIA PREVENTION: AN ANALYSIS OF LOT QUALITY ASSURANCE SURVEY AND ROUTINE HEALTH FACILITY DATA FOR CONFIRMED MALARIA CASES

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Mosquito net use is generally recognized as an effective protection against malaria infection globally (WHO 2017). This abstract compares net coverage, condition, use, and malaria test positivity rates (TPR) in five high-burden regions of Uganda: Acholi, Busoga, Karamoja, Lango, and West Nile. We analyzed Lot Quality Assurance Survey (LQAS) August 2022 - September 2023 household-level data of 7,224 respondents with 5,311 observed household nets and malaria TPR from 3,420,496 fever cases and 2,066,367 confirmed malaria cases for October 2022 - September 2023 health facility level DHIS2 data extract to understand the relationship between net use and malaria. Data was analyzed for key mosquito net coverage and use indicators: Proportion of households with at least one ITN for every two people; proportion of the population that slept last night under an ITN, correlated to conditions of ITN observed and annual regional malaria TPR from routine DHIS2 data. On average, nearly 81% (5,846) of households had a net, and at least 49% (3,541) of the households had a net for every two people; 74% (5,346) of the respondents had slept under a net the night before the survey and 5,311 mosquito nets were observed with 57% (3,049) in good condition and appropriately hung over beds. Analyzed DHIS2 data showed that higher malaria TPR was found in regions with lower observed nets in good condition and appropriately hung (62% TPR compared to 40% in Acholi and 52% TPR compared to 45% in West Nile, respectively) while lower TPR was found in regions with nets in good condition and appropriately hung (47% TPR compared to 69% in Busoga, 44% TPR compared to 51% in Karamoja, 62% TPR compared to 77% in Lango, respectively). Regardless of the proportion of availability of at least one ITN for every two people, high TPR was observed in the age groups 29 days-4 years and 10-19 years and lower TPR among 0-28 days and 20+ years of both sexes. Low malaria TPR may be associated with proper net maintenance, hanging and use as observed during the survey. Ensuring people at risk of malaria infection repair damaged nets, correctly and consistently use the nets can be an effective strategy for malaria prevention.

7305

LEVERAGING BEHAVIORAL SCIENCE FOR ENHANCED MALARIA PREVENTION IN UGANDA: HOUSEHOLD ACTION AGAINST MALARIA

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Malaria is the leading cause of illness and death in Uganda, despite being preventable and treatable. The PMI Uganda Malaria Reduction Activity (PMI MRA) builds community and household capacities to prevent malaria through the household action against malaria (HAAM) approach, adapted from the Ministry of Health's Mass Action Against Malaria. HAAM empowers communities to own malaria prevention at household level to achieve malaria smart home status: malaria-free for six consecutive months. Adhering to behavioural science principles—empowerment, inclusivity, community involvement, feedback loops, and collaboration—underpin HAAM success. HAAM is implemented in 12 high malaria-burden districts through health facility staff who line-list malaria cases from HMIS registers, map villages with >5 cases (high burden villages) and cluster households for all-village inclusion. Households are assessed for malaria transmission drivers using the HAAM assessment tool and action plans are co-created with household members to address them. Monthly follow up visits are conducted to monitor progress. During implementation, household malaria champions reinforce accountability and follow up malaria response plans. District/village health teams and other stakeholders are engaged to ensure community involvement. From October 2022-February 2024, 57,677 households were assessed, clustered and sensitized using the HAAM checklist. Results from HAAM assessment data show a reduction in household malaria episodes from an average of 61% to 32% from visit 1 to visits 3 or 4 in this time period. Households clearing breeding spots increased from 55% to 96%, while consistent net use among pregnant women increased from 85% to 100%. Households planting locally available mosquito repellents rose from 23% to 81%. By co-creating prevention actions with households based on locally available resources and strategies and, and clustering households for follow-up, HAAM fosters and local empowerment and community ownership for malaria prevention.

7306

CONTRIBUTION OF SOCIAL BEHAVIOR CHANGE THROUGH COMMUNITY HEALTH WORKERS AND LOCAL LEADERS IN REDUCING MALARIA INCIDENCE IN KAYONZA DISTRICT, EASTERN PROVINCE OF RWANDA

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Malaria remains a major public health problem in Rwanda and is considered among the leading cause of morbidity and mortality. The National Malaria Strategic plan objective five states that by 2024, 85% of the population at risk will have correct and consistent practices and behaviors towards malaria control interventions. In 2019, Kayonza district ranked in the top 10 with the highest malaria incidences nationwide requiring an integrated approach of malaria control. SFH in partnership with the Ministry of Health started implementation of social behavior change communication project complementing other existing interventions. Inclusive SBC intervention through different channels like community education, peer education and community outreach implemented by community health workers and local leaders at community level which yielded a significant reduction in malaria

incidence. These interventions are spearheaded by the theme "Zero Malaria Starts with Me" promoting community ownership in malaria prevention. We conducted a desk review to assess the contribution of SBC using Ministry of health data and reports from Health Management information System (HMIS) and score cards from 2019 to 2023. Data analysis showed that social behavior change complementing existing interventions has contributed to the significant reduction of malaria incidences in Kayonza district. Results show that malaria incidences reduced from 452 per 1000 population (total malaria cases =190,464) in 2019 to 12 (total malaria cases =5,277) in 2023. Social Behavior Change in Kayonza was proven to be a successful intervention towards adapting proper behaviors like use of Bed nets (LLINs), accepting Indoor Residual Spraying (IRS), early treatment seeking behavior and integrated vector control management (IVM) that yielded a substantial reduction in malaria incidences and thus contributing towards the goal of malaria elimination in Rwanda.

7307

TRENDS AND LEVELS OF MALARIA INCIDENCE DURING INDOOR RESIDUAL SPRAYING IN HOMABAY COUNTY, 2019-2023

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Malaria in Kenya accounts for 16% of all outpatient visits. Vector control interventions are implemented according to malaria risk stratification. Homa Bay County (HBC) is in a malaria endemic zone that has implemented indoor residual spraying (IRS) from 2018-2023 to supplement long-lasting insecticide nets (LLINs), resulting in high coverage rates over the 85% recommended by WHO for community effectiveness. We describe the trends of malaria incidence using reported program data during IRS intervention. This was a cross-sectional retrospective review of data from HBC extracted from the Kenya Health Information Systems (KHIS) and National Malaria Control Program activity reports from 2019-2023. Number of all suspected malaria cases and those tested were used to calculate test positivity rate (TPR) and malaria incidence was calculated as cases per 1000 population at risk. Geospatial maps were developed in QGIS to visualize incidence patterns over time. On average the IRS coverage was 93.8% and 95.8% of population targeted were protected. While there was an initial decline in incidence from 197.3 in 2018 to 106.7 in 2020, there was a gradual increase during the IRS period, up to 359.6 in 2023. TPR increased from 21.0% in 2019 to 42.2% in 2023. Number of malaria cases detected in the community increased from 16,690 in 2021 to 80,595 in 2023. The malaria incidence risk maps showed a gradual increase of malaria transmission intensity from 2019 that covered the whole county by 2023. The initial decline in malaria incidence may be attributable to IRS intervention. Due to implementation of community case management, the number of malaria cases detected in the community increased, contributing to increased incidence despite IRS. Comparing malaria incidence over time has limitations given its dependence on data completeness and quality. Reporting in KHIS have improved over time, resulting in what appears to be increased incidence. The malaria program data demonstrate that HBC is still receptive to malaria transmission and close monitoring of malaria data and insecticide resistance are critical in the period after IRS withdrawal.

7308

ENHANCING MALARIA DIAGNOSIS, TREATMENT, AND DATA MANAGEMENT THROUGH TRAINING AND SUPERVISION OF HEALTHCARE PERSONNEL IN SIX NORTHERN PROVINCES OF ANGOLA, 2018-2023

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Malaria remains a health challenge in Angola, with high incidence rates (267/1000 cases in 2023) and associated mortality. Effective diagnosis, treatment, and accurate data recording are key in malaria control efforts. Since 2018, a comprehensive training and supervision program was implemented targeting health workers (HWs) in 6 hyper-endemic provinces in Angola, with support from PMI. The program emphasized parasitological confirmation over clinical diagnosis, adhering to standardized treatment protocols, and improved data recording practices. In total 11,704 HWs were trained in-person or via the KASSAI online platform on rapid malaria diagnostics, 9,032 HWs were supervised on malaria diagnostics and 1,021 data verification visits to health units (HUs) were conducted. To assess the impact of this program, we used routine surveillance data from 2018 to 2023 and compared malaria diagnostic practices against 4 non-PMI provinces with high malaria burden. Results shows the percentage of clinically diagnosed cases declined from 16% to 2% in 6-PMI focus provinces from 2018 to 2023, as compared to no change (28%) in 4 non-PMI-focus provinces. Malaria incidence rates increased across all PMI-focus provinces: 207/1000 in 2018 and 467/1000 in 2023, likely due to improved case detection rather than a surge in actual cases, indicative of enhanced diagnostic practices, increased reporting rates (70.0% in 2018 and 92.0% in 2023) and improved data quality (quality scores rose from 84.3% in 2021 to 91.5% in 2023). The case fatality rate decreased from 0.28% in 2018 to 0.08% in 2023, suggesting improved treatment outcomes. The use of diagnostic tests over clinical diagnosis signifies a shift towards evidence-based practices, while improved data recording enhances the reliability of surveillance data for decision-making. The use of online platforms like KASSAI enhanced the scalability and accessibility of training initiatives. These findings underscore the importance of continuous training via multiple platforms and of target supervisions, in strengthening healthcare systems and combating malaria in resource-limited settings like Angola.

7309

BUILDING A LOCAL INSTITUTION WITH GLOBAL REACH: INVESTING IN AFRICA UNIVERSITY FOR ENTOMOLOGICAL SURVEILLANCE TO FIGHT MALARIA IN ZIMBABWE

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Localization is a commitment to shift program ownership and leadership to local institutions with the capability and credibility to drive positive change in their own countries and communities. We describe our multi-year journey to strengthen capacity to achieve rigorous entomological surveillance through Africa University in Zimbabwe. In 2017, the U.S. President's Malaria Initiative (PMI) began a stepwise, iterative process with Africa University, the National Malaria Program (NMP), and key partners to design activities, set performance milestones, and collaborate during implementation and monitoring. The key prerequisite was demonstrable success in conducting entomological surveillance as a sub-awardee under a global contract. In 2021, PMI awarded Africa University a three-year performance-based, fixed-amount cooperative agreement (total $1,650,000 USD). Concurrent

capacity strengthening included construction of an insectary and provision of equipment to the existing molecular laboratory. Existing and new cadres of field and laboratory staff received training. Entomological samples analyzed annually averaged 1,827 (range: 858-3,407) and increased to 8,872 post-localization (range: 6,453-11,291). Live reference colony mosquitoes supplied annually to the Health Ministry increased from a mean of 20,665 to 47,525. Direct upload of entomological data into the national database was established for program decision-making. Africa University also became a member of the Malaria Vector Control Subcommittee which provides technical support to NMP. Cost savings and capacity have permitted the geographical expansion of entomological and insecticide resistance monitoring. Building off this investment, Africa University has established a new malaria institute and entomological center of excellence with a new applied science curriculum for faculty and graduate student research, and student internships. Localization with Africa University is a model for improved local ownership and performance, cost savings, public-private partnership, impact, and sustainability of PMI investment.

7310

USING MALARIA ROUTINE DATA QUALITY AUDITS TO IMPROVE MALARIA DATA QUALITY IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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In the Democratic Republic of the Congo, malaria data are collected in DHIS2, the national platform for the collection and analysis of health information data. Despite continuous efforts by the National Malaria Control Program (NMCP) and its partners, data quality issues persist. To better understand root causes of this poor data quality, we conducted malaria routine data quality audits (mRDQA) in 61 health facilities in Haut Katanga, Kasai Central, Kasai Oriental, South Kivu, and Tanganyika provinces in 2023. Sites were selected based on accessibility and historically low performance on data quality metrics. The mRDQA is an open-source digital tool accompanied by a District Health Information System 2 (DHIS2) package used to collect information on data quality for routine malaria reporting from health facilities as part of routine supervision. mRDQA results revealed that 84 percent of sites had complete data in their reports, 66 percent did not use the standard national registers, and 67 percent did not have congruent data between the primary source documents and aggregate monthly reports for the period audited. We found that only 11 percent of health facility providers had received training on data collection and analysis in the past two years, and 77 percent of providers had poor understanding of malaria data elements and indicators used in DHIS2. Based on the mRDQA results, NMCP and partners identified and corrected 6,031 instances where cases were misclassified as malaria deaths and supported more than 278 providers in data analysis. The mRDQA revealed that inaccurate compilation from source documents, use of non-standard data collection tools, and lack of training contributed to observed data quality issues. Future efforts should focus on providing standard data collection tools to all 179 supported health zones, organizing targeted training in malaria surveillance, monitoring, and evaluation to improve data quality for informed decision making.

7311

INSECTICIDE RESISTANCE DATA TO INFORM INTERVENTION SELECTION AND TARGETING IN UGANDA

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Uganda represents 5.1% of the global malaria burden as per the World Malaria Report (2023). Long Lasting Insecticide Nets (LLINs) and indoor residual spraying (IRS) are core interventions utilized to disrupt malaria transmission and reduce illness in at-risk populations. Although existing strategies led to a decline in incidence by 48% between 2000 and 2015, incidence has plateaued to between 200 to 300 cases per 1,000 population alongside growing resistance to insecticides used in vector control interventions. Routine entomological surveillance is implemented in Uganda and includes insecticide testing for the presence, intensity, and mechanism of resistance to the common insecticide classes used for LLINs and IRS. Despite growing resistance to insecticides data collected at sentinel sites is underutilized. Understanding where resistance has developed helps the National Malaria Control Division (NMCD) to optimize procurement and distribute more effective nets where they will have most impact. To improve data-driven decision making, CHAI (Clinton Health Access Initiative) supports NMCD to collate, analyze, and interpret insecticide resistance data to tailor vector control interventions. The 2017 analysis identified increasing resistance to pyrethroids and was used to advocate for procurement of 25% Piperonyl-butoxide (PBO) nets for the 2017/2018 mass LLIN campaign. Analysis of 2021 data showed in 7/11 sites that submitted data, PBO did not restore susceptibility to pyrethroids. In 2022 data, 14/17 sentinel sites across the country had confirmed resistance to pyrethroids. These analyses informed a shift in procurement toward more dual active ingredient (AI) nets in the 2023 mass campaign from 0-19%, though due to cost implications most nets were PBO (71%) and the remaining 10% pyrethroid-only. Annual analysis and advocacy informed the latest global fund application where the country requested to increase the proportion of dual AI nets procured to 50% due to growing resistance. Routine use of entomological surveillance data is vital to ensure that resources are used to procure and deploy the most effective vector control tools.

7312

DECADAL TRENDS IN UNDER-5 MALARIA MORTALITY; INSIGHTS FROM AN ENDEMIC HDSS SITE IN RURAL WESTERN KENYA

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WRAIR AFRICA, KISUMU, Kenya

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causes, 878 were attributed to malaria (10.6%). Malaria mortality rates showed a decline from 180 deaths per 100,000 population in 2013 to 42 deaths per 100,000 population by the conclusion of 2023. Peaks in malaria mortality were observed in 2014 (337 per 100,000) and 2017 (203 per 100,000 population).

Conclusion: The real-world effectiveness of the various malaria interventions, as well as its impact on under-5 mortality in endemic settings, remains to be fully understood. As these interventions are rolled out in regions where malaria burden is high, it is essential to monitor its performance in reducing malaria-related deaths among children under five years old.

7313

NAVIGATING VILLAGE BOUNDARIES: A COMPARATIVE EXPLORATION OF THREE MAPPING TECHNIQUES

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Clear, well-defined village boundaries are vital for community-based intervention trials, vector control studies and malaria surveillance. They facilitate spatial analysis, capturing population denominators for more precise monitoring of infection transmission dynamics. Existing boundary mapping tools may not capture variations in land use or building characteristics (commercial vs residential). We examine three distinct techniques for mapping village-level spatial boundaries: i) village walk-around - traversing the entire village perimeter with a GPS receiver; ii) structure mapping- identifying and recording GPS coordinates for all physical structures in a village; and iii) centroid mapping - using a local expert to map perceived “centers” of the village and utilizing geospatial techniques to calculate centroids and Voronoi polygons to generate village boundaries. We evaluated practicality (ease of use, flexibility, precision, and scalability) and cost-effectiveness (operational cost analysis, time efficiency in data collection and processing) in various operational contexts, providing a detailed comparison for diverse field settings. Each technique presents unique advantages, challenges, and uncertainties, with practicality varying based on mapping objectives and study area characteristics. Structure mapping generates a fine-grained resolution dataset but is labor-intensive and at $112 per village is 5.3 times costlier than walk-around and centroid techniques. Boundary walk-around can be done relatively quickly (2 villages per day), but precision relies heavily on local area knowledge. Centroid mapping is an easy to deploy technique but may be limited by geographical orientation and estimation skills of local experts. Terrain complexity, population density, budget, and data processing timelines are key considerations in technique selection. Our findings offer valuable insights into technical aspects of village-level boundary mapping and provide a framework for selecting the most appropriate mapping method, optimizing spatial data collection and use.

7314

ASSESSING THE TRENDS AND CONCORDANCE OF MALARIA PREVALENCE BETWEEN PREGNANT WOMEN ATTENDING ANTENATAL CLINICS AND ASYMPTOMATIC INDIVIDUALS IN THREE REGIONS OF MAINLAND TANZANIA

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Tracking the burden and transmission of malaria using reliable data is crucial for designing and implementing effective control strategies and accurately monitoring the impacts of interventions and progress towards the elimination targets. Surveillance of malaria in Tanzania is based on different types of data including those obtained from screening of pregnant women at their first antenatal care clinic (ANC) visits since 2014. ANC malaria prevalence is highly correlated to prevalence in under-fives but the correlation with other age groups has not been established. This study assessed the trends and concordance of malaria prevalence between asymptomatic individuals of all age groups from community cross-sectional surveys (CSS) and pregnant women attending ANC clinics in three regions of Kigoma, Ruvuma and Tanga in Mainland Tanzania from 2021 to 2023. In both CSS and ANC clinics (from 2021 to 2023), testing for malaria was done using malaria rapid diagnostic tests (RDTs) and covered 8,096 asymptomatic individuals in CSS and 819,103 women. Malaria prevalence in CSS was 32.7% (95% confidence interval (CI), 31.7-33.7) in 2021, 36.8% (95% CI, 35.8-37.9) in 2022 and 30.5% (95% CI, 29.5-31.5-32.7) in 2023. The prevalence in pregnant women was 8.63% in 2021, 7.30% in 2022, and 7.93% in 2023 with higher prevalence among women aged <20 years (12.26%) compared to older women (7.14%). In both CSS and ANC, there was a significant positive correlation between malaria prevalence in CSS and ANC (r=0.719, P=0.03). The strongest positive correlation was among children <5 years and pregnant women aged <20 years (r=0.84,p=0.005); and school children aged 5-15 years and pregnant women aged >20 years (r=0.85, p=0.018). Malaria prevalence in pregnant women provided a close match to both under-fives and school aged children. The findings support previous studies and suggest that ANC data can be used as a sentinel surveillance group to monitor the trends of malaria prevalence in these groups rather than surveys that focus on presence or absence of asymptomatic infections in time points.

7315

TRANSFERRING CAMPAIGN DIGITIZATION EXPERTISE TO NATIONAL ENTITIES AND STRENGTHENING MALARIA CONTROL ACTIVITIES IN BENIN

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In 2022 malaria incidence was 21,7% among general population and 43,1% among under five children, in Benin. As the country is dedicated to achieving malaria elimination by 2030, it’s important to leverage on digital transformation to reach the target. Since 2019, the Ministry of Health has initiated campaign digitization initiatives with the technical support of Clinton Health Access Initiative. To ensure that the investments made in digitizing campaigns in Benin are sustainable, the Clinton Health Access Initiative, World Health Organization worked with the Ministry and other partners to expand and integrate the key components of campaign activities into disease control programs, while building capacities to lead digitization in the long term. The process of transferring the expertise on digitizing campaigns in Benin starts with strengthening and consolidating governance initiatives of the digitization campaign, led by the Information Systems Direction, followed by ensuring that the tool selection and deployment process leads to the adoption of suitable platforms and software addressing country specific needs, then, progressively improving digitization and integration of public health campaigns, and finally determine the sustainable ways to capacitate the government for the improvement of campaign operations. In result, leadership and coordination mechanisms were established, with steering committee that meets routinely to agree on the implementation plan for Integrated Campaigns Digitization across all Ministry of Health programs, departments and partners. The Information Systems Direction supported the malaria program to run nets distribution campaign and

Seasonal Malaria Chemoprevention campaign, engaged with technical and implementing partners to build a comprehensive platform to visualize, use and share the campaign data across programs, engaged steering committee and technical committee on design and requirements for review of existing tools and elaboration of new tools. Strengthening and transferring expertise to national entities ensure campaigns autonomous implementation by national stakeholders.

7316

UNDERSTANDING DHIS2 DATA LIMITATIONS FOR MALARIA BURDEN ESTIMATION: A COMPARISON WITH GOLD STANDARD MEASUREMENTS FROM A COHORT STUDY IN ZAMBIA

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To achieve public health goals and effectively respond to epidemics, robust health management information systems are indispensable. Platforms such as DHIS2, an open-source system, offer broad geographic coverage and timely disease incidence data, which can be helpful for malaria programming and intervention targeting. However, DHIS2 data inherently have limitations and may not provide a true estimate of community malaria incidence. Factors that contribute to these limitations include treatment-seeking behaviors, case management practices, and data quality concerns. This study aims to assess the differences in malaria incidence rates between passively-detected DHIS2 data and a gold standard measurement method, involving a prospective cohort with active case detection from a trial conducted in Western Province, Zambia for evaluating attractive targeted sugar baits (ATSB) from 2021 to 2023. Specifically focusing on children aged 12-59 months from the ATSB cohort that were cleared of parasites at the start of the malaria season and followed up monthly for 6 months to capture malaria incidence cases. These cases will be compared to the malaria incidence trends from matching health facility catchment areas using line plots. Concordance between the two estimates will be assessed via z-score scatter plots and Bland-Altman diagrams. Associations between health facility characteristics, patient preferences, and differences in estimates will be assessed through linear regression. Finally, Poisson regressions will be used to model the relationship between the outcome of monthly malaria incidence with both estimates, incorporating health facility characteristics and patient preferences. Examining the disparities between DHIS2 data and a gold standard measurement, and assessing the effects of contributing factors, may provide valuable insights into the limitations of DHIS2 estimates, aiding in their interpretation and informing their use in malaria programming efforts.

7317

CREATING COMMUNITY RESOURCES TO MAKE MALARIA GENOMIC DATA ANALYSIS MORE ACCESSIBLE BY EVALUATING, IMPROVING, AND HARMONIZING SOFTWARE TOOLS

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Major advances in *Plasmodium* sequencing approaches, pipelines, and data analysis tools have provided valuable insights from parasite genomic data on malaria epidemiology. However, translating genetic data into actionable information for NMCPs is still challenging. Important barriers still limit integration of these advances into a seamless data analysis ecosystem that produces standardized, interpretable results for use by NMCPs. The PlasmoGenEpi network convened 18 subject matter experts to landscape available tools, evaluate software standards, improve documentation, and evaluate next steps in the context of key use cases at the: **R**eproducibility, **A**ccessibility, **D**ocumentation, and **I**nteroperability **S**tandards **H**ackathon (RADISH23). We defined eight use cases for Plasmodium genetic data informing malaria surveillance, based on data analysis and functionality requirements. For each use case, we mapped out workflows with respect to information flow through each analysis functionality. In combination with the landscaping of tools and their functionalities, each step of the workflow can be mapped flexibly to available tools and can be used to identify gaps where new software is needed. These resources are available on **PGEforge** (mrc-ide.github.io/PGEforge), a community resource built during RADISH23. We identified 40 Plasmodium genomic analysis tools, of which 17 were prioritized for resource development. PGEforge contains the tool landscaping, software standard guidelines, and fully reproducible tutorials showing example usage of each tool using canonical target and whole genome sequencing datasets (empirical and simulated). Installation of R-based tools is simplified by our implementation of a centralized "R-universe" package repository. PGEforge now serves as a central, open repository for current and future resources for malaria genetic data and analysis workflows, greatly improving accessibility. Ongoing and future work will focus on rigorous benchmarking of tools and modular workflows to tackle the more ambitious goal of developing best practices in malaria genomic surveillance.

7318

USING ROUTINE SURVEILLANCE DATA TO ASSESS ADHERENCE TO MALARIA TREATMENT GUIDELINES IN THE COUNTY REFERRAL HOSPITALS IN KENYA

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The WHO recommends early diagnosis and prompt, effective treatment of malaria by observing appropriate weight-based dosing and rational use of antimalarial agents to reduce the spread of drug resistance. Kenyan malaria treatment guidelines recommend the appropriate dosage of Artemether Lumefantrine (AL) as the initial line of treatment for test-positive uncomplicated malaria. Cases are entered into registers; monthly summaries are uploaded to the Kenya Health Information System (KHIS). We assessed the adherence to the guidelines in Kenya's 47 County Referral Hospitals (CRHs) during the biannual commodity review meetings in November 2023. Suspected malaria cases are tested and recorded in a laboratory register (MOH 706); this information is replicated in the commodity summary report (MOH 743), which contains a summary of malaria tests, AL dispensed, and patients by weight category. A standard template was shared with the 47 counties to collect aggregated data from KHIS for Sept 2023, the most recent reporting month. Analysis of the total no. of patients who tested positive in both reporting tools, the total no. of patients treated with AL compared to the total no. of patients who tested positive in MOH 706 and MOH 743 for all CRHs. The conversion of doses dispensed to the number of tablets that should have been dispensed for the reported total no. of patients by weight category to cater for substitutions of AL packs. A total of 7,176 patients were treated with AL, yet only 3,080 (43%) tested positive for malaria, translating to overtreatment of

4,096 (57%) patients. A comparison of MOH 743 with MOH 706 (source document for laboratory test data), revealed over-reporting by 24% on the number of patients who tested positive. Only 580 (8%) of the total patients treated with AL were tested and treated correctly, with 11 CRHs (23%) giving correct dosing to positive patients. Data quality audits should be carried out to address data discrepancies, and data review meetings to be sustained for peer learning. Capacity building of health workers is also critical for rational drug use and inventory management.

7319

ADAPTING MALARIA INDICATOR SURVEYS TO INVESTIGATE TREATMENT ADHERENCE: A PILOT STUDY ON BIOKO ISLAND, EQUATORIAL GUINEA

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Adherence to antimalarial treatment regimens is an important aspect of understanding and improving the impact of malaria case management. However, both adherence to artemisinin combination therapies (ACT) and the factors driving it vary widely. While many other evaluation activities have been conducted on Bioko Island, until now adherence to antimalarial treatments, and in particular ACTs has not been evaluated. The implementation of a malaria indicator survey (MIS) conducted on Bioko in 2023 was leveraged to evaluate adherence to ACTs provided to individuals testing positive following the survey. A follow-up team visited the targeted households, physically observed treatment blisters where possible, and provided messaging to household members on the importance of adhering to the treatment guidelines to household members. The team used survey data from the targeted households to make messaging as relevant to the household's particular context as possible. Overall ACT adherence on Bioko Island was low, around 50%, and this varied demographically and geographically. Some of the highest transmission areas had exceptionally low adherence, but no systematic relationship between proper adherence and *P. falciparum* prevalence was detected. Estimates of adherence from follow-up visits were much lower than survey-based estimates in the same households (52.5% versus 87.1%), suggesting that lack of proper adherence may be a much larger issue on Bioko Island than previously thought. Anecdotally, the data-driven communication approach taken in this study was more effective in achieving desired behaviors than previous approaches focused on delivering a core set of messages to as many people as possible. The large discrepancy between adherence as measured in this study and survey-based estimates on Bioko Island suggests a health facility-based study to quantify adherence among the population receiving treatment for symptomatic malaria may be necessary.

7320

MALARIA OUTBREAK INVESTIGATION IN THE ARID NORTHERN WAJIR COUNTY, KENYA, DEC 2023-FEB 2024

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From Jan–Feb 2024, Wajir County reported 373 malaria cases, compared to an expected <10 cases, in what is considered a low transmission zone. Rainfall in Oct–Nov 2023 (2992mm) was significantly more than the same period in 2022 (110mm). We investigated the outbreak to ascertain the case characteristics and implement intervention measures. We reviewed data from Dec 2023–Feb 2024 in registers from health facilities that reported confirmed malaria cases higher than the sum of the median and 3rd quartile of cases reported in the past 5 years. We conducted a data quality audit (DQA) by comparing data in the registers against data in the Kenya Health Information System (KHIS). Key informant interviews were conducted with questionnaires to assess epidemic preparedness in coordination structures, surveillance, emergency commodities, and field response. Environmental risk factors were assessed in villages with the most cases and we evaluated community knowledge, attitudes, and practices on malaria. Frequencies and proportions were calculated for quantitative variables and qualitative data were analyzed thematically. Of the 710 positive cases investigated, 471 (66.3%) were male and 587 (82.7%) were ≥ 5 years of age. Most cases 499 (70.3%) were from Jan 2024, 2 months after the peak rainfall. There were 20 (2.8%) *P. vivax* cases, 57 (8.0%) severe malaria cases, and 4 deaths (CFR 0.6%). The county lacked epidemic preparedness and response coordination structures, and adequate stocks of key diagnostic and treatment commodities. Mosquito breeding sites were identified, and the community was aware of malaria treatment, prevention, and risk factors. DQA found only one-third of the suspected malaria cases were reported in KHIS. After the increased rainfall from Oct–Nov 2023, Wajir saw a >30-fold increase in malaria. Challenges included commodity stockouts, presence of *P. vivax* (new for the area), and lack of a coordinated county response. Strengthening diagnostic and treatment capacity, and improving data quality for surveillance to guide intervention strategies are key to minimizing morbidity and mortality in future malaria outbreaks.

7321

QUALITY OF MALARIA SERVICE DELIVERY BY HEALTH CARE WORKERS FOR PATIENTS PRESENTING WITH FEBRILE ILLNESS IN HEALTH FACILITIES IN SOUTHEASTERN TANZANIA, 2023

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High quality clinical management improves patient outcomes. Clinical management of febrile patients depends on the skills of health care workers (HCWs). To assess and improve malaria service delivery quality by HCWs in Tanzania, we supported the National Malaria Control Program to assess services via the Malaria Services and Data Quality Improvement (MSDQI) platform and conduct supportive supervision (SS). Using standard MSDQI checklists that generate composite competency scores in the areas of clinical history taking, physical examination, malaria testing, malaria diagnosis, malaria treatment, and provider counseling, we analyzed clinical observation data from 1,822 febrile patient visits collected from 590 health facilities in the high-burden southeastern PMI coverage regions of Lindi, Mtwara, Ruvuma, and Pwani from January to June 2023. If reporting data were complete for a given competency area, then the competency score for that area was analyzed descriptively, with the national competency standard defined as a score of >=75% ("good"). During 1,822 reported febrile patient visits, HCWs met area-specific national competency standards for 370/923 (40%) clinical histories, 717/1622 (44%) physical examinations, 1534/1615 (95%) malaria testing, 1596/1607 (99%) malaria diagnosis, 1522/1570 (97%) malaria treatment, and 1080/1790 (60%) counseling. HCWs met overall competency standards for all six categories in 948/1822 (52%) of visits. Despite high proportions of HCWs meeting competency standards for malaria testing, diagnosis, and treatment, we found that provider history taking, physical examination, and counseling contributed to degradation

of the overall quality of service delivery. Facility-based service delivery in southeastern Tanzania could be improved by identifying and intervening on factors contributing to weakness in these areas.

7322

OPERATIONAL FACTORS INFLUENCING TIMELY MALARIA CASE REPORTING BY PRIVATE HEALTH FACILITIES IN URBAN DISTRICT, UNGUJA ZONE, ZANZIBAR

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In Zanzibar, an area targeted for elimination, delayed reporting of malaria cases remains a challenge. Healthcare providers in public and private facilities are required to report malaria cases through the Malaria Case Notification system within 24 hours of diagnosis using a mobile reporting application. In 2021, reporting timeliness was 72.7%, and District Malaria Surveillance Officers observed private health facilities had lower malaria reporting timeliness. A cross-sectional explorative study using a phenomenological qualitative approach was conducted to examine operational factors impacting timeliness of case reporting among private health facilities in Urban Districts of Unguja. Sixteen study participants were selected using purposive sampling due to their reporting responsibilities. In-depth Key Informant Interviews were conducted using semi-structured guides, and thematic data analysis was performed using NVIVO software version 12. Of healthcare workers who participated in the study, 94% (15/16) demonstrated awareness of the reporting process and all (100%) received training on timely reporting. All participants also (100%) reported communicating with other staff at their facilities about reporting responsibilities, despite some challenges including effective communication, workloads, and lack of collaboration within facilities. Furthermore, 56% of healthcare workers reported receiving incentives including meeting allowance and best-performing rewards for timely reporting, which they found motivating. All respondents acknowledged operational resources like smartphone and internet bundles also played a role in reporting timeliness. The findings suggest that incentives, effective communication, and availability of resources can influence reporting timeliness for malaria cases from private healthcare facilities. Strategies to address communication challenges and ensure adequate provision of operational resources might be further assessed to enhance timely reporting of malaria cases, ultimately contributing to improved malaria surveillance and control efforts in Zanzibar

7323

RETROSPECTIVE ANALYSIS OF MALARIA INCIDENCE IN GUINEA 2018 TO 2022

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The objective of this study was to analyze the trend in malaria incidence in Guinea at the level of health districts and identify factors associated with high or low incidence. We used malaria surveillance data from 2018 to 2022, along with demographic data and results from national surveys (DHS 2018 and MIS 2021). The analytical methods included estimation of adjusted malaria incidences, time series decomposition, and the Mann-Kendall test ($p < 5\%$). We also employed Sen's slope to determine the direction and quantify the intensity of the trend, as well as multivariable analysis to identify factors associated with increased incidence. The results showed that nationally, between 2018 and 2022, the annual crude incidence increased by 36.7%, and adjusted incidence (completeness + testing) increased by 34.4%, with a variation rate ranging from 0 to 27% depending on the health district (HD) and year. In total, 27 out of 33 districts exhibited a significant upward trend (coef: 20 to 60%), 1 district (Siguiri) showed a significant downward trend (coef: -20 to -40%), and in 5 districts, the incidence trend was not significant. Multivariable analysis identified factors related to intervention and the healthcare system associated with high or low incidence in the districts. In summary, this study highlights a significant increase in malaria incidence in Guinea between 2018 and 2022, with notable variations among districts. The results suggest particular concern for the 27 districts showing an upward trend, and the identified factors associated with this increase provide factual insights to guide malaria control efforts in Guinea.

7324

COST-UNIT ANALYSIS OF VECTORCAM: A NOVEL COMMUNITY-BASED AI TOOL FOR VECTOR SURVEILLANCE TO IDENTIFY MOSQUITOES' SPECIES IN RURAL UGANDA

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Introduction: Advancements in digital tools have revolutionized mosquito surveillance for malaria control. VectorCam, is a novel tool that utilizes computer vision algorithms enabling low-cost, user-friendly mosquito identification at the village level. This study conducted collaboratively by the Johns Hopkins University, Makerere University, and the Ugandan Ministry of Health, aims to evaluate the cost per unit using VectorCam compared to traditional surveillance methods. **Methods:** In the randomized control trial in Uganda the village health team members (VHTs) in each arm collected mosquitoes using standard methods CDC light traps and pyrethrum spray catch from community households. Vector Control Officers in the control group, use microscopes and paper-based systems to morphological identify mosquitoes whereas in the study group, the VHTs employ the VectorCam app. Data in the control arm is manually transferred to the Ministry of Health's DHIS2 platform, whereas the study group's data is directly transferred via the app. **Preliminary Results:** Preliminary findings demonstrate VectorCam's ability to analyze a substantial volume of mosquitoes. Since September 2023, over 52,000 mosquitoes were imaged and analyzed, with 20.5k identified as *Anopheles* mosquitoes, of which 88% were female *Anopheles*. VectorCam's cost per mosquito analyzed was $0.50 per female *Anophelines* compared to the control arm of $0.64 per female *Anophelines*. **Conclusion:** Although both arms demonstrate an economy of scale the study arm maintains a consistently lower cost per unit. These findings highlight that in a country where scalability of their surveillance system is a priority, VectorCam could offer a financially advantageous alternative in high-volume settings than paper-based surveillance systems. VectorCam emerges as a robust tool for vector surveillance enhancing data collection and analysis, providing valuable insights for targeted interventions at the community level. This study highlights the importance of innovative digital solutions in advancing global health initiatives, particularly in resource-limited settings.

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ASSESSING THE FEASIBILITY OF IDENTIFYING AND VALIDATING SEROLOGICAL MARKERS OF RECENT LOW DENSITY *PLASMODIUM FALCIPARUM* INFECTIONS IN A PRE-ELIMINATION SETTING

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Serological markers of recent malaria infection are promising tools to measure malaria epidemiology. Previous work has identified serological markers of recent infection in moderate transmission settings; however, the generalizability of these findings to pre-elimination settings, where low parasite density infections elicit low antibody responses, remains unclear. Using a multiplex bead assay (MBA), we measured IgG responses to 19 *Plasmodium falciparum* antigens within a longitudinal cohort in Southern Province, Zambia. Monthly samples collected between October 2018 and September 2020 were tested for *P. falciparum* using ultrasensitive qPCR and quarterly samples with the MBA. The MBA was run on 1940 samples from 277 individuals, 59 of whom had at least one qPCR positive event with parasite density below 100 parasites per microliter. We found no differences in antibody responses to any antigens comparing participants with a qPCR positive event to those without, nor between pre- and post-qPCR positive events, demonstrating the limited feasibility of identifying markers of recent low-density infections. Using multilevel linear regression models, between person variability explained 63% to 86% of overall variability in antibody responses. Furthermore, while antibody responses of participants with no qPCR positive events overlapped with responses of serum from U.S. samples, the variability among serially negative participants was at least twice that of U.S. serum across all antigens suggesting that U.S. control serum fails to adequately capture the full range of antibody responses of negative serum from malaria endemic regions. Antibody responses of 56 participants showed variability in responses greater than 10 times the median within-host variability, this was not associated with age, sex, or infection. A timeseries analysis of antibody responses showed autocorrelation between -0.2 and 0.2 for all timepoints, suggesting random variation. These findings highlight the potential importance of incorporating longitudinal controls from malaria endemic areas, particularly in settings where biomarkers produce low signal.

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IMPACT OF ROUTINE DATA QUALITY AUDITS (RDQA) IN IMPROVING DATA QUALITY AND MALARIA MANAGEMENT STANDARDS IN HEALTH FACILITIES IN THE DEMOCRATIC REPUBLIC OF CONGO (DRC)

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The fight against malaria requires the production of quality data to monitor disease trends and enable evidence-based decision-making. An assessment of the DRC malaria surveillance system conducted in 2021-22 revealed significant inaccurate reporting of malaria data, with only about 20% accuracy. The NMCP, with support from PATH, has developed and piloted a decentralized approach to implementing Routine Data Quality Audits (RDQAs) in 36 health facilities in 4 health zones in Haut-Katanga Province. The approach favors ownership and accountability by the peripheral level of the health system around data quality. Health teams were trained on the RDQA approach, malaria data quality assurance procedures, and management of malaria interventions and indicators. During the pilot phase (June 2023-March 2024), purposive sampling was used for the selection of RDQA sites (n=36) for logistical reasons. The following indicators were included in the RDQA: outpatient consultation, suspected malaria, RDT performed, positive RDT, confirmed uncomplicated malaria, uncomplicated malaria treated according to national policy, confirmed severe malaria, and severe malaria treatment. Two RDQA rounds were carried out in each health facility in June 2023 and November 2023. During each visit, malaria data checks were carried out to compare data between registers, monthly HMIS reports, and data reported in DHIS2. During field visits, health workers were interviewed about malaria case management and a qualitative assessment of the data management system was conducted. Several data quality attributes were analyzed, including the average accuracy of all data elements for each round. The overall improvement in mean data accuracy from round 1 (30%) to round 2 (56%) was statistically significant ($p<0.0001$) by paired T-test. Given the promising results seen during the pilot phase, the NMCP is planning a national harmonization of RDQA approaches and developing RDQA malaria implementation manuals and training materials. Current efforts are focused on harmonizing and digitizing the RDQA tool in the country to facilitate further expansion beyond the pilot area.

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DESCRIPTION OF FACTORS ASSOCIATED WITH MALARIA PREVALENCE IN TWO TRANSMISSION SETTINGS IN SIAYA COUNTY, WESTERN KENYA (2022-2024)

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Malaria remains a public health challenge in western Kenya, with persistent transmission despite ongoing prevention and control efforts. Understanding the prevalence and associated factors among malaria cases is crucial for effective control. A continuous malaria indicator survey was conducted from April 2022 to March 2024 in Rarieda and Alego Usonga sub-counties, Siaya County, western Kenya. A total of 1,960 compounds were randomly selected from sub-county censuses to be surveyed. Demographic information, temperature, history of fever, and insecticide-treated net (ITN) use, were collected from consenting persons of all ages, and a malaria rapid diagnostic test (RDT) was administered. Correlates of malaria infection, including age, current fever, fever in the past 2 weeks, and ITN use were assessed using Poisson generalized linear regression models stratified by sub-county. In total, 7,490 (3,738 in Alego Usonga and 3,752 in Rarieda) individuals were included (1,008 (13.5%): <5yrs, 2,223 (29.7%): 5-14yrs and 4,259 (56.9%): 15+ yrs old). Malaria prevalence was 39.2% [95% CI: 38.1-40.3] with a higher prevalence in Alego Usonga (54.4% [95% CI: 52.7-56.0]) vs. Rarieda (24.1% [95% CI: 22.7-25.5]). Most cases were afebrile at the time of testing (99.6% [95% CI: 97.3% - 100%); 3.4% [95% CI: 3.0-3.8] reported fever in the past 2 weeks. Most (81.6%, 95% CI: 80.7-82.5) reported ITN use the night prior. Compared to those <5yrs, those 5-14yrs had higher risk (aPR: 1.31 [95% CI: 1.15 - 1.50] in Alego Usonga and 1.67 [95% CI: 1.37 - 2.06] in Rarieda) while those >15 had lower risk (aPR= 0.68 [95% CI: 0.60 - 0.78] in Alego Usonga and 0.71 [95% CI: 0.58 - 0.88] in Rarieda). Self-reported fever in the past 2 weeks was associated with an increased malaria risk (aPR: 1.51 [95% CI: 1.20 - 1.87] in Alego Usonga and 2.64 [95% CI: 2.09 - 3.28] in Rarieda). The findings highlight that children ages 5-14yrs remain a key risk group for malaria, emphasizing the need for additional tools and strategies to control transmission particularly targeting this key risk group. Given the high ITN use, factors including ITN quality, use duration, and time of entry and exit will be explored.

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IMPORTANCE OF A STRONG LOGISTIC MANAGEMENT INFORMATION SYSTEM TO REDUCE MALARIA COMMODITY LOSSES IN MADAGASCAR

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Between 2009 and 2020, Madagascar used a locally-designed, centrally-managed software called CHANNEL to facilitate the management of health sector commodities. Its specific purpose was to track stock levels and the movement of commodities between district pharmacies and health facilities with the aim of optimizing stock levels of essential commodities at both levels. In 2021, the Ministry of Health abandoned CHANNEL because it was inaccessible online and computer viruses destroyed the database behind the software. Since 2022, while awaiting the acquisition of new software for its logistics management system, which has been delayed, Madagascar has been using an ad hoc offline tracking platform centrally and peripheral health facilities continued reporting limited monthly stock data to DHIS2. Since 2009, the US President's Malaria Initiative has supported the Ministry of Health through an implementing partner to improve commodity management in all 115 districts. We assessed overall loss of malaria commodities through expiration, loss, or damage using data from DHIS2, comparing losses in 2022 and 2023 to those in 2021. Expiration, loss, or damage of 34,431 courses of Madagascar's first-line artemisinin-based combination therapy (ACT) and 49,715 malaria rapid diagnostic tests (mRDTs) was reported nationally in 2021. In 2022 and 2023, the number of ACTs that expired or were lost or damaged increased, respectively, to 142,925 courses (+315%) and 189,607 (+450%) courses. The number of expired, lost, or damaged mRDTs also increased in 2022 (198,471 mRDTs [+299%]) and 2023 (226,068 mRDTs [+354%]). The total procurement cost of these losses is equivalent to $24,730 in 2021, $90,532 in 2022, and $130,225 in 2023. In the absence of a supply chain management platform that integrates supply and demand data at all levels, Madagascar has experienced increased commodity loss. A supply chain system that tracks commodity movement, is accessible at all levels, and integrates supply- and demand-side data, and resources to redeploy excess stock, are crucial to improve the use of commodities in the context of limited resources and heterogenous transmission.

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MOLECULAR SURVEILLANCE OF MALARIA IN ENDEMIC REGIONS IN UGANDA REVEALS HIGH GENETIC DIVERSITY OF *PLASMODIUM FALCIPARUM* AND CORRELATION WITH TRANSMISSION INTENSITY

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Despite significant progress in genetic research enhancing our understanding of malaria, integrating these findings into practical strategies, especially concerning malaria transmission, remains underexplored. Although malaria epidemiology and parasite population genetics have developed distinct viewpoints, this study merges these perspectives. We explore the genetic diversity of P. falciparum and its link to transmission intensity using initial data from Uganda's first extensive molecular surveillance campaign in malaria-endemic areas. Our objective is to analyze the variability in transmission intensity across high endemic regions of Uganda, utilizing P. falciparum specific genomic data and epidemiological measures. We examined 2400 dried blood spot samples from symptomatic cases across 24 health facilities, averaging 100 samples per site. We calculated malaria incidence as cases per 1000 person-years over the three months before sample collection. The facilities represent varying transmission levels: high (over 500 cases per 1000 person-years in 9 centers), moderate (250-500 cases, 6 centers), and low (1-250 cases, 9 centers). We employed the MAD4HatTeR technique targeting 165 microhaplotypes and used MOIRE to assess infection complexity and within-host parasite relatedness. Early results showed a high average complexity of infection at 3.19, with significant within-host relatedness averaging 0.65. Interestingly, complexity decreased with patient age and increased with higher transmission levels, suggesting a link between transmission intensity and genetic diversity. These findings indicate potential superinfection and cotransmission rates, with ongoing analysis focused on identifying genetic indicators most predictive of local transmission intensities.

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THE INTEGRAL ROLE OF GIS IN THE SEASONAL MALARIA CHEMOPREVENTION CAMPAIGN TO IMPROVE MONITORING_A CASE STUDY OF TARABA STATE, NORTHEAST, NIGERIA

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Malaria in Nigeria is a persistent issue that requires strategic interventions. Mass Drug Administration (MDA) is crucial, especially in Taraba State, with a population of over 3.2 million. Seasonal Malaria Chemoprevention campaigns are key to malaria control. The Management Sciences for Health Global Fund Malaria has integrated geographical information systems (GIS) into MDA campaigns for better planning, implementation, and assessment. The study investigates the use of the Geographic Information System (GIS) in Taraba State's 2023 Seasonal Malaria Chemoprevention Campaign, to address inadequate supervision by monitors during mass drug distribution, focusing on intervention efficacy tracking, coverage examination, and monitoring at various levels. The SMC campaign used GIS technology to map and analyze key activities, including medicine delivery locations, demographic analysis, and malaria-prone regions. Geocoordinates were collected using platforms like Redrose and Kobocollect and placed on GIS platforms with basemaps from Google Maps and Google Satellite. SMC supervisors used handheld devices to take geo-coordinates at CDD drug administration sites. The GIS-based SMC campaign monitoring identified high-risk zones, streamlined logistics, evaluated campaign coverage, determined mass mop-up locations, and improved communication tactics. Monitoring of SMC supervisors' coverage. Real-time monitoring enabled aggressive responses to new challenges from 2021 to 2023, the supervisory coverage across supported wards increased from 60 to 90, resulting in a 65% to 89% increase. The 2023 Seasonal Malaria Chemoprevention campaign in Taraba State utilized GIS for targeted actions, logistics, and understanding of campaign dynamics. This demonstrates the potential of GIS in improving supervisors' coverage and visibility at sites, mass drug administration exercises, and providing crucial information for Nigeria's future malaria elimination plans. Consistent integration of GIS into MDA microplanning is recommended for long-term success.

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EXTENDED INTERVAL REGIMEN OF PREQUALIFIED MALARIA VACCINE R21 ADJUVANTED WITH 3M052 ELICITS HIGH AVIDITY ANTI-CIRCUMSPOROZOITE PROTEIN ANTIBODIES IN NON-HUMAN PRIMATES

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R21 is a WHO prequalified malaria vaccine targeting the pre-erythrocytic stage of *Plasmodium falciparum* (*Pf*) life cycle, exhibiting 74-77% efficacy in clinical trials in malaria endemic regions. By quantifying the binding kinetics of sera from multi-dose R21 immunized rhesus macaques to antigens (Ags) that include a recombinant *Pf* circumsporozoite protein (CSP), NANP6 (represent *CSP* central repeat region) and PF16 (represent *CSP* C-terminal region) measured using biolayer interferometry, we investigated whether varying adjuvants (3M052, GLA-LSQ or Matrix-M), immunization routes (subcutaneous (SC) or intramuscular (IM)) and/or vaccine schedules (standard regimen (weeks 0, 4, 8, and 62; SR) or extended interval regimen (weeks 0, 8, 23, and 72; ER)) influence R21-induced CSP targeting antibody (Ab) response and avidity. Among all combinations, IM groups with 3M052 or Matrix-M showed the highest Ab responses for CSP and NANP6 at post 3rd vaccination (PD3). Compared to Matrix-M IM-SR, the 3M052 IM-SR group showed comparable CSP and NANP6 responses but lower trending PF16 response, with the trend continuing at post 4th vaccination (PD4). Compared to 3M052 IM-SR, the 3M052 IM-ER group elicited >3 fold higher PF16 response but lower NANP6 response at PD3 and PD4 as well as showed 2.8-12.3 fold more retention of high Ab responses between PD3 and PD4 for CSP and PF16. Our avidity quantification further dissected the dissociation time course of Ag-sera interaction into components of different dissociation rates using Polyclonal Antibody Avidity Resolution Tool (PAART). Compared to 3M052-IM-SR, the 3M052-IM-ER group showed improved Ag occupancy by high avidity Abs at PD4 with 3 fold higher avidity over PD3 for NANP-targeting antibodies (binding to NANP6), despite low response at PD4. Additionally, for high responders in all 3M052 groups, high avidity Abs maintained >90% Ag occupancy between PD3 and PD4 despite decreasing Ab response. These results suggest that adjuvanting with 3M052 with an extended interval dosing schedule could increase the abundance and quality of R21-induced anti-CSP Abs and potentially improve Ab-mediated protection.

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IMPACT OF RTS,S MALARIA VACCINE ON *PLASMODIUM FALCIPARUM* INFECTION IN SCHOOL-AGED CHILDREN: INTERIM RESULTS FROM INDIVIDUALLY RANDOMIZED CLINICAL TRIAL IN MALAWI

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The burden of *Plasmodium falciparum (Pf)* malaria, including malaria-related anemia, is shifting towards school-aged children (SAC), who often have limited access to malaria interventions such as long-lasting insecticidal nets and prompt diagnosis and treatment. The RTS,S/AS01 malaria vaccine, the first vaccine recommended for under-five children in 2021, could potentially reduce the burden of clinical malaria in SAC. However, the effect of RTS,S/AS01 on SAC has never been assessed. As part of the first, individually randomized clinical trial assessing efficacy of RTS,S/AS01 in SAC, we evaluated the impact of the vaccine on *Pf* infection in children aged 6-15 years attending 5 primary schools in rural southern Malawi. This report is based on 3,884 children with median age 10 years (interquartile range [IQR] = 8-12 years), who were randomized to one of 4 intervention arms: 1) RTS,S/AS01 alone (963 children), 2) RTS,S/AS01 + parasite clearance with artemether-lumefantrine (AL) at enrollment (970 children), 3) parasite clearance with AL at enrollment alone (978 children), and 4) control receiving only Vitamin A (Vit A) (973 children). Participants were followed for detection of clinical malaria through a surveillance system at school clinics to which they reported whenever they felt symptoms. Malaria diagnosis was confirmed through microscopy (primary) and malaria rapid diagnostic test (mRDT). At this point, all participants in the 4 arms have received the 1st dose of the assigned intervention; 88% of participants in the two RTS,S/AS01 arms have received 2 doses and 82% all three doses of the vaccine. In 10 months of follow-up to date, median time to first mRDT positive malaria episode was 4 months (IQR: 2-6 months), with disease-free survival rates of 46% (95% CI: 42%-50%) overall, and 46% (95% CI: 37%-55%) RTS,S/AS01, 52% (95% CI: 42%-61%) RTS,S/AS01+AL; 48% (95% CI: 41%-55%) AL and 42% (95% CI: 36%-49%) Vit A. Thus far, neither of the RTS,S/AS01 arms show reduced time to *Pf* infection by mRDT. Results of an additional 7 months of exposure, and test results using both mRDT and microscopy, will be available from October 2024.

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ACCELERATED STABILITY STUDY OF CGMP DRUG PRODUCT INTERMEDIATE PVS230D1-EPA CONJUGATE

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Pvs230 is a promising *Plasmodium vivax* malaria transmission-blocking vaccine (TBV) candidate antigen. Pvs230 is expressed by gametocytes in the human host and displayed on the surface of gametes in the mosquito host. Antibodies generated against Pvs230 disrupt parasite development in the mosquito. To increase the immunogenicity of a *Pichia pastoris*-expressed domain 1 of Pvs230, recombinant Pvs230D1M was conjugated to the recombinant, non-toxic *Pseudomonas aeruginosa* ExoProtein A (rEPA), a carrier protein, in conformance with current good manufacturing practices (cGMP). To assess the stability of this conjugated vaccine candidate during storage, transportation and administration, an accelerated stability study was performed. The non-formulated cGMP Drug Product Intermediate, a 200 µg/mL Pvs230D1-EPA conjugate, was stored at -80ºC, -20ºC, 4ºC, 25ºC and 40ºC, and sampling was conducted at Days 0, 1, 3 and 7 for testing. The stability of the vaccine candidate was evaluated by appearance; pH; protein content by UV (A_{280}); SDS-PAGE with silver staining; Western blot with a transmission-blocking anti-Pvs230D1 monoclonal antibody 1H3, and an anti-exotoxin A polyclonal antibody; RP-UPLC; and size exclusion chromatography with multi-angle light scattering (SEC-MALS). Our results showed that the Pvs230D1-EPA conjugate is stable for at least 7 days after storage at 4°C and 25ºC. Storage at 40ºC showed a significant time-dependent decrease (Δ~15%, $p<0.05$) in molar mass of the conjugate when evaluated by SEC-MALS, although it is unknown whether this change impacts potency. Some changes by Western blot were observed including lower molecular weight bands when probed by both mAb 1H3 and the anti-exotoxin A polyclonal antibody after storage for 3 days at 40ºC. Storage at -20ºC showed a trend toward an increase in molar mass, suggesting minor aggregation after 1 day. These results indicate the Pvs230D1-EPA DPI maintains good stability characteristics when stored at various temperatures. More stability studies are warranted to better understand the implications of the observed changes and impact on vaccine efficacy in future formulations.

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DEVELOPMENT OF VACCINE CANDIDATES AGAINST PLACENTAL MALARIA USING PEPTIDE-DECORATED ANTIGENIC LIPOSOMES

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The WHO reported over 13 million pregnancies exposed to malaria infection in 2021, endangering both the mother and fetus. *Plasmodium falciparum* causes placental malaria by infecting red blood cells that accumulate in the intervillous space and bind to the syncytiotrophoblast of the placenta. Infected cells express the parasite virulence factor VAR2CSA that binds to chondroitin sulfate A (CSA) chains on proteoglycans in the placenta. The sequestration of infected red blood cells (iRBC) is associated with low birth weight, pre-term birth and fetal growth restriction. A vaccine against VAR2CSA is highly desirable to prevent these birth outcomes. In pre-clinical studies, we identified two peptides that mapped to conserved epitopes on VAR2CSA, P6 (in DBL3X) and P10 (in DBL4ε), and induced antibodies that prevented binding of iRBCs to CSA *in vitro.* We hypothesize P6 and P10 can be combined into a liposome-based multivalent peptide vaccine to induce synergistic inhibitory antibodies against VAR2CSA. Strain promoted azide-alkyne cycloaddition chemistry was employed to conjugate the peptides to a lipid linker prior to preparation of the liposomes via thin film hydration. We prepared single and multi-epitope liposomes with encapsulated ovalbumin to enhance the immunogenicity of the liposomes. The lipophilic adjuvant monophosphoryl lipid A was incorporated into the formulation as it is a TLR4 agonist and implicated in T cell activation. The resulting peptide-decorated liposomes were 189.8 nm (± 46.8) in size with a polydispersity index ranging from 0.2-0.4. Conjugation of both peptides to the liposomes was confirmed by ELISA. C57BL/6 mice were immunized subcutaneously with the antigenic liposomes and the sera will be tested for recognition of iRBCs infected with parasite strains expressing different alleles of VAR2CSA in an inhibition-based assay. Overall, our goal is to develop immunogenic liposomes against placental malaria to contribute to the urgent need for effective malaria vaccines.

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SAFETY AND REACTOGENICITY OF THE MALARIA VACCINE CANDIDATE ANAPN1 IN HEALTHY ADULTS IN GABON: PRELIMINARY DATA OF A RANDOMIZED, CONTROLLED, PHASE1 DOSE-ESCALATION CLINICAL TRIAL

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Malaria remains a major global public health issue in endemic regions. In preclinical studies, the recombinant AnAPN1 vaccine candidate has shown promising activity. Here, we assessed the safety, tolerability, and reactogenicity of three doses of the AnAPN1 vaccine, formulated with and without the GLA-LSQ (glucopyranosyl lipid containing QS21/saponin) adjuvant, administered to healthy adults. A randomized, double-blind, controlled, dose-escalation phase1 clinical trial was conducted in Lambaréné, Gabon among 33 healthy male and female volunteers aged 18-45 years. Participants were randomly assigned to one of 3 ascending dose groups. In each cohort, 9 participants received AnAPN1 with GLA-LSQ and 2 received the vaccine without adjuvant. The 20µg, 50µg, and 100µg vaccine doses were administered intramuscularly at days 0, 28, and 56-day in the first, second, and third cohorts, respectively. The vaccine's safety and reactogenicity were evaluated by means of close participant monitoring for any adverse effects occurring during and after vaccinations. The trial is registered with ClinicalTrial.gov, NCT05905432 and is still ongoing. Between October and December 2023, 55 participants were screened, of whom 33 eligible participants were recruited and allocated to either the 20µg, 50 µg, or 100µg dose in 3 sequential cohorts of 11 individuals each. The median age of enrolled participants is 27 years (range: 18-43 years). At the time of this analysis, participants in cohort 1 (n=10), cohort 2 (n=10) and cohort 3 (n=11) received the complete 3-dose vaccination schedule. The most frequently solicited local adverse events were mild to moderate injection site pain, representing 92% (44/48) of local events, and mild headache 36% (29/81) and nausea 19% (15/81) at a systemic level. There were no vaccine related serious adverse events reported. Overall, these preliminary results suggest that the administration of the AnAPN1 malaria candidate vaccine is safe and well tolerated in healthy Gabonese adults. Subsequent immunogenicity studies will determine whether it induces adequate IgG responses to justify a future phase2 clinical trial.

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CAREGIVER PERCEPTION AND ACCEPTABILITY OF THE MALARIA VACCINE RTS,S PRIOR TO INTRODUCTION IN THE FAR NORTH REGION OF CAMEROON

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Malaria is a recurrent public health challenge that requires a combination of strategies to address it in view of elimination. Currently, the malaria vaccine RTS,S vaccine is being introduced in several African malaria endemic countries while in Cameroon, the vaccine was introduced in January 2024. In view of interventions to evaluate the effectiveness of the RTS,S vaccine in Cameroon, pre-introduction caregiver perceptions and acceptability of the malaria vaccine was investigated in the Far North region, which poses the greatest risk of malaria related morbidity and mortality among under 5 children in Cameroon. A household survey was conducted in December 2024 involving 1240 parents/guardians in 4 randomly selected semi-urban and rural health areas of the Maroua 3 health district in the Far North region of Cameroon. The acceptability was explored. Quantitative data was analysed using regression analysis and qualitative data in Atla.ti using both inductive and deductive approaches. Among the 1203 participants, 79.3% were aged between 20 and 40 years and 71.1% had at most primary education. About 1 in 4 respondents were aware of the malaria vaccine Overall, 95.4% of caregivers interviewed were willing to accept the malaria vaccine if available. Confidence of vaccine efficacy,[5,78(aOR:1,27 ; 26,39), p=0.023], or were not concerned[aOR:3,75(1,09 ; 12,88)]. Believe in vaccine presenting low risk of serious reactions, independently affected acceptability. Community health workers were generally favorable to a combination of routine delivery through EPI and campaign style to implementation of the malaria vaccine given the high seasonality of malaria and experience with SMC. Overall, caregivers and community health workers expressed positive perception of the efficacy, health benefits and reduced out of pocket costs due to malaria infection of the RTS,S vaccine. Concerns on serious adverse reactions were expressed by <5% of respondents. Caregivers preferred vaccines delivered at home and community health care workers advocated for a hybrid approach to malaria vaccine delivery given their experience with other vaccines and SMC.

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EFFECTIVENESS AND IMPACT OF THE RTS,S/AS01$_E$ MALARIA VACCINE ONE YEAR AFTER THE PRIMARY VACCINATION IN REAL-LIFE SETTINGS IN THREE SUB-SAHARAN AFRICAN COUNTRIES: INTERIM RESULTS

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In the framework of the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP), the RTS,S/AS01$_E$ malaria vaccine was introduced in selected areas in Ghana, Kenya and Malawi through routine national immunization programs. Within selected MVIP areas, a prospective cohort

disease surveillance study (EPI-MAL-003, NCT03855995) is conducted to assess safety, effectiveness and impact of the RTS,S/AS01$_E$ vaccine in children under 5 years old. Children were followed up through home visits and continuous monitoring of outpatient visits and hospitalizations in selected sites where the vaccine was introduced (exposed clusters) and comparator sites where the vaccine was not initially introduced (unexposed clusters). Vaccine effectiveness and impact were assessed on the incidence of malaria, hospitalizations, anemia and mortality. Results (crude estimates) up to one year after the 3-dose primary vaccination are presented here. This interim analysis (study period: 2019-2023) included 44,912 children uniformly distributed between exposed and unexposed clusters. In the exposed clusters, the primary RTS,S/AS01$_E$ vaccination coverage was 85%. Incidence rate (IR, 95% confidence interval [CI]) per 100,000 person-years (PY) of severe malaria was 252.9 (182.3-341.9) in vaccinated vs 591.3 (489.9-707.6) in unvaccinated children (vaccine impact: 57%). IR (95% CI) per 100,000 PY of all-cause hospitalization was 8,713.0 (8,269.8-9,173.8) in vaccinated vs 10,644.3 (10,198.3-11,104.8) in unvaccinated children (vaccine impact: 18%). IR (95% CI) per 100,000 PY of malaria-attributed hospitalization was 2,342.3 (2,115.3-2,587.1) in vaccinated vs 3,513.3 (3,259.1-3,782.1) in unvaccinated children (vaccine impact: 33%). No vaccine impact was observed on anemia cases at hospital entry. Vaccine impact on all-cause mortality was 17% but did not reach statistical significance (IR ratio: 0.83 [95% CI: 0.64-1.08], p=0.162). The RTS,S/AS01$_E$ vaccine showed positive impact in reducing severe malaria, malaria-attributed hospitalization and all-cause hospitalization over one year after the primary vaccination in real-life settings.

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CHARACTERIZING HUMAN MONOCLONAL ANTIBODIES INDUCED BY VACCINES AGAINST PLASMODIUM VIVAX DUFFY-BINDING PROTEIN

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There are no licensed vaccines against *Plasmodium vivax*, the second most common cause of malaria in humans. Vaccine candidates targeting *P. vivax* Duffy-binding protein region II (PvDBPII), an antigen expressed during the blood-stage of the parasite life cycle, have recently been tested for efficacy in controlled human malaria infection trials in adults. These showed that delayed boosting with a protein-in-adjuvant vaccine partially inhibited parasite growth and that the level of *in vivo* growth inhibition correlated with antibody responses. However, the mechanism(s) of antibody-mediated parasite growth inhibition are not well defined. To determine the breadth of antibody responses that humans generate in response to PvDBPII-based vaccines and the mechanisms of protective antibody responses, we have isolated a large panel of over 150 IgG monoclonal antibodies (mAb) from humans vaccinated against PvDBPII. Anti-PvDBPII specific single cell sorted B cells were isolated from blood and recombinant mAbs were expressed in mammalian cells. The antibody variable gene sequences were analysed using IMGT V-quest. ELISA and high throughput surface plasmon resonance are being used to determine binding characteristics of each mAb and to identify mAb communities of with competitive epitope binding interactions. The functional activity of mAbs was assessed with an *in vitro* parasite growth inhibition activity (GIA) assay using transgenic *P. knowlesi* expressing PvDBP, which showed that the majority of mAbs are GIA positive over a range of potency. Data from this large panel of anti-PvDBPII mAb will be used to define characteristics that determine the functional potency of mAb across different epitopes within PvDBPII. This will help guide the rational redesign of new PvDBPII-based vaccines to improve on efficacy as well as development of prophylactic mAb against blood-stage *P. vivax*.

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COMPARATIVE STUDY OF ANTIBODY EFFECTOR FUNCTIONS IN UK INDIVIDUALS AFTER VACCINATION EITHER WITH RTS,S AS01$_B$ OR R21 MATRIX-M ENROLLED INTO CONTROLLED HUMAN MALARIA INFECTION STUDIES

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In 2022, malaria remained a leading cause of death in Sub-Saharan Africa, with more than 249 million cases and 608,000 deaths, *Plasmodium falciparum* (*Pf*) being the most widespread and deadly form of the parasite. Highly efficacious vaccines are valuable additions to core interventions to reduce malaria incidence and mortality. Recently, two pre-erythrocytic malaria vaccines based on a *Pf* antigen circumsporozoite protein (CSP), RTS,S/AS01$_B$, and R21/Matrix-M, have been licensed for the prevention of malaria in children. Vaccine-induced IgG antibodies against the central NANP repeat region of the CSP are known as the main driver of protection. The identification of the mechanism by which vaccine-induced antibodies provide protection at the individual level after CSP-based vaccines is still needed to facilitate rapid clinical development of new vaccine candidates. In this study, we performed a comprehensive antibody profiling using serum of UK adults enrolled in Controlled Human Malaria Infection studies and vaccinated either with RTS,S (N=24) or R21 (N=33), to provide information regarding the quantitative and qualitative functions of vaccine-induced antibodies associated with protection. Associations with protection were assessed for the two vaccines at the time of challenge (one month after three doses of vaccines). For RTS,S vaccinees, we observed higher FcγRIIIa binding (*P*=0.03) in protected compared with unprotected participants. For R21 vaccinees, we observed increased ability of antibodies to inhibit sporozoite invasion (*P*=0.04) in protected compared with unprotected participants. For both vaccines, complement deposition was higher in protected participants (RTS,S *p*=0.02; R21 *p*=0.04). In conclusion, antibody characterisation after vaccination at the time of challenge highlighted different functional humoral immune profiles between protected and non-protected participants across RTS,S and R21 vaccines. These findings may help to assess vaccine immunogenicity of new CSP-based vaccine candidates.

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SAFETY AND IMMUNOGENICITY OF THE MALARIA VACCINE R21/MATRIX-M™IN UGANDAN CHILDREN LIVING WITH HIV

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Malaria remains one of the main causes of mortality in children in Sub-Saharan Africa. Despite the initial success of preventive programmes, progress in reducing malaria incidence has stalled in recent years. A safe and highly effective vaccine is paramount to reduce malaria incidence in this population and to progress towards eradication. R21/Matrix-M™ malaria vaccine has been shown to be safe and highly effective in a phase 3 trial (73% vaccine efficacy [95% CI 70 to 76] to first malaria episode within 12 months) which resulted in the WHO recommendation in October 2023 and pre-qualification in December 2023. In sub-Saharan Africa, the areas most affected by malaria overlap substantially with the areas most affected by HIV. For successful deployment of R21/Matrix-M™, it is necessary to assess the safety and immunogenicity of R21/Matrix-M

in this vulnerable population. Although children living with HIV may have been enrolled in the R21/Matrix-M™ phase 3 trial as HIV-infection itself was not an exclusion criterion, this is the first trial to specifically assess the safety and immunogenicity of the R21/Matrix-M™ in this population. 100 HIV positive and 20 HIV negative children, aged 5-36 months, were recruited and received 3 doses of R21/Matrix-M™. We collected safety data for solicited adverse events for 7 days after each vaccination and unsolicited adverse events for 30 days after each vaccination. Serious adverse events are collected for the duration of the trial. Blood samples to assess immunogenicity were taken before enrolment, before administration of the third dose, and one, 6 and 12 months after the third dose and results will be presented in the meeting. R21/Matrix-M™ was well tolerated, and the adverse events observed were similar to the adverse events observed in previous R21/Matrix-M™ trial in children. Most of the solicited and unsolicited adverse events were mild or moderate, and short- lived. There were no observed trends in unsolicited adverse events. There were no serious adverse events assessed as related to the vaccine. These data support the safety of R21/Matrix-M™ in children living with HIV.

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A NOVEL *EX VIVO* ASSAY TO EVALUATE FUNCTIONAL EFFECTIVENESS OF *PLASMODIUM VIVAX* TRANSMISSION BLOCKING VACCINE USING PVS25 TRANSGENIC *P. BERGHEI*

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Plasmodium falciparum and *P. vivax* account for >90% global malaria burden. Transmission intervention strategies encompassing transmission-blocking vaccines (TBV) and drugs represent ideal public health tools to eliminate malaria at the population level. The availability of mature *P. falciparum* gametocytes through *in vitro* culture has facilitated development of a standard membrane feeding assay (SMFA) to assess efficacy of transmission interventions against *P. falciparum*. The lack of *in vitro* culture for *P. vivax* has significantly hampered similar progress on *P. vivax* and limited studies have been possible using blood from infected patients in endemic areas. The ethical and logistical limitations of on-time access to blood from patients have impeded the development of *P. vivax* TBVs. Transgenic murine malaria parasites (*P. berghei*) engineered to express TBV candidates of *P. vivax* offer a promising alternative for evaluation of *P. vivax* TBVs through *in vivo* studies in mice and *ex vivo* membrane feeding assay (MFA). In this study, we describe the development of transmission-competent transgenic *P. berghei* parasites expressing Pvs25 (TgPbvs25), and the optimization of parameters to establish a robust *ex vivo* MFA using TgPbvs25. We validated the reliability and applicability of this MFA for evaluating transmission-reducing activity (TRA) using two transmission-blocking mAbs targeting Pvs25. Furthermore, TRA of IgG from sera of mice immunized a Pvs25 DNA vaccine was demonstrated in *ex vivo* MFA using TgPbvs25, and the results were comparable to those tested in direct membrane feeding assay (DMFA) using *P. vivax*-infected patient blood in the field. This novel assay is expected to expedite Pvs25-based TBV development without dependence on blood from *P. vivax*-infected patients in endemic areas for evaluation. Additionally, the *ex vivo* MFA approach developed can be widely employed for various transgenic *P. berghei* parasites expressing different TBV antigens from both *P. vivax* and *P. falciparum*.

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MALARIA VACCINE INTRODUCTION REDUCED CLINICAL MALARIA IN KENYA: TIME-SERIES ANALYSIS OF ROUTINE HEALTH FACILITY SURVEILLANCE DATA (2020-2022)

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Following the introduction of RTS,S/AS01 (RTS,S) through the Malaria Vaccine Implementation Programme (MVIP) in Kenya, we examined monthly routine malaria surveillance data from the Kenya Health Management Information System (KHIS) to assess the impact of RTS,S on outpatient malaria cases in children <5 years of age. Due to KHIS data aggregation at <5 and ≥5 years, the proportion of vaccine age-eligible children (RTS,S doses at 6, 7, 9, and 24 months) among <5y was initially small but increased over time. The monthly number of confirmed malaria cases reported to KHIS from outpatient facilities and community health workers was included from 23 vaccinating and 23 comparator sub-counties. Analysis was restricted to facilities reporting at least 11 months each year from January 2015 through December 2022 (139 vaccinating; 141 comparator). We estimated the case reduction as the difference between monthly reported cases <5y and forecasted cases <5y (January 2020-December 2022). Forecasts were based on time-series models of pre-vaccination data (January 2015-December 2019). To account for factors unrelated to MVIP, such as decreased clinic attendance during the COVID-19 pandemic, IRS, and bednet distributions, the analyses included a covariate for malaria cases ≥5y, as well as adjustment for trends in comparator areas. The annual percent reduction in <5y cases in vaccinating facilities was 15% in year 1, 17% in year 2, 24% in year 3, and 18.4% across 3 years. Attributing the reduction of clinical malaria to RTS,S was supported by evidence that the impact was greatest (32.9% overall) when excluding 31 (22%) comparator facilities whose population may have received vaccine due to their proximity to a vaccinating facility (<5km). Routine health facility data may be an effective source for estimating vaccine impact following broad scale-up, but has several important limitations such as age aggregation to initially include vaccine ineligible children, assumptions about vaccination status based on population-level coverage, availability of data from comparable non-vaccinating facilities, incomplete reporting, and impact of non-vaccine factors.

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IMMATURE DENDRITIC CELL TARGETING MRNA VACCINE ENHANCES PROTECTION FROM *PLASMODIUM* LIVER STAGE INFECTION BY ENHANCING T CELL RESPONSES AND ANTIBODY TITERS AGAINST CSP REPEAT REGIONS

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In 2021, there were 247 million clinical cases and 619,000 deaths from malaria. RTS, S, the first and only WHO approved vaccine for malaria, targets the pre-erythrocytic stage antigen circumsporozoite protein (CSP) and provides only limited efficacy, reducing clinical malaria by a modest 30%. For RTS, S and other pre-erythrocytic stage targeting vaccines, the ability to produce a robust immune response, eliciting high antibody titers and engaging a strong T cell are the primary obstacles to achieving vaccine-induced protection. Here, we describe the creation of a novel CSP mRNA, chemokine fusion vaccine, designed to overcome these challenges. Vaccination with mRNA expressing full-length CSP fused to macrophage inflammatory protein 3 alpha (MIP3α), provided significantly greater protection against sporozoite challenge than vaccination with mRNA expressing full-length CSP alone. The CSP-MIP3α fusion vaccine enhanced antibody titers against highly neutralizing NANP repeat epitopes and stimulated both CD4+ and CD8+ T cell responses. Protection from sporozoite challenge correlated significantly with titers against NANP repeats and T cell stimulation, particularly CD4+ T cytokine responses.

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THE PVRBP2B-TFR1 INTERACTION IS NOT ESSENTIAL FOR RETICULOCYTES INVASION BY *PLASMODIUM VIVAX* ISOLATES FROM CAMBODIA

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Reticulocyte invasion by *Plasmodium vivax* (Pv) involves different receptor-ligand interactions. For decades, only the Duffy Binding Protein (DBP) was known to be critical for this process. Recently, the Reticulocyte Binding Protein 2b (RBP2b) has been described as an essential ligand for Pv invasion by binding the transferrin receptor 1 (TfR1) on the surface of reticulocytes. Anti-RBP2b mouse monoclonal and rabbit polyclonal antibodies (Abs) were shown to inhibit RBP2b-TfR1 binding as well as the invasion of a few clinical Pv isolates from Thailand and Brazil. Human monoclonal anti-RBP2b Abs have been isolated, epitopes determined, and shown to block the binding of rRBP2b to reticulates *in vitro*. However, their capacity to neutralize Pv invasion has not been evaluated. Here, we aim to determine if these same mouse, rabbit and human anti-RBP2b Abs can inhibit invasion of Pv isolates collected in Cambodia. Using a robust in vitro flow cytometry-based assay allowing unambiguous reticulocyte invasion scoring and a total of 49 different Pv clinical isolates, we show that none of the mouse monoclonal, rabbit polyclonal and human monoclonal Abs inhibit invasion even at high concentration (500 µg/ml), despite anti-DBP inhibited by nearly 60% invasion of Pv. The anti-TfR1 OKT9 Abs that inhibits the RBP2b-TfR1 binding does not inhibit Pv invasion either. Combinations at high concentrations of human monoclonal Abs targeting different RBP2b epitopes do not inhibit invasion. Combinations of anti-RBP2b with anti-DBP do not enhance invasion inhibition caused by anti-DBP Abs alone. We also show that invasion of Cambodian Pv is trypsin-resistant while TfR1 is trypsin-sensitive and we demonstrate that TfR1 is not recycled following trypsin treatment. We determined the RBP2b sequence of all isolates used in the invasion assays and analyzed polymorphism within epitopes recognized by anti-RBP2b Abs. We show that polymorphism does not explain the absence of neutralization. In addition, rabbit anti-RBP2b polyclonal Abs recognized all four isolates tested in IFA. Thus, RBP2b is not be essential for Pv isolates from Cambodia to invade reticulocytes.

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THE EFFECTS OF VACCINE ADJUVANTS & MAJOR HISTOCOMPATIBILITY COMPLEX (MHC) ON THE IMMUNOGENICITY OF A SUBDOMINANT EPITOPE IN *PLASMODIUM VIVAX* DUFFY BINDING PROTEIN

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We are developing a vaccine that targets a specific epitope within the *Plasmodium vivax* protein PvDBP. The challenge is that this epitope (in subdomain-1, or SD1) is subdominant & not immunogenic within the recombinant protein. We hypothesized that mutations in other regions of PvDBP (subdomains 2 and 3) may alter the immunodominance hierarchy to expose this epitope. To test this, we expressed various PvDBP mutants, measured their affinity toward a mouse monoclonal antibody (3D10 mAb) specific to SD1, & measured their immunogenicity in mice. Recombinant wild-type PvDBP (Sal1 allele) & four mutants (DEKnull, DEKnull-2, DEKnull-3, DEKnull-4) were expressed in *E. coli*, purified & refolded. The affinity of the 3D10 mAb against each recombinant protein was measured by mass photometry. BALB/c and C57BL/6 mice were immunized with Sal1 & the mutant proteins alone or with Titermax, GLA-SE, or Alum as adjuvants. Immunogenicity was determined by enzyme-linked immunosorbent assay (ELISA) against a synthetic SD1 peptide. Among the five proteins, the 3D10 mAb had the highest affinity for DEKnull-4. When comparing the IgG titers specific to SD1, vast differences were observed depending on the immunogen, strain of mouse and the choice of adjuvant. SD1 remained subdominant in BALB/c mice immunized with Sal1 without adjuvant or with Titermax, but was strongly immunogenic when adjuvanted with GLA-SE and Alum. The immunogenicity of SD1 was increased further when DEKnull-4 was adjuvanted with GLA-SE or Alum. Conversely, anti-SD1 IgG responses were significantly masked in C57BL/6 mice under similar immunization conditions, indicating an important contribution of the Major Histocompatibility complex (MHCII) to SD1 immunogenicity. Supporting this, immunization of B10.D2 congenic mice (BALB/c MHCII on a C57BL/6 genetic background) with either Sal1 or DEKnull-4 adjuvanted with Alum fully restored the immunogenicity of SD1. These results demonstrate that the antigen structure, the choice of adjuvant, & most significantly, MHC restriction, drive epitope-specific immunogenicity following vaccination with subunit vaccines.

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VACCINE DESIGNS TO ELICIT PROTECTIVE ANTIBODIES AGAINST *PLASMODIUM FALCIPARUM* CSP

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Vaccines and monoclonal antibodies (mAbs) that target the *P. falciparum* 3D7 circumsporozoite protein (CSP) have proven effective in blocking infection in humans but extending the length of protection likely requires improving immunogenicity and durability of CSP-based immunogens. CSP contains a central repeat region composed of 38 NANP tetramers and a minor repeat region composed of three alternating NVDP and NANP tetramers. The junctional region is located immediately upstream and is also a target of humoral immunity. Based on knowledge gained from structures of mAbs bound to these regions and with the goal of understanding and improving protection against infection, eight immunogens (IMV1-8) targeting the major and minor repeats and junctional peptide region have been designed and produced. Structural data have demonstrated that IMV1-8 display the proper structure and the anticipated antibody valency on the repeat regions. To promote immunogenicity, the purified recombinant immunogens were bound to the capsid virus-like particle (cVLP) AP205 using a split-protein conjugation system to generate stable isopeptide bound antigen-cVLP complexes. Groups (n=6) of female C57BL/6N mice were immunized three times at 3-week intervals with equimolar amounts (180 pmol) of cVLP-IMV1-8, using AddaVax as an extrinsic adjuvant. The calculated geometric mean titers, using 2A10 mAb as a reference, indicated immunogenicity was proportional to the length of the immunogen. To test infection blocking efficacy in vivo, immune sera against the different constructs were injected intravenously (IV) into mice, which were challenged IV with 2,000 tg*Pb-Pf*CSP sporozoites. Significant inhibitions were observed

for cVLP-IMV2 and cVLP-IMV8 at levels comparable to those induced by anti-RTS,S antisera. Thus, constructs presenting either the major (cVLP-IMV2) or the minor (cVLP-IMV8) repeats performed similarly to RTS,S/AS01 in producing infection blocking antibody responses in this mouse model. Whether such antibody responses might act in synergy is being investigated.

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AMA1-SPECIFIC HUMAN MONOCLONAL ANTIBODIES INHIBIT *PLASMODIUM VIVAX* PRE-ERYTHROCYTIC AND BLOOD STAGE INFECTION

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One-third of the human population is at risk of contracting *Plasmodium vivax* (Pv). Developing novel Pv-specific therapeutic options such as monoclonal antibodies is vital to decreasing the worldwide burden of Pv. Apical Membrane Antigen 1 (AMA1) is an essential invasion protein that when expressed binds to Rhoptry Neck Protein 2 (RON2), an interaction utilized by sporozoites and merozoites during host cell invasion. PBMCs from a Pv-exposed individual were screened for AMA1-RON2 blocking antibodies using a competition ELISA. 12 PvAMA1-specific human monoclonal antibodies (humAbs) were produced and their functional characteristics were analyzed. One humAb, 826827, blocks invasion of human reticulocytes using Pv clinical isolates *in vitro* (IC_{50}= 48 µg/mL). 826827 also inhibited sporozoite invasion of a human hepatocyte cell line and primary human hepatocytes (IC_{50} = 0.3 - 3.7 µg/mL). The crystal structure of recombinant PvAMA1 with the antigen-binding fragment of 826827 shows that 826827 partially occupies the highly conserved hydrophobic groove in PvAMA1 that binds its known receptor, PvRON2. Competition ELISAs confirm that 826827 competes with a PvRON2 peptide for PvAMA1 binding with a higher affinity, accounting for its potency. *In vivo* testing using a liver-humanized mouse model that supports Pv liver stage infection showed a log-fold reduction in parasite burden in the liver with 826827 compared to mice treated with an isotype control antibody (Mann-Whitney, P = 0.0143). 826827 binds to highly conserved residues on PvAMA1, explaining the observed strain-transcending properties. To our knowledge, 826827 is the first humAb reported specific to PvAMA1 and is one of the first antibodies to show potent inhibition against blood stages and pre-erythrocytic stages.

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DESIGN AND EVALUATION OF CHIMERIC *PLASMODIUM FALCIPARUM* CIRCUMSPOROZOITE PROTEIN-BASED MALARIA VACCINES

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Efficacy data on two malaria vaccines, RTS,S and R21, targeting *Plasmodium falciparum* circumsporozoite protein (*Pf*CSP), are encouraging. Efficacy may be improved by induction of additional antibodies to neutralizing epitopes outside of the central immunodominant repeat domain of *Pf*CSP. We designed four r*Pf*CSP-based vaccines in an effort to improve the diversity of the antibody response. We also evaluated *P. falciparum* merozoite surface protein 8 (*Pf*MSP8) as a malaria-specific carrier protein as an alternative to hepatitis B surface antigen. We measured the magnitude, specificity, subclass, avidity, durability, and efficacy of vaccine-induced antibodies in outbred CD1 mice. In comparison to N-terminal or C-terminal focused constructs, immunization with near full-length vaccines, r*Pf*CSP (#1) or the chimeric r*Pf*CSP/8 (#2), markedly increased the breadth of B cell epitopes recognized covering the N-terminal domain, junctional region, and central repeat. Both r*Pf*CSP (#1) and r*Pf*CSP/8 (#2) also elicited a high proportion of antibodies to conformation-dependent epitopes in the C-terminus of *Pf*CSP. Fusion of *Pf*CSP to *Pf*MSP8 shifted the specificity of the T cell response away from *Pf*CSP toward *Pf*MSP8 epitopes. Challenge studies with transgenic *Plasmodium yoelii* sporozoites expressing *Pf*CSP demonstrated high and consistent sterile protection following r*Pf*CSP/8 (#2) immunization. Noteworthy, antibodies to conformational C-terminal epitopes were not required for protection. These results indicate that inclusion of the N-terminal domain of *Pf*CSP can drive responses to protective, repeat, and non-repeat B cell epitopes and that *Pf*MSP8 is an effective carrier for induction of high titer, durable anti-*Pf*CSP antibodies.

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ASEPTIC, PURIFIED, VIALED *PLASMODIUM VIVAX* SPOROZOITES FOR CONTROLLED HUMAN MALARIA INFECTION

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Malaria caused by *Plasmodium vivax* (Pv) is 2nd to *P. falciparum* (Pf) in incidence and impact. Unlike Pf, chemoprophylactic measures against Pv do not prevent relapses due to re-activation of persistent liver-stage sleeping forms of the parasites called hypnozoites. Primaquine and tafenoquine are the only licensed drugs that target Pv hypnozoites, but cause life threatening acute hemolytic anemia in patients with G6PD deficiency. Drug and vaccine development are hampered by inability to propagate blood stages of Pv parasites *in vitro* and mosquitoes for controlled human malaria infection (CHMI) can only be generated with Pv-infected blood from patients. We produced Pv sporozoites (SPZ) of the Chesson strain by feeding infected blood from specific pathogen free (SPF) *Saimiri boliviensis* (Sb) monkeys to aseptic *Anopheles stephensi* mosquitoes and these PvSPZ were highly infectious to FRG mice with humanized livers and produced hynozoites. We then manufactured in compliance with GMPs 1) a master cell bank of Pv (Chesson) asexual RBC stage parasites in the blood of SPF Sb, 2) small lots of aseptic PvSPZ with all in-process samples of aseptic eggs, pupae, blood meals and adult mosquitoes, and the final product testing negative for microbial growth using U.S. Pharmacopeia USP<71> tests for sterility, and 3) One lot of aseptic, purified, vialed cryopreserved PvSPZ, Sanaria® PvSPZ Challenge (Chesson) that is aseptic, pure, and potent. Our pre-IND package to the FDA including our chemistry, manufacturing, and controls, quality control (QC) assays, and a proposal for a clinical trial, received positive feedback and recommendations. PfSPZ Challenge has revolutionized CHMI studies for Pf malaria. We expect PvSPZ Challenge will similarly provide the larger malaria community with a radically enhanced tool to assess anti-Pv interventions, as a safe quality-controlled reagent with minimal variability in potency, that is logistically simpler to administer, not subject to geographical limitations for application, compared to mosquito bite CHMI. The characteristics of the SPF Sb, aseptic mosquito infections, and GMP-produced PvSPZ will be presented.

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ANTIMICROBIAL RESISTANCE OF *SHIGELLA* AMONG CHILDREN UNDER FIVE YEARS WITH DIARRHEA OVER A DECADE IN THE GAMBIA

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Antimicrobial resistance (AMR) is a major public health concern globally, especially in low- and middle-income countries (LMICs). Resistance among the leading cause of bacterial diarrhea and dysentery, *Shigella* spp., limits antibiotic options for children vulnerable to mortality and linear growth faltering. A high burden of *Shigella* spp.-attributable diarrhea was found among African sites in the Global Enterics Multicenter Study (GEMS). We describe AMR among *Shigella* spp. from children with diarrhea enrolled in the GEMS (2007 - 2011), Vaccine Impact on Diarrhea in Africa (VIDA, 2015 - 2018) and Enterics For Global Health (EFGH) *Shigella* surveillance study (August 2022 - March 2024) in Basse, The Gambia. We enrolled children with diarrhea aged 6-35 months in the EFGH study and children with moderate to severe diarrhea (MSD) aged 0-59 months in the GEMS and VIDA studies. *Shigella* spp. isolated from stool and rectal swab samples by microbiological culture are reported. Antimicrobial resistance was assessed for 114, 214, and 99 *Shigella* spp. isolates from GEMS, VIDA and EFGH diarrhea cases, respectively. *S. flexneri* was the leading serogroup in all three studies constituting 69.0%, 67.6% and 57.3% of isolates in GEMS, VIDA and EFGH, respectively, followed by *S. sonnei* (20.7%; 18.2%; 36.9%), *S. boydii* (6.0%; 11.8%; 2.9%) and *S. dysenteriae* (4.3%; 2.3%; 1.0%). AMR in the GEMS, VIDA and EFGH studies was 93.9%, 93.0% and 97.9% to trimethoprim-sulfamethoxazole, 57.9%, 41.6% and 26.6% to ampicillin, 0.0%, 0.9% and 15.1% to nalidixic acid, 0.0%, 0.0% and 7.0% to azithromycin, 0.0%, 0.5% and 0.0% to ceftriaxone and 0.0%, 0.0% and 2.0% to ciprofloxacin, respectively. Resistance to pivmecillinam, only assessed in the EFGH study, was 10.0%. These findings suggest AMR patterns parallel drug usage, with AMR increasing in the recommended treatment for dysentery (trimethoprim-sulfamethoxazole, ciprofloxacin, azithromycin) and decreasing in ampicillin, which is no longer recommended. This emphasizes the importance and urgent need for *Shigella* vaccine introduction and implementation of strategies to prevent the further increase in AMR burden.

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COMPARING WHOLE CELL PSORALEN INACTIVATED SHIGELLA VACCINE VERSUS FORMALIN INACTIVATED SHIGELLA VACCINE IN MICE

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Shigella is responsible for approximately 600,000 annual deaths worldwide, predominantly among children, yet no licensed vaccines are currently available. This study evaluates the immunogenicity of a psoralen plus ultraviolet A-inactivated (PSIV) Shigella vaccine, which may enhance immunity by better preserving protein epitopes compared to traditional methods. We utilized a mouse model to compare the immunogenicity of PSIV versus formalin-inactivated (FIV) Shigella sonnei vaccines. Four groups of five mice each received one of the following treatments: PSIV with and without a double mutant heat-labile toxin (dmLT) adjuvant, and FIV with and without the adjuvant. Vaccinations were administered on days 0 and 28. Pooled sera from days 0, 28, and 49 were tested for the presence of anti-Shigella antibodies using whole-cell enzyme-linked immunosorbent assays. We found that PSIV with adjuvant resulted in the highest total antibody titer among the pooled samples, which was 30% higher than that of FIV. The mean fold change in antibody titer between days 28 and 49 across all arms was 13.5, indicating a strong booster effect. The PSIV Shigella vaccine is qualitatively superior and statistically non-inferior to an FIV Shigella vaccine in eliciting a broad antibody response. Further research is required to evaluate specific epitope responses. Our results suggest that PSIV may be an effective approach for developing a Shigella sonnei vaccine.

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ESTABLISHING CHOLERA SURVEILLANCE IN RURAL NEPAL DURING COVID-19 PANDEMIC: LESSONS LEARNED

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The ongoing upsurge of Cholera cases with multiple outbreaks, alarming numbers and mortality rates is a global public health concern. The situation underscores the importance of strengthened Cholera surveillance for accurate outbreak detection and response. Cholera outbreaks have been frequently reported in Nepal since early 1800's, but the country still lacks an effective surveillance system for its detection. Assessing the need, International Vaccine Institute (IVI) with the support of Global Disease Eradication Fund (GDEF) from Korea collaborated with Sudurpaschim Provincial Government of Nepal, to establish Cholera surveillance in Kailali district of Nepal in 2019. A network of 10 sentinel sites for enrollment and rapid laboratory testing of suspected Cholera cases and refurbishment of local laboratory to serve as regional reference laboratory for Cholera culture confirmation was planned. Throughout 2019, multiple engagements between stakeholders were held and project implementation was planned from 2020 through 2023 but had to be put on hold due to declaration of Covid-19 pandemic in March 2020. Finally, a collaboration agreement was signed on March 2022 after numerous virtual/on-site meetings even during Covid pandemic. Laboratory upgradation was completed in April 2023 and sentinel sites were trained on use of common protocol for diarrheal disease surveillance. The Cholera surveillance in Kailali formally kicked-off in June 2023 with the first culture confirmed Cholera case being reported in August 2023. Here we present our experience with lessons learned from planning and implementation of the project to reporting first case of Cholera from Kailali district of Nepal during Covid-19 pandemic.

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A COMPARISON OF SEROLOGIC, MOLECULAR, AND GENOMIC APPROACHES FOR SEROTYPING *SHIGELLA FLEXNERI* STRAINS ISOLATED FROM THE PERUVIAN AMAZON

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Shigellosis is one of the leading causes of bacterial gastroenteritis and dysentery in children under the age of 5 living in Iquitos, Peru. *Shigella* spp., a gram-negative bacillus, is the causative agent of this disease. Consequences of Shigellosis include persistent diarrhea, intestinal protein loss and intestinal inflammation, as well as linear growth faltering. Agglutination with antisera against lipopolysaccharide O-antigen is utilized as the gold standard for serotyping *Shigella flexneri*. However, molecular serotyping methods, including a qPCR-based approach, and a genomic based approach have been developed. In this study we compare the results obtained for serotyping *Shigella flexneri* isolates using serum agglutination, genomic sequencing, and qPCR of the matched rectal swabs. *Shigella* spp. isolates were obtained from the Enterics for Global Health Shigella Surveillance Study (EFGH) conducted in Iquitos, Peru. Between August 2022 and December 2023, 86 Shigella strains were isolated from unique rectal swabs from children with medically attended diarrhea. Of these, 78 had a matched qPCR result. Of these, 54 were identified as *S. flexneri*, 22 as *S. sonnei* and 1 as *S. dysenteriae*. Of the 54 *S. flexneri*, 37 (68.5%) ha a matched serotype assigned by agglutination and qPCR (1a (n=2), 2a (n=23), 2b (n=11), 3a (n=1), and 17 (31.5%) had discordant results by agglutination and qPCR. All strains were sequenced using Illumina based methods, and both reads and contigs were analyzed using ShigaTyper and ShigaPass bioinformatic programs. So far, of the 17 discordant pairs, sequencing results are available for three strains. Two of these were classified as 4a by agglutination, were not typed by qPCR and were classified as Yv by genomic serotyping. The third was classified as 1a by agglutination and 1b by qPCR and genomic serotyping. Sequencing will be completed in August 2024, and results of the pending matched and discordant serotyping will be presented at the meeting.

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INTERIM SAFETY DATA FROM A PHASE 1/2A, RANDOMIZED, CONTROLLED, OBSERVER-BLIND TRIAL TO EVALUATE THE SAFETY, REACTOGENICITY AND IMMUNOGENICITY OF A TRIVALENT VACCINE AGAINST INVASIVE NONTYPHOIDAL SALMONELLOSIS (INTS) AND TYPHOID FEVER IN HEALTHY EUROPEAN AND AFRICAN ADULTS.

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Invasive nontyphoidal Salmonellosis (iNTS) and typhoid fever are major public health concerns causing a significant burden, particularly in resource-limited settings of sub-Saharan Africa. There is no licensed vaccine for iNTS, and the licensed Typhoid Conjugate Vaccines (TCVs) are not widely used in Africa. A novel trivalent iNTS-TCV vaccine, aimed at preventing both diseases, is under development by GSK Global Health Vaccines R&D (GVGH). This abstract presents interim blinded safety results from an ongoing phase 1/2a study in healthy adults. In stage 1, 50 European adults were randomized in a 2:2:1 ratio to receive either iNTS-TCV vaccine and concomitant saline in different arms, or separate iNTS-GMMA and TCV vaccines in different arms, or placebo and saline in different arms intramuscularly, on Days 1, 57 and 169. Of these, 10 subjects received low doses of the study vaccines and 40 received full doses. In stage 2, 105 African adults were randomized in a 3:3:1 ratio to receive full doses of the same vaccines or comparators. Menveo, Boostrix and Typhim Vi are administered as controls for the 1st, 2nd and 3rd doses respectively. After all administrations in European adults and at least one administration in 92/105 (87.6%) African adults, majority of the adverse events (AEs) observed are of mild to moderate intensity. Injection site pain is the most reported local solicited AE, while myalgia, fatigue and headache are the most frequent systemic solicited AEs. Severe unsolicited AEs related to vaccination were reported in 4 subjects overall. No serious AE considered related to vaccination has been reported. In conclusion, based on available data, the anticipated benefit/risk profile of the iNTS-TCV vaccine continues to be positive, with no safety concerns precluding further clinical development. First immunogenicity results are expected later in 2024 and would be presented at the congress.

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POLYCHROMATIC FLOW CYTOMETRY PANELS TO CHARACTERIZE ANTIGEN-SPECIFIC MEMORY B-CELLS INDUCED BY ENTEROTOXIGENIC ESCHERICHIA COLI VACCINES

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Enterotoxigenic *Escherichia coli* (ETEC) is one of the significant pathogens causing moderate-to-severe diarrhea in travelers. ETEC is also a leading cause of morbidity in children under 5 years of age especially in resource-poor regions. Current approaches to ETEC vaccine development predominately target the colonization factors, which are involved in ETEC adhesion, and the diarrheagenic heat labile toxin (LT). Combination of colonization factor antigens and mucosal mutant LT adjuvants (mLT or dmLT) aim to induce systemic and mucosal immune responses capable of blocking infection and neutralizing LT. Here, we report on the development of antigenic probes to enable monitoring the induction and response rates of antigen-specific memory B cells induced by vaccination with intradermally administered subunit vaccine targeting the colonization factor antigen I (CFA/I) using the mLT adjuvant. This study was technically challenging due to the nature of the ETEC antigens (CfaE, LT), which bind to intestinal epithelial cells thus potentially resulting in non-specific binding to cells rather than to the antigen-specific B cell receptors. We summarize the various strategies applied to develop a highly specific and sensitive flow cytometric panel. The presentation will provide guidance on how to approach the design of antigenic probes for B cell analysis. The completed flow cytometric panel allowed simultaneous monitoring of LT- and CfaE-specific memory B cells, their functional status, and the expression of homing receptors associated with migration to intestines.

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RETAINING AZITHROMYCIN SUSCEPTIBILITY IN THE FACE OF INCREASING USE IN SUB-SAHARAN AFRICA-THE ROLE OF EFFLUX PUMP INHIBITORS

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Mass drug administration (MDA) of azithromycin is being considered to prevent child mortality in some high mortality settings. Although azithromycin resistance is uncommon in enteric bacteria in sub-Saharan Africa (SSA), resistance may rise with MDA. Azithromycin resistance in *Escherichia coli* (*E. coli*) can result from ribosomal mutations, macrolide-

modifying enzymes, or by efflux pumps expelling intracellular antibiotics. We sought to establish the minimum inhibitory concentration (MIC) of azithromycin and relative importance of efflux pumps in explaining azithromycin resistance in *E. coli* isolates cultured from children recently discharged from hospitals Western Kenya. *E. coli* was isolated from children aged 6-59 months enrolled in a randomized control trial testing post-discharge azithromycin efficacy against mortality and re-hospitalization. Azithromycin MICs were established by E-test in the presence or absence of 50µg/mL Phe-Arg-β-Naphthylamide (PAβN), an efflux pump inhibitor. *E. coli* was isolated from 1220 of 1400 enrolled children and 757 (62%) isolates were resistant to azithromycin (≥32 mg/L), with 565 (75%) having the highest MIC (≥256 mg/L). In the presence of PaβN, the prevalence of azithromycin resistance was reduced by more than half (357 [29%] isolates). MIC_{50} and MIC_{90} in the absence of PaβN were 128 mg/L and 256 mg/L respectively while in the presence of PaβN were 4 mg/L and 256 mg/L respectively. Almost 75% (908/1220) of the isolates had > 2-fold change in MIC values with PaβN, of these 300 (33%) had a 16-fold change in MIC. Azithromycin resistance in *E. coli* was common among children discharged after a non-traumatic hospital admission and highlights the importance of the potentiating effect of efflux pump inhibitors in azithromycin antibacterial activity in *E. coli*. Efflux pump inhibitors, or associated mechanisms such as increased membrane permeability, may hold promise for retaining azithromycin susceptibility in enteric bacterial infections in SSA.

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ESTIMATING THE COST-OF-ILLNESS RELATED TO CHOLERA IN MOZAMBIQUE AND NEPAL

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Cholera is endemic and epidemic in some developing countries. This disease not only tests a country's health systems resilience, but also has direct financial implication to patients and the country alike. Knowing the economic burden of cholera in different settings provides policymakers with appropriate evidence for development, budgeting, and implementation of the national cholera plan (NCP). We carried out a cost-of-illness (COI) study on cholera in Mozambique and Nepal. Using convenience sampling, confirmed cholera cases selected during active outbreak and endemic settings in these countries were surveyed in 2023. A structured questionnaire was used for collection of personal cost (direct medical, direct non-medical and indirect cost) associated with the disease. Healthcare provider costs were also collected. Total 204 and 119 patients were enrolled for COI survey in Mozambique and Nepal respectively. All patients in Mozambique were enrolled from inpatient ward, while 60.5% (72/119) of enrolled patients in Nepal were from emergency ward. Though patients in both countries received governmental subsidies for treatment, more people received subsidy in Mozambique (203/204; 99.5%) than Nepal (32/119; 26.9%). Compared to Mozambique (4/204; 0.019%) more participants from Nepal (19/119; 15.97%) visited pharmacy prior to seeking treatment at health facility. Average cost from patient perspective in Mozambique and Nepal was direct medical (USD0.33, and 52.42 respectively), direct non-medical (7.83, 9.30) and indirect cost (6.42, 35.92). In Mozambique, average total cost from patient perspective ranged from USD17.25 in Niassa to USD26.02 in Zambezia whereas in Nepal, for inpatient was USD153.93 and for outpatient USD47.28. There was substantial difference in cholera related COI in different settings within and between Mozambique and Nepal. If we compare these costs with the income of minimum wage workers, which is approximately USD62.5 for Mozambique and USD130 for Nepal, it becomes evident that cholera poses a considerable financial burden and also challenges in accessing affordable healthcare.

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SINGLE DOSE AZITHROMYCIN AMONG CHILD CONTACTS OF CHOLERA PATIENTS CAN REDUCE CHOLERA AT HOUSEHOLD LEVEL: A DOUBLE-BLINDED RANDOMIZED CONTROL TRIAL

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Vibrio cholerae causes 3 million cholera cases and 100,000 deaths annually with over half of deaths in children. Children who are household (HH) contacts of cholera patients are at high risk for cholera infection and are not well protected by cholera vaccines compared to adults. Azithromycin is an effective treatment for cholera and is widely used as prophylaxis against other childhood infections. Our objective of this trial is to determine whether a single dose of azithromycin given to children aged 1-15 years who are HH contacts of cholera patients will reduce the risk of *V. cholerae* infection. We are conducting a double-blinded cluster-randomized controlled trial of single-dose azithromycin (20mg/kg) compared with the non-antibiotic placebo group. After index cases are identified at icddr,b Dhaka hospital, we enroll HH children aged 1-15 years living in or around Dhaka city within 12 hours. HH contacts are assigned to receive azithromycin or a placebo. We then collect their rectal swab samples as well as clinical data with follow-up for up to 6 months post-intervention (days 1-7, day 30, and day 180). We initiated the study on 31st October 2021 and it is ongoing. A total of 1044 diarrheal patients were screened for *V. cholerae* through 29th February 2024 and 235 were cholera-positive by RDT. 84.26% of RDT-positive cases were positive by culture. Many index patients reported prior receipt of antibiotics, and 41.48% reported taking metronidazole. We enrolled 375 HH contacts from the 235 index cases. Among the HH contacts, 135 were <5 years of age, and 240 were 5-15 years of age. 36 HH contacts (9.6%) were culture-positive for *V. cholerae* O1 and only one was symptomatic. Baseline levels of antibiotic resistance, including macrolide resistance genes, were high among all participants. We report the early-stage results of a randomized clinical trial of single-dose azithromycin to prevent cholera in children. The results of the study when unblinded will inform the clinical management of close contacts of patients with cholera and provide new data about the impact of single-dose azithromycin on short- and long-term carriage of antibiotic-resistant bacteria.

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TYPHOID CONJUGATE VACCINE INTRODUCTION: DECISION-MAKING IN THE CONTEXT OF LIMITED DATA USING A BURDEN AND RISK ASSESSMENT FRAMEWORK

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Since WHO recommended typhoid conjugate vaccine (TCV) introduction in 2018 for all typhoid endemic countries, only six countries have introduced TCV. National decision-making for TCV introduction is limited by lack of typhoid burden data. To address this challenge, WHO and CDC, supported by a group of experts, developed a burden and risk assessment framework to provide a standardized approach to collating, scoring, and interpreting available typhoid data in six areas: incidence, prevalence, antimicrobial resistance (AMR), outbreaks, intestinal perforations, and risk factors. The framework underwent an iterative revision process through pilots in 4 purposively selected countries. Blood culture data and *Salmonella* serotype confirmation were available from tertiary hospitals, but quality and quantity varied by country. Typhoid diagnosis was frequently based on clinical symptoms and antigenic test results. AMR data were limited by the number

of available isolates and data quality varied by country. Intestinal perforation data lacked causality and outcome information. High quality WASH data were derived from national household surveys but were generally not available sub-nationally. Data on outbreaks were consistently lacking. Data collection comprised a desk review (incidence, outbreaks, risk factors) and health facility visits (prevalence, AMR, intestinal perforations), facilitated by an electronic tool, and focused on health facilities with blood culture capacity. Data collectors needed to have laboratory and moderate data management experience. Technical support and funding were required for implementation. Data interpretation required expertise in typhoid epidemiology and laboratory diagnostic methods and was nuanced to each country. The framework can help to provide an overall inference of typhoid burden in a country, even in settings where blood culture confirmation is not routine. Results may inform national typhoid control decision-making, including TCV introduction. However, technical support for implementation and data interpretation are necessary for success.

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MEASURING THE EFFECTIVENESS AND IMPACT OF TYPHOID CONJUGATE VACCINE FOLLOWING NATIONAL INTRODUCTION IN MALAWI (MITIMA)

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Typhoid conjugate vaccine (TCV) has demonstrated robust efficacy in randomized controlled trials in low- and middle-income countries, including Malawi. Liberia and Zimbabwe were the first sub-Saharan African countries to introduce TCV in April and May 2021, respectively. In May 2023, Malawi became the third African country to introduce TCV. We aim to measure TCV effectiveness and impact post-introduction in a typhoid-endemic sub-Saharan African setting and inform policy decisions across Africa. We are conducting passive blood culture surveillance for typhoid fever in Blantyre. Individuals aged 9 months to 45 years presenting with febrile illness (subjective fever for ≥72 hours, axillary temperature ≥38°C, or hospitalisation with a history of fever) have a blood culture. Vaccine effectiveness will be measured post-introduction among children age-eligible for vaccination (9 months to 15 years) using a test-negative study design. Cases are blood culture positive for *Salmonella.* Typhi (*S*. Typhi); controls are blood culture negative for *S.* Typhi. TCV impact will be assessed using an interrupted time series analysis of blood culture surveillance data collected from one-year pre-introduction and two years post-introduction. We will calculate changes in *S*. Typhi-positive blood culture incidence in vaccine-eligible and 16-45-year-old participants, using the latter as a comparator for temporal trends. TCV was introduced in Malawi from 15 May to 24 May 2023. Between 18 April 2022 and 12 Apr 2024, 240,062 participants were screened; 8537 met the febrile illness definition, 6762 were enrolled, and 6704 had blood cultures collected. The blood cultures yielded 190 *S.* Typhi and 23 *Salmonella* Typhimurium cases. Among the *S*. Typhi isolates, 94.8% were multidrug-resistant, 2.1% fluoroquinolone-resistant, and 3.1% susceptible to all or some first-line antibiotics. Blood culture surveillance before and after the TCV campaign has been consistent. The data are unadjusted for vaccine coverage or other temporal trends. Surveillance continues and will provide important data on TCV effectiveness and impact in an endemic African setting.

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EVALUATING THE IMPACT OF VACCINATION WITH ORAL CHOLERA VACCINE ON CHOLERA BURDEN IN HIGH TRANSMISSION AREAS OF DHAKA, BANGLADESH AN INTERRUPTED TIME SERIES ANALYSIS

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Bangladesh, a cholera endemic country, experiences two seasonal peaks: one from April to May, another from August to September. In 2022, Dhaka experienced the largest surge in cholera-related hospitalizations in last 60 years. More than half of the came from Jatrabari, Dakshinkhan, Sabujbagh, Mohammadpur-Adabor, and Mirpur regions. In response, the government of Bangladesh requested oral cholera vaccine (OCV) from the global stockpile. A targeted, two-dose vaccination campaign was implemented in the aforementioned areas in June and August 2022. This study aims to evaluate the impact of the OCV campaign on cholera burden in vaccinated areas. A pre- and post-evaluation was conducted using routinely collected surveillance data from the icddr,b hospitals. Since 1996, every 50th patient presenting for care with acute watery diarrhea is included and a stool sample is tested for cholera by culture. The proportion of cholera cases averted in the 5 vaccinated regions was calculated. An interrupted time series analysis compared the proportion of culture cholera confirmed cases in vaccinated and non-vaccinated areas of Dhaka. In the first year of the post-OCV campaign period (September 2022-September 2023), the culture confirmed cholera positivity among hospitalized diarrheal patients from vaccinated areas decreased by 46% compared to the pre-OCV campaign period (June 2017-May 2022; except 2020). In the five high burden vaccinated areas, the hospitalization rates per year during pre- and post-OCV campaign periods were 9.1 and 6.4 per 1000 population respectively. There was no significant difference in the positivity among patients from the unvaccinated areas during the same two periods. Also the cholera positivity in the post-OCV campaign period was 51.1% lower than predicted by the model. Both the cholera positivity and hospitalization rate among vaccinated areas in Dhaka decreased following the OCV campaign. While data on other factors that may have contributed to this reduction were not collected, this evaluation provides evidence to support the impact of cholera vaccination on burden reduction in the first year following vaccination.

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GENETIC DETERMINANTS OF EXTENDED-SPECTRUM BETA-LACTAMASE RESISTANCE IN *SHIGELLA* SPECIES IN KENYA

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Shigella spp have increasingly become resistant to mostly used antimicrobials, which account for over 165 million cases and 1.1 million deaths annually worldwide, significantly, due to its low infective dose and high transmission rate in areas with poor hygiene and in low income areas. The emergence of multidrug-resistant *Shigella* spp complicates the treatment and management of shigellosis which has put more strain to the already paltry resources in the developing countries. This study sought to detect the presence of Extended spectrum β-lactamases (ESBLs) resistance genes markers in *Shigella* spp. isolates from diarrheal patients in Kenya. A retrospective analysis of 515 *Shigella* spp stool specimens

initially tested for phenotypic antimicrobial susceptibility was performed using molecular PCR to detect resistance markers. Specifically, we targeted ESBL resistance gene markers, that included: TEM, SHV, OXA, OXA-48, CTX Groups 1, 2, 9, 8, and 25, CTX-M, ACC, FOX, MOX, DHA, CIT, EBC, GES, PER, VEB, IMP, VIM, and KPC. After results analysis, we found two major ESBL resistance gene markers in *Shigella* isolates; blaTEM and blaOXA in the same proportion 14% (71/515). Additionally, blaVIM was found in 1.4% (7/515) and blaIMP in 0.2% (1/515). The other gene markers were not detected from the isolates; SHV, OXA-48, CTX Groups 1, 2, 9, 8, and 25, CTX-M, ACC, FOX, MOX, DHA, CIT, EBC, GES, PER, VEB, IMP, and KPC. This study concludes that, blaTEM and blaOXA are the most commonly seen genes among the *Shigella* isolates from Kenyan patients. Further analysis using whole genome sequencing could be done to detect mutations or virulent genes that could be associated with the resistance conferred by *Shigella* isolates.

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MOLECULAR CHARACTERIZATION AND PHENOTYPIC ANTIMICROBIAL RESISTANCE PROFILE OF DIARRHEAGENIC *ESCHERICHIA COLI* ISOLATED FROM PATIENTS WITH ACUTE DIARRHEA VISITING KERICHO COUNTY REFERRAL HOSPITAL, KERICHO, KENYA.

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Diarrheal disease caused by diarrheagenic Escherichia coli (DEC) is the second leading (after pneumonia) cause of morbidity and mortalities in children under five years in low-income countries. The emergence of multi-drug resistant (MDR) variant of DEC poses a formidable challenge infection control efforts. This study aimed to determine the phenotypic antibiotic resistance profiles of DEC isolated from patients with acute diarrhea visiting Kericho County Referral Hospital between January 2022 to December 2023. A total of 149 stool samples were collected from patients presenting with symptoms of acute diarrhea over a two-year period, shipped to the Microbiology Hub Laboratory-Kericho, cultured and isolated. DEC pathotypes were identified by multiplex Polymerase Chain Reaction assays targeting nine virulence genes; *Enteroaggregative E.coli (*EAEC*_aatA,aaiC),* Enteropathogenic *E.coli (*EPEC*_eae,bfpA),* Enterotoxigenic *E.coli (*ETEC*_LT, ST),* Enterohemorrhagic *E.coli (*EHEC*_StxI,StxII)* and Enteroinvasive *E.coli (*ETEC*_ipaH).* DEC positive isolates were subjected to antimicrobial susceptibility testing using BD Phoenix Gram Negative NMIC/ID-431 panel run on the M50 identification system.15 out of 149 (10.10%) stool samples tested positive for DEC pathotypes. The most commonly isolated pathotype was EAEC 7/15 (46.67%), followed by EPEC in 5/15 (33.33%), and EIEC in 3/15 (20%). No ETEC and EHEC were detected during this period. Majority of the strains were resistant to trimethoprim/sulfamethoxazole 13/15 (86.66%), ampicillin 12/15 (80%), amoxicillin/klauvanate 6/15 (40%), cefazolin 6/15 (40%), cefuroxime 3/15 (20%), ceftriazone 3/15 (20%), imipenem 3/15 (20%), and tigercycline 3/15 (20%). 5/15 (33.33%) of the isolates were resistant to three classes of antibiotics. However, none of the isolates were resistant to amikacin, ceftolozane-tazobactam, gentamicin, piperallicin/tazobactam. Results showed that EAEC is the most frequently detected pathotype. While many of these isolates show resistance to commonly used antibiotics, there is still potential treatment options for diarrhea caused by EAEC.

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CAMPYLOBACTER SPP AND ANTIMICROBIAL RESISTANCE IN A DIARRHEAL CASE-CONTROL STUDY IN KENYA

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Campylobacter is one of the most commonly isolated enteric pathogens among patients with diarrhoea worldwide and has been listed among the WHO high priority pathogens due to emergence of fluoroquinolone resistant strains. Complications associated with campylobacteriosis are rare but infection may be concurrent with recurrent colitis, Guillain-Barré Syndrome (GBS), irritable bowel disease, pancreatitis, cystitis and reactive arthritis. We describe the results of surveillance of *Campylobacter spp* in a diarrheal case control study in Kenya between January 2013 and December 2020. A total of 4,062 stool samples from cases and controls were collected and cultured to determine bacterial diarrheal pathogens, including *Campylobacter spp*. *Campylobacter spp* were identified using biochemical tests and confirmed using the MALDI-TOF Mass Spectrometry System (Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility tests were performed using E-test and interpreted according to CLSI guidelines. *Campylobacter spp* was isolated from 91 (2.2 %) stool samples. Out of the 91 *Campylobacter spp* isolated, 55 (60%; p = 0.04) were from diarrheal cases while 36 (40%) were from controls. Majority of the *Campylobacter spp* were *C. jejuni* (78/91; 86%) which were mainly isolated from cases (46/78; 59%) as compared with controls. Additionally, the *Campylobacter spp* were mainly isolated from children ≤5 years (60/1705; 66%; p <0.0001). Antimicrobial susceptibility test was done for ciprofloxacin, chloramphenicol, ampicillin, azithromycin and tetracycline and they all showed 100% susceptibility. However, 24% of the isolates were resistant to trimethoprim sulphamethoxazole. Our results show that *Campylobacter sp*p disproportionately infects children ≤5 years and emphasizes the importance of continued surveillance and monitoring of antimicrobial resistance patterns to combat antimicrobial resistance.

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TIMING OF CHOLERA CASES ADMISSIONS AND IMPLICATIONS FOR CASE MANAGEMENT IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Clinical care for cholera is free in cholera treatment centers (CTCs) in many settings. In the DR Congo (DRC), where out-of-pocket payments significantly contribute to health facility revenues, CTCs attract few resources and attention from health care providers and managers. During night and weekend shifts, CTCs are often staffed by newly recruited or insufficiently trained nurses with limited access to pharmacy stocks including critical supplies for cholera treatment like rehydration solutions and antibiotics. We examined the drivers of night and weekend admissions in CTCs in Uvira, a cholera endemic city in eastern DRC. Between August 2021 and April 2024, 2,605 patients were admitted for cholera treatment, for whom time of admission data was available for 2,413. 40.5% of admissions were registered at night and 35.5% during weekends. There was no difference in age or sex between patients admitted during the day and night, but children < 5 years old were more likely to be admitted during weekends (OR 1.42; 95% CI: 1.11–1.83) than older individuals. Patients living closer to the CTCs were more likely to be admitted at night (OR 0.96; 95% CI: 0.92–1, distance measured in km). Those admitted at

night were more likely to be severely dehydrated (OR 1.16; CI 0.99–1.36) and were admitted for longer (≥ 2 days vs <1 day, 1.71; 1.23–2.38). The odds of seeking care within the first 24 hours of symptoms onset were 1.6 higher (95% CI 1.21–2.12) for patients admitted at night than those admitted during the day. During weekends, patients were twice as likely to be admitted at night than during the day (OR 2.06; CI 1.74–2.45). As both severe cases, for whom prompt and aggressive dehydration is crucial, and young children, for whom dehydration is more challenging, are more likely to be admitted to CTCs during night and weekend shifts, the provision of healthcare services in CTCs should be organized to ensure sufficient resources are available at all hours to improve clinical outcomes. Building CTCs in remote neighborhoods might improve access to cholera care in settings like Uvira, where public transport at night is sparse to non-existent and private pharmacies are closed.

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ANTIMICROBIAL RESISTANCE PATTERNS AT AN URBAN REFERRAL HOSPITAL IN BLANTYRE, MALAWI

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Antimicrobial resistance is one of the biggest new threats to global health security in Africa. Recent studies in Malawi document the emergence of carbapenemase-producing Enterobacter as well as other resistant pathogens. We obtained an antibiogram for positive blood and urine cultures from September 2021 through March 2022 at Blantyre Adventist Hospital, a 40-bed pediatric and adult hospital in southern Malawi which sees an average of 75,000 patients per year. A total of n=685 cultures were obtained, with 17.6% positive specimens. Findings were notable for 39.1% ceftriaxone resistance and 40.6% ciprofloxacin resistance in tested E. coli specimens. These findings were similar or worse in tested Klebsiella specimens (57.1% ceftriaxone and/or ciprofloxacin) and tested Proteus specimens (38.5% cefuroxime and/or 23.1% ciprofloxacin). A chi-square test of independence showed a correlation between ceftriaxone and ciprofloxacin resistance, both for all gram negatives (p=4.74E-06) as well as E. coli alone (p=1.77E-05). Of note, resistance to meropenem and/or imipenem was also seen in 14.3% of tested Klebsiella specimens and 15.4% of tested Proteus specimens. Additionally, a significant number of tested urine culture specimens displayed resistance to commonly prescribed outpatient medications, including trimethoprim (E. coli 30.9%, Klebsiella 57.1%, Proteus 38.5%) and less so nitrofurantoin (E. coli 11.6%, Klebsiella 14.3%, Proteus 53.8%). In addition, tested Staphylococcus species demonstrated significant resistance to some commonly used outpatient antibiotics (36.3% trimethoprim, 27.2% third-generation cephalosporins), less so other antibiotics (4.5% clindamycin, 9% second-generation cephalosporins). Further studies should attempt to develop a full program of antibiotic stewardship at Blantyre Adventist and other regional hospitals, assessing resistance genes, uniform identification and susceptibility testing across locations, and provider education.

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SPATIAL PATTERNS OF HANSEN'S DISEASE AND WASH RISK FACTORS IN MINAS GERAIS, BRAZIL

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The mode of transmission of *M. leprae*, the causative agent of Hansen's Disease (HD), remains uncertain due to the long incubation period of HD and the inability to culture *M. leprae* in the lab. Our research investigates the role of environmental and household-level water, sanitation, and hygiene (WaSH) factors on HD transmission. We conducted a cross-sectional study of 1,315 participants living in four municipalities of a HD-endemic area of Minas Gerais, Brazil. Data were collected on participants' *M. leprae* infection status and household WaSH factors. *M. leprae* infection was determined via antibody testing against LID-1, a recombinant *M. leprae* protein. Among the study population, the highest anti-LID-1 positivity rates were found in the municipality of Mantena (12.26%). Clustering of anti-LID-1 positivity was identified using the Kuldorff spatial scan statistic and relative risk surfaces. Due to the large areas between municipalities where data were collected, clustering was examined on both a regional scale encompassing all of the study data as well as at the municipality level. Examining the whole region, clustering of anti-LID-1 positivity was identified in the municipality of Mantena. Selected household-level WaSH factors were not significant using logistic regression controlling for residence in rural areas, suggesting other factors associated with rural residence may be driving HD transmission. To investigate this, we plan to incorporate neighbors' household WaSH characteristics and environmental characteristics including elevation and proximity to natural water source.

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THE IMPACTS OF THE CROSSTALK BETWEEN BACTERIAL VAGINOSIS ASSOCIATED BACTERIA AND *TRICHOMONAS VAGINALIS* ON THE PATHOGENESIS AND HOST IMMUNE RESPONSES

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Bacterial vaginosis (BV) is an enigmatic polymicrobial condition characterized by a depletion of health-associated *Lactobacillus* and an overgrowth of anaerobes. Trichomoniasis, caused by *Trichomonas vaginalis*, is a common infection of the urogenital system. Notably, BV-associated bacteria (BVB) and *T. vaginalis* are linked to adverse gynecologic outcomes, including an increased risk of sexually transmitted infections and cervical cancer. In this study, we aim to investigate whether BVB act as pathobionts of *T. vaginalis* infection by altering pathogenic capabilities of the parasite, focusing on adhesion to vaginal substrates and regulation of host immune responses. We established a co-culture system to investigate the interaction of *T. vaginalis* and vaginal bacteria (*Lactobacillus crispatus, Escherichia coli, Prevotella bivia*, and *Lactobacillus iners*), forming a polymicrobial infection on ectocervical cell (Ect). The gene expression of *T. vaginalis* adhesin AP65 was significantly increased after the interaction with *P. bivia*. Upon interaction with *P. bivia*, promoting *T. vaginalis*growth,and affected the survival of Ects, causing higher cytotoxicity and upregulation of IL-6, IL-8, CXCL1, and IP-10. However, *L. crispatus* suppressed the *T. vaginalis*-induced chemokines. Additionally, the crosstalk between *T. vaginalis* and *P. bivia*activated of PI3K, ERK1/2, and MAPKpathways, enhanced the EMT event (the loss of E-cadherin and increased expression of Snail) in Ect, and promoted the pathogenic effects of the parasite. Together, this study demonstrate the impacts of the crosstalk between BVB and *T. vaginalis* on the pathogenesis and host immune responses, and BVB accompanying by *T. vaginalis* infection function as pathobionts to enhance the pathogenic capabilities of this parasite.

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PHYLOGENETIC AND PHENOTYPIC CHARACTERIZATION OF *BURKHOLDERIA PSEUDOMALLEI* ISOLATES FROM GHANA REVEALS A NOVEL SEQUENCE TYPE AND COMMON PHENOTYPES

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We previously confirmed the presence of *Burkholderia pseudomallei* in the environment of Ghana, unmasking a new area of endemicity for this tropical pathogen. Here, we describe the genetic characteristics of isolates obtained from that environmental survey. Twenty-one isolates were subjected to whole genome sequencing and found to represent three discrete sequence types (ST), one of which was novel, and designated ST 2058. Phylogenetic analysis places this novel isolate within a *B. pseudomallei* clade that includes genomes derived from the Americas, although it is closely related to a sub-clade that includes isolates from Burkina Faso. Importantly, phenotypic characterization demonstrates common features including API20NE profiles and *B. pseudomallei* CPS to support existing diagnostics, and susceptibility to standard of care antibiotics often used in the clinical management of melioidosis. These findings add to our knowledge about the presence and distribution of *B. pseudomalle*i in Africa and represent the first published genomes out of Ghana.

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REAL TIME PCR-HIGH RESOLUTION MELTING ANALYSIS FOR PATHOGENIC *LEPTOSPIRA* SPP. IDENTIFICATION

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Leptospirosis is an important zoonotic disease widespread worldwide. The etiological agent, *Leptospira* spp., is a highly heterogeneous bacterial genus divided into pathogenic and saprophytic species. The high resolution melting (HRM) analysis was already described as an important tool for *Leptospira* spp. typing at the species and subspecies levels. The present study aims to evaluate the performance of real time PCR-high resolution melting (qPCR-HRM) analysis, targeting the housekeeping gene *mre*A, in the identification of pathogenic species of *Leptospira* spp. isolated from human cases of leptospirosis. Eighteen reference strains belonging to five *Leptospira* pathogenic species (*L. interrogans*, *L. kirshneri*, *L. noguchii*, *L. borgpetersenii* and *L. santarosai*) and six strains isolated from Brazilian human blood cultures were initially selected for this study. Human isolates were previously identified at species level by 16S DNA sequencing. All the strains were obtained from the *Leptospira* Collection/IOC/Fiocruz. Primer pairs *mre*A-1 and *mre*A-2 were designed based on the *in silico* analysis of the core genomes of these species deposited at the GeneBank. Amplification reactions were performed with 2X Type-it HRM PCR Kit (Qiagen) using the Rotor Gene-Q (Qiagen) instrument. HRM analysis was obtained using the software Rotor Gene Q Series version 2.3.2.(Qiagen). The qPCR-HRM assay using the primer pair *mre*A-2 was able to successfully distinguish *L. interrogans, L. kirshneri* and *L. noguchii*, although with low accuracy, and improvements in our qPCR-HRM assay are still necessary. On the other hand, primer pair *mre*A-1 produced distinct melting curve profiles for *L. borgpetersenii* and *L. santarosai* (Tm 84.4 and 85.6°C, respectively). This is an important finding since *L. santarosai* was already described as one of the predominant species in many countries from Central and South America. The qPCR-HRM assay we designed could be a simple tool for species identification, especially considering the prevalence of *L. santarosai* in Brazil.

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MULTI-DRUG THERAPY IS REQUIRED TO EFFECTIVELY TREAT *BARTONELLA* INFECTION IN DIFFERENT ENVIRONMENTS

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Bartonella is a gram negative, facultative intracellular bacterium that manifests as different clinical syndromes collectively known as bartonellosis. The well-known diseases caused by these bacteria are cat scratch disease (*Bartonella henselae*), trench fever (*Bartonella quintana*) and Carrion's disease (*Bartonella bacilliformis*). Excluding *B. bacilliformis*, which is evolutionarily more distinct than the 30+ other species, *Bartonella* infections often result in subclinical or undiagnosed disease that is left untreated. Individuals with compromised immune systems may experience life-threatening clinical manifestations. Bartonellosis can affect cardiac, circulatory, digestive and neurological function and needs to be treated with effective antibiotics. To date, there is no standard treatment course for these infections and many doctors prescribe antibiotics based on limited case studies. It has been shown that *Bartonella* can grow extracellularly, intracellularly, and in biofilms. To determine an effective antibiotic strategy, it is important to understand *Bartonella* susceptibility in each of these growth conditions. **We hypothesize that combination antibiotic treatments are required to effectively eliminate *Bartonella quintana* and *Bartonella henselae* growth, particularly in biofilm and intracellular environments**. Our previous work has shown that *B. henselae* treatment with single antibiotics in different media, as well as in DH82 canine macrophages, was ineffective in eliminating bacteria. We plan to expand this work with different antibiotics supported by case reports, as well as double and triple combination therapy in erythrocytes and biofilms. The following antibiotics were tested: doxycycline, gentamicin, azithromycin, azlocillin, rifampin, tobramycin and clarithromycin. We found that while monotherapy may inhibit growth extracellularly, it is ineffective when used against intracellular bacteria or pre-existing biofilms. The effectiveness of combination therapy supports the notion that *Bartonella* species utilize target cells and biofilms as an antibiotic tolerance strategy.

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EPIDEMIOLOGY OF INVASIVE *STAPHYLOCOCCUS AUREUS* IN PATIENTS SEEN AT AN OUTPATIENT CLINIC IN THE GAMBIA

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Staphylococcus aureus is a major cause of infection globally, particularly in low-and middle- income countries. In The Gambia, *S. aureus* is a common cause of infection in children. However, comprehensive data on the epidemiology of and antibiotic susceptibility of *S. aureus* is limited. We describe the epidemiology and antibiotic susceptibility of invasive *S. aureus* causing invasive disease in The Gambia. 134 *S. aureus i*solates obtained from clinical specimens of patients seen between 2018 and 2020 at the MRCG at LSHTM outpatient clinic in Fajara, The Gambia were analyzed. *S. aureus* strains were characterized using Multilocus Sequence Typing (MLST) and antimicrobial susceptibility was determined using the Kirby-Bauer disc diffusion method. 60.3% of strains were recovered from males while children < 2 years contributed the highest number of isolates (65.0%). 82.6% of the isolates were obtained from blood cultures. Antibiotic susceptibility to trimethoprim-sulphamethoxazole, chloramphenicol, cloxacillin and methicillin was 12.7%, 97.0%, 97.0% and 96.3% respectively. MLST identified 10 Sequence Types. Our study has provided essential information on invasive *S. aureus* strains in The Gambia. Antibiotic susceptibility patterns show that invasive *S. aureus* infections can be successfully treated with widely available antibiotics in The Gambia. Methicillin Susceptible *Staphylococcus aureus* (MSSA) strains continue to be the major cause of invasive staphylococcal infection in The Gambia. Discovery of Methicillin Resistant *Staphylococcus aureus* (MRSA) strains although in small numbers emphasizes the need for continuous surveillance and better antibiotic stewardship to avoid increase in antibiotic resistance.

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CLINICAL CHARACTERIZATION OF HUMAN LEPTOSPIROSIS IN A REGION OF THE COLOMBIAN CARIBBEAN

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Leptospirosis is the emerging and re-emerging zoonosis with the highest distribution and prevalence worldwide with important repercussions on human and animal health. A prospective longitudinal descriptive study was carried out, with non-probabilistic sampling, which included 339 patients suspected of leptospirosis during July 2017 to February 2021. The cases were confirmed by the Microagglutination Test (MAT) and Polymerase Chain Reaction (PCR). The 16S rRNA gene amplification products obtained from blood or urine samples of confirmed patients were sequenced. 67 cases of the 339 suspects were confirmed. The most frequent serogroups associated with acute cases were Sejroe, Australis and Pomona. The 16S rRNA gene sequences showed L. *interrogans* and L. *borgpetersenii* as species associated with acute cases of leptospirosis. At the time of admission, the symptoms reported by the positive patients showed that 86.6% (n=58) presented the triad of symptoms: fever, headache and myalgia. In 40.3% (n=27) of cases, the triad was accompanied by jaundice and in 17.9% (n=12) by hepatomegaly. For the operational case definition, there is a greater possibility of having leptospirosis when patients presented hepatomegaly, jaundice, conjunctival injection, triad plus jaundice and triad plus hepatomegaly with statistically significant differences. In the early stages of the disease, patients with the presence of the triad (fever, headache and myalgia) associated with conjunctival injection were more likely to suffer from the disease. This symptomatology must be taken into account for the operational case definition in the study area. Leptospirosis clinical protocols in Colombia should include not only diagnostic but also clinical algorithms that guide the timely and adequate management of the disease, whose transmission is not only occurring in rural areas as has traditionally been described, but also in the urban environment.

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SEROLOGICAL ASSESSMENT OF *HELICOBACTER PYLORI* INFECTION AND ITS ASSOCIATED RISK FACTORS IN ASYMPTOMATIC GHANAIAN PATIENTS, ATTENDING AGONA GOVERNMENT HOSPITAL

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Helicobacter pylori infection poses a considerable global health challenge, exhibiting high prevalence rates in developing countries. This disease lacks a definitive treatment in Ghana and is often treated with a combination of antibiotics— posing risk of antibiotic resistance. Evidence suggests that gastric cancer risk might increase due to helminths colonizing the gastric epithelium following H. pylori-induced gastric atrophy. We carried out a cross-sectional clinical survey in Ghanaian asymptomatic patients to determine the exposure rate of *H. pylori* infection, the presence of intestinal helminthic flora, and identify related risk factors for gastro-duodenal diseases. A 2ml venous blood and 3 g stool samples were collected from 275 asymptomatic patients (mean age: 29.4 ± 9.2 years) for serological tests that detected *H. pylori* serum antibodies (human IgG) and stool antigens. A portion (1 g) of the stool samples was analyzed for intestinal helminthic flora using the formo-ether concentration technique. Structured questionnaires were utilized to collect demographic information and assess risk factors. Serum antibody testing revealed *H. pylori* exposure in 63.3% of participants, while 71.3% tested positive for *H. pylori* stool antigens. Females exhibited higher positivity rates for both tests (72.3% for stool, 65.1% for serum). More individuals (60.7%) tested positive for both *H. pylori* serum antibodies and stool antigens. Microscopic examination showed that 90.6% of the participants had no intestinal helminths. Employment status did not significantly affect *H. pylori* positivity rates (X^2=01.92; p=0.908). Logistic regression identified a long-term high-fat diet as a significant predictor of *H. pylori* occurrence (p=0.003). The high exposure and occurrence of asymptomatic *H. pylori* infection in the study area highlights the need for routine screening and early intervention to prevent the development of serious gastro-duodenal diseases. Targeted public health efforts should address modifiable risk factors like dietary habits to reduce the burden of *H. pylori*-related morbidity.

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ASSESSING PROGRESS TOWARDS THE ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF SYPHILIS IN PERU

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To eliminate and control the mother-to-child transmission (MTCT) of Syphilis, the World Health Organization (WHO) recommends meeting the following targets: (1) 95% coverage of syphilis screening during pregnancy, (2) reducing the incidence of congenital syphilis in less than or equal to 0.5 cases per 1000 newborns, and (3) 90% reduction in the incidence of maternal syphilis between 2018 and 2030. We evaluated the progress in the Peruvian context at the national and department level. A retrospective epidemiological analysis was performed using national data collected by the Peruvian Ministry of Health of reported cases of congenital and maternal syphilis from 2015 to 2022. The incidence rates were calculated by dividing the number of cases over the number of live births each year by department. Syphilis screening and sociodemographic data were obtained from The Demographic and Health Survey (DHS). In addition, we described departments with higher rates of congenital and maternal syphilis and higher percentages of extreme poverty and low maternal education (primary or no education). In 2022, nationwide syphilis screening during pregnancy was 82.6% (95% CI: 80.7% - 84.5%), the congenital syphilis rate was 0.82 cases per 1000 newborns, and the maternal syphilis rate increased by 53.7% from 2018. At the department level, only one department achieved all targets; 14, either target (2), (3) or both; while 10, didn't meet any targets. Among those living in extreme poverty, the jungle region exhibited the highest rate of congenital syphilis. Additionally, for maternal syphilis, this trend extended to include the highlands. When stratified by low maternal education, the jungle showed the highest rate of congenital syphilis, whereas for maternal syphilis, the north coast of Peru stood out. This study found that none of the Syphilis MTCT targets proposed by the WHO were met in Peru in 2022. Decentralized strategies are needed to achieve the goals of syphilis screening coverage and reduction of syphilis incidence by 2030.

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BACTERIOLOGICAL PROFILES OF DIABETIC ULCERS IN CASES OF MAJOR LIMB AMPUTATION: INSIGHTS FROM SOLOMON ISLANDS

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Solomon Islands is a Pacific island country with a 19.8% estimated diabetes prevalence. Diabetic patients there face limited access to medical care leading to poor glycemic control and increased risk of diabetic ulceration. This retrospective study describes the microbiota of diabetic ulcers in cases of major limb amputation in Solomon Islands. It is the first report

of microbiological data from diabetic ulcers in the nation. Demographic, microbiological, and outcomes data was collected from the records of patients with diabetes who underwent major limb amputation in Solomon Islands between 2018-2023. Summary and univariate analysis were conducted. Among 338 adults who underwent major limb amputation during the study period, 33% (N=113) had microbiological data available for abstraction. The median age was 53 (range: 22-83) and 58% were male (N=65). A total of 20 species were identified via pus and tissue culture. The most common species were *Pseudomonas aeruginosa* (N=27, 24%), *Enterococcus* spp. (N=25, 23%), and *Klebsiella pneumoniae* (N=18, 16%). MRSA was identified in one patient. 55% (N=62) of cultures demonstrated resistance. Resistance against ampicillin (N=31), amoxycillin (N=31), gentamycin (N=21), and Trimethoprim/sulfamethoxazole (N=21) were most common. On univariate analysis, colonization with *E. coli*, *K. pneumoniae*, and *Enterococcus* spp. was significantly associated with antibiotic resistance. The relative predominance of *Pseudomonas*, *Enterococcus*, and *Klebsiella* species is consistent with prior research on the microbiota of diabetic infections. Despite limited data, cultures from this cohort were diverse, including rarer opportunistic species such as *P. agglomerans* and *P. gergoviae*. The high percentage of resistance is concerning given the limited access to next generation antibiotics in Solomon Islands. Data gaps prevented assessment of the appropriateness of antibiotic selection. Further research is needed to better understand local infection management practices, factors contributing towards resistance, and clinical outcomes from antibiotic-resistant infections in Solomon Islands.

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HANSEN'S DISEASE (LEPROSY) IN THE UNITED STATES OF AMERICA: A SYSTEMATIC REVIEW

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Hansen's disease, also known as leprosy, is a chronic infectious disease that is caused by the bacteria *Mycobacterium leprae* and, more rarely, by *M. lepromatosis*. It is primarily spread through respiratory droplets from person to person but can also be transmitted zoonotically from nine-banded armadillos and some other mammals. The condition commonly affects the skin, peripheral nerves, mucous membranes, and extremities and occasionally impacts internal organs. Patients often face chronic impairments in both their physical and mental health. A systematic review of all published U.S. cases of leprosy has not been undertaken prior. This study's aim was to characterize all scientifically published case reports and case series of leprosy diagnosed in the U.S. Four databases were searched for relevant studies published in English up to 6/2/2023. A total of 133 case reports and series, from 1896 to 2023, met selection criteria. From these, 328 unique cases were identified. Median age was 43 years (range: 3.5 - 87 years). Most were male (79.9%) and White (51.5%), followed by 13.4% Asian and 10.4% Black. One-third presented to the National Hansen's Disease Program (NHDP) in Louisiana. State of residence and state of diagnosis trends aligned. A majority identified the U.S. as their country of origin and resided in regions providing NHDP resources. Prior to 1960, most cases were linked to military service abroad (86.5%); however, mode of transmission was usually unknown. A growing proportion of cases has been linked to zoonoses (22.8%) since 1980. Skin biopsy remained the dominant diagnostic modality (61.6%) through 2023, with PCR utilized more since 2000. By Ridley-Jopling classification, most cases (47.3%) were lepromatous. By WHO classification, when information was reliably available, 21.8% were multibacillary and 8.3% were paucibacillary. Multi-drug regimens have dominated treatment protocols since 1980, but other antibiotics have been increasingly used over the past decade. Studies reporting leprosy in the U.S. are limited overall. This systematic review comprehensively informs on past and present trends of leprosy in the U.S.

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COXBASE GOES WIKI - HOW TO CREATE SUSTAINABILITY FOR GENOMIC Q FEVER DATA.

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Q fever is a wordwide distributed zoonotic disease, caused by the Gram-negative bacterium *Coxiella burnetii*. It primarily affects livestock and animals but can also be transmitted to humans through direct contact with infected animals or contaminated animal derived materials in the environment via aerosols. CoxBase (https://coxbase.q-gaps.de/) is an online platform for epidemiological surveillance, visualization, analysis and typing of Coxiella brunetii genomic sequence and for tracking outbreak. It is maintained and closely monitored by a small team of experts from German Interdisciplinary Program "Q-GAPS - Q fever GermAn Interdisciplinary Program for reSearch" (https://q-gaps.de/). It aims to gather and display information about isolates discovered all around the world. The dataset of CoxBase provides a deep dive into epidemiological information about a bacterium and its distinctive resilience little is known about. Wikibase is a versatile open-source software platform developed by the Wikimedia Foundation. It provides the infrastructure and tools needed to create, manage, modify and query data. The best known instance is Wikidata (https://www.wikidata.org/), which host more than 1 Billion items and is maintained by a large, global community of contributors. Wikibase offers an easy to use web-interface to enter the primary structured data and can be efficiently queried via SPARQL (SPARQL Protocol And RDF Query Language.) and connected to other knowledge graphs.Here we would like to present how the genomic data of CoxBase was integrated into a dedicated Wikibase instance. The resulting resource offers all the benefits of Wikibase including an easy way to curate data collaborativly, querying it with a powerful language and connecting it with other resources. In addition we hope that this would be a model for the future to produce sustainability for genomic data - independent from research projects and their grants.

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ROLE OF ACRAB AND OQXAB EFFLUX PUMPS IN AMIKACIN AND CIPROFLOXACIN RESISTANCE AMONG CLINICAL ISOLATES OF KLEBSIELLA PNEUMONIAE IN LIMA, PERU

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Klebsiella pneumoniae is the most significant pathogen and is associated with one of the highest global mortality rates, with an average pooled mortality. The WHO has designated this bacterium as a top-priority target for research on novel antimicrobials, due to its raising antibiotic resistance. We conducted is study to determine the prevalence of the AcrAB and OqxAB efflux pumps in clinical isolates *K. pneumoniae* and their role in amikacin and ciprofloxacin resistance. The clinical samples identified as *Klebsiella pneumoniae* collected from in patients hospitalized from Lima, Peru. Antimicrobial susceptibility testing was conducted using the microdilution method. The susceptibility to antibiotics was evaluated in the presence and absence of the inhibitor CCCP and PaβN efflux pumps. Efflux pump resistance genes AcrA, AcrB, OqxA, and OqxB were amplified using the polymerase chain reaction amplification technique. We found that 100% of the isolates of *K. pneumoniae* were resistant to amoxicillin-clavulanic acid, cefotaxime, ceftazidime, cefuroxime, ertapenem, gentamicin, imipenem, meropenem and tobramycin. The 93.75% were

resistant to ciprofloxacin and piperacillin/tazobactam; 87.5% were resistant to trimethoprim/sulfamethoxazole; 56.25% were resistant to fosfomycin; 25% were resistant to levofloxacin and 18.75% to amikacin. The exposure to the PaβN inhibitor, an increase in susceptibility was observed in clinically resistant strains to amikacin, and strains resistant to ciprofloxacin show susceptible with both inhibitors. In the case of CCCP addition to ciprofloxacin, 18.75% exhibited a fourfold decrease and 56.25% displayed a threefold decrease in MIC, with 25% remaining unchanged. The prevalence of resistance genes show AcrA gene was detected in 43.75% isolates, the AcrB gene in 56.25%, OqxA in 31.25%, and OqxB in 25.00%. In conclusion, our findings suggest that efflux pumps are major mechanisms for ciprofloxacin and amikacin resistance in *K. pneumoniae*, with the AcrAB and OqxAB systems being significant contributors to this resistance

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PREVENTION AND CONTROL OF HYDATID CYST: STRATEGIES, CHALLENGES, AND FUTURE DIRECTIONS

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Background: Hydatid cyst, caused by the larval stage of Echinococcus tapeworms, is a significant public health concern worldwide but mainly in Africa. Understanding the strategies, challenges, and future directions in hydatid cyst prevention is essential for developing effective interventions and promoting global health.Objective: This abstract aims to provide an overview of the current strategies employed for the prevention and control of hydatid cyst, highlight the challenges faced in implementing these measures, and discuss potential future directions for improved prevention strategies.Methods: A review of the literature was conducted by searching electronic databases including PubMed, Scopus, and Embase. Relevant articles published between 1960 and 2021, including research studies, reviews, and public health reports, were analyzed and synthesized to provide a comprehensive overview.Results: Various prevention strategies have been implemented to combat hydatid cyst, including public health education, surveillance and control programs, veterinary interventions, and improved sanitation and hygiene practices. Future directions for hydatid cyst prevention include the development of novel diagnostic tools, vaccines, and targeted interventions, as well as strengthening collaboration between human and veterinary health sectors.Conclusion: Prevention and control of hydatid cyst necessitate a multi-faceted, integrated approach that addresses the complex interplay between human, animal, and environmental factors. Collaboration between researchers, policymakers, healthcare professionals, and communities is crucial to achieving sustainable prevention and control efforts.Keywords: hydatid cyst, echinococcosis, prevention, control, interventions, strategies, challenges, future directions.

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CLINICAL MANAGEMENT AND RECURRENCE OF HUMAN CYSTIC ECHINOCOCCOSIS IN A SECONDARY HEALTHCARE CENTER OF A HIGHLY ENDEMIC AREA IN THE ANDES OF CUSCO, PERU

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Cystic echinococcosis (CE) management in low- and middle-income countries remains a challenge due to advanced disease at presentation, limited resources and lack of standardization of care. Surgical outcomes including recurrence rates are unknown. Up to 45% CE patients in tertiary hospitals of Cusco City are referred from the Sicuani District. We reviewed medical records of 115 patients with CE admitted to a secondary care hospital in Sicuani from January 2010 to December 2019. The median age was 25 years (IQR, 16-46) and 60.5% were female. Fifty-six patients (48.7%) were referred from primary care centers. Liver cysts were diagnosed in 106 patients (92.2%), lung cysts in 5 (4.3%), and combined liver/lung cysts in 4 (3.5%). The median duration of symptoms was 21 days (IQR, 3-89 days). The median length of stay was 7 days (IQR, 5-10). Pre-surgical complications were documented in 46 cases (40%). One hundred seven patients (93%) had an ultrasound, identifying 134 liver cysts. The median largest liver cyst diameter was 13 cm (IQR, 9.2-15.2). Eighty-four patients (62.7%) had single cysts, 19 had two cysts, and 12 patients had 3 cysts. Eighty-one cysts (58.3%) were staged: 28 (34.6%) were Gharbi I, 31 (38.3%) Gharbi II, 17 (21%) Gharbi III, and 5 (6.2%) Gharbi IV. Of the 102 (88.7%) surgically treated patients, 57 (55.9%) received albendazole (ABZ) after surgery, 27 (26.5%) before and after surgery, 7 (6.9%) did not received it, 6 (5.9%) before surgery, and in 5 the timing was not specified. Anti-spillage measures were documented in 11 (9.6%) patients. Fourteen out of 110 (12.7%) were readmitted to the hospital, 8 for cyst recurrence (new cyst, same site), 4 for complications, 3 for elective two-stage treatment, and 1 for a new cyst (different site). Considering past medical history, readmissions, and follow-up, the recurrence rate was 16/115 (13.9%). The patients admitted to this secondary care hospital in a highly CE endemic area presented advanced disease and complications. Surgery was the main stage-specific treatment implemented. The high recurrence rate created a burden that could be effectively reduced with spillage prevention and peri-operative ABZ.

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SUBARACHNOID NEUROCYSTICERCOSIS: CLINICAL, SEROLOGICAL AND NEUROIMAGING EVOLUTION AFTER ANTIPARASITIC TREATMENT

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Neurocysticercosis (NCC) presenting in the subarachnoid space, represents the most aggressive form of the disease. The cysts' growth within this space tends to be uncontrolled and diffuse, often resulting in mass effects and triggering immune responses in surrounding tissues, that may lead to arachnoiditis or even vasculitis. Data on the efficacy of antiparasitic treatment in subarachnoid NCC remain scarce, leaving healthcare providers and patients without clear guidance on therapeutic outcomes. This cross-sectional study assessed the clinical, serological, and imaging evolution of 80 individuals with a history of subarachnoid NCC who received antiparasitic treatment at least two years before. Seventeen participants (23.6%) continued presenting subarachnoid NCC lesions. From these, 15 (82.35 %) had positive levels of circulating parasite antigen, most of them at high levels (11/15, 73.3%, with rations above 20, and 4 (26.6%) with ratios between 1-3). All cases continued having positive antibody responses on EITB (western blot), with 11 reacting to all 7 diagnostic bands. Univariate analysis showed that individuals with high antigen levels had 43.1 times the OR compared to those who have a negative antigen ratio, individuals with 60 years more have 6.75 the OR of having lesions compared to those age less than 45 years (CI 95% 1.33-34.26, p=0.02), patients with continuous crisis have 3.9 (CI 95% 1.03-15.03, p=0.04) times the OR compared to those who did not have seizure activity per every increase in one reactive antibody band on EITB the OR of having lesions increases by a factor of 2.9 (CI 95% 1.7-4.9, p<0.001). Multivariate analysis showed strong evidence that those who have high antigen ratio have 39.9 times the OR of having lesions compared to those who have a negative result p=0.017, when adjusted by sex, age, clinical symptoms (headache and seizures) and WB. Incomplete cure of subarachnoid NCC occurs in a sizable proportion of

patients, and serological results (in particular very high antigen levels) are strong predictors of treatment failure.

Keywords: subarachnoid, neurocysticercosis, evolution, recurrence

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EXPERIMENTAL INFECTIONS DEMONSTRATE CONCOMITANT IMMUNITY AGAINST *TAENIA SOLIUM* IN PIGS: QUANTIFYING THE IMPACTS OF AGE AND PRIOR INFECTIONS ON THE NUMBER OF CYSTS

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Taenia solium is a major cause of epilepsy in low- and middle-income countries. Important efforts have been made to control and eliminate this parasite but, due to the high costs of large-scale field testing, it is difficult to experimentally validate the optimal strategy. Mathematical models are therefore also used to help design cost-effective strategies, but knowledge gaps around the existence and extent of pig immunity hamper the representation of transmission in endemic settings. In this study, we show that pig immunity constrains cyst development, and we quantify this effect. In a first experiment focusing on the impact of age, six groups of pigs (48 pigs in total) between 4 and 22 weeks old were infected with 20,000 eggs each. In a second experiment focusing on the impact of prior infections, 80 pigs were either infected with 100, 1,000, 5,000 or 20,000 eggs at 4 weeks old and reinfected after 12 weeks with 5,000 or 20,000 eggs, or infected only once, at the time of the first or second infection. To decrease the variability in results, pigs were infected in individual pens with eggs coming from a pool of up to 10 tapeworms with more than 75% of activated oncospheres. The first experiment showed that the ratio of viable cysts to eggs ingested first increased with age at infection, up to approximately 10-16 weeks old, then declined drastically in older pigs (KW test p=0.008). The second experiment showed that first exposure with as few as 100 eggs, almost entirely prevents the development of more cysts at reinfection, even with high re-exposure doses, with no statistical differences between infected and reinfected pigs. Despite extensive efforts to control for variability in infective doses, the number of cysts varied a lot between individual pigs within each group. In conclusion, age at infection and prior exposure affect cyst development in pigs. These factors may explain why low number of cysts are routinely found in endemic regions, usually fewer than 10 per animal, despite high transmission levels. The parameters we have obtained will be incorporated into simulation models to replicate the distribution of cysts found in pigs from endemic settings.

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ECHINOCOCCOSIS: ASSESSING SURVEILLANCE NEEDS FOR AN EMERGING INFECTIOUS DISEASE IN THE UNITED STATES

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Echinococcosis is caused by several species of zoonotic tapeworms and affects dogs and wild canids worldwide; sheep, cervids, and rodents are intermediate hosts. Two main species, *E. granulosus* and *E. multilocularis,* affect humans, who are accidental hosts. Infection causes enlarging lesions in multiple organs; rupture of cystic lesions can lead to anaphylaxis and death. During 1980-2010, no locally acquired human cases were described, but since 2010, nine such human cases have been identified in three states, along with infections in wild canids and domestic dogs. Recently, echinococcosis consultations to CDC increased from 32 in 2022 to 61 in 2023. Echinococcosis is not nationally notifiable and is reportable in only two states: Texas and Washington. Key stakeholders were identified from states where echinococcosis is reportable (n=2) and states with locally acquired human or animal cases (n=6). Stakeholders were interviewed during September-December 2023 using a semi-structured questionnaire and participated in group discussions. Responses were analyzed for thematic patterns around surveillance. The most common themes were desire for multi-state collaboration (n=8), interest in improving surveillance (n=7), and need for a One Health approach (n=6). No states had outreach materials, although the need was recognized (n=4). Surveillance in states where echinococcosis is reportable began in 2016 (Texas) and 2023 (Washington). Clinical criteria differ between these case definitions, and one state noted difficulty applying the criteria. Given the limited number of cases in any state, the need for a coordinated approach was identified. Subsequently, two multi-state working groups were established to develop a standardized case definition and outreach materials for pet owners, hunters, farmers, veterinarians, and public health professionals. Because this emerging disease is rare, aggregating standardized human case data at CDC would help stakeholders understand the risk for transmission in the US and develop prevention strategies. Further, outreach materials would raise awareness around reporting potential cases.

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POVERTY LEVELS ASSOCIATED WITH THE PREVALENCE OF LIVER CYSTIC ECHINOCOCCOSIS IN A PERUVIAN RURAL COMMUNITY

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Human cystic echinococcosis (CE) is a zoonotic parasitic disease categorized among the most neglected diseases. It detrimentally impacts the economy and the quality of life of affected individuals. While associations with poverty-related factors have been observed, these relationships have not been thoroughly assessed using appropriate methods. The current study aims to determine the influence of poverty on the prevalence of CE within the livestock-rearing community of Canchayllo, Peru. For this analysis, a secondary examination was conducted on a convenience sample of 138 individuals selected from a dataset of 232 subjects. The selection criteria included only those who responded to the survey designed to measure the Wealth Index. A generalized binomial regression model with a log link function was used to evaluate the association between the presence of liver CE and levels of poverty. Poverty was classified into two categories: high poverty (1st and 2nd wealth index quintiles) and non-high poverty (3rd to 5th wealth index quintiles). The analysis adjusted for screening coverage and other covariates. The findings indicate a liver CE prevalence of 13.04% (95%CI: 7.42 - 18.66) and a prevalence ratio (PR) of 2.35 (95%CI: 1.17 - 4.73, p=0.016) between groups with high levels of poverty compared to those with non-high levels of poverty, after adjusting for sex, gender, and screening coverage. Some variables like sheep raising were excluded from the model due to multicollinearity with the wealth Index. The results demonstrated a significant correlation between the level of poverty and the prevalence of liver cystic echinococcosis, thereby confirming the influence of poverty on the development of the disease.

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ALVEOLAR ECHINOCOCCOSIS: NOT JUST IN ENDEMIC COUNTRIES

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Alveolar echinococcosis (AE) is a zoonosis caused by the larval form of *Echinococcus multilocularis*, a cestode endemic in Asia, especially China, Turkey and north-eastern European countries. *E. multilocularis* has a sylvatic life cycle, where foxes act as definitive hosts and rodents as intermediated hosts. When the intermediate host ingests eggs of *E. multilocularis* excreted by the definitive host with feces, the larval stage can develop. Humans are accidental intermediate hosts, after ingesting contaminated foods. Until 2023, no cases of AE had ever been reported in Italy, and the first case was reported in February 2024. Here we report a second case of AE diagnosed in Italy. A 87-year-old Swiss woman living in Italy, was seen in a Hospital in northern Italy for a painful epigastric mass ,not dissociable from the gastric wall, pancreas and liver, with peripheral contrast enhancement at CT scan. An esophagogastroduodenoscopy excluded the gastric origin of the mass. The patient was diagnosed with liver neoplasm of unknown origin. Chemotherapy was excluded due to her age and performance status. No biopsy was performed. However, serology for CE returned positive and she was referred to our center. Ultrasound showed a roundish inhomogeneous mass 11 x 7 x 12 cm in diameter, with ill-defined margins, anechoic central areas, calcifications and small cystic images within. While this appearance was not consistent with CE, the Swiss nationality of the patient prompted us to inquire about contact with foxes in her home country, which she reported. AE was therefore suspected and confirmed by serology. The patient was referred to a center for AE in Switzerland where she was staged as P4 N0-1 M1 for the presence of metastatic lesions in the lung. Albendazole at 100 mg/die was started for the presence of biliary tree compression, with of resolution of epigastric pain after few weeks . She is clinically stable and asymptomatic at the time of this writing. AE is a rare but potentially fatal parasitic disease if not diagnosed and left untreated and should be included in the differential of neoplastic lesions in selected cases also in non-endemic areas.

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SURGICAL TECHNIQUES AND COST ANALYSIS OF PULMONARY ECHINOCOCCOSIS: A SINGLE CENTER EXPERIENCE

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Surgery is the established therapy for thoracic echinococcal cysts, but there is no consensus about the optimal surgical method. Options include lobectomy, segmentectomy, or cystostomy with closure of bronchial openings and capitonnage. The choice depends on several factors such as cyst integrity, quantity, location in the lung, associated lung tissue damage, and costs. Each surgical approach carries its own disadvantages and potential benefits, and a careful assessment of the individual patient's condition and the medical team's expertise is crucial. We report our experience with surgical techniques and costs in the treatment of thoracic echinococcosis (TE). We reviewed hospitalization expenses and surgical techniques used in the treatment of 11 patients with TE admitted to the Thoracic Surgery Ward at 'Santi Antonio e Biagio e Cesare Arrigo' Hospital in Alessandria, Italy from May 2023 to March 2024. The total expenditure for a single hospitalization, encompassing both hospital stay and surgical intervention, ranged from €7754.387 to €19160.987. Cystostomy with closure of bronchial openings and capitonnage was the primary surgical approach. Our data indicate that a more conservative approach, such as cystostomy, yields superior surgical outcomes, consistent with the literature. Despite incurring slightly higher costs than with lobectomy, the benefits offered by cystostomy outweigh this marginal expense difference. Given the relatively similar costs between the two procedures, opting for the more conservative surgery appears to be a prudent and therefore best choice.

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FORMALIN INJECTION LEADING TO CHEMICAL CHOLANGITIS IN SURGERY FOR ECHINOCOCCAL CYST: A CASE REPORT

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Cystic echinococcosis (CE) is a debilitating chronic infection predominantly affecting the liver and lungs. Various surgical options, including conservative (endocystectomy) and radical approaches (pericystectomy or segmentectomy), are employed in treatment. However, the intracystic administration of scolicidal agents is contraindicated in cases where connections to the biliary system are present, due to the risk of chemical cholangitis, a severe and feared complication.In this report, we present a case involving an Italian patient who, in 1993, underwent surgical resection of a hepatic CE cyst. The procedure involved the injection of formalin into the cyst cavity, followed by aspiration of its contents and pericystectomy. This outdated method led to the development of chemical cholangitis and multiple biliary strictures, necessitating the placement of several stents over time. The patient's condition progressively deteriorated, culminating in a liver transplant in 2016. Complications from this procedure included embolization of a hepatic artery pseudoaneurysm, ultimately necessitating a second transplant shortly thereafter.While no consensus exists on the optimal surgical technique for treating liver CE—owing to variables such as cyst stage, size, segmental location, and presence of complications—adhering to fundamental safety principles is imperative to prevent dire outcomes.

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A RARE CASE OF NEUROCYSTICERCOSIS WITH THE NORTHERN HEMISPHERE TAPEWORM *TAENIA CRASSICEPS*

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Neurocysticercosis occurs mainly in South America and Sub-Saharan Africa and is usually caused by larvae of *Taenia solium*. In Europe neurocysticercosis is not a common differential diagnosis for intracerebral lesions. In rare cases *Taenia crassiceps*, a tape worm, that is endemic in the northern hemisphere can cause neurocysticercosis. We present a case of *Taenia crassiceps* neurocysticercosis in a 72-year-old immunocompetent male.The patient presented in the emergency room with symptoms, that were suspected to be a stroke. There was no relevant medical history, especially no immunosuppression. A CT scan showed a cerebral lesion with atypical haemorrhage. Neurological symptoms resolved without intervention, hence a follow-up cerebral MRI scan of the lesion was performed after three months. This showed increasing perifocal oedema so that surgery was indicated. Macroscopically it appeared as a lesion with a rough shell and a fluid core. Histopathology showed no malignancy but the remnants of a cystic lesion with signs of chronic inflammation and small calcified bodies. A detailed travel and exposure history made the diagnosis of a parasitic disease highly likely. Neurocysticercosis seemed a potential differential diagnosis, however neither MRI nor histopathological findings were typical. Serology for cysticercosis was negative. A biopsy specimen was sent for a specific cestode PCR. The result showed DNA of the tapeworm species *Taenia crassiceps*. Given the paucity of published clinical case reports, therapy with praziquantel and albendazole was started, prednisolone was added. Therapy was well tolerated. *Taenia crassiceps* tapeworm infections have been described rarely in humans. Diagnosis is difficult on the basis of MRI-imaging and histopathological findings and needs high index of suspicion. Specific serological testing is not available; hence we are depending on molecular diagnostics. An immuncompromised host is not a precondition for infection. Reasons for the increasing number in infections as well as therapy can be discussed and need further investigation.

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PYROPTOSIS CELL DEATH IN RAT BRAIN TISSUE WITH NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is a parasitic disease affecting the central nervous system (CNS), whose infectious agent is the larval form of the parasite *Taenia solium*. The pathology of the disease is not fully understood, as it is a chronic disease affecting humans. Clinical manifestations include headache, dizziness, seizures and memory loss or cognitive deficits. During treatment, the clinical manifestations are exacerbated by the death or degeneration of the parasite. The clinical picture of NCC resembles other neurodegenerative diseases such as Alzheimer's, Parkinson's and multiple sclerosis, clinical manifestations that are associated with pyroptosis processes. Pyroptosis is a type of programmed cell death that plays a protective role against infections, but excessive pyroptosis can cause neuronal damage and be detrimental to normal cells and tissues. Therefore, in this research we determined whether the larval stage of *T. solium* causes pyroptosis cell death in the central nervous system in an animal model of NCC. Brain tissues from rats with NCC, untreated and treated with antiparasitic drugs, and a control group of brain tissues from non-infected rats were used. Immunoreactivity in tissues around the cyst was determined by immunohistochemistry for markers associated with programmed cell death: NLRP3 inflammasome, Caspase-1 (Casp1), Gasdermin D (GSDMD) and IL-1β. The immunoreactivity to GSDMD was elevated in all NCC-infected tissues, being statistically significant compared to brain tissues from non-infected rats. While immuoreactivity to NLRP3, Casp1, GSDMD and IL-1β markers was elevated in 30% of infected brain tissues, being the pattern of immuoreactivity different from the control. Our data suggest that there is pyroptosis-programmed cell death due to immuoreactivity to GSDMD in rat brain tissues with NCC.

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A ONE HEALTH SYSTEMATIC REVIEW OF ECHINOCOCCAL INFECTIONS IN CANADA

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Echinococcus canadensis and *multilocularis* are parasitic agents transmitted among animals, occasionally infecting humans. Despite being classified as neglected tropical diseases, echinococcal infections are believed to be emerging within the ranges of their wild definitive hosts across Canada. This study aims to consolidate and systematically review estimates of parasitic zoonoses frequency available in Canada. Considering that these parasites infect various host species and involve stages in the soil, an integrated One Health approach is imperative for obtaining an accurate epidemiological overview. A systematic review on the frequency of *E. canadensis* and *E. multilocularis* in humans, animals, and soil in Canada is currently underway following the PRISMA guidelines. We have developed a search query encompassing the names of the two parasites, the diseases they cause, and the Canadian provinces and territories. Three databases were searched for relevant articles. Subsequently, articles were imported into Covidence© software for assessment by two independent reviewers in two phases (title and abstract screening, followed by full-text review) following predetermined inclusion and exclusion criteria. These articles will undergo evaluation using modified JBI quality assessment checklists tailored for One Health studies. Data will be extracted on general study characteristics, population demographics, study design, diagnostic tests, and estimates for the outcome variable (prevalence, incidence, count). A total of 1152 unique articles were identified spanning from 1962 to 2023, of which 965 were deemed irrelevant after screening titles and abstracts. The remaining 187 articles are currently undergoing full-text review. This presentation will demonstrate the geographic distribution of the selected articles, the number of case reports for each host group, and where possible, the frequency trends over time for each host group. Additionally, the limitations of the existing JBI tools in addressing frequency measures concerning domestic and wild animals and the environment will be highlighted.

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COMPARISON OF THE DIAGNOSTIC ACCURACY OF LIVER ULTRASONOGRAPHY AND COMPUTED TOMOGRAPHY FOR CYSTIC ECHINOCOCCOSIS IN A NATURALLY INFECTED SHEEP MODEL

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Cystic echinococcosis (CE) is a major zoonotic disease in Peru's central highlands, where controlling this disease in animals requires significant interventions. Imaging methods are favored over serological tests for diagnosing CE due to the latter's cross-reactivity with other parasites. To evaluate the diagnostic accuracy of liver ultrasonography (US) and

computed tomography (CT) for detecting cystic lesions in sheep, using necropsy as the gold standard. We assessed the sensitivity and specificity of US and CT in sheep over four years old from an endemic area. Diagnostic criteria for US positivity were defined as any suspicious lesion, lesions ≥20 mm regardless of WHO stage, lesions in early stages (CE1, CE2, CE3) irrespective of size, and lesions ≥20 mm in stages CE1, CE2, and CE3. Necropsy data served as the basis for sensitivity and specificity estimates. Necropsy showed a CE prevalence of 82.3% (79/96). US sensitivity ranged from 18.4% to 84.6%, with specificity from 62.2% to 100%. CT sensitivity was between 26.5% and 92.3%, and specificity ranged from 35.6% to 100%. Concordance between US and CT varied from 41.4% to 89.7%, indicating significant variations depending on diagnostic criteria listed above. This study highlights the variability in the sensitivity and specificity of US and CT depending on the applied criteria. The results underscore the importance of non-invasive imaging in diagnosing CE in sheep and suggest potential applicability in human diagnostics

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STUDY OF THE PREVALENCE OF CYSTIC ECHINOCOCCOSIS IN LIVESTOCK COMMUNITIES OF CUSCO, PERU

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Cystic echinococcosis (CE) poses a significant public health challenge worldwide, particularly in regions where livestock is a major economic activity and human-animal interaction is frequent, such as in Peru. The liver and lungs are the most commonly affected organs, with a previous studies performed in Peru indicating a prevalence ratio of 3:1. This study aimed to analyze the prevalence of liver CE in three endemic communities in the southern highlands of Cusco, Peru—Acopia, Combapata, and Pomacanchi—and to examine the spatial distribution of cases within these communities. We conducted an abdominal ultrasound survey across the three communities, enrolling a total of 811 participants. Epidemiological and clinical data were also collected to identify relevant risk factors. Ultrasound evaluationindicated prevalence levels of 3.4% (95% CI: 0.1% - 6.8%), 7.9% (95% CI: 4.1% - 11.7%), and 6.5% (95% CI: 4.4% - 8.7%) in Acopia, Combapata, and Pomacanchi, respectively. Geospatial analysis revealed that the spatial risk of liver CE was primarily concentrated on the peripheries of each community, where informal slaughter practices are common. The study highlights the ongoing challenge of CE in endemic regions and underscores the importance of spatial analysis in understanding the distribution of health risks. Addressing informal slaughter practices may be key to reducing the prevalence of CE in these communities.

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IMMUNOHISTOCHEMICAL IDENTIFICATION AND SPATIAL DISTRIBUTION OF TWO ANTIGENS IN CEREBRAL PORCINE NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC), invasion of the central nervous system by *Taenia solium*, stands as the predominant cause of acquired epilepsy worldwide. In viable phase, cyst actively produces/releases sets of antigens that stimulate a host immunological response and can induce inflammation. However, the antigen distribution across cyst stages (viable, degenerating, and calcified) is unknown. Using anti-*T.solium* monoclonal antibodies (moabs), targeting total cyst, vesicular fluid and excretory/secretory (E/S) antigens, we explored its localization in brain tissue samples of treated naturally infected-NCC pigs in different cyst stages. We selected two clones of moabs for each antigen type based in our western blots results against well-defined recombinant antigens related to anchoring, scaffold formation, and secretion (rGP50, rT24H and sTsRS2-sTs14/18, respectively). Moabs against total cysts principally targeted rGP50, rT24H and sTsRS2, while the others recognized sTs14/18 and sTsRS2. Four moab-based immunohistochemistry techniques (IHC), two against anchoring antigens (TsW5/TsW8) and two against E/S (TsV3/TsE1) were standardized and tested with viable, degenerating, and calcified cysts from 17 pigs. IHC results determined two distinct antigen patterns: moabs TsW5/TsW8, directed against total cysts were detected in the cyst walls, vesicular fluid, and the spiral canal in viable cysts, while TsV3/TsE1, directed against E/S, in cyst walls and vesicular fluid only. Both were detected in the surrounding tissue. In calcified cysts TsW5/TsW8 recognized antigens within the cyst, while TsV3/TsE1 stained antigens in the surrounding parenchyma (500µM). Residual antigens were detected until 12-months after antiparasitic treatment with a gradual decrease in immunoreactivity percentage (4-months:30.8%, 8-months:7.5%, 12-months:1.8%). These findings demonstrate the dynamic nature of antigen distribution. The presence of antigen in the tissue, even in calcified lesions, suggests an antigen diffusion mechanism from parasite E/S to brain cells that can potentially cause structural alterations.

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EVALUATION OF DAMAGE IN AXONAL TRANSPORT THROUGH THE IMMUNOREACTIVITY OF THE MOTOR PROTEINS KINESIN AND DYNEIN IN BRAIN TISSUE OF RATS WITH NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is a parasitic disease of the CNS that causes acquired epilepsy in people from endemic countries in Latin America, Africa and Asia, generated by the larval form of the cestode *Taenia solium*. It is a chronic disease, which in symptomatic patients is characterized by seizures and epilepsy that make it impossible for them to carry out their daily activities. Infection studies in laboratory rats have identified that in NCC there is axonal damage characterized by the accumulation of proteins (neurofilament, amyloid precursor protein) in areas of axonal swelling or axonal spheroids, which could be related to a probable deterioration in the axonal transport and would contribute to the degeneration and death of neuronal cells. Therefore, in this study, the reactivity of the motor proteins kinesin and dynein in brain tissue of rats with NCC treated and not treated with antiparasitics at different post-treatment sacrifice times (up to 12 months) was evaluated by immunohistochemistry. It was identified that rats with NCC present accumulation of kinesin and dynein in the axonal spheroids surrounding the parasite, with no significant difference between the treated and untreated group; with absence of spheroids in the control group. Likewise, there is a greater number of axonal spheroids reactive to these motor proteins in gray matter than in white matter. These results indicate that in NCC there is damage in axonal transport characterized by the pathological accumulation of these proteins that would contribute to the process of neuronal degeneration, and that is maintained over time indicating irreversible axonal damage.

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IDENTIFICATION OF PROTEINS WITH TGF- β FUNCTION IN THE EXCRETORY SECRETORY PRODUCTS OF *TAENIA SOLIUM* LARVAL STAGE

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Helminth parasites have the ability to modulate the host's immune response through their secretory excretory products (ES) that activate TGF-β

signalling. *Taenia solium* is a cestode helminth whose larval stage affects the central nervous system in humans, causing neurocysticercosis which is associated with seizures. The mechanism that this parasite uses to establish itself and remain in its host is not yet known. The aim of this study was to identify proteins with TGF- β function. For these, the ES products were fractionated by ion exchange chromatography, then each fraction was incubated in MFB-11 cells that release alkaline phosphatase enzymes in the presence of TGF-β-like proteins (TGF- β bioassay). Each fraction was also observed using SDS-PAGE and silver stain. Protein fractions positive in the TGF-β bioassay were analyzed by LC-MS/MS. The results showed a total of 12 fractions of the ES products, and 4 fractions were positive in the TGF- β bioassay. In the SDS-PAGE, we observed differences in the banding pattern in each fraction. Besides, we evaluated these fractions by immunoblot using an anti-TGF β antibody, and we observed that no band was recognized by this antibody, suggesting that these proteins have TGB function but are structurally different from TGF β. These positive fractions were evaluated by LC-MS/MS.

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DEFINING THE CELLULAR COMPOSITION OF THE CSF IN SUBARACHNOID NEUROCYSTICERCOSIS THOUGH MULTIDIMENSIONAL SPECTRAL FLOW CYTOMETRY

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The most severe manifestation of neurocysticercosis is subarachnoid disease (SANCC), causing chronic relapsing-remitting inflammation, arachnoiditis, and significant morbidity and mortality if untreated. Improved understanding of the inflammatory milieu in the central nervous system (CNS) may improve targeted immunomodulation as an adjunct to anthelmintic therapy. To characterize the cellular nature of the CNS inflammation, fresh CSF was obtained from patients at their entry to care ("pre-treatment"), prospectively every 3-6 months ("mid-treatment"), and at the time of presumed cure (CSF antigen and qPCR tests for *T. solium* were negative) from 2022-present. Cells were analyzed by multidimensional spectral flow cytometry. In the 7 pre-treatment CSF, each had elevations of leukocytes (GM 10 leukocytes/μL; normal 0-5/μL). Lymphocytes were the primary cells present, with CD3+ T lymphocytes making up 66.4% (GM 2.3/μL, normal 0.15-1.83/μL) and B cells forming the next largest group of cells identified in all specimens at 14.1% (GM 0.43/μL, normal 0-0.03/μL). CSF from untreated SANCC was characterized by expansion of a sizeable effector memory (Tem) CD4+ T population (84.8% of CD4+ cells, GM 1.2/μL, normal 0-0.02/μL), with smaller populations of TEMRA (GM 0.04/μL, normal 0.00-0.02/μL), T regulatory (FoxP3+, GM 0.03, normal 0.00-0.12/μL), T central memory (GM 0.03/μL, normal 0.05-1.6/μL) and naïve T cells (0.3%, 0.003/μL, normal 0.00-0.08/μL). CXCR3+/CD4+ cells (Th1) made up 38.4% of the Tem cells (39.4%). Among B cells, plasmablasts represented 5.4%, naïve B cells 7.5%, and central memory B cells 5.4%. Cluster analysis (FlowSom) identified a CD3+/TCRgd-/CD4-/CD8- population as being notably expanded (GM 6.7% of T cells, range 1.8-35.8%) along with a CD3-/CD19+/CD27-/IgD- population (GM 14.7% of B cells, range 7.9-42.1%), both of which have been shown to be associated with other non-infectious autoimmune inflammatory disease. Post cure analyses are underway using paired samples (n=2) but await additional subjects. Our data help provide a single cell landscape that underlies some of the contributors to pathology seen in SANCC.

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SARS-COV-2 EXPOSURE BEFORE OR AFTER PLASMODIUM VIVAX INFECTION EXACERBATES THE HUMORAL RESPONSE AGAINST THE LATTER

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Loreto is a region of the Peruvian Amazon with a high risk of transmission of malaria whose health system suffered deeply early in the COVID-19 pandemic. Previously it has been shown that a *Plasmodium* infection diminishes the humoral response against respiratory viruses. We hypothesize that symptomatic (Sym) acute malaria and asymptomatic (Asym) malaria reduces pre-existing natural IgG antibody levels against SARS-CoV-2 in people living in the Peruvian Amazon. This study performed a multiplex assay in a Luminex platform to analyze IgG antibody levels against a 11-antigen (Ag) panel of *P. falciparum*, 10-Ag panel of *P. vivax* (*Pv*) and a 6-Ag panel of SARS-CoV-2. The study population was a total of 93 individuals. Samples of healthy endemic controls from Iquitos city (n=9) (no history of malaria in the past 3 years and no confirmed *Plasmodium* infection); Asym (n=24) and Sym (n=34) Amazonian subjects with only a confirmed *Pv*-infection; subjects with a *Pv*-infection first and a latter SARS-CoV-2 exposure (n=20) and the opposite sequence: exposure to SARS-CoV-2 first and a latter Pv-infection (n=6) were evaluated. *Pv*-infection was determined by positive microscopy and/or qPCR and SARS-CoV-2 exposure by positive antigenic, serological, or molecular testing or vaccination against COVID-19 self-reported by the subject. MFI (mean fluorescence intensity) log-transformed data was compared between study groups for each antigen by permutation ANOVA. Individuals with SARS-CoV-2 exposure before or after *Pv* exposure have lower IgG anti-PvEBPII and anti-PfMSP1 and higher IgG anti-PvMSP1-19 and anti-PvMSP8 levels compared to the only *Pv*-infected Asym group. In addition, these individuals have higher IgG anti-Spike, anti-RBD, and anti-NP levels for the Wuhan and Omicron strains compared to the only *Pv*-infected group whether they were Asym or Sym. This analysis shows that SARS-CoV-2 exposure before or after *Pv* exposure has an Ag-dependent effect on the response against *Pv* and that the order of coexposure to *Pv* and SARS-CoV-2 does not affect the response against SARS-CoV-2.

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EVALUATION OF NEUROCYSTICERCOSIS PRESENTATION AND MANAGEMENT IN HOUSTON, TEXAS

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Neurocysticercosis (NCC) is a neglected tropical disease affecting 2-8 million people globally and results in ~30% of epilepsy cases in endemic countries. While the causative agent, Taenia solium, is not endemic in the United States (US), experts estimate 4,000 annual US cases. Data from our health system in Houston, TX, describe >10 new NCC diagnoses yearly. Infectious Disease Society of America (IDSA) guidelines recommend treatment based on location and viability of cysts in the central nervous system (CNS). Here we describe NCC cases presenting to our system serving at-risk patients in Houston, TX between 2017-2021. We retrospectively identified patients ≥18 years old tested for NCC in the Harris Health System [HHS], systematically extracted demographic, clinical, imaging, and treatment variables from the patients' records, and recorded this data via a REDCap instrument. We classified NCC patients by NCC type and performed descriptive statistics. Of the 113 unique patient NCC records found, most were born in Mexico (n=65, 57%) and lived in the US for >5 years prior to NCC diagnosis (n=66, 58%). 67 (59%) initially presented as inpatients. 72 had calcified parenchymal lesions and 57 (50%) had viable cysts (24 with extra-parenchymal NCC [EPN]). Patients with calcified disease frequently reported chronic headaches (n=29, 56%), whereas patients with viable parenchymal NCC (VPN) more often presented with seizures (n=18, 55%). Considering IDSA guideline-directed management, 25 (76%) of patients with VPN cysts received corticosteroids. 16 (66%) of 22 patients with 1-2 VPN cysts received albendazole monotherapy, and 5 (56%) of 13 patients with >2 VPN cysts were treated

with dual anti-parasitic therapy for at least 7-14 days. Regarding patients with EPN, only 15 (63%) received corticosteroids and only 8 (33%) received dual anti-parasitic therapy of which 4 (50%) were treated with shorter duration (7-14 days). In summary, in our healthcare system, management of NCC varied greatly and often did not follow IDSA guidelines. Improving frontline provider education on NCC may enhance adherence to guideline-based treatment and neurologic outcomes.

7400

ASSOCIATIONS BETWEEN C-REACTIVE PROTEIN, MALARIA, AND MALNUTRITION AMONG CHILDREN WITH FEBRILE ACUTE RESPIRATORY ILLNESS IN UGANDA

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C-reactive protein is a useful biomarker in differentiating bacterial from viral acute respiratory illnesses (ARI) in resource-constrained settings. In malaria endemic regions, however, CRP production may be influenced by malaria infection. The relationship between nutritional status and CRP levels is unclear. We conducted a posthoc analysis of data from the intervention group of a stepped-wedge cluster-randomized controlled trial evaluating the use of a clinical algorithm including a CRP rapid diagnostic test (RDT) to guide antibiotic treatment among children with febrile ARI. We enrolled 1220 children aged 2 months to 5 years old evaluated by a village health worker (VHW) in the Kasese district of western Uganda. CRP was measured by a semi-quantitative rapid test (<10, 10-40, 40-80, 80+ mg/L). Malnutrition status was assessed using MUAC (mid upper arm circumference). Participants were tested for malaria using an antigen RDT specific for *Plasmodium falciparum*. The association between CRP and malaria RDT results was assessed with a Cochran-Mantel-Haenszel chi-squared test. We accounted for the sensitivity and specificity of the CRP RDT. The association between CRP and MUAC was assessed with a Kruskal-Wallis chi-squared test. Of the 632 children evaluated during intervention periods, both CRP and malaria RDT results were available for 629 children. 50.4% tested positive for malaria. Malaria positive children tended to have higher CRP levels compared to those who were malaria negative ($p<0.0001$). Among those with MUAC measurements, 12.7% had severe or moderate malnutrition (MUAC < 13.5 cm). CRP levels were similar between those with severe or moderate malnutrition and those without ($p=0.24$). CRP levels among children with malaria in our study tend to be elevated and may be like those observed with bacterial infection. Additionally, CRP levels among children with severe or moderate malnutrition were like those without malnutrition. The presence of malaria should be considered when designing treatment algorithms to guide antibiotic decisions for febrile children in malaria-endemic regions.

7401

UNRAVELLING THE ENIGMA: HOW SIMULATION-BASED CLINICAL TRAINING ENHANCES THE DIAGNOSIS OF VIRAL ENCEPHALITIS - INSIGHTS FROM GHANA'S SECOND LARGEST REFERRAL HOSPITAL

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Viral encephalitis poses a significant global health challenge, particularly in developing countries like Ghana. However, accurate diagnosis is hindered by low rates of essential lumbar puncture (LP) and cerebrospinal fluid (CSF) analysis. A 3-year retrospective study at Ghana's second largest tertiary hospital showed that only 26% (15/57) of patients with suspected Central Nervous System infection underwent LP subsequent CSF fluid analysis. To address this, clinical skills training was implemented to enhance healthcare professionals' proficiency in lumbar puncture. Training materials were developed using the Modified Delphi Approach. Pre- and post-training knowledge assessments were conducted using online data collection forms. The training was conducted by expert clinicians and included didactic and hands-on practice sessions. Customized mannequins were used for LP simulation training, with intracranial pressure (ICP) measuring devices utilized to demonstrate proper techniques. All training items were donated to the hospital's skills development and simulation centre for continuous skills enhancement. Twenty-one healthcare professionals participated in the training. The pre-training assessment showed that 85% (18) clinicians encountered more than 3 suspected cases of viral encephalitis monthly but were likely to request LP in only 10% of cases. Barriers to LP performance included contraindications (15, 71%), absence of intracranial pressure (ICP) measuring devices (7, 33%), inadequate tools (6, 29%), and lack of expertise (6, 29%). After the training, participants experienced notable improvements: 90% (19) reported fulfillment of training expectations, 81% (17) gained confidence in LP, and 77% (16) enhanced their LP skills. LP performance surged from 15 to 77 over 3 years, representing a 413% increase. The improved LP proficiency led to identifying viral agents causing encephalitis for the first time in Ghana. This advanced medical knowledge and diagnosis strengthened the healthcare system, and potentially improved patient outcomes.

7402

SEVERE *PLASMODIUM FALCIPARUM* MALARIA WITH SYMMETRIC PERIPHERAL GANGRENE: A REPORT OF TWO CASES

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Malaria remains a leading cause of morbidity and mortality in sub-Saharan Africa, particularly in its severe forms. Symmetric peripheral gangrene (SPG) occurring with disseminated intravascular coagulation (DIC) during severe *Plasmodium falciparum* malaria is a rare and serious event, more commonly reported in Asia than in West Africa. SPG is defined as symmetric distal ischemic lesions on two or more sites without major vessel obstruction. The pathophysiological mechanisms involve complex consumptive coagulopathy, which is increasingly understood.We report two cases from the medical intensive care unit at the Principal Hospital of Dakar, Senegal. The patients, aged 60 and 66, presented with severe malaria evidenced by blood smears showing >10% parasitemia with *P. falciparum*. Both developed DIC with multi-organ failure (neurological, hemodynamic, renal, hematological, hepatic, and metabolic) requiring supportive treatments. They subsequently developed SPG affecting all four limbs, leading to bilateral lower limb amputations for one and disarticulation of fingers for the other. The use of anticoagulants (unfractionated heparin for Case 1 and low molecular weight heparin for Case 2) played a crucial role in managing the coagulation-inflammation cycle. Early diagnosis of infection, prompt antimalarial treatment, intensive care management, and anticoagulation therapy are critical for improving prognosis in patients with severe malaria complicated by SPG.

7403

PERFORMANCE OF QUANTITATIVE POINT-OF-CARE TESTS TO MEASURE G6PD ACTIVITY: A META-ANALYSIS

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the main risk factor for severe haemolysis following treatment with 8-aminoquinolines (8AQ). The WHO recommends G6PD testing prior to 8AQ-based hypnozoitocidal treatment. We undertook an individual level meta-analysis of the performance of commercially available quantitative point of care assays (PoCs) compared to reference spectrophotometry. A systematic literature search identified 588 articles of which 14 (2.4%) fulfilled pre-defined inclusion criteria and were included; 3 unpublished datasets were also included. In total 12,545 paired measurements were included, 10,313 (82.2%) by STANDARD G6PD Test (SD Biosensor, RoK, "SDB"), 2,042 (16.3%) by CareStart G6PD Biosensor (AccessBio, USA, "CSA"), 150 (1.2%) by CareStart Biosensor (WellsBio, RoK "CSW"), and 40 (0.3%) by FINDER (Baebies, USA, "FBA"). The pooled sensitivities of the SDB when diagnosing G6PD activity <30% of normal were 0.82 (95%CI: 0.72-0.89) and 0.93 (95%CI: 0.73-0.98) for capillary and venous blood samples, respectively. The corresponding values for diagnosing <70% G6PD activity were 0.93 (95%CI: 0.67-0.99) and 0.87 (95%CI: 0.70-0.95), respectively. The pooled specificity of the SDB was high (>98%) for all blood samples and thresholds. Irrespective of the blood samples and threshold applied, the sensitivity of the CSA did not exceed 62%, although the specificity remained high at both the 30% and 70% thresholds (>88%). Only one study each from CSW and FBA were included. Sensitivity of the CSW was 0.04 (95%CI: 0.01-0.14) and 0.81 (95%CI: 0.71-0.89) at the 30% and 70% thresholds, respectively (venous blood samples). Sensitivity of the FBA was 1.00 (95%CI: 0.29-1.00) and 0.75 (95%CI: 0.19-0.99) at the 30% and 70% thresholds (venous blood samples). The specificities of the CSW and FBA were consistently high (>90%) at both diagnostic thresholds. The SDB performed significantly better than other tested PoCs except for the FBA. More evidence is available for the performance of the SDB compared to other PoCs, giving higher confidence in its utility in diagnosing G6PD deficiency.

7404

UNBIASED METAGENOMIC SEQUENCING OF ACUTE ENCEPHALITIS AND MENINGOENCEPHALITIS FOR IDENTIFICATION OF INFECTIOUS ETIOLOGIES IN NEPAL

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The burden of acute encephalitis syndrome (AES) and meningoencephalitis is significant in Nepal. Their causative agents mostly remain unknown because of use of conventional approach which fails to identify the etiologies, leading to delays in treatment, causing morbidity and mortality. We hypothesize presence of several organisms, including vaccine preventable etiologies causing AES, meningoencephalitis and febrile illness, when identified directs public health efforts for prevention and surveillance. This study employs unbiased metagenomic sequencing to investigate infectious etiologies causing AES, undiagnosed febrile illness and meningoencephalitis, in 200 subjects (3mth-75yr) from east Nepal. Cerebrospinal fluids (190) were collected, during May-Dec'23, with process controls from skin and procedure area and clinical metadata. Until now, 38 CSF have been sequenced using Illumina iSeq100. The initial clinical diagnoses of the subjects were meningoencephalitis, AES and sepsis with fever, seizure and vomiting. Most of these subjects had elevated WBC (>11×10^9/L) but normal CSF cell-count (≤5WBC/mm^3) indicating infectious etiology, which was confirmed by sequencing: *Enterovirus C* (5), *Pseudomonas putida* (2) and *Elizabethkingia meningoseptica* (2). The *Enterovirus C* was closely related to isolates from outbreaks in Pakistan and northeast India, near to our enrollment site. Other studies have linked these pathogens as etiologies: *E. meningoseptica* reported as emerging hospital-based pathogen causing meningitis and *P. putida* as a rare pathogen causing central nervous system infections. The subject infected with *P. putida* had high CSF glucose indicating early infection and possible disruption of blood-brain barrier due to sepsis. Another subject which had coinfection of all 3 pathogens, showed higher CSF protein, confirming viral etiology. This novel study was able to identify several etiologies, including depiction of co-infection. Further, this study elevates the utilization of unbiased metagenomic sequencing to complement diagnosis, identify coinfections, conduct surveillance and track transmission.

7405

ENVIRONMENTAL ENTERIC DYSFUNCTION IN NON-SLUM-DWELLING WELL-NOURISHED WOMEN IN DHAKA CITY, BANGLADESH

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Environmental Enteric Dysfunction (EED) is a subacute inflammation of the gut mucosa associated with undernutrition and prevalent in regions with inadequate sanitation facilities. Previous investigations indicated a high prevalence of histologically confirmed EED among undernourished women residing in the slums of Dhaka, with over ninety percent exhibiting the condition. However, scant data exist on histology-confirmed EED among well-nourished women residing outside of slum areas. In the present study, we screened normal Body Mass Index (BMI) (20-24.9 kg/m2) non-pregnant non-lactating women (18-45 years), residing in non-slum areas of Dhaka, who presented with functional dyspepsia according to the ROME IV criteria. Participants consenting to the study underwent upper gastrointestinal endoscopy, with mucosal biopsies obtained from the distal duodenum and subsequently subjected to histopathological examination for EED. Diagnosis of EED was established based on the following criteria: Mild EED, characterized by the presence of at least one EED feature (i.e., lymphocyte infiltration); Moderate EED, defined by the presence of two EED features (comprising mild features along with villous atrophy or crypt hyperplasia); Severe EED, identified by the presence of all three aforementioned features. Between October 2, 2022, to March 30, 2024, a total of 888 women were screened for eligibility, among whom 33 participants provided consent for endoscopic evaluation. The mean age of the participants was 28.7±6 years with a mean BMI of 23.2±1.4 kg/m2. Histological examination revealed that 21% (n=7) of the participants exhibited features indicative of EED, whereas the remaining 79% (n=26) exhibited no histological evidence of the condition. Among those diagnosed with EED, five individuals demonstrated mild EED, while two exhibited moderate EED. This study contributes novel insights into the epidemiology of EED, suggesting a lower prevalence among well-nourished women residing in non-slum areas. Furthermore, it underscores the pivotal role of environmental sanitation and nutritional status in the pathogenesis of EED.

7406

ADAPTIVE DENGUE ANTIVIRAL PLATFORM TRIAL (ADAPT): A RANDOMIZED, ADAPTIVE, OPEN LABEL TRIAL FOR ANTIVIRAL SCREENING IN PATIENTS WITH EARLY SYMPTOMATIC DENGUE

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Dengue virus infection is the most abundant and rapidly spreading vector borne disease globally (est. 105million cases/year). Climate change is driving disease emergence in altitudes and latitudes not previously endemic. There are currently no licensed antiviral therapies. Severe manifestations occur between day 4-6 of illness, allowing only a brief window to intervene with a directly acting antiviral drug. There is no consensus pharmacometric approach to evaluate antivirals in early symptomatic dengue. Previous phase 2 trials have used either time to viral clearance or area under the viraemia curve, but these are insensitive measures and generalise poorly. We will present the protocol for our multi-center, phase 2 open label, randomised adaptive platform trial for the rapid screening and dose optimisation of antiviral drugs in early symptomatic dengue. This will be a continuously running adaptive platform, with capacity to add new intervention arms as therapeutic agents become available, and terminate arms if efficacy/futility endpoints are met. We will enrol participants with dengue confirmed by positive NS1 antigen test, and <48hrs of symptoms. Where safety data is available for individual drug candidates, we will recruit children ≥10yrs. Patients will be randomised 1:1 to eligible intervention arms, or the control arm (supportive care, no placebo). Initial therapeutic candidates include a monoclonal antibody (Serum Institute of India), Baricitinib and Molnupiravir. After enrolment, participants will have serial plasma samples collected for viral load measurement every 12 hours for 5 days. The primary virological endpoint will be rate of viral clearance estimated under a hierarchical log-linear model fit to serial viral load measurements. The initial efficacy endpoint will be a ≥10% increase in viral clearance rate in the intervention arm relative to control arm. We anticipate that this trial will provide proof of concept for the rapid assessment of in-vivo antiviral activity for dengue using rate of viral clearance, and provide evidence to justify progression of promising antiviral agents to phase 3 trials.

7407

SURVIVING SNAKEBITE ENVENOMING: DECADES-LONG WAR WITH CHRONIC KIDNEY DISEASE: A CASE SERIES FROM RAJASTHAN, INDIA

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Snakebite envenoming is a neglected tropical disease. Vipers- *Daboia russelii*, *Echis carinatus* and *Hypnale hypnale* are commonly responsible for Acute kidney injury (AKI) that resolves with antivenom and supportive care. However, antivenom ineffectiveness in Rajasthan poses a special challenge. Here, we report 2 young patients who developed CKD decades following probable *Echis carinatus sochureki* envenoming. *Case 1:* A 22-year-old lady with a snakebite at 5y of age, and again at 11y of age presented to us with status epilepticus. She had experienced local swelling on both occasions but developed a superadded infection, requiring incision and drainage during the second bite. She did not receive any antivenom for either event. Her pregnancy (18 y) was complicated by preeclampsia. She had elevated urea, creatinine, bilateral contracted kidneys, hypocalcemia (4.2 mg/dL) and raised PTH (1409 pmol/l). Symptoms resolved with parenteral calcium. She is currently on bi-weekly maintenance haemodialysis (HD) for CKD. *Patient 2*: A 30-year-old lady, CKD on maintenance HD, presented with MRSA central-line associated blood stream infection (CLABSI) complicated by spinal epidural abscess (C7-T1 destruction), cord compression and spastic quadriparesis. She had a snakebite at 18y of age during complicated by bleeding and anuria. She improved with antivenom, 2 HD sessions and remained asymptomatic for 10 years before developing CKD. She further developed *Pseudomonas* CLABSI. She received daptomycin, meropenem and brief empirical anti-tubercular therapy. Despite this and change of HD catheter thrice, she succumbed to septic shock. Throughout her medical journey, CKD was a focal point, significantly impacting her prognosis and contributing to her eventual demise. CKD is reported in 26-37% after Russell's viper bites. Though, AKI occurs in ~20% of *Echis* bites, to our knowledge, this is the first report of CKD after possible *E. c. sochureki* bite. We highlight the long-term productivity loss, financial burden and suffering of snakebite survivors.

7408

PREVALENCE OF *PLASMODIUM FALCIPARUM* INFECTION AMONG CHILDREN HOSPITALIZED WITH ACUTE RESPIRATORY ILLNESS IN WESTERN UGANDA

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Previous studies suggest malaria co-infection with influenza in sub-Saharan Africa is uncommon, but coinfected children are more likely to experience more severe illness. However, the prevalence of malaria in influenza-infected children in sub-Saharan Africa may have changed due to the expanded global efforts to decrease the burden of malaria in the past decade. From July to November 2022, we enrolled 265 children aged 2 months to 18 years admitted to the inpatient departments of one rural (Bugoye Health Centre [BHC]) and one semi-urban (Rukoki Health Center [RHC]) health facility in Kasese District, Uganda with acute respiratory illness defined as onset of documented fever (≥38°C) and respiratory symptoms (i.e., cough, respiratory rate > 30 breaths per minute, and/or oxygen saturation < 90%) in the prior 7 days. All participants were tested for influenza A and B, respiratory syncytial virus (RSV), and SARS-CoV-2 by polymerase chain reaction (Cepheid, Inc., GeneXpert platform). Rapid Plasmodium falciparum malaria HRP-2 antigen testing (mRDT) was performed on capillary blood. A total of 12 participants were excluded because of missing data. Overall, 36% (86/253) of children tested positive for Influenza A (24%) or B (13%), while 42% (106/253) had a positive mRDT. Among influenza-positive children, 48% (41/86) had a positive mRDT, compared to 39% (65/167) of influenza-negative children. Influenza was not significantly associated with a positive malaria RDT, (Unadjusted Prevalence Ratio: 1.2, 95% CI: 0.90, 1.78). When stratifying by study site, 54% (36/67) of influenza-positive children at the rural site had a positive malaria RDT whereas the prevalence of co-infection at the semi-urban site was lower at 26% (5/19). Our findings demonstrate that malaria parasitemia among children hospitalized with acute respiratory illness in western Uganda is frequent, but similar between influenza-positive and influenza-negative children. These results highlight the need for further research assessing the impact of malaria co-infection on the transmission and pathogenesis of influenza.

7409

IMPROVING INFECTION PREVENTION AND CONTROL COMPLIANCE IN CAMEROONIAN HEALTHCARE FACILITIES USING THE WORLD HEALTH ORGANIZATION CORONAVIRUS SCORECARD TOOL

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Infection prevention and control (IPC) is a clinical and practical evidence-based-approach aiming at protecting patients, health workers and visitors from avoidable infections. We conducted a study to determine the baseline level of infection prevention and control and to determine if repeated evaluations of healthcare facilities after prior trainings of healthcare workers could lead to the improvement of IPC. The study took place

from March 2020 to November 2023. Trainings of healthcare workers in selected healthcare facilities were followed by baseline assessments and reassessments. From 2020 to 2023, we evaluated and analyzed 2,188 IPC assessments from 1,358 healthcare facilities during the 3-year period. IPC assessments included 1,358 (62%) at baseline, 485 (2%) IPC first reassessment, 234 (1%) IPC second reassessment, 65 (0.3%) IPC third reassessment, 33 (0.1%) IPC fourth reassessment, 7 (0.03%) IPC fifth reassessment, 5 (0.2%) IPC sixth reassessment and 1 (0.04%) IPC seventh reassessment. Among all the healthcare facilities evaluated, only 497 (36.5%) have been evaluated more at least 2 times. The median IPC score was 52.4% at baseline and increased to 88.1% in some facilities. Between the baseline and reassessments, there were significant differences in the median IPC score between healthcare facilities, translating a better compliance after trainings. These differences were maintained during the multiple reassessments. Our findings are in accordance with previous studies in other sub-Saharan African countries which found a significant association between the ownership status and IPC performance, an improvement in the median IPC score from baseline and higher IPC scores in healthcare facilities dedicated to COVID-19. Our findings could guide policy implications, since there is a recognized low utilization and effectiveness of validated IPC tools in low- and middle-income countries, particularly in Sub-Saharan Africa. Emergencies are opportunities to improve and monitor IPC compliance in LMIC.

7410

COULD EARLY CARE SEEKING AND INCREASED ACCESS TO COMMUNITY-LEVEL HEALTH SERVICES STOP THE INCREASING MALARIA-RELATED DEATHS IN ZIMBABWE?

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Mashonaland Central and East provinces are among the highest malaria burden provinces in Zimbabwe with an average annual incidence of 24/1000 in 2023. During the peak period January to June, there were 42 malaria deaths in 2022 and 94 deaths in 2023; the case fatality rate increased 63% from 0.08% to 0.13%. A retrospective review of deaths reported in Mashonaland Central and East provinces was completed using a structured investigation form to extract patient data from clinical charts, including demographics, reasons for delays in care, appropriate clinical management, and associated complications. Out of 94 malaria-attributed deaths, 88 (94%) had records available and were reviewed. Overall, 14% were <5 years, 24% were aged 5-14 years, 43% were aged 15-59 years, and 19% were ≥60 years. Males accounted for 52% of all deaths. Seventy-seven percent of all deaths obtained care more than 24 hours after the onset of malaria symptoms, and 28% of these delayed reaching a healthcare provider because of a lack of transportation. Most cases (68%) first sought care at a health facility, while 25% sought care first from a community health worker. Seventy-four percent of the cases were diagnosed as severe malaria at the initial presentation. Shortages in diagnostic equipment and consumables for assessing kidney function, blood glucose levels, parasite levels, and temperature were reported in 30% of deaths. Ninety-one percent of deaths occurred at the health facility, while 9% were in the community. The most commonly reported complications requiring specialized care were impaired consciousness (64%), acute respiratory distress (40%), and acute kidney injury (17%). A lack of specialized services and expertise for intensive care and hemodialysis to manage associated complications was reported in 36% of deaths. The clinical courses of individuals dying secondary to malaria infection suggest that use of community health services may play a role in reducing mortality by preventing delays in seeking care. Limited resources and expertise to manage complications of severe malaria disease may be a contributing factor and could represent a target for intervention.

7411

ESTIMATES AND SPATIAL PREVALENCE OF *TRYPANOSOMA CRUZI* INFECTION AMONG CHILDREN IN NEW YORK CITY

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Chagas disease, caused by the protozoa *Trypanosoma cruzi*, is the leading cause of parasitic death in Latin America. Humans are primarily infected when a Triatomine bug defecates while feeding and the feces are scratched into the bite; other modes include vertical transmission, ingestion of contaminated food, transplantation, and blood transfusion. Acute *T cruzi* infection is typically asymptomatic and undiagnosed. If untreated, however, nearly 30% of individuals progress to debilitating chronic Chagas disease decades later after initial infection. In 2023, it is estimated that 37,500 migrants younger than 18 years of age arrived in New York City (NYC) primarily from *T cruzi* endemic countries in Latin America. To date, there has not been a large-scale pediatric prevalence study of *T cruzi* in NYC.*T cruzi* infection in NYC's Latin American pediatric migrant population is highly variable and dependent of socio-demographic factors, country of origin, and built environment. We aim to screen roughly 300 pediatric migrants of Latin American origin for *T cruzi* at Mount Sinai affiliated outpatient pediatric clinics as well as to administer a demographic survey to identify risk factors for exposure. We will develop risk profiles for *T cruzi* infection and create a statistical model to extrapolate prevalence estimates for the five boroughs of NYC using geo-located information on migrant age structure and origin. This work represents an initial step in developing a cost-effective pediatric *T cruzi* screening protocol for NYC.

7412

EPIDEMIOLOGY OF NEUROCYSTICERCOSIS: A 30 YEAR PILOT STUDY OF HOSPITALIZED PATIENTS IN FLORIDA

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Neurocysticercosis (NCC) is a parasitic disease of the CNS caused by the pork tapeworm, *taenia solium*, and is the leading cause of acquired seizure disorder worldwide. Although there have been international and out-of-state studies characterizing the epidemiology of patients presenting with NCC, this study is the first to characterize the burden of NCC in Florida. The inclusion criteria for this retrospective chart review included any patient presenting to UF Health Shands Hospital, Gainesville, FL, with symptomatic NCC (defined as one or more of the following symptoms unexplained by another disorder: seizures, focal neurologic deficits, headaches, hydrocephalus, nucal rigidity, psychiatric disturbances, and altered mental status plus or minus systemic symptoms) between June 1993-June 2023 given an ICD-9 or ICD-10 code of NCC. 34 patients in total met this criteria. Demographic characteristics of these patients included country of origin (76% non-USA, 24% unspecified), sex (59% Male, 41% Female), ethnicity (65% Hispanic, 32% non-Hispanic, 3% unspecified), age (68% 21-50, 18% 51-70, 15% 0-20), race (47% white, 12% black/AA, 9% Asian, 3% AIAAN, 29% unspecified), insurance status (41% uninsured, 21% insured, 38% unspecified), language preferred for medical correspondence (47% Spanish, 38% English, 6% other, 9% unspecified), and per capita income of Florida county of origin (53% bottom 50%, 41% top 50%, 6% unspecified). Selected hospitalization outcomes were also collected and compared between groups. 97% of patients reported NCC symptoms prior to receiving an NCC diagnosis and 72% of patients presented to at least one healthcare facility for similar symptoms without receiving a diagnosis of NCC. 21% of patients were readmitted at least once for NCC symptoms or complications. 18% of patients stayed in the hospital for more than 10 days. Although the power of this study is limited, this research identifies

delays in patient presentation and diagnosis and may aid clinicians in identifying common patient presentations associated with NCC in order to promote prompt diagnosis and close follow-up for these patients.

7413

TARGETED CLINICAL MENTORSHIP IMPROVES PERFORMANCE OF MALARIA SERVICES IN ZIMBABWE

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The PMI-funded Zimbabwe Assistance Program in Malaria II (ZAPIM II) project uses targeted clinical mentorship to improve case management and malaria in pregnancy service provision in health facilities (HFs) with observed service provision gaps. In September 2022, ZAPIM II conducted a malaria quality standards assessment (QSA), using a structured tool, to evaluate facility readiness and 108 health workers' (HWs) clinical performances at 70 HFs in Mashonaland Central and Mashonaland East provinces. The project assessed HF readiness to provide malaria services, including availability of material and human resources trained in malaria case management, HW clinical skills, and use of standard operating procedures (SOPs) for diagnosis, classification, and treatment of malaria cases. Action plans were made for assessed health facilities to address identified gaps through mentorship. Fifty-two health facilities received onsite mentorship, 15 virtual mentorship and 3 onsite supportive supervision between October 2022 and August 2023. In September 2023, ZAPIM II conducted another QSA at the same 70 HFs and 124 HWs were assessed to document the improvements in malaria service delivery after mentorship. There was a 21% significant decrease in the proportion of HWs trained in malaria case management (CI: 17%-24%, p<0.0001) due to newly recruited HWs. Overall, HW clinical skills scores improved by 9.3% (CI: 5.6%-13.1%; p =0.000) despite the decrease in the percentage of providers trained in malaria case management. Use of SOPs during rapid diagnostic testing for malaria increased by 10% (CI: -24.9%-7.5%; p =0.272). Correct classification of malaria cases, documentation of treatment doses and duration, and explanation and advice on malaria prevention given to patients increased by 10.6% (CI: -48.8%-27.6%; p=0.5322). Lack of statistically significant increases in these parameters could be due to the high number of untrained new staff in the second assessment. Findings suggest that targeted mentorship can improve HW malaria case management clinical skills. More analysis is needed to assess the overall impact on malaria services.

7414

A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL PROGNOSTIC MODELS AMONG CHILDREN WITH SEPSIS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Sepsis is the leading cause of child death worldwide, with the majority of these deaths occurring in low- and middle-income countries (LMICs). The aim of this systematic review and meta-analysis was to describe clinical prognostic scores and models for pediatric sepsis outcomes and assess the performance of these scores for predicting mortality in LMICs. Ovid Medline, CINAHL, Cochrane Library, EBSCO Global Health, Web of Science, were searched through September 2022 for citations related to the development or validation of a clinical prognostic score or model among children with sepsis, conducted in an LMIC. Titles, abstracts, and full texts were screened by two independent reviewers and data extracted regarding population characteristics, variables included, outcomes, and model performance. Risk of bias was assessed with the Prediction Model Risk of Bias Assessment Tool (PROBAST). 4,251 titles/abstracts and 315 full-text studies were screened, with 12 studies meeting inclusion criteria. Study countries included India, China, Egypt, Indonesia, Tanzania, and a multi-site study in Latin America. Prognostic scores/models included existing scores such as PELOD-2, pSOFA, PRISM, P-MODS, refractory shock criteria. There was high risk of bias in all studies. Meta-analysis was possible for pSOFA and PELOD-2 with pooled area under the receiver-operator characteristic curve of 0.86 (95%CI 0.78-0.94) and 0.83 (95% CI 0.76-0.91), respectively. Relatively few clinical scores and models have been externally validated for prognostication and risk-stratification among children with sepsis in diverse LMIC settings. Notably there were no studies from low-income countries. Some potentially relevant studies were excluded due to lack of clarity regarding the presence of sepsis in the study populations. More widespread and standardized use of sepsis criteria may aid in better understanding the burden of sepsis and prognostic model performance among children in LMICs. Further research to externally validate, implement and adapt these models is needed to account for challenges in use of these scores at the bedside in resource-limited settings.

7415

STRONG HEARTS: A NOVEL PRIMARY-CARE BASED DIAGNOSIS AND TREATMENT SUPPORT PROGRAM FOR CHAGAS DISEASE IN EAST BOSTON, MA, USA (2017-2023)

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Chagas disease is a neglected infection of poverty estimated to affect 300,000 people in the US, with a prevalence of 49 per 100,000 in Massachusetts. If left untreated, it progresses to irreversible heart disease and death in 20-30%, but <1% of the infected in the US receive treatment. Strong Hearts is a Chagas disease diagnostics and treatment initiative centered at the East Boston Neighborhood Health Center (EBNHC) in Boston, MA, whose goal is to uphold the preciousness of every person and the human right to healthcare. We present the program structure, diagnostics uptake, local epidemiology, and Chagas care continuum. Following provider and East Boston community information sessions, a protocol for EBNHC was developed and approved by its Board. Confirmed Chagas patients were referred to Boston Medical Center for evaluation and treatment. Our chart reviews identified continuum of care barriers, addressed by Strong Hearts' care navigators. 14,354 patients were screened at EBNHC from Mar 2017-May 2023. 3.4% of screening tests were positive. After confirmation, the overall population prevalence was 0.7% (95% CI: 0.6% - 0.9%) with no sex difference. Steep barriers at most steps of the care continuum would have been insurmountable for most patients without a care navigator. Of 90 patients diagnosed at EBNHC Mar 2017-Sep 2022, 44 (49%) began and 28 (31%) completed antiparasitic therapy. Major barriers to diagnosis and treatment were complexity of the confirmation process for positive screening results, number of steps between referral and initial appointment, challenges for patients taking time from work and traveling for appointments, lack of insurance, and medical bills. While some barriers to care are specific to Chagas disease and its lack of optimal diagnostic and treatment modalities, others exemplify barriers faced by many low-income Latin American community members in accessing medical care in the US. We identified important barriers to care that could be attenuated by medical institutions. We find that motivated primary care clinicians provide Chagas care when support for confirmatory testing and care navigation are in place.

7416

BURULI ULCER CASE DETECTION AND DIAGNOSIS IN THE OBOM SUB MUNICIPAL IN GA SOUTH MUNICIPALITY OF THE GREATER ACCRA REGION, GHANA.

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Mycobacterium ulcerans is the cause of Buruli Ulcer Disease (BUD), a chronic, debilitating condition that mostly affects the skin and sometimes the bone. Patients who have BUD may have long-term disability, irreversible deformity, and a decline in their quality of life. There is no known way to prevent M. ulcerans, mode of transmission is yet unknown. BUD is still a public health concern in Ghana's endemic communities. Hence, there is the need for periodic assessment in endemic areas to control the diseases. The current study examines Buruli ulcer prevalence, case detection, and diagnosis in the Obom sub municipality of the Ga South Municipality in the Greater Accra Ghana.**A** community-based cross-sectional study was conducted. The Obom community, Konkon Lebene, Nyormishie, was specifically chosen because to its history of Buruli ulcer endemicity. Residents who had resided in the research area for the previous six months and were present throughout the study's duration were the study's potential participants. The survey used simple random sampling to choose participants from houses. Furthermore, health screening was done to look for Buruli ulcer case in the community. Samples from potential participants were taken for laboratory testing. To identify the possible variables linked to Buruli Ulcer case detection, information on demographic traits, awareness of Buruli ulcer, health-seeking behaviour. Tables and figures were used to report the findings.All the 32 suspected buruli ulcer samples tested negative for buruli ulcers using both PCR and microscopy. About 6% of participants had no knowledge about Buruli Ulcer while males are 10 percent less likely to be knowledgeable about the Buruli Ulcer compared to females in the community with an odds ratio of OR = 0.9(95%C. I, -1.2 – 1.3). The study concludes zero prevalence of Buruli ulcer within the study area. The knowledge of Buruli ulcer is high among community members and majority of individuals visits health facilities upon detection of symptoms of Buruli ulcer. The study recommends targeted public health programs that address diverse beliefs and practices related to BU detection in Obom community.

7417

DENGUE SEVERITY PREDICTION IN A HYPERENDEMIC REGION IN COLOMBIA

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Early detection of severe dengue (SD) warning signs is crucial in preventing life-threatening complications. Despite its importance, comprehensive knowledge about these early indicators is still limited. This study aims to identify predictors of SD in a hyperendemic region of Colombia. A cross-sectional analysis was conducted using data from 2018 to 2022, encompassing 233 patients. Utilizing the 2009 World Health Organization dengue classifications, cases were differentiated between severe dengue (SD) and non-severe dengue (non-SD). Among these, 47 were confirmed as SD. Associations between clinical, demographic, and laboratory data and disease severity were examined using Fisher's exact tests or the Mann-Whitney U test ($p<0.05$). Profiles for SD and non-SD cases were established through multiple correspondence analysis, and a logistic regression-based predictive model was validated using training and test sets. The model's performance was evaluated using the area under the receiver operating characteristic curve (AUC-ROC), accuracy, sensitivity, F1-score, and precision. Differences in place of residence, comorbidities, type of infection, and signs and symptoms were observed between the severe dengue (SD) and non-severe dengue (non-SD) groups. Median levels of platelets, white blood cells (WBC), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were found to be higher in the SD group compared to the non-SD group. Key hematological markers, including neutrophils, leukocytes, platelets, AST, and primary infection, were identified as significant predictors of SD. The model demonstrated an area under the receiver operating characteristic curve (AUC) of 0.91 (95% CI, 0.85-0.96). The developed predictive model significantly assists clinicians in assessing SD risk and optimizing triage, which is particularly crucial during dengue outbreaks.

7418

ACCIDENTS BY CATERPILLARS IN THE VALLEY OF CARACAS, VENEZUELA: AN OUTBREAK STUDY

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Most accidents by caterpillars are mild, self-limited hypersensitivity reactions and occur in tropical areas with limited access to medical care, making the epidemiology of lepidopterism poorly understood. Several clinically important species are subject to dramatic variations in density, resulting in infestations of large numbers of caterpillars or moths and subsequent outbreaks of coincident cases. In August 2023, an unexpected increase in accidents by caterpillars was observed in the valley of Caracas, Venezuela, including a small group with cardiovascular alterations. This outbreak study describes the clinical cases of accidents and analyzes the geographical behavior of the reported caterpillar sightings during the study period. A total of 32 sighting reports were recorded, with 117 caterpillars observed, including 13 accidents. Most reports occurred in Miranda state (n=115, 98.2%). Most of the caterpillars were identified as belonging to the family *Saturniidae*, genus *Dirphia* (*n*=101; 86.3%) and *Automeris* (*n*=11; 9.4%). Two (1.7%) caterpillars were identified as *Megalopygidae Megalopyge*. More than half of the accidents occurred in children under 9 years of age (53.8%). Accidents occurred more frequently in residential gardens and parks (*n*=7; 53.8%), and public parks and pedestrian paths (*n*=4, 30.7%). In addition to all of them presenting skin lesions, six patients presented systemic symptoms, the most common being fever (n=3) and palpitations (*n*=3). A 9-year-old child showed an EKG with a negative T wave from V1-V4; a 5-year-old boy presented bradycardia, atrial extrasystoles, and CK-MB elevation; another child under 2 years old presented CK-MB elevation; and a 31-year-old girl had T-wave repolarization disorder. All these alterations were resolved in the follow-up control. This study describes a period of occurrence of caterpillar accidents consistent with multiple sightings of different caterpillars in the Valley of Caracas. It describes not only cutaneous alterations but also previously undescribed electrocardiographic and cardiac enzyme alterations.

7419

POTENTIAL RISK INCURRED BY HEALTH CARE PROVIDERS ATTENDING TO MALARIA PATIENTS ACROSS KENYA

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Management of malaria patients necessitates close monitoring, which exposes healthcare providers (HCPs) to increased risk. In many malaria-endemic regions, effective mosquito control is inadequate. Research shows a higher mosquito affinity for individuals infected with the gametocyte stage of malaria. This situation risks increasing the population of malaria-infected mosquitoes within healthcare facilities. Further, recent changes in mosquito feeding patterns reveal peaked activity during daylight hours—a time that coincides with patient visits. The potential for health facilities to become malaria transmission hotspots due to these combined factors needs further investigation. Understanding the infectiousness of individuals seeking malaria treatment is crucial for assessing the risk to HCPs in Kenyan hospitals. This knowledge helps in formulating guidelines for countermeasures aimed at reducing transmissions within hospitals. Between January 2023 and March 2024, 991 blood samples were collected from individuals with naturally acquired *Plasmodium* species infections presenting with uncomplicated malaria from six different sites countrywide. 295 samples from Busia, 50 from Kericho, 238 from Kisumu, 224 from Kombewa, 51 from Kisii, and 133 from Marigat. These samples were diagnosed for the presence of *Plasmodium species* before downstream screening for *P. falciparum* gametocyte life-cycle stage composition using real-time PCR. About 78.3% (766/991) of individuals tested positive for malaria by PCR. 87.37% (678/766) of these harbored gametocytes lifecycle stage comprising Marigat 93.41% (85/91), Kombewa 88.54% (170/192), Busia 87.39% (194/222), Kisii 86.05% (37/43), Kericho 85% (34/40) and Kisumu 84.04% (158/188). The substantial proportion of gametocytes in infections indicative of potential for patients to infect mosquitoes roosting within the hospital poses a risk of transmission of the disease to health workers. There is need for effective preventative strategies to protect healthcare providers exposed to malaria patients from possible transmission while in the health care facilities.

7420

EXPLORING ACUTE UNDIFFERENTIATED FEVERS AT A TERTIARY CARE HOSPITAL IN INDIA: ETIOLOGICAL PROFILE, CLINICAL CHARACTERISTICS AND BIOMARKERS

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This observational study was conducted at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi to determine the seroprevalence and clinical & laboratory profiles of malaria, scrub typhus, leptospirosis, typhoid, hepatitis A, hepatitis E, chikungunya, and dengue among patients presenting with acute undifferentiated fever (AUF). From July 2022 to November 2023, 18,362 patients with febrile illnesses lasting 2-14 days were included. Blood samples were tested for malarial parasites, dengue NS1 antigen, antibodies against typhoid, dengue IgM, Leptospira IgM, Scrub typhus IgM, Chikungunya IgM, hepatitis A IgM, and hepatitis E IgM antibodies. Additionally, C-Reactive Protein, Procalcitonin levels, and complete blood counts were assessed. Cases were defined according to IDSP, 2019 P and L form criteria. Out of 18,362 febrile patients screened, 4,259 tested positive for at least one of the 8 pathogens studied. Among these cases, 75% had single infections, while 25% had co-infections. Dengue was the most common single infection (2,049 cases), followed by typhoid (667) and chikungunya (353). Symptoms varied by pathogen, but fever was universal. Anaemia was observed in 85% of malaria and 82.5% of scrub typhus cases. Thrombocytopenia was seen in 15.9% of dengue and chikungunya cases. Higher CRP levels (4.8 mg/dl) were predominantly found in bacterial infections, followed by malaria, dengue, and chikungunya. Procalcitonin levels were elevated in scrub typhus, typhoid, malaria, and leptospirosis cases, indicating PCT to be a poor indicator of viral infections Dengue emerged as the most common mono-infection, while dengue-typhoid combination was the most frequent co-infection. This study offers robust epidemiological data on AUF, providing valuable insights for diagnosing single as well as multiple infections. The comprehensive data on clinical and laboratory findings in conjunction with levels of biomarkers presents valuable tools for improved diagnosis, management, and awareness of AUF and its associated aetiologies.

7421

SUBCUTANEOUS MYCOSES: ENDEMIC BUT NEGLECTED AMONG THE NEGLECTED TROPICAL DISEASES IN ETHIOPIA

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Subcutaneous mycoses are a chronic infectious disease of the skin and underlying structures endemic in tropical countries. The disease has serious medical and socioeconomic consequences for patients, communities and health services in endemic areas. The inclusion of mycetoma and other deep fungal infection in the list of Neglected Tropical Diseases by WHO highlights the need to assess the burden of these diseases and establish control programs where necessary. In Ethiopia no strategies can be devised because of a lack of epidemiologic information. To address this evidence gap, we performed a national rapid assessment of the geographic distribution of subcutaneous mycoses. We conducted a rapid retrospective assessment using hospital records to identify all suspected and confirmed cases of subcutaneous mycoses in 13 referral hospitals across the country between 2015 and 2022. In each hospital the logbooks were reviewed for diagnoses of deep fungal infections, as diagnosed per routine practice. Descriptive analysis was done. From 12 hospitals we extracted 85 cases of subcutaneous mycoses, registered from July 2018 to September 2022. 60 (70.6%) patients were diagnosed as mycetoma, 21 (24.5%) as chromoblastomycosis and the remaining 4 (4.7%) as sporotrichosis. The median age of patients was 35 years (IQR=18). 61 (71.8%) patients were male and 80.8% patients were farmers. 30 (36.9%) cases were from the Amhara national regional state. 56 (65.9%) patients had information on diagnostic microscopic evaluation: for mycetoma histopathologic evaluation and fine needle aspiration cytology have a higher positivity rate while for chromoblastomycosis Potassium hydroxide (KOH) staining had abetter yield. The main clinical presentations were nodules, sinuses and infiltrative plaques on the skin. Mycetoma and other subcutaneous mycoses are endemic in Ethiopia, with cases reported from almost all regions albeit with variation in case distribution. A routine program and systems should be developed to identify and document the burdens of subcutaneous fungal infections in the country.

7422

IMPACT OF INTESTINAL PARASITE INFECTIONS ON HUMAN PAPILLOMA VIRUS INFECTION AND REPRODUCTIVE HEALTH: EXPLORING ALTERATIONS IN INTESTINAL AND CERVICOVAGINAL MICROBIOME

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Intestinal parasite infections (IPIs) pose significant public health risks in areas with limited sanitation and healthcare, like the Peruvian Amazon. As they establish chronicity in the human gut, they downregulate host immunity to ensure survival, potentially facilitating the establishment of other pathogens, like HPV. While helminths clearly impact the gut microbiome, a major regulator of the systemic immune system, their impact on the cervicovaginal (CV) microbiome is uncertain. *Lactobacillus* spp. comprise >70% of CV microbiota in healthy women and promote protective immunity. Severe or prolonged CV dysbiosis, characterized by predominance of non-*Lactobacillus* spp., has been linked to increased HPV risk. This study aims to investigate intestinal and CV microbiome changes among Peruvian women aged 30–50 with and without IPIs, to understand IPI impact on these microbiomes and their association with HPV infection risk. We enrolled 353 women undergoing cervical cancer screening in Iquitos, Peru, between August 2022 and November 2023. Participants provided demographic, clinical, and risk factor information; underwent sexually transmitted infection (STI) and stool ova and parasites testing; and submitted CV and stool specimens for microbiome analysis via 16s rRNA sequencing. We used multiple logistic regression to evaluate IPI risk factors. Of 353 participants, the median age of sexual debut was 17 years [IQR 16-18], 6% were smokers, and 1.7% reported prior STI. CV infection frequencies were: HPV 21% [71/336], HIV 0.5% [2/353], syphilis 0.5% [2/353], chlamydia 0% [0/50], BV 32% [112/345], and TV 3.2% [11/342]. 312 submitted stool specimens. 41% had IPI; 7.4% had helminths (69.5% [16/23] *Ascaris*, 13.04% [3/23] hookworm, 8.69% [2/23] *Enterobius* and 8.69% [2/23] *Hymenolepis*) and 37% had protozoa (99.1% [114/115] *Giardia* and 65% [75/115] *Entamoeba histolytica*). Comparative analysis of CV and intestinal microbiota distributions is ongoing. We expect CV *Lactobacillus* spp. will be less abundant in women with IPIs. Study results will pave the way for a larger longitudinal analysis.

7423

DOES THE RUN- IN PHASE ADD WHEN ASSESSING SAFETY OF TRYPANOCIDAL THERAPIES? THE EXPERIENCE OF THE EQUITY TRIAL

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The run-in phase is a design tool seeking to select compliant participants in randomized trials. This may be relevant when assessing long-term interventions or those with low tolerance, such as trypanocidal therapy. The EQUITY trial tested a 120 day treatment including Nifurtimox, Benznidazole or placebo (PBO) among *T. cruzi* seropositive young adults with no cardiomyopathy. Treatments were assigned in two consecutive 60 day periods, with participants receiving either active treatments or PBO in a blinded fashion. Before randomization, participants underwent a 10 day run-in phase with PBO. Only those showing acceptable tolerance or adherence (>80% of treatment) were randomized. The treatments assigned over the study periods led to four possible situations after introducing, continuing, or interrupting the active treatment (OFF-ON, OFF-OFF, ON-ON, or ON-OFF). We recorded the occurrence of adverse events (AE) defined as moderate to severe symptoms, including those leading to additional prescriptions, dose reductions or study treatment discontinuation. Participants were assessed in the first 20 days of each study period (day 20 and 80 after the run-in). We computed McNemar's chi square statistics for 2x2 tables of paired observations (appearing/disappearing events) for each situation. After the run-in phase, 44 (12.5%) of 351 candidates were excluded (34 due to diverse complaints). In 307 randomized, when introducing active treatments (the OFF-ON group, n=232) AE appeared/receded in 64/18 participants (X^2 25.8, p <.001). These figures differed by the continuation of PBO (groups OFF-OFF, n=126, 15/10, X^2 1.00, p 0.31) or active treatment (ON-ON, n=110, 16/12 X^2 0.571, p 0.45) and its interruption (ON-OFF, n=44, 6/7, X^2 0.076, p 0.78). Using a run-in period in this trial allowed a better estimation and discrimination of AE after introducing active treatments, suggesting causality. Twenty days may not be enough to notice receding symptoms after stopping active treatment. At the cost of inducing some nocebo effect and excluding some candidates, the run-in improves the risk-benefit assessment of therapies for neglected tropical diseases.

7424

BRUGIA IMPACT SURVEY AS AN ALTERNATIVE METHOD FOR LYMPHATIC FILARIASIS TRANSMISSION ASSESSMENT SURVEY IN INDONESIA

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Indonesia's 236 districts endemic with *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* worms require at least five years of mass drug administration (MDA) to interrupt lymphatic filariasis (LF) transmission. The subsequent transmission assessment surveys (TAS) determine whether an evaluation unit (EU) can safely stop MDA. Indonesia has a current backlog of surveys in districts with *Brugia spp* due to global supply challenges with diagnostic tests. As such, the World Health Organization (WHO) recommended the Brugia impact survey (BIS) as an alternative method to TAS. The traditional TAS employs rapid tests among students in sampled schools, whereas the BIS requires night blood collection from adults for microscopic identification of microfilaria. Indonesia has conducted BIS in 42 EUs in 41 districts since September 2022; 41 EUs used a method-specific complex cluster sampling and 1 smaller EU used systematic sampling. The median sample size in EUs using cluster sampling was 1050 while the smaller EU had a sample size of 794; all surveys met required minimum sample sizes. Microscopists identified microfilaria in 17 EUs (range 1-12 positive samples). The threshold for passing the BIS was 4 or fewer positive samples; 2 EUs were over this threshold and therefore failed. The collection of microfilariae from randomly selected adults in the BIS makes it a robust methodology but challenging to implement. To be used as an assessment survey, the BIS needs to be a reliable proxy indication of low enough transmission to safely stop MDA, and Indonesia's experience has shown feasibility with proper training and supervision. However, the BIS had increased costs and higher refusals due to overnight sampling, required accurate population registers, and relied on a network of 76 skilled lab technicians with prior night blood sample experience. Indonesia's experience may be useful for other settings considering microfilaria testing in combination with rapid tests. The BIS implementation also established a precedent for other emerging methodologies with complex sampling; such novel approaches are essential to maintain momentum towards LF elimination.

7425

ASSESSMENT OF DISABILITY AND HEALTH-RELATED QUALITY OF LIFE USING WHODAS 2.0 TOOL IN A POPULATION LIVING IN *LOA LOA* ENDEMIC AREAS OF THE REPUBLIC OF CONGO (THE MORLO PROJECT)

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Loa loa filariasis, a parasitic infection endemic to Central Africa, is considered a frequent cause of medical consultation in this region. To evaluate the quality of life (QoL) of individuals living in loiasis endemic areas, we enrolled 991 subjects (one-third being microfilaremic) in the general population of a rural area of the Republic of Congo. WHODAS 12-items and information on the number of eye worm (Ew) and Calabar swellings episodes experienced throughout their lives, were collected. We analyzed the overall WHODAS score and its six domains (mobility, self-care, cognition, life activities, social activities, and participation). Nested analyses of baseline data showed that individuals with more than 10 Ew episodes had significantly higher scores than those without such history, which was particularly significant in the domains of mobility, cognition, and social participation. These individuals had also an increased risk of experiencing moderate (score >25/100) and severe impairment (score > 50/100) by nearly 3-fold (adjusted OR = 3.13, 95% CI 1.28-7.64, P = 0.012) and 2.69-fold (95% CI 1.41-5.13, P = 0.003), respectively, compared to individuals without any history of Ew. No other variable related to loiasis (Calabar swelling frequency, *L. loa* microfilaremia, and positivity to *L. loa* antibody rapid test) was associated with the various scores. Assuming that the frequency of Ew episodes throughout life could be a suitable proxy for overall exposure to the infection and/or the number of adult worms present in the individuals, the impact of loiasis on daily QoL appears to be primarily attributable to adult worms rather than to the microfilarial density. Adult worms would primarily affect everyday activity through peripheral symptoms, such as joint-related discomfort (with notable mobility impairment), while microfilariae would primarily induce organ dysfunction. Further studies are needed to better understand the respective clinical impacts of adult worms and *L. loa* microfilariae.

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BASELINE EVALUATION OF ONCHOCERCIASIS TRANSMISSION IN FIVE DISTRICTS OF BENIN

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Onchocerciasis, or river blindness, is a disease caused by the filarial parasite, *Onchocerca volvulus*. Achieving the World Health Organization (WHO) recommended Ov16 seroprevalence threshold of <0.1% in children under 10 to stop mass drug administration (MDA) is a major challenge for most endemic countries. Modeling studies suggest that the seroprevalence threshold could be increased to ≤2%. To evaluate the 2% threshold, Benin conducted serological and entomological surveys in five onchocerciasis-endemic districts where seroprevalence by Ov16 rapid diagnostic test (RDT) in 2020 was ≤2%. If the baseline survey shows an Ov16 seroprevalence ≤2% in children 5–9 years and blackfly infectivity by O150 PCR meets the WHO threshold, MDA will be stopped, and the area monitored for recrudescence. Results from the entomologic survey are not available and will not be discussed here. Samples were collected from children aged 5–9 years in the districts of Ouaké, Tchaourou, Bassila, Bante and Savè in 2023. Villages were selected by probability proportional to estimated size method, plus one additional first-line village. In villages, a multi-stage random sample of children was enrolled with parental authorization. Dried blood spots (DBS) were prepared from venipuncture samples, then eluted for analysis using the DBS Ov16 RDT method. From the 5 districts, 51 villages were selected and 1,884 children were enrolled: 53% were girls and 47% boys. In Bantè, no children had positive RDT results. Seroprevalence by RDT was 0.41% [95%CI: 0.00–1.21] in Ouaké, 0.54% [95%CI: 0.01–1.07] in Tchaourou, 0.98% [95%CI: 0.02–1.95] in Bassila, and 3.26% [95%CI: 0.88–5.63] in Savè. Overall seroprevalence was 0.9% [95%CI: 0.5%–1.4%]. The results in Savè might suggest an increase in seroprevalence between the 2020 and 2023 studies. These results need to be confirmed by Ov16m ELISA and analyzed with the results of the blackfly qPCR analysis to decide whether to discontinue MDA in the districts that have met the serological criteria. Demonstrating that transmission is interrupted at a higher serological threshold would facilitate progress towards the WHO targets for 2030.

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SUBSTANTIAL PROGRESS TOWARDS ENDING LYMPHATIC FILARIASIS AS A PUBLIC HEALTH PROBLEM IN DELTA STATE, NIGERIA

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Lymphatic filariasis (LF) is a neglected tropical disease endemic in Nigeria. In Delta state, in southern Nigeria, 16 of 25 districts were found to be LF-endemic with prevalence of circulating filarial antigen (CFA) by immunochromatographic test ranging from 1- 4% in baseline mapping (2005-2011). Annual mass drug administration (MDA) with ivermectin and albendazole delivered by community directed distributors (CDDs) started in 2014 in the 16 districts. Pre-transmission assessment surveys (Pre-TAS) were conducted in 16 districts in 2022 using filariasis test strips (FTS) among 22,400 people ≥ 5 years in each of 32 sites (one sentinel and one spot-check per district). Among 9,251 people tested, 9,246 (99.9%) were negative, and all 16 districts had <2% positive by FTS meaning they passed Pre-TAS and progressed to TAS-1 in 2023. The 16 districts were grouped into 11 evaluation units (EUs) based on geographic and epidemiological similarity. An average of 45 schools per EU were randomly selected for sampling from a list of registered schools. Students were sampled according to WHO guidance using survey sample builder. Refusal rate was low (0.6%), likely the result of a multi-pronged approach that engaged Parent Teachers Association (PTA) meetings in every selected school to obtain consent and dispel rumors and radio and television jingles to combat misinformation in addition to typical community mobilization for surveys. Valid FTS results were available for 16,887 children from 497 schools; only 6 children (0.04%) were CFA-positive. No EU had more than 2 positives, less than the critical threshold in each EU (range 14-18). Thus, all 11 EUs passed TAS-1, stopped MDA, and entered post-treatment surveillance for LF. Over 2.9 million people in the 16 districts no longer require LF MDA, representing a significant achievement toward national LF elimination. The national LF elimination program and partners should sustain the involvement of health workers and stakeholders like PTAs in subsequent TAS to support high participation in these surveys.

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MIXED TREATMENT STRATEGIES ARE AN EFFECTIVE HEALTH CAMPAIGN TO IMPROVE DRUG COVERAGE FOR RIVER BLINDNESS ELIMINATION IN INSECURE AREAS OF EDO STATE, NIGERIA.

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The region of Edo state, Nigeria along the Osse River has ongoing transmission of onchocerciasis and perennially low coverage of semi-annual mass drug administration (MDA) treatments. To improve MDA coverage, a health campaign involving mixed treatment strategies was deployed between November and December 2023 in six districts in Edo, bordering Ondo state. Methods consisted of integrating traditional house-to-house community-directed treatment with ivermectin (CDTI) with the immunization program's outbreak response (OBR), use of mobile health teams, providing medicines house-to-house, at fixed locations, and special teams of health workers, along with indigenous residents with security operatives to treat insecure areas termed "hit and run". This special strategy included identifying safe periods when intervention teams could travel to the security-compromised areas. A total of 990,813 treatments were distributed in the mixed strategy approach in the 6 districts November-December 2023—an 8.5% increase over the 913,367 treatments distributed in the prior June 2023 CDTI-only MDA. Correspondingly, the reported coverage increased from 65% overall in June 2023 (districts ranged from 54 – 70%) to 71% in December 2023 (districts ranged from 68 – 74%). Independent coverage surveys across all 6 districts confirmed this increase with significantly higher coverage in December 2023 than in the prior round (76.2% vs. 66.8%, $p<0.001$). Mixed treatment strategies were an effective health campaign that enhanced MDA coverage over CDTI alone in this area of Nigeria with persistently low coverage and offer a way to hasten disease elimination in other areas where terrain and insecurity pose challenges to house-to-house CDTI.

7429

POST-TREATMENT SURVEILLANCE FOR LYMPHATIC FILARIASIS SUPPORTS CESSATION OF TRANSMISSION IN HISTORICALLY CLASSIFIED ENDEMIC FOCI IN THE DOMINICAN REPUBLIC

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The Dominican Republic aims to eliminate lymphatic filariasis (LF) as a public health problem by 2025. Nationwide baseline mapping using lot-quality assurance sampling identified 3 endemic foci in need of mass drug administration (MDA) - Southwest, La Ciénaga, and East. By 2018, prevalence of circulating filarial antigen (CFA) was < 2% in all foci, meeting the criteria to stop MDA and begin post-treatment surveillance (PTS). The World Health Organization (WHO) recommends a minimum 4-year period of PTS to confirm that LF prevalence remains significantly below sustainable transmission levels. A community-based transmission assessment survey (TAS-3) was conducted in the East focus from December 2023-February 2024, six years after the halt of MDA in 2018 and two years after a TAS-2. In total, 154 bateyes (agricultural settlement villages targeted for MDA in the East region) were visited to exceed the target population of 909 children ages 6-7 years to test for CFA by Filariasis Test Strip. The threshold to pass TAS was 11. CFA was not detected among any of the 933 children tested with valid results, and the TAS passed. Similarly, CFA was not detected among 811 "adults" (85% female; age range [15-93 years], mean: 37 years) also invited for testing in the same household with valid results. WHO criteria to validate a country as having eliminated LF as a public health problem includes alleviating suffering through morbidity management and disability prevention (MMDP). A morbidity assessment was concurrently conducted in these bateyes where 4 members of 3 HHs self-reported lymphedema, all from the same province. These results, combined with finding no CFA-positive children or adults in the most recent PTS surveys conducted in the Southwest (2020) and La Ciénaga (2021) foci, indicate that LF transmission has been eliminated in all historically-classified endemic foci in the Dominican Republic. Remaining steps include scaling up MMDP services, dossier submission to WHO for validating elimination of LF as a public health problem, and maintaining post-validation surveillance until LF transmission is interrupted across Hispaniola.

7430

COMORBIDITY BETWEEN LYMPHATIC FILARIASIS AND HYPERTENSION AND DIABETES: A PROSPECTIVE CASE-COHORT STUDY IN KENYA

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Lymphatic Filariasis (LF) can lead to unilateral or bilateral swelling (Lymphoedema) in the legs, which in its advanced stage is known as elephantiasis, one of the world's leading causes of permanent and long-term disability. Due to its disfiguring nature, LF may directly or indirectly interfere with a person's mobility, predisposing a patient to a sedentary lifestyle and thus increasing the risk of non-communicable diseases like Type 2 diabetes and hypertension. A prospective case-cohort study was conducted in Kwale County in Kenya among 123 lymphoedema patients to screen them for type-2 diabetes and hypertension. Socio-demographic data, nutrition status, tobacco use, and physical activity (PA) levels were collected. Blood pressure and diabetes assessment was done over two subsequent days. PA assessment followed the Global Physical Activity Questionnaire (GPAQ) guidelines, with metabolic equivalent (MET) scores calculated based on frequency and type of exercise. Participants were grouped into diabetic/non-diabetic and hypertensive/normotensive categories. Those with either disease were treated as cases, while the rest were controls. Most of the study participants were female (60.2%), with the majority aged above 60 (61.8%). All of them were either minimally active, 19.5% (95% CI: 13.1 - 27.8), or moderately active, 80.5% (95% CI: 72.2% - 86.9%), with none classified as health-efficient physically active. The prevalence of hypertension was 79.7% (95% CI: 71.3 - 86.2), while 17.1% (95% CI: 11.1% - 25.1%) were diabetic, with hypertension higher among women and diabetes higher among men. Linear model revealed significant association between lower MET scores and presence of disease (hypertension and diabetes) (Estimate: -264.4; 95% CI: -437.8 to -91.0; $p=0.003$) among lymphoedema patients. This study demonstrates that lymphedema patients need to be enrolled in PA under the guidance of physiotherapists to improve their MET scores and prevent them from secondary diseases like type 2 diabetes and hypertension. If already diagnosed with both conditions, they should be targeted for glycaemic and blood pressure control, respectively.

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ONCHOCERCIASIS SEROPREVALENCE IN BIÉ PROVINCE, ANGOLA: A CROSS-SECTIONAL SURVEY TO GUIDE EFFORTS TOWARDS ELIMINATION

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Despite intensive control efforts in many countries, it is estimated that onchocerciasis still affects over 19 million people globally and continues to be a cause of considerable morbidity including blindness. Recently, a program of mass drug administration (MDA) with ivermectin was introduced to areas of Angola including Bié province that had been determined to be endemic through surveys conducted between 2003 and 2015 using either nodule palpation or microscopy of blood specimens. In Bié, prior to the initiation of MDA, we conducted a cross-sectional survey across three areas to determine suitability for a planned cluster-randomised trial of moxidectin versus ivermectin MDA. We randomly selected 10 villages in each area, with 10-12 households randomly selected per village, aiming to enrol 50 participants aged one year and above with informed consent per village; to reach a total of 500 participants in each study area. Finger-prick blood samples were collected from consenting participants for dry blood spots (DBS) and thick blood smears for onchocerciasis and *Loa loa* diagnosis, respectively. The Ov-16 rapid diagnostic test was conducted on the DBS eluates, with results read 24 hours later. Thick blood smears were stained with Giemsa and examined under light microscopes for *Loa loa* detection. Additionally, participants aged 15 years and above were invited to respond to a questionnaire on black fly exposure. We also conducted an exploratory entomological survey, assessing blackfly breeding sites along rivers in the study areas and collected blackfly larvae for subsequent laboratory analysis. Preliminary findings of Ov-16 seroprevalence adjusted for clustering at village and household level revealed it varied across the three study areas, ranging from 8.2% to 46.6%. Older age groups had higher Ov-16 prevalence. One *Loa loa* case was detected. The breeding site assessments confirmed the presence of blackfly larvae in all three study areas. Our findings confirm the urgent need for MDA against onchocerciasis in this province.

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POST-TREATMENT SURVEILLANCE FOR LYMPHATIC FILARIASIS IN HAITI: RESULTS FROM TRANSMISSION ASSESSMENT SURVEY (TAS-3) IN NIPPES AND SOUTH-EAST.

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Lymphatic filariasis (LF) is a leading cause of permanent disability globally with over 882 million people in 44 countries at risk for infection. Haiti is one of 4 remaining LF-endemic countries in the Americas. Baseline mapping determined that 88% of Haiti's districts were endemic, however, the Haitian Ministry of Public Health and Population decided to implement nationwide annual mass drug administration (MDA) of diethylcarbamazine and albendazole. The World Health Organization recommends transmission assessment surveys (TAS) to determine whether the prevalence of circulating filarial antigen (CFA) is below 2%--the putative threshold for interrupting *Wuchereria bancrofti* in *Culex* or *Anopheles* transmission areas. Repeated TAS are recommended at 2-3-year intervals during 4-5 years of post-treatment surveillance (PTS). Nippes and Sud-Est *departments* (regions) of Haiti's southern peninsula halted MDA after passing TAS-1 in 2014-2015. Following successful TAS-2 surveys in 2017, TAS-3 was conducted in November and December of 2023 in 21 districts grouped into 3 evaluation units (EUs): Miragoane (a single district in Nippes), Nippes (the remaining 10 districts), and Sud-Est (10 districts). A total of 4,610 children aged 6-7 years old were tested for CFA by filariasis test strips in community-based TAS: 1,416 children in 30 localities in Miragoane, 1,607 children in 39 localities in Nippes, and 1,587 in 64 localities in Sud-Est. Among these, 3 (0.21%), 1 (0.06%), and 0 (0%) were CFA-positive—all beneath the critical cut-off values (range 16-18) for each EU. All 4 CFA-positive individuals were microfilaria-negative in follow-up night blood testing. Children were also tested for malaria by rapid diagnostic test, with prevalence estimates of 0.07% (1/1,414), 0.44% (7/1,608), and 0.13% (2/1,587) in Miragoane, Nippes, and Sud-Est, respectively. Results indicate that LF and malaria are rare in these areas. Passing TAS-3 fulfills the epidemiological criteria for eliminating LF as a public health problem, yet follow-up is needed to investigate persistent CFA-positive signals and to maintain PTS given displacement and insecurity in Haiti.

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HIGH MORTALITY AMONG PERSONS WITH SUSPECTED EPILEPSY: A FOCUS ON ONCHOCERCIASIS-ENDEMIC COUNTIES OF SOUTH SUDAN

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Onchocerciasis, a neglected tropical disease, has been consistently associated with epilepsy. We investigated epilepsy prevalence and mortality in four onchocerciasis-endemic counties in South Sudan: Maridi, Mvolo, Mundri and Wulu. House-to-house cross-sectional surveys from 2021 to 2024 identified suspected persons with epilepsy (sPWE) and ascertained deaths among sPWE and individuals without epilepsy (IWE). Epilepsy diagnoses were confirmed by trained clinicians. Epilepsy prevalence ranged from 3.3% in Mundri (86/2588) to 4.5% in Mvolo (672/15092), with Maridi (586/14402) and Wulu (55/1355) having a rate of 4.1%. In Maridi and Mundri, with access to free antiseizure medication (ASM) at a treatment centre, ASM adherence was 91% and 95%, respectively, compared to Wulu (9%) and Mvolo (23%) without such access. The median age of death for sPWE varied from 19 years in Maridi to 22 years in Mundri. sPWE mortality rates per 1,000 person-years were 44 in Maridi (95%CI: 36-55), 46 in Mvolo (95%CI: 38-56), 66 in Mundri (95%CI: 37-113) and 70 in Wulu (95%CI: 34-133). In comparison, IWE mortality rates per 1,000 person-years were significantly lower, ranging from 5 in Mvolo (95%CI: 4-5) and Mundri (95%CI: 4-8) to 10 in Wulu (95%CI: 7-15) and Maridi (95%CI: 9-11). The resulting mortality rate ratios indicated that sPWE were 4-12 times more likely to die than IWE. Limitations include potential recall bias on mortality data and the cross-sectional design preventing confirmation of epilepsy diagnoses among deceased sPWE. Additionally, self-reported ASM access may be inflated in the counties with treatment centres due to social desirability bias. Our study highlights a significant mortality burden among PWE in onchocerciasis-endemic areas. The observed high mortality burden may be explained by the combination of high epilepsy prevalence and related mortality, exacerbated by a substantial epilepsy treatment gap. Thus, more advocacy is needed to strengthen onchocerciasis elimination programmes associated with decreased epilepsy incidence in endemic areas and ensure uninterrupted free access to ASM in primary healthcare settings for all PWE.

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INTEGRATED LYMPHATIC FILARIASIS, SCHISTOSOMIASIS AND SOIL TRANSMITTED HELMINTHIASIS IMPACT ASSESSMENT IN OHAUKWU, EBONYI STATE, NIGERIA

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Lymphatic filariasis (LF), Schistosomiasis (SCH), and soil-transmitted helminthiasis (STH) are co-endemic in Ohaukwu local government area of Ebonyi State and have been treated by mass drug administration (MDA) since 2014, 2015, and 2014, respectively. Impact assessments for SCH/STH are recommended every 2-3 years, but none have occurred since baseline surveys in 2013 due to funding constraints. We integrated an SCH/STH assessment into a planned LF transmission assessment survey (TAS-1) in Ohaukwu to attempt cost-effective impact assessment. LF TAS-1 was conducted in January 2024 according to standard WHO protocol, with filariasis test strips (FTS) used for all children from classes 1 and 2 (~age 6-7 years) in 40 systematically selected schools from the LGA. The target sample was 1,380 with a critical cut-off of 16 positives. We randomly included 10 selected schools in the SCH/STH survey, and purposively added the 5 still-extant schools from the 2013 baseline survey. Urine and stool samples were collected from a target of 50 school-aged children (SAC) aged 5-14 years in each school and 50 adults in each surrounding community and microscopically examined with urine filtration and Kato-Katz methods. None of 1,473 SAC had positive FTS results, meaning that Ohaukwu passed TAS-1 and qualifies to stop LF MDA. Of 701 adults, 36 (5.1%) were positive for any STH and 12 (1.7%) for SCH. Of 736 SAC, 64 (8.7%) were positive for any STH and 68 (9.2%) for SCH. The prevalence in SAC reflects a reduction in SCH from 19.7% in 2013 and in STH from 58.4%. In the 5 resurveyed villages, SCH prevalence reduced in 4 and increased in 1, while STH reduced in all 5. We estimate that the integrated survey reduced costs by approximately 19% compared to the costs of conducting the TAS and SCH/STH surveys separately. We conclude that integrating SCH/STH impact assessment into an LF TAS is feasible and reduces costs, and that SCH/STH control and LF elimination efforts in Ohaukwu have been successful.

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COMPREHENSIVE ASSESSMENT OF ONCHOCERCIASIS TRANSMISSION DYNAMICS AND COMMUNITY PERCEPTIONS: A CASE STUDY IN HYPO-ENDEMIC COMMUNITIES OF OGUN STATE, NIGERIA

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Onchocerciasis persists as a significant neglected tropical disease in Africa, causing notable morbidity and socioeconomic strain, leading to a rise in disability-adjusted life years. Control efforts have mainly focused on preventive chemotherapy (PC) in moderate to high endemic areas. However, extending PC to hypo-endemic regions is crucial for meeting 2030 elimination targets. An epidemiological and entomological survey was conducted in hypo-endemic areas of Ogun State to assess onchocerciasis prevalence, associated risk factors, and blackfly vectors' abundance and infectivity over 12 months. 230 participants aged 5-70 were recruited from three communities within hypo-endemic implementation units (IUs). Parasitological and entomological surveys, along with questionnaires, were employed, and findings revealed a 10.04% and 15.79% prevalence microscopically and via O-150 screen pool analysis, respectively. Visual impairment (4%), Onchodermatitis (6.27%), and nodules (10.45%) were observed among adults aged 50 and above, with no significant gender difference. 418 blackflies were collected, with higher numbers during the rainy season (27% wet, 56% dry), notably in November and December. Larvae were absent upon dissection. Biting rates surged during early rainfall (April-June 2023) and continued rising till December, paralleled by an increase in blackflies' parous level. Participant interviews highlighted symptoms caused by microfilariae, but a lack of knowledge regarding blackfly breeding sites (69%) and prevention methods (87%). Traditional remedies were commonly used post-bites, while anti-malarial drugs, herbs, and local concoctions were mentioned for treatment. This study underscores the onchocerciasis status in hypo-endemic communities, stressing the need for intensified control efforts aligned with WHO objectives.

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INTESTINAL HELMINTHIASIS IS NOT ASSOCIATED WITH CLINICAL AND THERAPEUTIC ASPECTS OF DISSEMINATED LEISHMANIASIS CAUSED BY *LEISHMANIA BRAZILIENSIS* IN AN ENDEMIC AREA OF BRAZIL

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Disseminated leishmaniasis (DL) is an emerging but poorly characterized form of cutaneous leishmaniasis (CL) caused by metastatic infection with *Leishmania braziliensis*. We recruited participants with PCR-confirmed CL (n=99) and DL (n=20) between January and December 2017 at a dedicated leishmaniasis center in Bahia, Brazil. At enrollment, participants provided a stool sample, which was evaluated for presence of intestinal helminth infection and the number of helminth ova per gram of stool was quantified. Initial clinical examination consisted of an evaluation of the size and number of cutaneous lesions. Upon 60- and 90-day follow-up, participants were evaluated for the appearance of new lesions and response to treatment of existing lesions. Participants were considered cured by the presence of complete re-epithelialization of all lesions after the initiation of antimonial treatment. The median age of participants was 26 years (13-69) and 76.5% were male. Individuals with DL were significantly older than those with CL (42 vs 24 years; p=0.02), though univariate analysis among individuals with DL did not demonstrate a correlation between age and time to cure (R^2 0.06, p=0.5). The cure rate after 90 days of treatment was significantly lower in individuals with DL compared to those with CL (30% vs 65.9%; p=0.003), and the median time to cure was significantly longer (154.5 vs 65 days; p<0.001). There was no significant difference in the median number of lesions, median area of largest lesion, cure rate at 90 days, or median time to cure between DL patients with or without intestinal helminthiasis. The prevalence of intestinal helminthiasis was 40.3% (48/119), with no difference between the CL and DL populations. The most commonly identified organisms were *Necator americanus* (23/119), *Trichuris trichiuris* (19/119), and *Ascaris lumbricoides* (14/119). Coinfection with *L. braziliensis* and intestinal helminths does not affect clinical aspects or response to therapy in DL. Compared to individuals with localized cutaneous leishmaniasis, those with DL are significantly older.

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AN INVESTIGATION OF MUCOSAL LEISHMANIASIS IN THE U.S. MILITARY HEALTH SYSTEM

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Leishmaniasis is a protozoal infection with an increased risk of transmission to those serving in the United States (U.S.)military due to theaters of

operation in endemic regions.There has, in recent decades, been robust experience with old-world leishmaniasis in the MilitaryHealth System (MHS); however, new-world leishmaniasis, which may result in mucosal leishmaniasis, has been less studied. A total of 88 patients from 2012-2022 with diagnosis codes for "mucocutaneous leishmaniasis"or "leishmaniasis, unspecified"were identified in the Military Data Repository and reviewed. Within this cohort, there were two validated cases of mucosal leishmaniasis. Case one was a 28-year-old Active Duty (AD) male with recent travel to Belize who presented with a mucosal lip lesion that was biopsied and had inconclusive species confirmation, but was thought to be either *L. braziliensis* or *L. mexicana*. The second case involved a 30-year-old AD male with a history of travel to French Guyana who had a cutaneous lesion on his left hand that was identified as *L. guyanensis*, a causative species for mucosal leishmaniasis. Neither had evidence of any further mucosal involvement on otolaryngologic evaluation, and both subsequently received systemic therapy with a good clinical response. Although only two cases were identified over this period, this disease remains an important medical consideration when conducting military operations within endemic regions as both cases had recent military-specific travel to these areas.

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FIRST DETECTION OF *LEISHMANIA MAJOR* IN DOGS LIVING IN AN ENDEMIC AREA OF ZOONOTIC CUTANEOUS LEISHMANIASIS IN TUNISIA

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Dogs are considered the main domestic animals reservoir for *Leishmania infantum* parasite, the agent of Zoonotic Visceral Leishmaniasis (ZVL) in several Countries of the World. Dog may host other *Leishmania species* but its epidemiological role in the maintaining and spreading of these parasites is not completely elucidated. Zoonotic Cutaneous Leishmaniasis (ZCL) caused by *Leishmania major* affects thousands of people every year in North Africa. In ZCL endemic Countries few reports of *Leishmania major* positive dogs have been reported, probably because most human cases occur in poor rural areas where the social role of the dog and its medical management is not well considered. The aim of the present study is to add information on the possible involvement of domestic dog in the epidemiology of ZCL. Our research focused on a well-established endemic focus of ZCL, in the area of Echrarda, Kairouan Governorate, Central Tunisia. Fifty-one dogs with no apparent clinical signs of vector borne diseases were selected in small villages where human cases of ZCL are yearly present. Most of them appeared not well managed and were infested by ticks and fleas. All dogs were sampled for the *Leishmania spp*. diagnosis, by using the following procedures: blood sample for serology and buffy coat qPCR, popliteal fine needle aspiration and cutaneous biopsy punch for lymph node and skin qPCR. The results demonstrated a high percentage (21.56%) of dogs positive at least at one or more test, the most sensitive technique was the lymph node qPCR that detected 8/11 positive dogs. Nine, out of the eleven positive dogs, resulted infected by *Leishmania infantum*; ITS1-PCR-sequencing allowed *Leishmania major* identification in the remaining 2 cases, both from the popliteal lymph node samples that can suggest a possible visceral spread of a cutaneous *Leishmania* species in dog. Interestingly, one of the two *Leishmania major* positive dogs was living in the same house where 6-year-old children showed cutaneous lesions referred to ZCL. To our knowledge, this is the first report of *Leishmania major* positive dogs in Tunisia, the epidemiological role of which remains under investigation.

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SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF LIPOSOMAL AMPHOTERICIN B (AMBISOME) EFFECTIVENESS DATA FROM CLINICAL TRIALS FOR THE TREATMENT OF VISCERAL LEISHMANIASIS IN SOUTHEAST ASIA

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Leishmaniasis is transmitted by sandflies and caused by obligate intracellular protozoa of genus *Leishmania*. Visceral leishmaniasis (VL) is a neglected tropical disease, lethal if untreated, with 50 000- 90 000 cases/ year, caused by *L. donovani* in South-East (SE) Asia and East Africa, and *L. infantum* in Latin America and Mediterranean regions. The regimen of AmBisome approved by FDA in 1997 for VL is intravenous (IV) 3 mg/ kg, on D1-5, 14, and 21 (total: 21 mg/kg). This currently recommended regimen was based on studies with VL patients with *L. infantum* infection where AmBisome was administered in various regimens. Since then, in SE Asia, multiple studies have been run to optimize the treatment regimen in patients with *L. donovani*. Since 2014 in India, the treatment of choice for primary, immunocompetent patients with VL by the national elimination program has been IV 10mg/kg single dose AmBisome (SDA), in line with WHO recommendation. Systematic literature review and meta-analysis were conducted to review efficacy of 10mg/kg SDA. The estimate of clinical efficacy of 10mg/kg SDA obtained from this meta-analysis will inform future phase 3 studies. Following the systematic literature review, the meta-analysis limited inclusion to those studies conducted in the last 37 years on primary VL patients treated with AmBisome in SE Asia. Analysis of all 13 studies, totaling 3563 patients, based on Intent to Treat (ITT) set was conducted. These studies included treatment of patients at various doses and regimens of AmBisome and revealed cure rate of 92% at six months (CI 91-93%). A subsequent analysis of six of the 13 studies including 2768 patients treated with the SE Asia current treatment of choice, SDA 10mg/ kg, revealed cure rate of 93% at six months (CI 92-94%). The systematic literature review identified a significant number of studies conducted in the region, with over 3000 VL patients treated with AmBisome. The meta-analysis showed consistently high effectiveness of 10mg/kg SDA (>90%), which is the treatment of choice for VL patients in SE Asia, and is in the same range as multiple dose regimens of AmBisome that have been tested.

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GENOTYPING OF *BLASTOCYSTIS* SP. ISOLATES FROM FECAL SAMPLES FROM CHILDREN OF THE EDUCATIONAL INSTITUTION "128 LA LIBERTAD" (SAN JUAN LURIGANCHO), LIMA, PERU

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Diseases caused by intestinal parasites are among the most common public health problems, mainly in developing countries. *Blastocystis* sp. It is a single-celled, cosmopolitan intestinal protozoan that affects the intestinal tract of humans and various animals. *Blastocystis* sp. is considered commensal and is currently recognized as an emerging, opportunistic, zoonotic agent with broad genetic diversity. Its extensive diversity is evidenced by the 39 subtypes identified to date, whose assignment depends on the sequence analysis of the RNA gene (*SSU-rRNA*). This study aimed to genotype and characterize the subtypes of *Blastocystis* sp. from isolates of fecal samples from children in Lima, Peru. Seventy-two fecal samples from school-age children were analyzed, corresponding to 53% (38/72) and 47% (34/72), respectively, with age ranges ranging from 6 to 11 years. Four diagnostic techniques were used: direct examination,

culture in Jones medium, spontaneous sedimentation, and staining with Gomoris Trichromic. The 72 stool samples were cultured in Jones culture medium, from these samples, 35 positive cultures were obtained for *Blastocystis* sp.; likewise, DNA extraction was carried out using the commercial kit "High pure PCR Template Preparation". *Blastocystis* sp. was identified through PCR- SSU-rRNA gene. The genotypes of *Blastocystis* sp. were identified by RFLP using the restriction enzymes AluI and HinfI. For the identification of subtypes, specific primers. By direct observation and culture of Jones, *Blastocystis* sp. was the most prevalent species with 36% (26/72) and 48.6% (35/72) in the positive samples, respectively. An 1800 bp band evidenced the presence of *Blastocystis* sp. The RFLP with the two restriction enzymes (*Alu*I and *Hinf*I) showed varied band patterns; the ST3 subtype was the most predominant. *Blastocystis* sp., the RFLP allowed the identification of genotypes, and the ST1, ST3, and ST5 subtypes were also identified; these results suggest a genetic diversity associated with pathogenesis and zoonosis of the parasite.

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EPIDEMIOLOGICAL DYNAMICS OF LEISHMANIASIS IN THE SOUSS-MASSA REGION, MOROCCO (2017-2022)

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Leishmaniasis, identified as the second leading cause of mortality among global parasitic diseases, represents a significant public health challenge in Morocco, particularly in the Souss-Massa region. This study aims to elucidate the epidemiological dynamics of leishmaniasis within this region. We analyzed data from 1,103 cases across the six provinces of Souss Massa recorded between 2017 and 2022, using Jamovi software version 2.3.2.1 for statistical analysis. The vast majority of these cases were cutaneous leishmaniasis, accounting for 98% (1,084 cases) of the infections, with visceral leishmaniasis making up only 1.7% (19 cases). A notable 88% of the cases occurred in rural areas. The leading causative agent was *Leishmania major*, responsible for 56% (619 cases) of the infections, followed by *Leishmania tropica* at 42%, and *Leishmania infantum* at 2%. The average age of the affected individuals was 15.6 years, with a standard deviation of 16.4 years, indicating a wide age range among patients. The median age was 11 years. Males showed a statistically significant higher incidence, representing 56.1% of cases, compared to 43.9% in females ($p < 0.05$). Peaks in the number of cases were observed in May and January, while lower case numbers were typically seen in October and November. Tata province was identified as the main hotspot, contributing 57% of the cases, primarily due to *Leishmania major*, with an epidemic center in Akka. In Agadir province, accounting for 20% of all cases, 52% were attributed to *Leishmania tropica*, with a new epidemic focus in Drarga. These findings suggest a potential correlation with climate change and highlight the need for targeted public health interventions sensitive to the region's demographic and environmental factors influencing the spread of leishmaniasis. Alongside climate change, urbanization also emerges as a significant factor affecting disease dynamics. Passive screening played a crucial role, detecting 66.4% of the cases and proving essential for effective disease surveillance.

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THE EFFECTS OF ADVERSE ENVIRONMENTAL EXPOSURES ON RISK FOR CONGENITAL CHAGAS TRANSMISSION AND ADVERSE BIRTH OUTCOMES IN SANTA CRUZ, BOLIVIA

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Nearly 8 million people in Latin America are infected with *Trypanosoma cruzi* (*Tc*), the parasite causing Chagas disease, and most infections are initially asymptomatic and go undiagnosed. Chagas results in ~12,000 deaths annually, which is ten-times the number of deaths caused by Malaria in this region, making it the leading cause of parasitic death in the Americas. While treatable if diagnosed early, left untreated, *Tc* evades the immune system and decades later becomes a chronic cardiac, gastrointestinal, and/or neurological disease. *Tc* is also known to cause adverse birth outcomes in infants born to infected mothers, and congenital transmission occurs in about 5% of these births and can result in delayed childhood development. How *Tc* evades the immune system to traverse the placental barrier and establish congenital infection isn't well known. One theory is that a complex interaction between parasite, placenta, and inflammatory and oxidative stressors weakens the placental barrier from repeated activation of the innate immune system allowing the parasite to cross the placental barrier. Similarly, it is known that environmental exposures during pregnancy can have deleterious effects on birth outcomes. Repeated gestational exposure to ambient PM2.5 has been shown to result in adverse birth outcomes due to oxidative and inflammatory stress and PM2.5 can cross the placental barrier resulting in placental maladaptation. Extreme heat exposure can also have negative effects on pregnancy. Studies indicate that a 1°C increase in temperature correlates to double the risk for both pre-term and stillbirths. This ongoing study leverages two existing congenital chagas cohorts with ~10,000 mother-child dyads with a maternal *Tc* prevalence of 23.7% combined with freely available girded remote sensing environmental data to identify the effect of environmental exposures on congenital Chagas transmission and negative birth outcomes in Santa Cruz, Bolivia. This is a status update on an ongoing pilot-study and to our knowledge this is the first study to investigate the effects of environmental exposures on congenital Chagas transmission.

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MODELING CLIMATE DRIVERS OF CUTANEOUS LEISHMANIASIS INCIDENCE IN NORTHERN SYRIA

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Modeling climate drivers of cutaneous leishmaniasis incidence in northern SyriaLeishmaniasis is a Neglected Tropical Disease of global epidemiological importance caused by *Leishmania* parasites. Leishmaniasis is associated with high morbidity and impacts on quality of life, as it results in large open wounds during infection, which are associated with severe social stigmatization. In northern Syria, cutaneous leishmaniasis (CL) is endemic and its incidence exhibits significant geographic and temporal variation. Furthermore, CL incidence in northern Syria is dependent on the presence of the dipteran vector, which displays high variation in relation to environmental factors and public health vector control interventions. This study examines historical associations between CL due to *Leishmania tropica* and *Leishmania major* and environmental variables including rainfall, temperature, humidity, and vegetation cover in 63 subdistricts in 21 districts in the Al-Hasakeh, Aleppo, Raqqa, Deir-ez-Zor, and Idlib Governorates of northern Syria. Specifically, this study employs a time-lag generalized linear model to examine the relationship between the environmental variables and CL incidence over 479 weeks between December 2014 and March 2024. Weekly case counts varied from zero cases per week in many subdistricts to 2185 cases per week in the Ras Al Ain subdistrict in the 45th week of 2021. On the governorate level, over the study period, CL cases were highest in Al-Hasakeh governorate, peaking at 2216 cases in the 45th week of 2021. Seasonal trends were particularly apparent in Deir-ez-Zor governorate, where cases peaked in January every year between 2018 and 2022. This study found significant intra-governate and intra-district variability

in weekly case counts. Variations in temperature, rainfall patterns, humidity, and vegetation cover associated with climate change are likely to have a significant impact on future CL transmission patterns in endemic regions. These models suggest that climate monitoring is an important tool in the control and prediction of future CL incidence.

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SPECIES IDENTIFICATION OF CUTANEOUS LEISHMANIASIS CAUSING PARASITES IN NEPAL

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The ongoing Kala-azar elimination programme in Nepal is based on anthroponotic transmission of Kala-azar caused by the protozoan parasite *Leishmania donovani*. In recent years, a shift of reported cases from classical lowland foci in the east to hilly and mountainous areas of the western and far western regions of Nepal was well documented by the national control programme. In addition, cutaneous leishmaniasis cases are increasingly being reported, mainly from the west of the country, though the causative parasite species is not yet fully elucidated. Hence, to support of the ongoing country disease programme and to generate further evidence on the causative parasite species for cutaneous leishmaniasis in Nepal, a study was set up, in which we collected detailed patient information as well as skin biopsies from several hospitals located in the western and far western regions of Nepal. Altogether, 24 skin samples were collected and subjected to PCR and sequencing to determine the infecting parasite at species level. Samples were obtained from 11 different hilly districts, all from patients who didn't have a travel history outside of the country. Out of 24 skin samples, PCR detected *Leishmania* infection in 13 samples. Further molecular analysis confirmed the presence of *L. donovani* in 12 of them. Although these findings do not exclude other causative species to be involved in cutaneous leishmaniasis in Nepal as well, the confirmation of *L. donovani* in these cutaneous leishmaniasis patients could have important implications for the Kala-azar elimination programme. Furthermore, there is no evidence yet that this particular *L. donovani* strain could also cause visceral leishmaniasis, there is a clear need for genomic surveillance of visceral and cutaneous leishmaniasis cases in Nepal to rule out any potential threat to the Kala-azar elimination initiative in the region.

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BLASTOCYSTOSIS INFECTIONS AMONG CHILDREN ATTENDING FOUR HOSPITALS IN WESTERN KENYA

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Blastocystis spp, is a common intestinal parasite affecting both humans and animals worldwide. Although the role of Blastocystis *spp* as an enteric pathogen is disputed, it has been associated with infections including gastrointestinal discomfort. *Blastocystis spp* is thought to have harmful functions in the presence of certain enteric pathogens, in addition, having a potential pathogenic role in the gut, affecting growth and development in children. This study determined the prevalence of *Blastocystis spp* infection or carriage in children 15years and below, characteristic symptoms and association of infection with water source and water treatment. Faecal microscopy was conducted on 976 stool samples (488 symptomatic, 488 asymptomatic) from children enrolled in a case-control study in four County Hospitals in western Kenya. The samples were processed using Mini Parasep SF Faecal Parasite concentrator. Blastocystis *spp* was detected in 73/ 976 (7.5%) of the stool samples from both symptomatic and asymptomatic subjects with a distribution of 36/488 (7.4%) infections in cases and 37/488 (7.6%) in controls. Among the 73 infections, 56 /73 (76.7%) were Mono-infections while 17/73 (23.3%) were co-infections. Of the 73, 34/73 (46.6%) were females while 39/73 (53.4%) were males. General gastrointestinal symptoms reported were mainly; abdominal pain/ cramps (42.5%), diarrhea (15.1%), and loss of appetite/vomiting (12.3%). Additionally, cough (15.0%) and fever (12.3%) were reported as secondary symptoms, while headache (6.8%) was less frequently reported. The highest number of infection 35/73(47.9%) was among subjects who used municipal/tap water, followed by 30/73 (41.1%), 28/73 (38.4%) and 7/73 (9.6%) among those who used water from the river/springs, rainwater and borehole/well respectively. 50/73 (68.5%) of the *Blastocystis spp* were found in subjects who did not treat water. However, 23/73 (31.5%) infections were found in those who treated water. There is asymptomatic carriage of *Blastocystis spp* in children of up to 15years of age is 7.5%, however, no follow-up was done to see if the participant got diarrhea or not.

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THE GROWING PROBLEM OF LEISHMANIASIS IN TUSCANY, ITALY: AN INVESTIGATION OF UNDERREPORTED HUMAN CASES AND COMPARISON WITH CANINE INCIDENCE USING A MULTIDISCIPLINARY APPROACH.

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The Mediterranean basin, including Italy, hosts endemic areas for leishmaniasis, mainly attributable to the presence of sand flies. Leishmaniasis has gained importance in Europe, fuelled by factors such as climate change, globalisation and migration. For at least 10 years in Tuscany (Italy) there has been an important discrepancy between official notifications on reports of human visceral and cutaneous leishmaniasis cases and the number of hospital admissions, highlighting an important underreporting, despite the Italian reporting obligation. Moreover, official reports have increased alarmingly over the last three years. Human leishmaniasis is a disease that does not always require hospitalisation: it often presents cutaneous manifestations, whereas in the immunocompetent individual it may not manifest itself at all. For this reason, it is reasonable to assume that the number of cases is higher than the number of hospitalisations. The project aims to investigate the underreporting of human leishmaniasis cases from 2014 to 2023 by analysing laboratory diagnoses (considering any laboratory test that according to the guidelines of the Italian Ministry of Health is useful in identifying a 'confirmed case', thus serological tests; parasitological tests; culture tests; PCR). To estimate the extent of the underreporting, the capture-recapture method will be used, taking into account laboratory data, official reports and hospital data. Subsequently, a comparison will be made with the incidence, in the same territory, of veterinary cases, particularly in dogs, using data obtained from the Lazio-Tuscany Zooprophylactic Institute, to compare the trend of human and canine cases over time. Analyses are in progress and currently confirm a significant underreporting of up to five times the official number of notifications. The results will be presented at the conference. Poor surveillance leads to ineffective prevention policies. The impact of the project is to strengthen the leishmaniasis surveillance system in Tuscany in order to reinforce prevention systems and face emergencies.

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UNTANGLING THE LEISHMANIASIS THREAT: A MULTIFACETED ANALYSIS OF TRANSMISSION NETWORKS, ECOLOGICAL FACTORS, AND GEOGRAPHIC IMPLICATIONS IN A LEISHMANIASIS ENDEMIC REGION IN THE EASTERN MEDITERRANEAN

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The Leishmaniases, a group of neglected tropical diseases exhibiting significant anthropo-zoonotic transmission, are experiencing a worrying upsurge across the Mediterranean and Middle East, particularly in Israel. This review delves into the multifaceted factors driving this concerning trend.Israel, a Leishmaniasis hotspot within the Middle East, presents a unique case study. Four Leishmania species (*Leishmania major*, *Leishmania tropica*, *Leishmania infantum*, and the recently identified *Leishmania donovani*) co-exist, each engaged in intricate zoonotic cycles involving specific sandfly vectors and mammalian reservoirs. This intricate interplay between specific Phlebotominae sand flies of the genus *Phlebotoums*, diverse mammalian reservoirs, and Israel's varied ecological landscapes results in a spectrum of clinical presentations in both humans and animals. This complex transmission web underscores the critical need for in-depth research to develop effective control strategies.Factors such as cross-border transmission, the detection of novel transmission cycles, local conflicts, and evolving transmission dynamics all contribute to the escalating risk. Climate change adds another layer of complexity by potentially altering sandfly distribution and parasite development.This work emphasizes the urgent need for further investigation into the dynamic interplay between Leishmania parasites, sandfly vectors, animal reservoirs, and environmental factors. Only through a comprehensive approach can effectively combat the growing threat of Leishmaniasis in the Middle East and beyond.

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ASSESSING *TOXOPLASMA GONDII* SEROPREVALENCE AMONG IMMUNOCOMPETENT AND IMMUNOCOMPROMISED INDIVIDUALS LIVING IN PERU: A COMPARATIVE STUDY BETWEEN LIMA AND IQUITOS

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Toxoplasmosis, caused by *Toxoplasma gondii*, is a disease that may produce severe consequences among immunocompromised individuals. The seroprevalence of Toxoplasmosis among immunocompromised patients has not been well studied in Peru. Our study aimed to: 1) evaluate the performance of an in-house ELISA using the commercially available Vircell ELISA kit as a reference; 2) estimate the seroprevalence of Toxoplasmosis among individuals living in Lima, located in the coastal region of Peru, and Iquitos, in the Peruvian Amazon basin; and 3) evaluate factors associated with *T. gondii* seropositivity. We enrolled HIV positive individuals with neurological signs in hospitals in Lima (n=50) and Iquitos (n=50), and healthy individuals working at a university from Lima (n=73) and from houses randomly selected in Iquitos (n=108). We processed 90 randomly selected samples for performance evaluation of our in-house ELISA. Our ELISA showed 98.3% and 100% positive and negative percent agreements, with the Vircell ELISA kit. In Iquitos, individuals had a median age of 38.5 (IQR 27-51), with 77 (48.7%) males and 50 (31.65%) HIV positive. In Lima, individuals had a median age of 26 (IQR 23-34), with 70 (56.9%) males and 50 (40.65%) HIV positive. Toxoplasmosis seroprevalence was 88% in Iquitos (139/158) and 29.3% in Lima (36/123). In Lima, older individuals (PR 1.04, [95% CI 1.03-1.06]) and in Iquitos, males (PR 1.13, [95% CI 1.01-1.27]) showed higher seropositivity rates. HIV positive individuals from both study sites were more likely to be seropositive (PR 2.29, [95% CI 1.30-4.05] for Lima; and 1.18, [95% CI 1.07-1.29] for Iquitos). Our in-house ELISA presented a high performance. Future studies should determine the performance of this in-house test with other human and animal samples. Our results highlight important seroprevalence levels of Toxoplasmosis in Iquitos, Peru. Although this seroprevalence was not low among HIV negative persons living in Lima (14/73, 19.2%) and Iquitos (90/108, 83.3%), it was even higher among HIV individuals (22/50, 44%; and 49/50, 98% in Iquitos), which represents a risk for neurological complications among these patients.

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DEFORESTATION, LAND REVERSION, AND *TRYPANOSOMA CRUZI* INFECTION IN DOGS LIVING IN RURAL COMMUNITIES IN CENTRAL PANAMA

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Given dogs' roles as sentinels and reservoirs for *Trypanosoma cruzi*, the etiologic agent of Chagas disease, it is important to understand host and environmental factors associated with *T. cruzi* infection in dogs. The objective of our study is to measure *T. cruzi* infection in dogs from 12 rural communities and to evaluate intrinsic (e.g., sex, age, body condition, hemogram) and environmental (e.g., land cover) relationships between *T. cruzi* infection in dogs. We hypothesized that deforestation and land reversion influence *T. cruzi* infection rates in dogs and that *T. cruzi* infection will be higher in areas dominated by secondary forest growth. We performed physical examinations and sampled blood from 483 dogs from 203 households. We collected epidemiological variables (e.g., age, sex, body condition score) and performed rapid immunochromatographic tests, western blot, indirect immunofluorescence, and multiplex microsphere immunoassay to evaluate previous *T. cruzi* exposure. Additionally, we evaluated *T. cruzi* parasitemia by conventional PCR using S35/S36 targeting the 330bp region of the kinetoplast. Dogs positive for two or more serological tests or PCR were considered positive. Preliminary results show that across the communities,15.21% (95% CI, 11.89-19.04) (63/414) of dogs were positive for two or more *T. cruzi* serological tests. In addition, 3.54% (95% CI, 1.63-6.62) (9/254) had *T. cruzi* parasitemia confirmed by PCR. Overall, there were no significant associations between *T. cruzi* infection in relation to dog sex, body condition, and age. However, there were community level differences in *T. cruzi* infection/exposure in dogs- communities surrounded by secondary forest growth had positive associations with *T. cruzi* prevalence. Preliminary results suggest that complex interactions between land cover types around communities and households influence *T. cruzi* infection in dogs.

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KNOWLEDGE ABOUT CHAGAS DISEASE AMONG HEALTHCARE PROFESSIONALS

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The knowledge of health professionals about Chagas disease among health professionals is essential for controlling this Public Health problem. We aimed to identify the knowledge about this public health problem among these Primary Health Care professionals. We performed a cross-sectional, exploratory study, with 257 professionals between April and September 2023 in Irecê city, Brazil. Data were collected using a standardized questionnaire and data were analyzed descriptively. From the total number of professionals, 87.9% recognized the etiological agent is a protozoan, and identified the following forms of transmission: vector (100%), blood transfusion (55.3%), and oral (61.9%); the main organs affected were: heart (99.2%) and spleen (58.4%). The signs/symptoms identified in the acute phase were fever (76.6%), adenomegaly (59.4%), edema (85.2%), splenomegaly (68.0%), hepatomegaly (65.2%), Romaña sign (50.4%); at chronic cases, it was recognized that it may occur asymptomatically, but electrocardiographic changes (99.2%), megacolon (64.6%), megaesophagus (59.1%), congestive heart failure (99.2%) may be present.), thromboembolic phenomena (58.4%), and respiratory distress (80.9%). Regarding etiological treatment, 72.0% recognized its existence, but 47.5% were unable to inform which medication was recommended; and for 73.5% of participants, the disease is incurable. Regarding the insect vector, 81.7% recognized it. When asked about the service where triatomines should be sent, 65.7% recognized the Zoonosis Control Center. The care to be taken when handling triatomines was to use gloves or protect your hands with a plastic bag (92.2%); the guidance to be given when faced with an insect bite in humans was to carry out serological tests (91.8%) and personal access to information occurred informally in everyday daily work (30.0%) or during the training course in the health area (28.8%). It is of fundamental importance that health professionals are trained on Chagas disease for early recognition and specific treatment, and that health surveillance and vector control actions are effective.

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IMPACT OF *BLASTOCYSTIS* SUBTYPES ON POLYPARASITISM IN COLOMBIAN CHILDREN

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Polyparasitism is prevalent in developing communities and peri-urban areas of large cities. Factors contributing to persistent polyparasitism include recurrent environmental exposure and reinfection. Identifying the primary risk factors is crucial for effective intervention. *Blastocystis* is a common intestinal protozoan with a contested role as a human pathogen, with pathogenicity dependent on the *Blastocystis* subtype. In a peri-urban area of Medellín, Colombia, stool samples were taken from 202 children under five years old, and we conducted stool-based multi-parallel real-time quantitative PCR. Preliminary results revealed that 57.9% of children tested positive for *Blastocystis* DNA, 20.3% *Cryptosporidium*, 20.3% *Giardia intestinalis,* 9.4% *Necator americanus,*1.9% *Trichuris trichiura,*1.9% *Entamoeba histolytica*, and 1.5% *Ascaris lumbricoides*. No positive samples were found for *Ancylostoma duodenale* and *Strongyloides stercoralis.* We found varying degrees of polyparasitism, with 57.2% of children testing for one parasite, 34.9% for two, and 7.9% for three. The children infected with *Blastocystis* and a helminth had a significantly different burden of *N. americanus*, *T. trichiura*, and *A. lumbricoides* (0.011 vs 0.12 vs 0.59, p = 0.0018). There is a greater burden of *G. intestinalis* within *Blastocystis* negative children than *Blastocystis* positive children (1.36 versus 0.26 fg/µl, p = 0.0340). Also, a significant positive correlation was identified between *Blastocystis* and *G. intestinalis* with Spearman R = 0.37898, p = 0.0385. These findings suggest *Blastocystis* is a valuable indicator of GI parasite exposure rates. Given its reported transmission through fecal-oral contamination and cyst-infected water sources, further studies will explore *Blastocystis* subtypes and their associations with helminth/protozoan infections.

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IMPACT OF EDUCATIONAL ACTIVITIES AND AN ELECTRONIC MEDICAL RECORD TEMPLATE ON CHAGAS DISEASE SCREENING

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Given a lack of comprehensive screening programs or standardized screening recommendations for clinicians, the estimated prevalence of 300,000 people with Chagas disease in the United States (US) is likely an underestimate. In 2021, clinicians and public health experts began the Implementing Novel Strategies for Education and Chagas Testing (INSECT) study at Boston Medical Center (BMC) to improve awareness and knowledge of Chagas disease and enhance healthcare provider screening. As a quality improvement initiative, we examined the influence of educational activities and implementation of an electronic medical record (EMR) template on changes in screening rates at BMC. Educational sessions were conducted in the BMC departments of internal medicine, obstetrics/gynecology, pediatrics, and family medicine and sections of nephrology, transplant nephrology, cardiology and infectious diseases. Audience members included medical students, resident, fellow and attending physicians, nurses, midwives and public health experts. From 2014 to the start of BMC educational activities in 2021, 729 tests were ordered, including screening and confirmatory testing at the Centers for Disease Control and Prevention. The top five ordering departments were obstetrics/gynecology (OB/GYN) (152, 21%), adult inpatient medicine (123, 17%), transplant surgery (92,13%), cardiology (80, 11%), and infectious diseases (60, 8%). From 2021-2024, INSECT study members conducted 23 Grand Rounds and lectures to approximately 870 individuals at BMC. Since INSECT implementation, 3,731 tests were ordered (2021-April 17, 2024), displaying increased testing overall and a shift towards more primary care testing. Top ordering departments included OB/GYN (1802, 48%), transplant surgery (844, 23%), adult outpatient primary care (407, 11%), adult inpatient medicine (159, 4%), and family medicine (116, 3%). With the implementation of educational programming for providers and an EMR template for ordering ease, we increased testing for Chagas disease at BMC. We anticipate that other sites with at-risk patients may benefit from similar activities.

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BIBLIOMETRIC META-ANALYSIS OF CHAGAS DISEASE AND EQUITABLE ACCESS TO HEALTH CARE

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Chagas disease, transmitted by *Trypanosoma cruzi*, has been historically reported in endemic areas of Latin America. However, an increasing

presence of this disease is currently observed in urban habitats with domestic transmission cycles and adapted to different ecological environments. Currently, the total burden of Chagas disease is approximately 7 million cases worldwide. The objective of the study was to investigate the vertical transmission of *Trypanosoma cruzi*, its presence in blood banks and donors, its epidemiological distribution in urban areas, and its appearance in non-endemic regions. We conducted a bibliometric meta-analysis through searches in Scientific Technical Health Literature of Latin America and the Caribbean (LILACS), PubMed, multilingual collaborative health evidence database (epistemonikos), Cochrane, and Scopus. The search for scientific articles was conducted in English, Portuguese, and Spanish, with a cutoff date of December 27, 2022. The data network was constructed using VOSviewer software to: a) visualize any possible overlapping between the analyses by applying the association strength normalization technique, and b) analyze the information by a clustering technique, with relevant co-authorship publications between countries. The distance from one country to another reflects the strength of co-authorship each country exerts. The obtained results highlighted trends and patterns on Chagas disease research, its transmission, and epidemiology in the context of current knowledge and its implications for public health, especially in urban areas and non-endemic regions. In conclusion, this analysis focused on the infection of the parasite *T. cruzi* and its association in urban environments of both endemic and non-endemic countries, based on data collected from various studies published in scientific journals. The results underscore the need to strengthen disease surveillance and control programs in urban settings, and to implement strategies for early detection and timely treatment.

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CAPACITY-BUILDING IN MOLECULAR SURVEILLANCE OF INFECTIOUS DISEASES: PROGRESS AND ACHIEVEMENTS OF THE INSTITUTE OF RESEARCH IN TROPICAL DISEASES IN AMAZONAS, PERU

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Amazonas is a northeastern region located between the Andean mountains and the Amazon plain with a population of 429 483 inhabitants. This region has seven provinces with areas where native communities do not have access to public services such as electricity, drinking water or sewage. Amazonas is affected by several infectious and tropical diseases such as malaria, leishmania, Chagas, HIV, dengue and other arbovirus. The UNTRM was the first university in Amazonas to implement, in collaboration with the Regional Direction of Health, molecular tools for the research of infectious diseases that constitute a severe burden to the region. By January 2020th, the IET was created with three main laboratories: molecular epidemiology and genomics, cell culture and advanced therapies, and biosensors and biomedical devices. Molecular confirmation tests for the previously mentioned diseases were implemented and by September 2020th the COVID-19 laboratory for molecular diagnosis and genome sequencing received its operating license, becoming the first in the region. Additionally, we made major progress in implementing a surveillance platform for parasitic diseases such as malaria, reporting an outbreak of *Plasmodium falciparum* and a recent clonal expansion in the district of Rio Santiago, with its vector *Anopheles benarrochi*. We also managed to implement a reader device for electronic differential measurement to detect nucleic acid of Plasmodium in blood samples to be used in the field. On the other hand, the immunomodulatory cytokine profile of the secretome of mesenchymal stem cells cultured in the presence of Leishmania antigens was characterized. As a result of these investigations, over 15 papers have been published so far and several undergraduate and graduate students have participated and benefited by performing their thesis and dissertations. In conclusion, the UNTRM in collaboration with partner institutions was successful in building an institute with the latest technology in a hard-to-reach area, transferring capabilities to improve the diagnostic capacity of infectious diseases in Amazonas.

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TSLP UPREGULATES IFN-GAMMA PRODUCTION IN CUTANEOUS LEISHMANIASIS PATIENTS

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Patients with cutaneous leishmaniasis (CL) due to *Leishmania braziliensis* infection develop ulcerative skin lesions that are associated with inflammatory response. Activation of macrophages by IFN-gamma is the main mechanism of *Leishmania* parasite killing, whereas Th2 environment with IL-5 production is associated with parasite replication. Our previous results show intense inflammatory infiltrate with high production of TNF and IL-1-beta in lesions from CL patients. Thymic stromal lymphopoietin (TSLP) is an epithelial cell-derived cytokine expressed in skin, gut, lungs, and thymus that induce Th2 cytokines and is produced during helminth infection and atopy. Our aim was to assess the production and effect of TSLP in cells from CL patients. By analyzing single-cell RNAseq we found that TSLP is not significantly expressed in lesion C57BL/6 mice upon infection with *L. major*, or in lesion from CL patients due to *L. braziliensis* infection. To assess the effect of TSLP on CL patients we added recombinant (r) TSLP to Soluble *Leishmania* Antigen (SLA)-stimulated peripheral blood mononuclear cells (PBMC) from CL patients. Surprisingly, addition of rTSLP increased IFN-gamma in SLA-stimulated PBMC culture supernatants without affecting the production of TNF, IL-5 and IL-10. Our data suggest that presence of TSLP may benefit CL patients by increasing IFN-gamma production, thus contributing to parasite killing.

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FOLLICULAR T HELPER (TFH) VERSUS HYBRID TH1/TFH CELLS AND THE OUTCOME B CELL RESPONSE IN *TRYPANOSOMA CRUZI* INFECTION OF SUSCEPTIBLE AND RESISTANT MICE

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Trypanosoma cruzi is the etiologic agent of Chagas disease (CD). Endemic to Latin America, CD affects 6 to 7 million people worldwide and is responsible for over 800,000 disability-adjusted life-years due to digestive and cardiac manifestations. Immune response studies in the context of *T. cruzi* infection are mostly focused on T cells, due to their well-known role associated with better outcomes by the generation of a CD4$^+$ T helper Th1 profile and a strong CD8$^+$ T response that is, however, unable to resolve the infection. Contrarily, B cell response in CD models has been overall under investigated. It's known that *T. cruzi* infection induces a polyclonal B lymphocyte proliferation with unspecific antibody response unable to clear the parasites, resulting in chronic infection. In this work, we performed a thorough characterization of the B cell immune response and Follicular T helper (Tfh) cells, a subset of CD4$^+$ T cells required for the T-dependent germinal center (GC) response, in *T. cruzi* infection. Comparing two different mouse models: C57BL/6 mice described as a resistant model to *T. cruzi* infection, and BALB/c mice, susceptible. Female mice of both strains were infected with 5000 blood form trypomastigotes of the bioluminescent H1 *T. cruzi* strain. Flow cytometry analysis showed that C57BL/6 mice model, associated with type I immunity, produced hybrid Th1/Tfh cells with reduced expression of the transcription factor Bcl6 and increased expression of IFN-γ. Comparatively, BALB/c mouse model, associated with type 2 immunity, produced mainly classic Tfh cells with increased Bcl6 expression leading to IgG 1 hypergammaglobulinemia and an exacerbated expansion of germinal center B cells. In both models, the expression of Bcl6 in germinal center B cells, associated with the production of high-quality antibodies, is delayed appearing only 28 dpi. These results point to the development of different evasion mechanisms by the parasite with the late production of specific high-affinity antibodies.

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GALNAC AND GLCNAC CARBOHYDRATES INCREASE THE PRESENCE AND ACTIVITY OF THE MYELOPEROXIDASE ENZYME DURING *ENTAMOEBA HISTOLYTICA* AND NEUTROPHIL INTERACTIONS, POSSIBLY BY BLOCKING AMEBIC ADHESION

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The present study analyzes the effect of the presence of carbohydrates N-acetyl-D-galactosamine (GalNAc) and N-acetyl-D-glucosamine (GlcNAc) on the myeloperoxidase (MPO) activity of neutrophils during their interaction (mouse model of resistance to amebiasis) with trophozoites of *Entamoeba histolytica* (*E. histolytica*). GalNAc and GlcNAc block the amoebic 260 kDa and 220 kDa lectins, respectively. *E. histolytica* trophozoites (5×10^4 amebas/ml) were interacted with mouse neutrophils (1×10^6 cells/mL) in presence of the carbohydrates at 25 mM and the effect was evaluated at 20, 40, 60, and 90 min. MPO activity was explored with the addition of TMB (chlorhydrate of 3,3', 5,5'-tetramethylbenzidine) and hydrogen peroxide solution. The microscopy analysis was carried out with an anti-ameba polyclonal rabbit IgG antibody, which was detected with a secondary donkey anti-rabbit IgG (H + L) antibody Alexa Fluor-647. MPO was detected with an anti-MPO polyclonal rabbit IgG conjugated to the Alexa Fluor-350 antibody. The samples were counterstained with SYTOX green to observe the DNA and images were collected and analyzed with confocal fluorescence microscopy. A significant increase was observed in the activity and presence of MPO at the different times of the interactions in presence of the carbohydrates compared with the interactions in absence of the carbohydrates. The greatest increase in MPO activity was found in the presence of GalNAc. The increase in the activity and presence of MPO in ameba/neutrophil interactions in the presence of carbohydrates suggests that MPO could be involved in amoebic damage by blocking amebic adhesion, thus making it possible for the MPO of neutrophils to be activated.

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LACK OF INFORMATION AS A REASON FOR NON-PARTICIPATION IN MASS DRUG ADMINISTRATION TARGETING ONCHOCERCIASIS: A MIXED METHOD STUDY

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The World Health Organization recommends mass ivermectin administration to eliminate onchocerciasis as a public health problem. However, despite efforts to achieve sufficient coverage over time, some targeted individuals report never receiving information about the mass drug administration (MDA) campaigns. Our study aimed to understand why some individuals in endemic areas did not receive information about the MDA campaign over multiple rounds in KA-05, one transmission zone in Mali. We conducted a mixed method study, combining community surveys with qualitative and participatory methods. Data collection took place in February 2023 in the health districts of Sagabari, Kita, and Kenieba. We interviewed participants aged 18 years and above using a pre-established questionnaire to collect sociodemographic characteristics and the reasons associated with the lack of information, such as the main source of income, health districts, the travel history, and level of knowledge of the disease. We also conducted individual interviews and focus group discussions using an interview guide. Finally, we performed a thematic analysis for qualitative data using NVIVO v14. We used SPSS v26 to conduct a binary logistic regression for quantitative data to identify factors associated with the lack of information about the MDA campaign. Lack of information was the most frequently reported reason for non-participation in onchocerciasis targeted MDA [20% (187/921)]. People who knew nothing about onchocerciasis were 1.93 times more likely to be unaware of the campaign as compared to those who had heard of onchocerciasis (CI: 1.18 - 3.14). Qualitative study revealed that this lack of information can be attributed to various factors, such as the lack of awareness, education, seasonal movements, rumors, and available communication channels. Despite many years of MDA for onchocerciasis in this location, some people remain unaware about the disease and the MDA. As programs reach the endgame of elimination, new approaches are needed to reach the unreached.

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EVALUATION OF SOIL-TRANSMITTED HELMINTHIASIS AND SCHISTOSOMIASIS COVERAGE FOLLOWING SIX YEARS OF MASS DRUG ADMINISTRATION IN FIVE NIGERIA STATES

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Achieving the WHO recommended treatment threshold during every round of preventive chemotherapy (PC) is essential to reach elimination of parasitic worm infections as public health problems. Reported administrative coverage data, though essential for program monitoring, can sometimes vary from the actual treatment coverage due to weaknesses in health information systems (use of outdated population census data, inaccurate count of persons treated etc). WHO recommends Coverage Evaluation Surveys (CES) to understand reporting accuracy and to determine if there are data reporting problems. This study evaluates CES conducted post-PC in 55 implementing units (IUs) across five Nigerian states for soil transmitted helminths (STH; 38 IUs) and schistosomiasis (SCH; 17 IUs), from 2018 - 2023. Following the WHO CES protocol, households and schools in 1,650 communities were visited and 62,683 individuals surveyed to estimate treatment coverage over six years. The surveyed coverage showed that 45.5% (25; STH- 16, SCH-9) of IUs met/exceeded the 75% target treatment threshold with 95% CI ranging from 75% - 97%, an adequate marker for a well-functioning programme and successful MDA. Only 3% (1,894) of individuals did not swallow the medicines when offered, indicating high compliance. The reported administrative coverage ranged from 42% - 133% in the 55 IUs, but were similar to the surveyed coverage in only 13% (7) and validated in 7% (4) of the IUs, evidence of critical data reporting issues across board. A significant 23% (14,457) reported they were not offered medicines during the PC round; predominant reasons include absence on deworming day (26.4%); school did not participate or receive medicines (20%); and lack of awareness of the PC (11.5%). Data quality assessment post-PC is recommended to check issues around the variances between the survey and reported coverage and strengthen PC reporting. Additionally, strengthening community engagement and sensitization, as well as proper program planning to address medicine quantification and positioning will be necessary to improve awareness and boost participation in PC.

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CHALLENGES IN MEASURING AND DISCUSSING ELIMINATION GOALS: FROM MODELLING TO POLICY

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The World Health Organisation (WHO) have targeted *gambiense* human African trypanosomiasis (*g*HAT) for elimination of transmission (EoT) by 2030. Unfortunately, it is not possible to directly observe new infections, so a proxy indicator is needed to be able to measure progress towards this target. The WHO HAT elimination Technical Advisory Group have recently defined the indicator for EoT as five years of no cases, along with a sufficient level of surveillance. To support programs in achieving this goal, mathematical modelling is being used to predict and quantitively evaluate the effectiveness of interventions and measure progress towards elimination. Unlike in the real world, modelling can find the exact point at which transmission ceases in the model and many papers have been published using this modelled point of EoT to predict when real-world EoT will be reached. Unfortunately, despite sharing a name, these two definitions of EoT are not the same, and in fact can differ very significantly. In this presentation we discuss the difference between these indicators and show with some examples how severely these indicators can disagree. Similarly, models can predict the exact point at which there is no more infection in the population – Elimination of Infection (EoI), an even stronger criterion than EoT, and also not directly measurable in the real world. The difference between EoT and EoI is particularly pertinent for *g*HAT, which has a very long infection time (often multiple years, sometimes over a decade) meaning that cases can be found substantially after infection was first transmitted to the patient. While this presentation focuses specifically on these three benchmarks for *g*HAT, the general points made here about seemingly trivial differences in the definition of elimination and its indicators could have significant consequences on decision making for any infections approaching the endgame. Modellers and policymakers, both in *g*HAT and beyond, need to work closely together and communicate clearly to ensure that they are in alignment when discussing elimination.

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COVERAGE EVALUATION SURVEY OF LYMPHATIC FILARIASIS RE- MASS DRUG ADMINISTRATION AFTER PRE-TAS FAILURE IN 4 DISTRICTS OF MOZAMBIQUE, 2023

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The Department of Disease Prevention and Control conducted a post-lymphatic filariasis (LF) MDA coverage evaluation survey (CES) from August to September 2023 in Cuamba, Murrupula, Mulevala & Ile. The survey aimed to validate the reported coverage and explore factors affecting MDA implementation. The CES is a community-based cross-sectional survey where 30 clusters are randomly selected using probability proportionate to estimate size (PPES), segmented, and then households are selected for interviews based on a numbered list. Surveyed coverage ranged from 64.1% to 83.5% across the four districts, with only Mulevala failing to meet the WHO coverage threshold of 65%. Across all districts, the main reasons for not consuming drugs were “not being at home during distribution”, “unaware of the MDA”, or “distributors did not visit their house, school, or distribution point”. Respondents that were unaware of the MDA ranged from 23% to 44% across districts and 48% to 90% of participants indicated drugs were received during a household visit. Those that had never participated in an LF MDA ranged from 10% to 26%, and despite upwards of 10 years of treatment in some districts, 52% to 87% indicated that they participated only once. Of the 120 clusters surveyed, 32 failed to meet the coverage threshold, suggesting a more focal issue. When cluster coverage data was compared to daily monitoring reports from the MDA, it revealed potential implementation and data quality issues at the community level. Despite sufficient coverage at the district level, low surveyed coverage in some clusters underscores the need for a more targeted, community-based approach. Future MDAs should focus on community preparation & sensitization, engaging community leaders in planning and pre-MDA meetings, ensuring robust IEC, and implementing innovative strategies to reach the absent people. Enhancing CDD training, conducting daily data monitoring at the community level, and planning for post-MDA mop-up in low coverage communities will ensure more uniform coverage across the districts, as missed populations may sustain LF transmission despite achieving recommended thresholds.

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COMPLETING THE TRACHOMA MAP IN SOUTH SUDAN: RESULTS OF THREE BASELINE PREVALENCE SURVEYS IN EASTERN EQUATORIA STATE, 2023-2024

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Estimating the baseline prevalence of trachoma is required for trachoma control programs to determine a district’s eligibility to receive SAFE (Surgery, Antibiotics, Facial cleanliness, and Environmental improvement) interventions. The Ministry of Health of the Republic of South Sudan (MoH-RSS) is dedicated to eliminating trachoma as a public health problem and since 2001 has implemented aspects of the SAFE strategy in parts of the country. However, as of 2022, three counties (districts) in Eastern Equatoria State (EES) had not completed baseline mapping. From 2023-2024, the three counties of Torit, Magwi, and Ikotos were surveyed by the MoH-RSS Trachoma Control Program using a multistage cluster-randomized sampling design. Trained and certified graders examined participants for trachoma clinical signs and county level prevalence was estimated. Dried blood spot (DBS) specimens were collected from individuals one year of age or older in all three counties. In addition, ocular swabs for *Chlamydia trachomatis* (*Ct*) infections were collected from children ages 1-9 years in Torit. During the 2023 surveys of Torit and Magwi, a total of 59 clusters with 6,222 individuals from 1,577 households were examined for trachoma, with 6,213 DBS and 1,346 swabs collected. Prevalence of trachomatous inflammation—follicular (TF) among children ages 1-9 years was 0.8% (95% confidence interval [CI]: 0.4-1.7%) in Magwi and 7.3% (95% CI: 3.3-15.7%) in Torit. Trachomatous trichiasis (TT) in adults 15 years and older was 1.05% (95% CI: 0.59-1.86%) in Magwi and 1.41% (95% CI: 0.81-2.44%) in Torit. The analysis of the 2024 Ikotos survey results, and the results of the infection and serological analysis, will be complete by summer 2024. Based on these results, Torit is slightly above the World Health Organization elimination thresholds of TF<5% and TT<0.2% and will require all SAFE interventions, whereas Magwi will only require S, F, and E interventions until TT levels are <0.2%. With the completion of baseline surveys for all counties in EES, the MoH-RSS has the data needed to drive progress towards the elimination of trachoma.

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ANALYSIS OF THE SITUATION OF LEPROSY CASES IN CHILDREN AGED FROM 5 TO 14 YEARS FROM 2022 TO 2023 IN CONAKRY (GUINEA)

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Depuis 2010, la Guinée a atteint le seuil d’élimination de la lèpre comme problème de santé publique, avec moins d’un cas pour 10 000 habitants dans toutes les préfectures du pays. Malgré les efforts du Ministère de la Santé et de l’Hygiène Publique à travers le Programme National de

Lutte contre les Maladies Tropicales Négligées avec Prise en Charge des Cas (PNLMTN-PCC) en collaboration avec les partenaires techniques et financiers, il y a eu une sous-déclaration ces dernières années dans tous les centres de prise en charge des cas du pays. pays. Plusieurs facteurs peuvent expliquer cette sous-déclaration, notamment un dépistage retardé entraînant une proportion élevée de cas multibacillaires (MB), un nombre important d'invalidités de grade 2, un financement insuffisant pour une surveillance solide de ces maladies et le départ à la retraite du personnel qualifié. Fin 2022, 185 nouveaux cas ont été recensés, dont 4 cas chez les enfants (2,2%). En 2023, 244 nouveaux cas ont été détectés, dont 6 cas chez des enfants, tous scolarisés (1,8%). La moitié de ces enfants résident à Conakry. Plusieurs indicateurs clés mettent en évidence les défis rencontrés pour mettre en œuvre la stratégie de l'Organisation mondiale de la santé visant à interrompre la transmission. Le pourcentage d'enfants supérieur à 1% constitue un indicateur crucial signalant la présence persistante de la maladie dans la population, notamment dans la région de Conakry et ses deux villes du nord. La proportion croissante de cas multibacillaires (80 % et 88 % en 2022 et 2023, respectivement) parmi les nouveaux cas signifie un risque accru de transmission de la maladie au sein de la population, notamment dans les milieux éducatifs où les étudiants interagissent étroitement pendant des périodes prolongées. Seize de ces cas provenaient de Conakry, dont 3 cas impliquant des enfants (19%). Une évaluation de la situation indique une résurgence potentielle de la lèpre en Guinée. Face à ce scénario, il est essentiel d'intensifier les efforts de détection précoce de la lèpre.

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ADDRESSING "LEAVING NO ONE BEHIND" IN AN NTD PROGRAMMATIC CONTEXT: EXPERIENCE FROM THE DEWORMING INNOVATION FUND

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As NTD endemic countries implement the World Health Organization Sustainability Framework for Action Against NTDs 2021-2030, the need to ensure all at risk populations are reached has become urgent. Kenya is implementing interventions on Schistosomiasis (SCH) and soil transmitted helminthiasis (STH) in the Western Region with a view to reaching affected communities with information and services and influence adoption of positive behaviors by prioritizing inclusivity, equity and social justice. One aim of the Kenya NTD Master Plan 2023 -2027 is to interrupt transmission of SCH and STH through adopting comprehensive approaches, one being, leaving no one behind (LNOB). Under the Deworming Innovation Fund, a community consultative process was applied to identify people at risk of infection and the their social networks, while survey data were used to determine effective channels of communication. Key groups identified as needing special attention included street families, prisoners, people in remote areas, persons with disabilities, older persons and minority groups. Tailor-made strategies were implemented including: identifying and sensitizing influencers and change agents; developing culturally acceptable sensitization materials with NTD messages such as religious training manuals with Muslim and Christian groups; collaborating with other sectors such as prisons and social services departments; holding community dialogue forums; working closely with community-based organizations and private sector in implementing social behavior change and social mobilization initiatives. These actions resulted in improved access to information, treatment and increased avenues for structured in-depth conversations triggering behavior change. Quarterly monitoring reports in 2022/23 show increased levels of knowledge and a consistent high uptake of treatment (over 80%). Success stories have been documented in the intervention sites to demonstrate how the program is positively changing lives. Implementing targeted social mobilization and treatment interventions are key strategies to leaving no one behind.

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FACTORS ASSOCIATED WITH PERSISTENT AND RECRUDESCENT ACTIVE TRACHOMA: RESULTS FROM ADAPTIVE COVERAGE EVALUATION SURVEYS IN UGANDA

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Through implementation of the surgery, antibiotics, facial cleanliness, and environmental change (SAFE) strategy, Uganda has made progress towards elimination of trachoma with 59 of 61 previously endemic districts having stopped mass drug administration (MDA). Moroto and Nabilatuk have persistent and recrudescent active trachoma. The population in these districts are predominantly nomadic pastoralists where coverage of water, sanitation, and hygiene (WASH) is low and hard to reach, making MDA campaigns challenging. We investigated the factors associated with trachomatous inflammation-follicular (TF) in children aged 1–9 years following completion of MDA. Trachoma examination was added onto a routine coverage evaluation survey conducted one month after MDA. A two-stage sampling design was used to select 30 clusters and 10 to 12 households per cluster. MDA coverage was assessed in all eligible household members using standard WHO tools while trachoma examination was undertaken by graders certified using Tropical Data standards. Univariate and multivariate logistic regression analysis was used to explore association of TF and explanatory variables. A total 1806 children were included in the analysis and majority (51%) were male. In the univariate analysis, factors associated with increased odds of TF were residing in Moroto district, odds ratio (OR)=6.0 (95% confidence interval [CI] 2.3-16.1); not attending school, OR=9.6 (95% CI=1.3-71.2); not treated during MDA, OR=12.9 (95%CI=5.8-25.5); and low access to water source (p-value<0.001). Adjusting for age and gender, factors independently associated with TF were: residing in Moroto, OR=3.6 (95% CI1.1-9.2); not treated during MDA, OR=8.4 (95%CI=3.1-23.2); and low access to water source (p-value=0.002). The results showed lack of participation in MDA was an important driver of persistent trachoma, especially in Moroto district. The findings also suggest that low access to WASH remains an important driver of trachoma in these mobile and migrant pastoralist populations. Enhanced MDA and WASH interventions are needed to eliminate trachoma in Moroto and Nabilatuk.

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DETERMINANTS FOR UPTAKE OF MASS DRUG ADMINISTRATION FOR SCHISTOSOMIASIS CONTROL IN BUTIABA, UGANDA

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Schistosomiasis is targeted for elimination in Uganda by 2025 through Mass Drug Administration (MDA) using praziquantel. To achieve this, WHO estimates indicate that MDA coverage and uptake of 75% is required. However, coverage remains suboptimal. There is need to add to the body of knowledge to enable more robust mitigation measures. This study aimed to assess the uptake of praziquantel for MDA and associated factors in Butiaba sub-county along the shores of Lake Albert in Uganda. A cross-sectional study was conducted in five randomly selected villages between July and September 2021 using quantitative and qualitative approaches. Semi-structured questionnaires were administered to 450 adults, with two

Focus Group Discussions and Key Informant interviews held with village and district leaders. Self-reported uptake of praziquantel within twelve months of the most recent MDA exercise was 71.56% (95% CI: 67.14 - 75.68). Of all the participants, 5.78% reported having never swallowed praziquantel in their lifetime and 75% (96/128) of participants who didn't swallow praziquantel in the last twelve months reported having at least swallowed the drug in the last ten years. Respondents were less likely to have swallowed praziquantel if they had no knowledge about schistosomiasis signs (AOR= 0.18, 95% CI: 0.08-0.39) and more likely if they were between the ages 30-39years (AOR= 2.31, 95% CI: 1.35-3.95) or 40 years and above (AOR= 2.86, 95% CI: 1.45 - 4.95). Operational challenges such as inadequate supply of praziquantel and financial constraints also influence uptake of praziquantel during MDA in Butiaba sub-county. Uptake of praziquantel was high but still below the WHO target of 75%. People with limited knowledge on schistosomiasis symptoms and those aged 18 - 29 years were less likely to take Praziquantel. Irregular drug supply was also a key challenge. Rigorous health education and ensuring continuous supply of Praziquantel are key in improving MDA uptake.

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FORECASTING OF ONCHOCERCIASIS PREVALENCE IN WEST AFRICA THROUGH TIME SERIES MODELING

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Act to End NTDs | West is a five-year USAID-funded program that aims to eliminate or control five Neglected Tropical Diseases across 11 West African countries. WHO's roadmap for NTD elimination targets five diseases for preventive chemotherapy: Lymphatic Filariasis (LF), Trachoma, Onchocerciasis (OV), Schistosomiasis, and Soil-Transmitted Helminth. Disease prevalence is assessed by population-based surveys.As LF and Trachoma are near elimination in several West African countries, the focus of funders and governments is increasingly shifting to eliminating OV. Therefore, this paper sets out to forecast OV prevalence using forecasts through modeling. Utilizing ESPEN site-level prevalence data spanning from 1975 to 2018, we focused on seven countries: Burkina Faso, Benin, Cote d'Ivoire, Ghana, Guinea, Mali, and Togo. Maximum prevalence at the site level was utilized to summarize the data for each year across the selected countries. In instances of missing data, prevalence from the preceding year was used.Various time series modeling techniques, including Autoregressive Integrated Moving Average (ARIMA), Generalized additive model (GAM), Generalized linear model (GLM), and Facebook's Prophet models, were employed using RStudio (version 3.3.0). For these models, we set a calibration period of 43 years and a forecasting horizon from 2019 to 2030 (12 years). Data management was facilitated through MS Excel pivot tables. Despite ARIMA and GAM models showing a minimal decline in prevalence, GLM and Prophet model forecasts suggest that by 2030, OV prevalence will decline to 0% (with a 95% prediction interval of 0% to 2.8%) across the seven countries, indicating the achievement of onchocerciasis elimination by 2030. The Prophet model demonstrated the best fit based on fit statistics, including average Mean Absolute Error (MAE), Prediction Interval Coverage, and Weighted Interval Score (WIS).This talk will additionally explore more complex models, such as the n-sub epidemic and spatial wave framework, for future analyses to forecast OV prevalence. Finally, we aim to expand our analysis to provide country-specific forecasts.

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MIND THE GAP: GENDER DIFFERENCES IN PREVENTATIVE TREATMENT OF SEVEN NEGLECTED TROPICAL DISEASES

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Ensuring gender equity is a core goal of USAID as well as of Act to End NTDs | West, a USAID-funded program supporting Ministries of Health in 11 West African countries to manage seven neglected tropical diseases (NTDs). A key strategy of NTD management is mass drug administration (MDA) of preventative chemotherapy (PC) to populations at risk. Determining the presence and magnitude of gender disparities in MDA is crucial both to ensuring health equity, and to identifying pathways of ongoing NTD transmission. This study assessed 3,832 USAID-funded MDA events covering the seven PC-NTDs across 792 districts in 11 countries from 2019 to 2023, disaggregated by sex. We estimated sex-disaggregated program coverage rates for each MDA by dividing reported male and female treatment data by estimated male and female target populations, respectively. The distributions of, and differences between, male and female coverage rates were analyzed by country and targeted disease. Broadly, NTD programs appear to achieve high MDA coverage, but differences between males and females do exist. Average coverage across all MDA events was 92.8% for females and 85.1% for males. However, 355 MDA events (9.3%) had differences of at least 20 percentage points, and 41 (5.2%) of the 792 districts studied had differences of at least 20 percentage points in three or more MDA held during the study period. Coverage differences vary by the disease being treated, and across countries. MDA treating schistosomiasis had the smallest differences (female coverage exceeded that of males by 6.5 percentage points) while those treating lymphatic filariasis had the largest (female coverage exceeded that of males by 10.6 percentage points). The lowest country-level average difference was 3.3 percentage points, while the highest was 15.2 percentage points. This study will explore country- and disease-specific context to interpretate the drivers of coverage differences that must be addressed to improve gender equity in future MDA programming.

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TRACHOMA ZONES OF CONCERN: IDENTIFYING AREAS OF TRACHOMA RISK BEFORE AND AFTER ELIMINATION USING NOVEL GEOSPATIAL ANALYSIS

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Enhanced analysis methods can help identify areas at high risk for persistent and/or recrudescent active trachoma within and between trachoma endemic Evaluation Units (EUs). Geospatial analysis could identify "zones of concern" likely to have above-threshold trachomatous inflammation—follicular prevalence in children aged 1-9 years (TF1-9) within and between EUs, including within and between countries. This study is a secondary data analysis using trachoma baseline, impact (TIS), and surveillance (TSS) survey data collected with Global Trachoma Mapping Project (GTMP) and Tropical Data support from 2012 to 2022 in Uganda, Kenya, and neighboring countries. Previous work has explored the spatial distribution of trachoma and the spatial relationship of trachoma to spatial covariates in these countries. Leveraging these results and an understanding of trachoma geospatial dynamics, a new analysis approach was developed. The approach borrows information from nearby survey clusters within a certain distance or buffer of a survey cluster and uses these data to estimate a zonal mean TF1-9 prevalence for each survey cluster area. This approach was piloted in several areas of Uganda with different epidemiological and survey profiles. Data from the most recent survey in one area of was used to identify a "zone of concern" with several overlapping 10-kilometer cluster buffers of more than 5% TF1-9 across several districts in the study area. In another area, the results show several zones of concern, including a large zone overlapping international borders. Trachoma is highly focal in distribution, and spatial models need to be tailored to each area of interest. The spatial scale of analysis, including

considering the use of data beyond the borders of a single EU or even country, could be important in some areas. Simple geospatial analysis, such as this "zone of concern" approach, may provide initial information for programs to target interventions in areas at risk of persistent and/or recrudescent trachoma or for post-validation surveillance activities.

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IMPROVING THE QUALITY OF MASS DRUG ADMINISTRATION IN GHANA USING ELECTRONIC DATA CAPTURE.

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Ghana has conducted Mass Drug Administration (MDAs) as a means of controlling neglected tropical diseases for over two decades. These MDAs have used traditional community registers and community drug distributors (CDD) as a channel to distribute essential MDA medicines to community members. Data from these MDAs are sometimes not reported in a manner that is timely, complete, inaccurate and hence NTD programs have challenges making informed decisions timely for improved or quality MDA. This shortcoming leads to even dire consequences as the deficiencies are only discovered a few months after implementation making introduction of strategies to improve MDA during the period impossible. At the implementation level supervisors are constrained in identifying areas with low coverage whiles MDA is ongoing because data does not get to them in real time. The Ghana NTD program is piloting the use of the Lymph App's MDA module for the annual integrated Lymphatic Filariasis (LF) and Onchocerciasis (OV) MDA. The main objective of the study is to demonstrate how the Lymph App MDA module can help improve MDA data accuracy, completeness and timeliness and provide adequate data to support supervisors with the identification of underserved areas. There will also be a rapid assessment of the acceptability and convenience of the app to CDDs and health workers. Five LF and OV endemic sub districts will be purposively selected for this pilot. Supervisors and CDDs in these sub districts will be trained on the use of the app. After training and pretesting, there will be an initial registration of all community members in all study sites. This registration will capture the bio data of all household members and household's geo coordinates. This data which forms the registration for the communities will be cleaned thoroughly and will be used as the community register. MDA medicines given will also be recorded as part of this register. Data from the app will be downloaded, cleaned, analyzed, and presented as maps and tables daily and shared with supervisors to facilitate the identification of areas with poor coverage and address MDA issues immediately to ensure maximum coverage.

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OCULAR *CHLAMYDIAL TRACHOMATIS* INFECTION IMMEDIATELY FOLLOWING AN ENHANCED MASS DRUG ADMINISTRATION STRATEGY FOR TRACHOMA IN AMHARA, ETHIOPIA: THE CHILD MDA PILOT STUDY

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The Ministry of Health of Ethiopia has recently recommended an enhanced mass drug administration (MDA) strategy, "Child MDA" for trachoma, consisting of a standard community-wide round of MDA followed by a child only round (ages 6 months to 9 years) 4 weeks later. Child MDA was piloted in the Amhara region in 2023 in 2 districts, Lasta and Wadilla. As of 2022, the trachomatous inflammation-follicular (TF) prevalence among children ages 1-9 years was 30.0% in both districts, and the *Chlamydia trachomatis* (*Ct*) infection prevalence among children ages 1-5 years was 15.5% in Lasta and 9.4% in Wadilla. This study's aim was to determine the prevalence of *Ct* infection 3 weeks post-Child MDA intervention by embedding conjunctival swabbing within MDA coverage surveys. A period of 3 weeks was chosen to allow for enough time for infection to clear and to be recent enough to minimize recall bias. The surveys used multi-level sampling, selecting 30 communities and 30 households within each community. Following household and individual level MDA questionnaires, one swab was collected per child ages 1-9 years. All swabs were tested for *Ct* infection in Amhara. The July 2023 coverage surveys interviewed 1,752 children ages 1-9 years across the 2 districts to assess self-reported MDA coverage for both rounds, and 1,632 (93%) children were swabbed. The MDA coverage among children was >82% at all rounds in both districts. The district-level prevalence of *Ct* infection was 3.5% (CI: 1.7-7.3%) among children ages 1-9 years and 4.6% (CI: 2.3-8.9%) among children ages 1-5 years in Lasta. In Wadilla, the *Ct* prevalence among children ages 1-9 years and children ages 1-5 years was 1.7% (CI: 0.5-5.7%) and 1.3% (CI: 0.4-3.9%) respectively. Across both districts, the *Ct* prevalence among children who reported not taking either dose of MDA (n=95) was 15.9% (CI: 8.0-29.2%), and among those who reported taking both doses (n=1,343), it was 1.2% (CI: 0.7-2.2%). The *Ct* infection prevalence was lower after the Child MDA treatment, however, considerable infection remained 3 weeks post-treatment. One year of Child MDA treatment is likely not sufficient in highly endemic settings.

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ANTIBODY-OMICS REVEALS BIOMARKERS OF SCHISTOSOMIASIS AND CROSS-TALK WITH TUBERCULOSIS.

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Lack of accurate accessible diagnostics for Schistosomiasis (schisto) is a critical bottleneck in its elimination. In the absence of microscopic evidence of parasite, antibody (Ab) tests cannot distinguish past from current infection. Recently developed antigen detection tests (CAA) are promising for detection of current infection but not widely available. Additionally, schisto is associated with higher risk for Tuberculosis (TB), although the mechanism for this is not clear. We have developed a multiplexed 'Ab-omics' platform for deep characterization of a broad set of antigen-specific Abs (isotype, subclass, glycosylation and Fc receptor binding). Machine-learning applied to these data can reveal unique Ab signatures predictive of disease state and outcome. Here, sera from subjects (n=41, from Kenya), previously screened using a CAA test, were characterized with the Ab-omics workflow, using multiple *S. mansoni* (SEA, Sm25, Sm29, MEG, CD63, Calumenin), *M. tuberculosis* (PPD, Ag85A, ESAT6, CFP10 HspX, PstS1, LAM) and other helminth and non-helminth antigens. Antigen-coated barcoded beads were incubated with serum and probed. With a total of 270 measured Ab features from each subject LASSO-based feature selection led to a unique biomarker to differentiate CAA+ from CAA- individuals accurately (AUC>0.9). These findings suggest that a purely Ab-based biomarker, including Sm-29 specific IgG2, Ab galactosylation and Sm25-specific Ab FcR2b binding can achieve accurate diagnosis of current schistosome infection in endemic areas. Further, this approach was also able to distinguish early, late and past infection. Mtb-specific Abs also showed different Ab Fc profiles between CAA+ and CAA- individual's, specifically higher Ab sialylation, galactosylation and Fc2b binding. This is indicative of an anti-inflammatory tuning of the Fc profiles of Mtb-specific

Abs in Schisto patients, which has been earlier shown to be correlated with reduced Ab function and higher risk of reactivation of TB infection to active TB.

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IMMUNOLOGICAL BIOMARKERS FOR DETECTING SUBCLINICAL LEPROSY INFECTION: CROSS-TALK BETWEEN LID-1 AND PGL-1 IN INDIVIDUAL IMMUNE RESPONSES

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Brazil ranks second globally in the number of annual new leprosy cases. Active surveillance is ideal for early detection and interruption of the transmission chain. In this context, identifying immunological biomarkers for the detection of subclinical infection represents a strategy to achieve this goal. A random sampling strategy was utilized to select 1315 asymptomatic individuals residing in hyperendemic municipalities in eastern Minas Gerais. Blood samples were collected and tested to detect antibodies against the *Myocbacterium leprae* protein (LID-1) on a multiplexed beaded assay. Following categorization into anti-LID1+ or anti-LID- groups, individuals were paired based on age and sex, resulting in a total of 160 participants. Immunological assays assessed chemokines (CXCL8, CCL2, CXCL9, CCL5, and CXCL10) and cytokines (IL-6, TNF, IFN-ϒ, IL-17, IL-4, IL-10, and IL-2) using PBMC culture supernatants stimulated by M. leprae antigens. Participants were evaluated for clinical disease, with 14 diagnosed, and an additional serological test for anti-phenoglycolipid-1 (PGL1) was performed. IFN-γ was able to identify LID1+ well (AUC= 0.73, p= 0.01, sensitivity= 71.79%, specificity = 86.30%) indicating its potential as a biomarker for subclinical infection. Conversely, the chemokine CCL2 demonstrated superior characterization of the LID1- group (AUC= 0.61, p= 0.02, sensitivity= 34.18%, specificity = 88.31%), albeit with low sensitivity. The analysis of PGL-1 showed that anti-PGL-1(-) subjects had higher CXCL10 levels. Also, the network correlation between the biomarkers, showed a specific pattern in the IFN-γ, TNF and IL-17 correlation among the subgroups [LID(-)PLG1(-), LID(-)PLG1(+), LID(+)PLG1(-) and LID(+)PLG1(+)]. Overall, the differential biomarker profile and correlation between the groups suggest a promising avenue for developing future diagnostic tests for subclinical infection. Despite being asymptomatic, the participants in this study reside in regions with high endemicity, underscoring the critical need for early leprosy diagnosis. Financial support: CNPq, FAPEMIG, NIH.

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EXPLORING THE IMPACT OF DECENTRALIZATION IN IN THE LEPROSY ENDEMIC REGION OF EASTERN MINAS GERAIS USING GEOSPATIAL AND QPCR TECHNIQUES

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Many studies have explored the qPCR technique for leprosy diagnosis, having successfully identified undiagnosed cases or sites of disease outbreaks. In parallel, the techniques of spatial epidemiology have also been making significant contributions to leprosy control, highlighting differences in the spatial distribution of the disease between regions, states, and municipalities, where places of greater social inequality and accessibility to health services can impact local epidemiology. This study aimed to map asymptomatic individuals examined at the reference center - CREDEN/PES (spontaneous demand or referral) with skin smears positive for the RLEP gene of *M. leprae* in Governador Valadares. Additionally, through a network analysis using point interpolation algorithms, an estimation of the coverage areas of primary health units (ESF/UBS) was conducted in the census sectors of the municipality. Using quantum GIS 3.14 Pi software, maps were created using shape files of census sectors, streets, and sociodemographic data sourced from the Brazilian Institute of Geography and Statistics (IBGE). Individuals' qPCR+ were heterogeneously distributed across census sectors, with a higher proportion of female individuals ($p = 0.0451$), predominating literate individuals ($p = 0.0405$), black ($p = 0.0072$) and mixed race ($p = 0.0020$). Around 70% of the urban area of GV is covered by a health unit. However, only 41.2% of qPCR+ individuals lived in these areas. The remaining 58.8% of qPCR+ individuals lived in areas without coverage by a Health Unit. The estimated average distance traveled by participants to the nearest ESF/UBS was 0.515 km, while the distance to CREDEN-PES (reference center) was 3.77 km. In conclusion, combined molecular and geoprocessing techniques proved effective in identifying critical areas for disease control in Governador Valadares. This study highlighted the importance of expanding ESF/UBS and potentially decentralizing leprosy care, particularly in regions inhabited by individuals from lower socioeconomic strata.

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MYCOBACTERIUM LEPRAE AND *SCHISTOSOMA MANSONI* CO-INFECTION IN COMMUNITIES OF EASTERN MINAS GERAIS, BRAZIL

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Leprosy, caused by *Mycobacterium leprae*, exhibits varied clinical forms depending on the immune response, Th1 or Th2. The coexistence of infections by parasites, particularly *Schistosoma mansoni*, and micronutrient deficiencies with leprosy is observed in endemic regions of Brazil. S. mansoni infection is known to negatively modulate the Th1 response, favoring M. leprae infection and progression to severe clinical forms. In this sense, the identification of risk factors associated with leprosy includes socio-demographic, immunological, and parasitological factors. A random sampling strategy was utilized to select 1315 asymptomatic individuals residing in hyperendemic municipalities in eastern Minas Gerais. IgG reactivity tests to Leprosy IDRI diagnostic antigen 1 (LID-1) and anti-PGL-1 IgM were conducted to identify individuals potentially infected by M. leprae without clinical manifestations. Tests for presumptive detection of schistosomiasis, including Detection of Circulating Cathodic Antigen (CCA) in urine and detection of anti-SEA and anti-SWAP antibodies in serum, were performed. Preliminary results showed 79 participants had anti-LID IgG, designated LID+. Among 156 sera evaluated for anti-PGL-1, 47 were positive (30.12%). ELISA assays revealed 28 sera (17.72%) reactive for SEA and 27 (17.0%) for SWAP. Using the rapid CCA test, 83 urine samples were collected, revealing co-infection in ten cases (12.05%), where patients tested positive for both LID+ (leprosy) and CCA (schistosomiasis). Notably,

14 new cases of leprosy were confirmed among LID+ individuals. Ongoing clinical evaluation and monitoring of participants are crucial for immediate treatment of newly diagnosed cases.

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MODEL-BASED GEOSTATISTICS TO SELECT SITES FOR MONITORING LYMPHATIC FILARIASIS TRANSMISSION INTERRUPTION FOLLOWING MASS DRUG ADMINISTRATION WITH IVERMECTIN, DIETHYLCARBAMAZINE AND ALBENDAZOLE IN EAST NEW BRITAIN, PAPUA NEW GUINEA

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After two rounds of mass drug administration (MDA) with ivermectin, diethylcarbamazine, and albendazole (IDA) for lymphatic filariasis (LF) elimination, the World Health Organization (WHO) recommends the IDA Impact Survey (IIS) to assess if LF transmission has ceased. This involves population proportional sampling (PPS) of 30 sentinel sites to assess LF infection parameters in those ≥20 years. Model-based geostatistics (MBS) is also recommended if capacity exists, but only some countries have used MBS for IIS. Here we used MBS for IIS sentinel site selection in East New Britain province (ENB), Papua New Guinea (PNG). ENB completed two rounds of IDA MDA in 2019 and 2022, with 82% and 67% epidemiological coverage, respectively. We conducted IIS from June 2023 - February 2024 and examined the impact of MDA on sites (villages) with known high LF infection before MDA. Subsequent selection with MBS prioritized sites whose LF infection probability was most uncertain based on prior data. In selected sites we sampled approximately 110 adults ≥20 years with filarial test strips (FTS) followed by night blood smears for microfilaria (Mf) if FTS positive. We tested 4,164 individuals in 42 sites across ENB. Sites were selected based on prior LF infections (N=10), MBS (N=26), and convenience where MBS villages became inaccessible (e.g. weather, security, etc, N=6). The sampled individuals averaged 38 years old, and 42.8% were male. 193 individuals were FTS positive, with a mean of 4.5%, (95% CI 1.8, 7.2). Fourteen of the 26 MBS sites contained FTS-positive individuals, with two containing Mf positives. Overall, ten Mf positives were identified with a mean Mf positivity across ENB of 0.24%, (95% CI 0.02, 0.45). Two sites exceeded 1% Mf positivity. Thus, MBS selected unrecognized sites of FTS and Mf positivity, mainly in remote areas where LF transmission and poor MDA coverage are more likely. We showed that LF transmission has been interrupted across most of ENB. PPS IIS is now underway, and results can be compared to MBS. We will work with the provincial health authority to administer additional MDA in smaller evaluation units encompassing sites with >1% Mf positivity.

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LONGITUDINAL ANALYSIS OF THE PREVALENCE OF MINOR *PLASMODIUM* SPP. INFECTING HUMANS THROUGH SEQUENTIAL INTERVENTIONS IN NORTHERN GHANA

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Current interventions targeting malaria control are focused on *Plasmodium falciparum*, the major species infecting humans. Despite renewed efforts for malaria elimination in sub-Saharan Africa, little attention has been paid to the neglected parasites, *P. vivax, P. malariae,* and *P. ovale* spp. and the impact of interventions, like indoor residual spraying (IRS), and/or seasonal malaria chemoprevention (SMC) on these minor *Plasmodium* spp. To address this research gap, this study was undertaken to assess the efficacy of IRS and SMC combined with long-lasting insecticidal nets (LLINs), on minor *Plasmodium* spp. infections in an area characterized by high seasonal transmission in northern Ghana. Using an interrupted time-series study, five age-stratified surveys, each of ~2,000 participants, were undertaken at the end of the wet seasons between 2012 and 2022. Across this 10-year study period infections with *P. malariae* and *P. ovale* spp. were detected using a species-specific PCR targeting the *18S rRNA* gene, while no *P. vivax* was detected. In 2015, following IRS, the prevalence of the minor *Plasmodium* spp. declined in all ages, with participants being significantly less likely to be infected with *P. malariae* (1.4% vs. 13.7%) and *P. ovale* spp. (0.4% vs. 5.7%) compared to 2012. Despite this decline, in 2017, 2-years after IRS was withdrawn and SMC was introduced, the prevalence of *P. malariae* (2.9%) and *P. ovale* spp. (4.0%), rebounded 2- and 10-fold, respectively. Finally, when we examined this population in 2020 and 2022 after sustained use of SMC, the prevalence of *P. malariae* continued to increase (7.4% and 5.8%), while the prevalence for *P. ovale* spp. declined (2.6% and 1.3%). The rebound in the minor species was observed in all age groups, except for the younger children (1-5 years) targeted by SMC where no *P. malariae* or *P. ovale* spp. infections were detected in 2017 to 2022. Results show that the transmission of *P. malariae,* and to a lesser extent *P. ovale* spp., were affected by the interventions deployed in Bongo District. However, infections with minor species rebounded following the discontinuation of IRS in the age groups not targeted by SMC.

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OPTIMIZING DRUG DISTRIBUTOR PERFORMANCE IN NEGLECTED TROPICAL DISEASE MASS DRUG ADMINISTRATION PROGRAMS; RESULTS FROM A MULTI-COUNTRY EVALUATION

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Community drug distributors (CDDs) and other similar cadres of lay and professional staff are the backbone of neglected tropical disease (NTD) mass drug administration (MDA) programs. These personnel often volunteer time or receive minimal financial incentive for their work. These individuals are often selected to serve their own communities and are asked to participate in periodic trainings to deliver health promotion and counseling, drug distribution, and adverse event monitoring services. There is minimal information available about the characteristics of CDDs associated with program performance, defined as the proportion of individuals accepting treatment from a CDD when offered. We tracked this information in the DeWorm3 project, a large cluster randomized trial testing the feasibility of interrupting transmission of soil-transmitted helminths (STH) in Benin, Malawi, and India. We documented CDD attributes during six rounds of biannual community-wide MDA and, using electronic data collection, linked CDD attributes to treatment coverage for households assigned to a given CDD. We conducted multivariate logistic regression with an interaction term to determine if treatment refusal varied by gender of participants and

CDDs. We engaged 444 CDDs total (113 in Benin, 57 in Malawi, and 274 in India). CDDs were 35% (Benin), 63% (Malawi), and 87% (India) female. In Malawi, CDDs were professional Health Surveillance Assistants while in Benin the majority (21%) worked in agriculture and in India 41% identified as housewives. In Benin and India, the majority of CDDs were ages 18-29 while in Malawi the majority were older (30-39 years). CDDs were able to reach a range of 15.3 (median) households per day in urban areas of Benin and up to 30.4 (median) in rural areas of Malawi. In Benin, women were more likely to refuse treatment from male CDDs as compared to female CDDs (p=0.03). In Malawi, both men and women were more likely to refuse treatment from male CDDs (p<0.001) as compared to female CDDs. These findings are useful for other NTD programs as they consider opportunities to recruit, finance and plan for CDD engagement and to optimize CDD performance.

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ASSESSMENT OF QUALITY OF ONCHOCERCIASIS MASS DRUG ADMINISTRATION, INSIGHTS FROM A COVERAGE SURVEY IN NINE DISTRICTS OF OROMIA REGION, ETHIOPIA

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Onchocerciasis control with community distributed treatment with ivermectin started in 2001 in Ethiopia, with mass drug administration (MDA) expanding to new endemic districts as they are identified until recently. MDA began in nine newly identified districts from 2019 to 2022. Cross-sectional community-based coverage surveys were conducted in the nine districts one month after MDA in 2023 to validate reported MDA coverage, assess service quality, and identify factors affecting ivermectin intake in these new program areas. Two-stage random sampling was used, starting with the random selection of 8 villages per district (72 villages in total). Then, within each selected village, at least 16 households (1,431 households in total) were chosen using systematic random sampling. All household residents were asked whether they took ivermectin during MDA. Overall, surveyed ivermectin coverage was 78% (95% CI 77-79%), with districts ranging from 56% to 86.9%. Three districts reported coverage that was higher than that surveyed by 11% to 26% and 6 districts reported coverage lower than that surveyed by 6% to 7%. Six districts from East and West Hararge zones met the acceptable coverage threshold of ≥80%, but 3 (Girar Jarso and Aleltu of North Shoa zone and Digalona Tijo of Arsi zone) did not. There were high rates of underdosing in Digaluna Tijo (16%) and Aleltu (12%) and high rates of overdosing in Oda Bultum (17%) and Habro (14%) and Melka Belo (13%). Individuals who received health education had 7.6 times the odds of swallowing ivermectin as those who did not (95% CI: 6.6-8.8). In summary, underdosing and overdosing were identified in specific districts, highlighting the importance of quality assurance during MDA campaigns. Health education was strongly associated with ivermectin intake. Based on the observed discrepancies, enhanced training on dosing and reporting for drug distributors is required. Areas of North Shoa and Arsi zones with sub-standard coverage require improvements in both coverage and quality through increased community engagement and empowerment of Community Drug Distributors.

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PRODUCTIVITY RETURNS FROM TEN YEARS OF THE KENYAN NATIONAL SCHOOL BASED DEWORMING PROGRAM

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Many areas of Kenya are endemic for soil-transmitted helminths (STH) and schistosomiasis (SCH). Preventive chemotherapy (PC) among school-aged children (SAC) has been applied to endemic counties since 2012 as part of the National School Based Deworming Program (NSBDP). Providing PC to endemic children results in long-term productivity gains. Previous evaluations of PC my underestimate impact of intestinal helminths, as they often only focus on short-term morbidity without addressing productivity. We aim to quantify total productivity gains from the NSBDP and compare them to estimated program cost for a return on investment from 10 years of the NSBDP's operation. We first constructed a deterministic epidemiological model using a series of ordered differential equations to estimate child time-months spent in different intensity classes of STH/SCH, when subject to different levels of PC. The model was calibrated to national prevalence and coverage data with parameters derived from existing literature. An annual 2022 productivity gain range was estimated and assigned to each class of infection. Total cumulative lifetime productivity gains were estimated for averted child-years of infection from the assumed beginning of a dewormed child's productive life to 20 years in the future. Detailed program costing records were consulted to estimate total costs of the program implementation over 10 years. Overall, $1,100,000,000 2023 USD cumulative productivity returns are estimated to be realized 2012 to 2042 due to 10 years of operation (2012-2022) of the Kenyan NSBDP. The total spend on the program was estimated at $27,000,000 2023 USD suggesting a $30 return on investment for every $1. These results are conservative due to a limited time frame, do not include infections averted through reduced environmental contamination, and do not include other avoided costs such as to the health system. They highlight substantial impact which can be achieved through preventing STH/SCH infections in SAC. Deworming in Kenya and in other endemic countries remains a sound investment due to very high returns comparable to many other health and development programs.

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MORBIDITY MANAGEMENT OF LYMPHATIC FILARIASIS: STRENGTHENING SURGICAL APPROACHES TO FILARIAL HYDROCELES IN KENYA

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Lymphatic Filariasis (LF) is prevalent in Kenya's coastal region, where hydrocele cases have been documented. Due to inadequate local capacity to manage hydroceles, the Ministry of Health Neglected Tropical Disease program partnered with Amref Health Africa, the University of Nairobi Department of Surgery, and the African Filariasis Morbidity Project (AFMP) to train local surgeons and medical officers on a new technique involving total excision of the tunica. We sought to evaluate the impact of the training camp and surgical outcomes of treated patients. Community Health Promoters screened and referred patients with scrotal swelling from LF-endemic counties in May and October 2023. Health workers from endemic

counties underwent training modelled on the AFMP protocol. The training incorporated didactic sessions, selecting eligible patients, and practical theatre sessions in 8 health facilities. Follow-up was done upon discharge on day 3 and in the subsequent training camp. Data collected included the number of cases performed, intraoperative findings, and post-operative complications. Descriptive statistics was used to summarize the findings. Overall, 105 health workers underwent training, including 3 urologists, 5 general surgeons, and 33 medical officers. Furthermore, 22 clinical officer anaesthetists and 42 theatre nurses were trained in perioperative management of hydrocele patients. Of 166 referred patients, 111/166 (66.9%) underwent surgery, 70/111 (63.3%) in May, and 41/111(36.9%) in October 2023 respectively. The median age was 58 years (IQR 52.5 years), with 45 (40.5%) having bilateral hydrocele and 30 (27%) presenting with both hernia and hydrocele. All patients with hernias underwent repair in addition to hydrocelectomy. No post-operative complications were noted upon discharge; minimal complications were noted in 2/37(5.4%) followed up after 5 months. All follow up patients self-reported improvement in psychosocial and overall health status. The training camps increased the local capacity of healthcare workers to manage hydroceles. We recommend continued use of the new technique to manage hydroceles.

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FACTORS ASSOCIATED WITH FAILING ASSESSMENTS TO STOP MASS DRUG ADMINISTRATION FOR ONCHOCERCIASIS IN KONTA SPECIAL WOREDA, SOUTHWEST ETHIOPIA PEOPLE'S REGION

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Mass drug administration (MDA) with ivermectin is the key strategy in the elimination of onchocerciasis in Ethiopia. Community ownership and health education through community drug distributors (CDDs) and community supervisors play a vital role in achieving quality MDA and high coverage. Mapping data from 2000 reported a baseline nodule prevalence of 14.4% in Konta Special Woreda, classifying it as hypoendemic. MDA began in 2015. This district is surrounded by endemic districts of Kaffa, Jimma and Dawuro zones, all bordering the Gojeb river. An impact assessment in 2020 found 1% prevalence of Ov16 antibodies by ELISA, prompting a full stop-MDA evaluation in 2022. The stop MDA survey tested 3,200 children 10 years of age and under. With 23 Ov16 positives (0.7%), the woreda failed to meet the stop-MDA threshold of <0.1%. While MDA continued, the program conducted a retrospective investigation into factors that might have contributed to the failure by evaluating data from MDA coverage surveys conducted in the woreda in 2019 and 2022. Two-stage cross-sectional community-based surveys were done to assess MDA coverage and other CDTI activities. In 2019, from the total 697 participants, 535 were treated with therapeutic coverage of 76% (95% confidence limits [CL] 73-79%), which was lower than the recommended 80%. Of untreated eligible people, 78 (46%) participants in 2019 and 25 (28%) of participants in 2022 were not treated due to absenteeism. From total 127 household (HH) participants in 2022, 22 (14%) of the HH heads participated in MDA site selection. Community participation in CDD selection declined from 2019 (24%) to 2022 (15%). Of those treated in 2019 and 2022, 50 (9%) and 72 (15%) of participants, respectively, did not have their height measured for dosing, and 144 (16%) and 155 (31%) did not get the right dose. The program should work on strengthening community participation in MDA activities as well as focus on overall program quality and responsiveness. Since the district has high density of *Simulium damnosum* along the Gojeb river, further epidemiological and entomological investigation could identify hotspots for special intervention.

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OPTIMIZATION APPROACHES FOR INTEGRATION OF NEGLECTED TROPICAL DISEASES INTO HEALTHCARE SYSTEMS IN KENYA

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Kenya strategy for incorporating Neglected Tropical Diseases (NTDs) into its healthcare systems reflects a notable departure from previous practices, aiming for sustainability and self-reliance in combating these ailments. By adhering to WHO guidelines and aligning with Kenya's health agenda, the country has taken proactive measures to ensure that NTD programs are efficiently managed and seamlessly integrated into existing healthcare structures. A crucial aspect of this integration involves transitioning from isolated approaches to a more comprehensive one. Through the utilization of WHO's health system building blocks and alignment with Kenya's Bottom-up Economic Transformation Agenda (BETA), the Ministry of Health – NTD Programme has facilitated the provision of comprehensive NTD treatment and care by integrating it into the Social Health Insurance Fund (SHIF). This was by engaging the health financing and SHIF team in an NTD costing workshops. This transition not only secures sustainable funding but also underscores the importance of embedding NTD interventions within broader healthcare frameworks. Furthermore, involving implementing and development partners in integrating NTD indicators into Kenya Health Information Systems (KHIS) exemplifies a commitment to evidence-based decision-making and transparency. To improve the timely referral of suspected NTD cases by Community Health Promoters (CHPs) and to ensure efficiency, accountability, and effective supervision during mass drug administration, the NTD program has integrated essential indicators into electronic Community Health Information System (eCHIS) platform which feeds into KHIS. This integration facilitates better monitoring and evaluation of NTD interventions while ensuring efficient resource allocation. Additionally, integrating NTD components into the country's community health strategy training modules and formulating a draft integrated vector management strategy showcases a multifaceted approach to disease control. By bolstering vector surveillance and control in collaboration with other health programs like the National Malaria Program, Kenya is optimizing resources and addressing the interconnected nature of vector-borne diseases. The accomplishments described above have been made possible through the strict adherence to a well-designed NTD coordination framework, which serves as a guiding document for the coordination of NTD integration efforts throughout Kenya.In summary, Kenya's integration approach serves as a model for other nations seeking to incorporate NTD interventions into their healthcare systems. By prioritizing sustainability, efficiency, and collaboration, Kenya is well-positioned to accelerate progress toward NTD elimination and eradication goals, all while alleviating strain on health systems, especially amidst reduced external financing.

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EMPOWERING WOMEN IN BIHAR, INDIA TO ELIMINATE LYMPHATIC FILARIASIS

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Lymphatic Filariasis (LF) poses a significant threat to Bihar, India, affecting over 130 million individuals across its 38 districts. Administering anti-LF drugs through Directly Observed Therapy (DOT) to the eligible 120 million population is a formidable task. Leveraging the State Rural Livelihood Mission's (SRLM) network of 11.6 million women's collectives (Self-Help Groups - SHGs), which touch every other household in rural Bihar, presents a promising solution. A pilot study in 2023 demonstrated the efficacy of SHG platforms, with SHG members exhibiting a 74% DOT compared with 45% among non-SHG members. Building on this success, in February 2024, 24 districts with 6.3 million SHG members were targeted for Mass Drug Administration (MDA). Prior to MDA, SHG members were educated on LF and MDA during their weekly meetings, to disseminate information

to their families and communities. The SHGs were engaged in various awareness activities, including discussions, oath-taking ceremonies, slogan competitions, and community rallies, fostering preparedness for anti-filarial drugs at the household level. Post-MDA, SRLM reported a 66% drug consumption rate among SHG members, contributing to a 6% increase in DOT overall. Further assessment of the intervention revealed that SHG households exhibited a 40% higher unadjusted DOT compared to non-SHG households. Within the SHG network, community mobilizers played a crucial role, increasing the odds of DOT compliance by 12 times (OR: 12.07, p: 0.00, 95% CI: 3.4-42.7) when promoting MDA activities. Moreover, timely information delivery (received 10-20 days before MDA), doubled the odds of DOT (OR: 2.52, p: 0.04, 95% CI: 1.2-2.1). This success underscores the potential of SHGs in enhancing anti-filarial drug compliance and aiding LF elimination efforts. Leveraging millions of women's networks could serve as a model for other endemic regions, amplifying outreach and impact. To mainstream women's involvement in LF elimination, capacity-building initiatives for SRLM staff and cadre could be implemented by health departments.

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STATUS OF LYMPHATIC FILARIASIS TRANSMISSION IN PASTORALIST AREAS OF SOUTH AND SOUTHWEST ETHIOPIA

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Lymphatic filariasis (LF) is targeted for global elimination through treatment of endemic populations with annual mass drug administration (MDA). WHO guidelines call for a transmission assessment survey (TAS) after at least five effective MDA rounds to determine if MDA can be stopped. LF commonly affects pastoralist areas and tends to be persistent since these areas are often hard to reach and have low access to and coverage of MDA. Five rounds of MDA were conducted in pastoralist areas of South and West Omo zones in Ethiopia between 2018 and 2022 with reported average coverage of >81% in all districts, achieved through close follow-up, monitoring, and support with expanded house-to-house attention by community directed distributors (CDDs) given the nomadic nature of the populations. Pre-TAS and TAS1 were conducted in 2023 in pastoralist communities of eligible districts of South and Southwest Ethiopia regional states. Pre-TAS involved sampling ~300 people aged 5 and older in each of sentinel and spot-check communities per evaluation unit (EU) in Hammer, Turmi, and Selamago districts. TAS-1 involved community-based surveys to sample children aged 6-7 years cluster sampled in 322 villages from 570 total villages in pastoralist woredas in South Ari, Surma, Hammer, Turmi, and Selamago districts. Samples were tested for LF antigen by Filarial Test Strips (FTS), and survey data were collected electronically with open data kit software. Pre-TAS included 1,939 FTS results, of which there was one positive from Hammer and one from Selamago. The prevalences in Hammer (0.15%), Selamago (0.15%), and Turmi (0%) were all less than the WHO threshold of 1%, and the EUs proceeded to TAS-1. TAS-1 included FTS results for 4,164 children, of which all were negative. LF transmission has been successfully reduced below sustainable levels such that MDA can be stopped in South Ari, Surma, Hammer, Turmi, and Selamago districts, with ~339,206 people at risk. This reflects the success of program implementation for these hard-to-reach pastoralist populations, though strong post-treatment surveillance is required to ensure that transmission does not recrudesce.

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OUTCOME OF SNAKEBITE VICTIMS MANAGED BY TRAINED HEALTH ASSISTANTS AT A SNAKEBITE TREATMENT CENTER IN NEPAL

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Snakebite envenoming is a neglected tropical disease. The World Health Organization (WHO) roadmap on snakebite envenoming targets snakebite related death reduction to 50% by 2030. Strengthening the health system is one of the four pillars of WHO snakebite strategy for snakebite prevention and control. Unfortunately, skilled physicians are scarce in the areas where snakebite is prevalent. Empowering health assistants (HA) for task sharing to manage snakebite may help prompt management of snakebite and reduce mortality. The aim of this study is to evaluate the outcome of snakebite cases managed by trained HAs at a snakebite treatment center. The study is a fifteen years (2008 AD to 2023 AD) retrospective audit of outcome of snakebite victims from a snakebite treatment center, Damak Red Cross, Damak, Nepal. A six-week training course organized for Health Assistant, to identify the features of envenomation, management, early identification of adverse reactions to anti-venom and need of referral were the focus of the training. Management of snakebite cases were done as per protocol provided by Ministry of Health and Population, Nepal. Anti-venom and other essential medicines were made available by the center itself. Six HA received training in 1998. Two to four days reinforcement of training was provided in subsequent years. HA had access to telephonic consultation with a faculty of medicine at B.P. Koirala Institute of Health Sciences. All records were kept in a structured case record and outcomes were analyzed using SPSS Version 26. A total of 30 HAs were trained. A total of 15,513 snakebite cases were managed in the center. Among the envenomation cases, neurotoxicity was the predominant manifestation. Majority of snakebite victims improved (98.4%), with a low referral rate (0.6%), and case fatality rate (1.2%). Mortality was found to be lower in comparison to national figures and other centers managing snakebite. Structured training and task sharing with paramedics may contribute to reduction in snakebite-related death.

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GENDER AND AGE MODULATING THE HEMATOLOGICAL PROFILES OF LEPROSY PATIENTS: ADISCURSIVE ANALYSIS

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Leprosy is a chronic infectious disease characterized by slow progression. Theobjective of this study was to analyze how age and sex can modify hematological data,as well as plasma levels of Vitamin A and D in patients with leprosy. The study groupcomprised 77 patients, being 44 (57,14%) males, diagnosed at the Reference Centerfor Endemic Diseases and Special Programs (CREDEN-PES/SMS/GV) in GovernadorValadares, eastern Minas Gerais, Brazil, age between 5 to 86 years old and exhibitingclinical forms classified as Paucibacillary (PB) and Multibacillary (MB) according to theWHO's operational classification. Mean values, standard deviations, and confidencelimits were stratified by age group and by gender. Significant differences were observedin the global leukocyte count in both genders (males - p=0.047 and females p=0.043),with higher values observed between 5-30 years old, with significant differences forglobal lymphocyte count (p-0.025) and basophils (p=0.028) only in males, with highervalues between 2-20 years and lower values between

31-40 years. Hematologicalvalues for RBC, hemoglobin and hematocrit were significantly higher in males (p<0.001)than in females. Age significantly modulated only the hematocrit (p=0.033) in males,while it significantly modulated the values for Hgb (p=0.041), HCT (p=0.037), MCV(p=0.015) and MCH (p=0.007) in females. Age significantly modulated the absoluteplatelet count only in males, with higher values between 21-30 and lower valuesbetween 41-50 years. Age significantly modulated only vitamin A values, this beingsignificant only in females (0.016), with the lowest levels between 5-20 years old. Thesefindings underscore the importance of considering variables such as age and gender inthe interpretation of hematological results in leprosy patients. However, further studiesare needed to better understand these differences and their clinical impact on diseaseprogression and management.

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SPATIOTEMPORAL DISTRIBUTION AND DIVERSITY OF AIRBORNE RESISTANT BACTERIA: AN EXPLORATORY ONE HEALTH STUDY IN THE URBAN AND RURAL ENVIRONMENTS OF BANGLADESH

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Antimicrobial resistance (AMR) is a widespread One health issue with planetary impacts. However, there is dearth of knowledge and scientific evidence on the magnitude of resistant bacteria in air and their transmission pathway. Therefore, an exploratory observational study in Bangladesh was conducted to quantify the clinically significant drug resistant bacteria in air with their spatial diversity. This study employed the collection of air samples from both urban and rural settings in four distinct environments – i) Urban live bird markets (LBM) ii) Urban residential area (URA) iii) Commercial poultry farms(CPF) and iv) Rural households (RHH). MacConkey agar supplemented with 3rd generation cephalosporin (3GC) and meropenem respectively was used to obtain 3GC resistant (3GCr) and carbapenem resistant *Enterobacteriaceae* (CRE). Mannitol Salt agar supplemented with oxacillin and Slanetz-Bartley medium supplemented with vancomycin were utilized to obtain Methicillin (Oxacillin) resistant Staphylococci (MRS) and Vancomycin resistant Enterococci (VRE). The bacterial identification and susceptibility testing were conducted by VITEK 2 system. The presence of 3GCr, CRE, MRS and VRE in 85%, 60%, 100% and 80% air samples was observed respectively. 3GCr, CRE and MRS were highest in CPFs and VRE in LBMs. The abundance (>90%) of MRS, VRE and 3GCr in URA is alarming whereas the air samples from RHHs were heavily burdened with 3GCr and MRS (60-100%). The CRE in poultry environment also establishes the threat added by current farm practice. The diversity and richness of resistant organisms were measured by Shannon diversity index, which was higher in both seasons at LBMs and CPFs (H-2.17-2.21 and H-1.99-2.03 respectively). Considering the organism family, the major bacteria were Staphylococcaceae (35%), Pseudomonadaceae (20%), Enterobacteriaceae (15%), Moraxellaceae (10%), Lactobacillaceae (7%) and Enterococcaceae (6%). This study findings emphasize on the inclusion of air in the system approach and surveillance to tackle AMR due to its high potential for acting as both reservoir and medium of spread of resistance.

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FINDINGS FROM A SIMULATION EXERCISE UTILIZING THE ONE HEALTH TRANSBOUNDARY ASSESSMENT FOR PRIORITY ZOONOSES (OHTAPZ) TOOL TO MEASURE HEALTH SECURITY PREPAREDNESS, DETECTION, AND RESPONSE CAPACITIES AT THE JORDAN-IRAQ BORDER

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Strengthening global health security efforts for the prevention, detection, and response to transboundary zoonotic diseases (TZDs) within and between nations requires multisectoral and multilateral approaches. The One Health Transboundary Assessment for Priority Zoonoses (OHTAPZ) tool is a published methodology that engages human, animal, environmental, and border health stakeholders at various levels to assess and prioritize One Health (OH) capacities at points of entry (POEs), where the exchange of people, livestock, goods, and infectious diseases often takes place. The OHTAPZ tool, which encourages bilateral collaboration between two neighboring nations; includes the development of an agreed joint list of priority TZDs; stakeholder mapping through an interactive tabletop exercise; and completing a POE self-assessment which provides a baseline of the current OH capacities at the POEs assessed. Through implementation of the methodology in Jordan and Iraq, our team at Johns Hopkins University then conducted a simulation exercise (SimEx) that tested the self-evaluated OH capacities at each POE. The SimEx assessed current preparedness and response communication and coordination mechanisms within and between the formal land border POEs for during a TZD event, resulting in not only the first bilateral assessment of OH capacities across formal land borders in Jordan and Iraq, but also demonstrating this methodology fills an important role in the global health security research and practice spheres.

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PHARMACOKINETIC PROPERTIES AND MOSQUITO-LETHAL EFFECTS OF A NOVEL LONG-LASTING FORMULATION OF IVERMECTIN IN CATTLE

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Ivermectin is an antiparasitic drug, used in human and animals for decades. It has recently been developed as a novel vector control tool for malaria as ivermectin-treated humans and animals are lethal to blood-feeding *Anopheles* mosquitoes. The aim of this work was to characterise the population pharmacokinetic (PK) and pharmacodynamic (PD) properties of a newly developed long-acting ivermectin formulation (BEPO® technology) in cattle. Two PK studies were conducted in Burkina Faso (Study 1: n=20 and Study 2: n=24). Plasma samples were shipped to Thailand for drug quantification by LC-MS/MS and for membrane feeding mosquito-killing evaluations. Plasma samples were mixed with fresh red blood cells obtained from cattle for mosquito feeding experiments. Only ivermectin and one major human metabolite (M1) were detectable in plasma samples and combined with mosquito mortality data, and evaluated using population PK/

PD modelling (i.e. nonlinear mixed-effects modelling; NONMEM). Specific emphasis was placed on characterising the absorption properties of this novel formulation. Mosquito mortality was modelled using a sigmoidal Emax model. A three-compartment disposition model for ivermectin and a two-compartment disposition model for M1 were used to describe the observed drug concentration data. The final population PK model adequately described the dual absorption processes of fast and slow first-order absorption after subcutaneous injection. The estimated IC_{50} of ivermectin and its metabolite was 12.9 nmol/L for *Anopheles dirus* mortality and 1.48 nmol/L for *Anopheles minimus*. The developed novel formulation demonstrated sustained mosquito mortality after a single injection. Translational simulations were also conducted to inform a prospective first-in-human clinical study. Body weight-scaled doses used in cattle (0.6, 1, 1.5 mg/kg) were predicted to result in sustained ivermectin exposure and sustained *dirus* and *minimus* killing for >35 days and >90 days, respectively, after a single injection. This could be a promising novel tool for transmission blocking of malaria and for the treatment of NTDs in humans.

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MOLECULAR CHARACTERIZATION AND PHYLOGENETIC ANALYSIS OF BOVINE *FASCIOLOSIS* IN UPPER EAST REGION, GHANA

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Fascioliasis, a disease transmitted between animals and humans, is caused by liver flukes. The primary cause of this ailment are two species: *Fasciola gigantica* and *F. hepatica*. These parasites can have a severe impact on both public health and the livestock industry due to their prevalence. To understand the occurrence and genetic properties of these *Fasciola* parasites in the Upper East Region of Ghana, a study was conducted. The research involved examining 246 cattle from this region to determine the presence of *Fasciola* infections. The scientists utilized the polymerase chain reaction (PCR) technique and sequenced a specific portion (290 bp) of the nad5 gene. The findings revealed that around 23.58% (58 out of 246) of the cattle were infected with Fasciola. However, after analyzing the data, no significant correlation (with a p-value greater than 0.05) was found between Fasciola infection and the animals' gender or age. Interestingly, a noteworthy and statistically significant relationship (with a p-value of less than 0.001) was discovered between Fasciola infection and the animals' body condition scores (BCS). When the obtained DNA sequences were compared using the BLAST tool, it was confirmed that the isolated *Fasciola* specimens belonged to the *F. gigantica* species. Five distinct haplotypes were identified, with one haplotype showing similarities to those found in Niger's haplogroups. Notably, two of these haplotypes were previously undocumented.

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POSITIVE ASSOCIATION OF ORAL INFECTION BY *TRICHOMONAS TENAX* WITH PERIODONTITIS IN THE DOMESTIC DOG

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Trichomonas tenax, an anaerobic protozoan, colonizes the oral cavities of humans and animals, particularly in individuals with compromised oral hygiene and periodontal disease. Transmission occurs through droplet spray, kissing, or exposure to contaminated utensils and water. The established association between *T. tenax* and periodontal disease in humans is noteworthy, given the global prevalence of this inflammatory condition leading to tooth loss, impaired chewing function, aesthetic concerns, social disparities, and reduced quality of life. In humans, periodontal disease ranges from 1-57%, while in domestic dogs, it varies from 15-25%. Recognized as a parasite and potential zoonotic agent, *T. tenax* raises concerns about cross-species transmission between humans and their pet dogs. This study aims to correlate *T. tenax* infection with periodontal disease in domestic dogs by comparing its prevalence in dogs with periodontitis to that in healthy dogs. Oral swabs were collected from the gumline of dogs on St. Kitts between October 2023 and January 2024. A total of 50 samples underwent microscopy for *T. tenax* detection. The dogs were categorized into healthy (Stage 0-1, with or without gingivitis) and diseased (Stage 2-4, with periodontitis) groups based on periodontal disease severity. Three swabs were obtained from each dog: two for culture using the classic Diamond media and a newly modified Diamonds media, and one in alcohol for LAMP. *T. tenax* was detected in 14% of all dogs (7/50), specifically, 33% prevalence in the diseased group (7/21) compared to 0% in the healthy group (0/29). Statistical analysis revealed a significant association between *T. tenax* presence and diseased dogs (P=0.0008). The newly modified media exhibited greater sensitivity, detecting 14% of samples (7/50), compared to the classis Diamonds media, which detected only 2% of samples (1/50, P=0.0270). Subsequent LAMP analysis of alcohol-preserved samples will further compare the prevalence and sensitivity of the two detection methods, contributing valuable insights to the observed statistical significance between periodontitis and *T. tenax* infection in mouth.

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BEHAVIORAL AND BIOLOGICAL SURVEILLANCE OF EMERGING INFECTIOUS DISEASES AT THE HIGH-RISK HUMAN-ANIMAL INTERFACE IN BANGLADESH

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Human-animal interactions are the key drivers of zoonotic spillover, highlighting the better understanding of human behaviors to mitigate disease emergence at high-risk communities. Hence, we conducted an integrated biological and behavioral surveillance to detect novel and known zoonotic viruses in potential high-risk populations and identify risk factors for viral spillover in Bangladesh. Between 2017 and 2019, we enrolled a total of 1106 participants for behavioral interviews at three communities and one hospital site. We obtained biological specimens (throat swab, rectal swab, urine, and blood) from 862 participants and tested for coronaviruses, filoviruses, flaviviruses, influenza viruses, and paramyxoviruses using pan (consensus) RNA Virus assays. Overall, 64/862 (7.4%) tested positive for viral families including influenza viruses (51.6%), coronaviruses (20.3%), flaviviruses (12.5%), and paramyxoviruses (15.6%). Participants reported highly contact with poultry (92.4%) and domestic animals (74.6%) comprising raising, handling, slaughtering, scratched or bitten. A significant percentage of participants also reported consuming sick animals' meat (44.3%) and raw meat (5.9%). In case of wild animal, participants had high level of rodent contact (92.5%) and having rodent feces near their food (75.9%), followed by 6.3% contact with bat hunting and processing. Moreover, 17.5% of participants kept the bitten or scratched wound open. Lasso regression model revealed that most salient risk factors of self-reported influenza-like illness (ILI) in the past year were slaughtering animals, had contact with poultry, scratched or bitten by animals and most prominent protective factors were living in urban areas having a smaller family (less than 5 person). The findings underscore the significant level of interaction between humans, livestock, and wildlife in communities, which might lead to transmit emerging pathogens in Bangladesh. We recommend One health surveillance and to develop targeted interventions to mitigate the risk of zoonotic disease spillover at animal-human interface in Bangladesh.

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MYCOBACTERIUM AVIUM SUBSP. *PARATUBERCULOSIS* AND MICROBIOME: A ONE HEALTH CONCERN

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Mycobacterium avium subsp. *paratuberculosis* (MAP) causes the notifiable disease in ruminants, Johne's disease, or paratuberculosis (PTB). Besides, it is a potential zoonotic pathogen as it is implicated in inflammatory bowel disease and many other chronic conditions in humans. Also, MAP is thought to change the gut microbiome, which in turn is connected to some MAP- linked diseases. Animal health and welfare, economic impacts and public health concern are key drivers of PTB control; however, such programmes are costly and hindered by lack of sensitive diagnostics. Microbiome could serve as footprint for MAP infection and/disease; indeed, it could be targeted to control MAP- attributed inflammation. A dairy cattle herd with history of clinical PTB was investigated by serology and molecular detection of MAP in the faeces for 10 months. Also, 103 faecal samples were obtained from patients with chronic gastrointestinal conditions after they consented to participate. Faecal metagenomic analysis was performed using Oxford Nanopore Sequencing Technology. All animals were positive in MAP test(s) except two, while in humans, MAP DNA was detected in 8.7% and MAP was isolated from 28.2%. Most species were depleted from faecal microbiome of MAP positive subjects. In MAP- positive patients, firmicutes and proteobacteria dominated and the colitogenic bacteria, *Klebsiella pneumoniae*, was enriched. In animals, firmicutes and bacteroidetes were highly enriched with a small contribution of proteobacteria. Furthermore, animals with increasing frequency of MAP positivity showed comparable microbial content. Overall, richness and evenness indices decreased with increasing MAP positivity rate. These findings reflect a potential influence of MAP on faecal microbiome, also, demonstrated the unique microbiome of the animals progressively shed MAP in their faeces, the highly infectious animals. This of significance in control such zoonotic pathogen, thus remains for further investigations.

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ONE HEALTH AWARENESS, INTERPRETATION AND PRIORITIZATION IN THE GAMBIA: A PARTICIPATORY SITUATIONAL ANALYSIS OF NATIONAL STAKEHOLDERS ACROSS GOVERNMENT, ACADEMIA AND CIVIL SOCIETY

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The Gambia currently lacks active and coordinated One Health (OH) institutional frameworks or a national strategic plan. Despite the formation of multisectoral task forces *ad hoc* in response to national health emergencies, OH activities remain siloed within a group of governmental and academic bodies, and have lacked the momentum, resources, cross-sectoral engagement and political will to operationalise OH in a sustainable and equitable manner. At the community level, OH beneficiaries are mostly excluded from stakeholder exercises. This study identified national OH stakeholders across government, academia, health agencies and civil society. Semi-structured interviews and focus group discussions were conducted with engaged stakeholders at national and regional levels. Inductive thematic analysis was conducted to identify themes relating to OH interpretation, awareness, prioritisation and operationalisation in The Gambia. Study outcomes were rapidly disseminated to stakeholders at an in-person meeting and in a policy briefing document. Interconnected themes were identified relating to: awareness of the OH concept; OH definition in the context of the participants' working, study or community environment; national activities or frameworks related to OH; community, regional and national level collaborations between OH stakeholders; OH priority areas; and barriers and solutions to OH operationalisation. Awareness levels of the term OH were variable between stakeholder groups, with overall low awareness demonstrated by community and student groups. Upon explanation of OH, the majority of stakeholders successfully related the concept to their diverse working, study or community environments. Between sectors and disciplines, and varying levels of society, shared and diverging OH interpretations, awareness levels, priority areas and challenges were demonstrated. This study provided novel evidence of OH awareness and prioritisation in The Gambia, which could be used to inform OH participatory research activities, policies and national frameworks.

7496

BRUCELLOSIS SEROPREVALENCE AND RISK FACTORS AMONG HIGH-RISK GROUPS AT TWO URBAN SITES IN KENYA

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Brucellosis is a zoonotic bacterial disease that can affect humans and animals. It is often transmitted to humans through the consumption of contaminated animal products or by direct contact with infected animals. In Kenya, data on human and animal brucellosis are limited. To investigate the seroprevalence of human brucellosis in Kenya, we randomly selected from the participants had possible animal exposure and tested 348 out of 2,779 human blood samples, from a longitudinal cohort study of dengue and chikungunya exposure in western (Kisumu) and coastal (Ukunda) Kenya. The inclusion criteria consisted of those who demonstrated positive responses to any of the following risk factors: ownership of livestock or ruminants, usage of raw animal blood, consumption of raw milk (either fresh or fermented), involvement in animal butchering, and providing of animal care. Our study included 126 males (36%), 222 females (64%) in

different age categories, and 61 children aged 16 years and younger (18%), with an overall median age of 29.5 years [2 -75-year age range]. Samples were tested by Abnova Brucella IgG ELISA Kit (KA0954). Of the tested individuals, anti-Brucella IgG antibodies were detected in 96 (28%) in 348 randomly selected participants. Brucella exposure was not associated with study site, gender, age, socioeconomic status, specific livestock ownership (cattle, goats, and sheep), or consumption of raw animal products. Highly educated individuals were more likely to have brucella exposure (OR = 2.02, 1.20-3.41, *P = 0.01)*. In comparison to previous seroprevalence-based studies conducted in non-pastoral Kenyan communities, our study revealed significantly higher seropositivity. This study highlights the neglected significance of brucellosis exposure among urban human populations in Kenya, which could serve as a baseline to guide future research on brucellosis in humans.

7497

THE HIGHEST MPOX OUTBREAK EVER REPORTED IN CAMEROON; THE CASE OF MBONGE HEALTH DISTRICT OF THE SOUTH WEST REGION: A CROSS SECTIONAL ANALYTICAL STUDY, JUNE 2023.

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Human mpox is a viral zoonotic disease endemic in Central and West Africa. On May 10th 2023, a laboratory confirmed case was notified in the South West Region. We conducted an investigation to assess the outbreak. We carried out a cross-sectional analytical study in Mbonge District from May 15th to June 3rd 2023. Community-health-workers and leaders were engaged after being trained on simplified case definitions, active case search and sensitization. We reviewed registers in five major hospitals. A suspected case was anybody in Mbonge District between April 19th and May 14th 2023 with acute fever >38.3°C, headache, lymphadenopathy, followed after one to three days by maculopapular rash. Swabs and blood samples were collected from suspected cases. A line-list for all suspected and confirmed cases was analyzed for descriptive epidemiology and binary logistic regression for associated factors. We identified 48 suspected cases of which 15(31,2%) were confirmed positive, 8(53,3%) were Clade-II. Amongst confirmed cases, 7(46,6%) were females and median age was 33 years, [3-52]. Persons who spent at least two-weeks in the bush had four times the likelihood of getting mpox (P:0,007, C.I [0,006 - 0,443]). Sensitization on preventive measures while in the bush and engagement of community actors in a crisis zone remains vital.

7498

SURVEILLANCE AND HOME RANGE ANALYSIS OF OLIVE BABOONS TO INFORM PROGRAMMATIC DECISIONS FOR GUINEA WORM ERADICATION IN GAMBELLA, ETHIOPIA

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The first Guinea worm infection in Olive baboons (*Papio anubis*) in Ethiopia was reported in 2013. Since then, questions have been raised about the role of Olive baboons in ongoing Guinea worm transmission among both humans and domestic dogs in Ethiopia. In support of eradication and to better understand transmission risks, the Ethiopia Dracunculiasis Eradication Program (EDEP) conducts active surveillance activities among Olive baboon troops in the Gambella region considered high risk for Guinea worm due to previous infections or proximity to human or other animal infections. Surveillance includes weekly tracking of baboon movement and water source use, as well as trapping and sedation of baboons to physically check for emerged worms or signs of Guinea worm. Since 2021, EDEP has screened more than 200 baboons for Guinea worm through active surveillance. During trapping in March 2024, we screened 68 baboons for Guinea worm among nine troops, with no Guinea worm detected. In response to the 2023 animal infection detected in Ethiopia, EDEP is expanding the number of baboon troops under surveillance, with additional trapping sessions planned for July and October 2024. In March, we placed GPS collars on baboons from five troops, and plan to place more collars on baboons during the July trapping. Data from GPS collars, captured year-round, will clarify baboon movement, and troop overlap with both nearby baboon troops and water sources used by communities. Preliminary results indicate variation in total troop home ranges between 2.2 and 7.9 kilometers squared. Daily averages for the troop with the largest total home range during the peak dry season varies from 0.2 to 2.0 kilometers squared. These results are programmatically meaningful given baboon home ranges encompass water sources used by humans and domestic dogs, which could have implications for Guinea worm transmission. EDEP is leveraging findings from baboon surveillance activities to inform programmatic implementation strategies, including surveillance intensity, community mobilization, and water treatment to prevent Guinea worm transmission.

7499

(UN)SUSTAINABLE SCIENCE: ENVIRONMENTAL FOOTPRINT OF RESEARCH, CLINICAL MICROBIOLOGY AND VETERINARY LABORATORIES LOCALLY AND GLOBALLY

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Recently, the scientific and healthcare research communities have increased their efforts to study the causes, implications, adaptation, and mitigation strategies for climate change. It is also important to address our fields' contributions to climate pollution. In this review, we present the scale of the problem, potential interventions, and a case study on waste management from hospitals in Kenya to give a global perspective. Research laboratories produce 12 billion pounds of plastic waste each year and use up to 70% of their institutions' energy despite occupying a significantly smaller proportion of their institutions' total space. –80°C freezers and fume hoods alone use energy that is equivalent to a single and 3.5 households, respectively, and a single laboratory can have multiple freezers and hoods. Clinical microbiology laboratories have significant carbon footprints that can be reduced through diagnostic stewardship, a process focused on ensuring the collection of the right test from the right patient at the right time. Opportunities exist for reducing reagent waste in frequently ordered clinical tests such as complete metabolic panels. Veterinary laboratories also contribute significant carbon emissions from excessive waste from phlebotomy supplies, packaging, animal carcasses, and other biohazardous waste. Green initiatives have been shown to decrease the carbon footprint of laboratories, provide cost savings, and do not have to be resource- or time-intensive. Reducing waste production by purchasing reusable and refillable materials, autoclaving for reuse whenever possible, participating in recycling programs, using low-faucet valves to reduce water use, shutting off hoods and other equipment when not in use, and increasing freezer temperature from –80°C to –70°C are some eco-friendly practices laboratories might adopt. In addition to reducing carbon footprint and saving costs, these practices can also help advance health equity as waste is often disposed of in areas proximal to marginalized communities causing human morbidity and mortality.

7500

AVIAN VACCINATION VIA RECOMBINANT *LACTOBACILLUS*-BOUND BIRDSEED TO CURB THE SPREAD OF WEST NILE VIRUS

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West Nile virus (WNV) is the leading cause of domestically acquired mosquito-borne disease in the United States. Despite significant investment, no effective human WNV vaccines have been developed, so current mitigation efforts remain limited to environmentally toxic insecticidal sprays. While humans and other animals can develop disease, they are dead-end hosts because they do not develop high enough viremia to infect other mosquitoes. Rather, propagation of WNV is primarily maintained between mosquitoes and birds. We hypothesize that immunizing WNV-susceptible birds will reduce WNV transmission to mosquitoes, protecting both people and animals from infectious bites and disease. To this end, we are genetically modifying strains of the probiotic *Lactobacillus acidophilus* (LA) to express WNV antigenic proteins premembrane (prM), envelope (E), and non-structural protein 1 (NS1). The bacteria will be administered orally to deliver intact viral protein to mucosal immune inductive sites in birds. Immunogenicity is enhanced by the addition of a dendritic cell targeting peptide (DCpep). Protein expression by the LA-based vaccine (rLA-WNV) will be assessed by Western blot and flow cytometry. Immunogenicity will be measured by vaccinating chickens and assessing development of anti-WNV antibodies via ELISA-based techniques and plaque-reduction neutralization assays. We will lyophilize rLA-WNV and bind it to seed to assess its environmental stability and immunogenicity. We selected this strategy because 1. it is only practical to immunize wild birds orally with food baits in WNV endemic areas, and 2. LA can be lyophilized, allowing for preservation and binding to bird seed. The strategy, if successful, will result in an innovative and cost-effective strategy for control of vector-borne disease.

7501

THE FINANCIAL IMPACT OF LIVESTOCK SCHISTOSOMIASIS AND UNDERSTANDING THE IMPORTANCE OF POLICY BUY-IN ON INTERVENTION SUCCESS

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Schistosomiasis is a neglected parasitic disease that poses major threats to human and animal health, as well as the economy, especially in sub-Saharan Africa. It is second only to malaria in its socioeconomic and public health importance with an estimated 1.864 million disability-adjusted life-years (DALYs) lost, 240 million people infected globally and estimated productivity losses due to human schistosomiasis at $11.9 billion/year for 2021-2030. It also has debilitating effects on animals. However, knowledge about the impact of the disease on economic livelihoods and how policy buy-in at various stakeholder levels affects interventions and economic outcomes is limited. A One Health financial analysis of livestock schistosomiasis was conducted to estimate the financial impact of the disease in northern Senegal. Stochastic partial budget models were developed for traditional ruminant farmers in 12 villages. These models were parameterised using data from a cross-sectional survey, focus group discussions (FGDs), scientific literature, and available statistics. Two scenarios were defined: scenario 1 modelled farmers who tested and treated their livestock for schistosomiasis, while scenario 2 modelled no tests or treatment. Sensitivity analyses were conducted to assess the impact of uncertain variables on disease costs. Results revealed that livestock schistosomiasis has a substantial impact on farmers. Schistosomiasis in a herd reduces the farmers' livelihood and may lead to an inability to meet basic needs. Therefore, treating livestock schistosomiasis has the potential to generate considerable benefits for farmers and their families. These findings will be discussed in the context of policy buy-in across stakeholders. They will be presented alongside work on a literature review and community surveys, where we are identifying current interventions in affected communities; measuring the impacts, accessibility, and cost-effectiveness of these interventions through empirical research; and assessing barriers and facilitators to policy buy-in for intervention uptake and success through FGDs and in-depth interviews.

7502

COMPARATIVE ANALYSIS OF STEROID-RDV COMBINATION THERAPY VERSUS STEROIDS ALONE IN HOSPITALIZED COVID-19 PATIENTS: A SARS-COV-2 VIRAL LOAD DYNAMICS STUDY

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Treatment with steroids and/or remdesivir (RDV) are standard treatments in hospitalized COVID-19 patients. Studies with conflicting findings have investigated how steroids and/or RDV affected SARS-CoV-2 viral load (VL) dynamics in the upper respiratory tract (URT). Our studies in hospitalized patients showed that elevated SARS-CoV-2 in peripheral blood (PB), but not the URT, are predictors of severe disease. To investigate the influence of standard treatments on PB and URT VL dynamics, we examined the impact of steroids alone or in combination with RDV in hospitalized COVID-19 patients (n=475) recruited between 4/2020-12/2021 at the University of New Mexico Hospital. To account for the influence of disease severity, only severe COVID-19 patients (n=190), defined by ICU requirements and/or death, were included in the study. Severe patients were stratified into those who received steroids alone (n=37, 19.5%) or steroids/RDV (n=130, 68.4%). Patients (12.1%) who did not receive treatment due to RDV unavailability, contraindications to steroids and/or RDV, completion of prior therapies, or undergoing alternative treatments were excluded. PB and URT VLs at enrollment and cumulative VLs across 14 days were similar between treatment groups. Refined analyses with linear mixed-effects models were employed to analyze the general trend and individual variations in VL changes over time. VLs in PB (P=4.40E^{-9}) and URT (P=9.00E^{-10}) decreased in both groups across 14 days. Patients who received steroids/RDV had higher initial PB VLs (P=0.049) that decreased at a faster rate (P=0.0019). In contrast, patients treated with steroids/RDV had comparable initial URT VLs (P=0.31) and similar decreases across time to those treated with steroids alone (P=0.406). Importantly, patients receiving combination therapy had a shorter average length of stay (20 vs. 23 days) vs. steroids alone (P=0.041). Collectively, findings presented here indicate that severe COVID-19 is defined by higher PB VLs across time and that combination therapy (steroids/RDV) is more effective than steroids alone for reducing SARS-CoV-2 in blood, as well as length of hospitalization.

7503

MULTIPLE VIRAL COINFECTIONS IN TUBERCULOSIS PATIENTS IN BAMAKO, MALI

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Tuberculosis (TB) infection is often found with other chronic pathologies. While morbidity and mortality fromopportunistic diseases have declined recently, some infections such as cytomegalovirus (CMV), TB, andhepatitis B remain significant health issues in person living with HIV (PLWH). Viral co-infections can disrupthost defenses which may impact the risk of developing active TB disease. Thus, our study aimed todetermine, on an exploratory basis, the frequency of other viruses in patients co-infected with TB and CMVin Bamako, Mali using VirCapSeq-VERT. We conducted a cross-sectional study by enrolling TB patients atthe University Clinical Research Center (UCRC) in an IRB approved protocol between October 2018 andOctober 2019. TB was confirmed by positive culture, and sera were tested for viral coinfections. The originalstudy was designed to look at the impact of CMV on TB. IgM/CMV was determined from all samples usingELISA. For this exploratory analysis, only positive serum samples were extracted using the DNA/RNA MiniKit (Qiagen, Hilden, Germany) and then unbiased metagenomic sequencing for viruses was performed usingVirome Capture Sequencing for vertebrate viruses (VirCapSeq-VERT) followed by captured amplification andsequencing with the illumina NextSeq 2000 system. Out of 100 TB patients enrolled, the prevalence ofIgM/CMV was 17%. Among the 17 TB+/CMV IgM+ participants, 11 were male and the mean age was 26.29years old. VirCapSeq-VERT detected various viruses in the 17 participants: Tenovirus/Teno-midi virus(N=11), hepatitis B (N=9), Human Herpes virus (HHV)-4/SEN virus (N=5), GB virus C (N=4), HHV-8/HHV-5(N=2). HHV-6A, HIV, Betapapillomavirus 1, Human endogenous retrovirus, Murine leukemia virus, TilapiaLake virus, Gemycircularvirus NP were all identified in a single participant. While the pathogenicity of mostdetected viruses remains uncertain, VirCapSeq-VERT was useful in detecting a diverse set of viruses.Further research using VirCapSeq-VERT in all TB patients could provide a more comprehensive profile ofviral coinfections in TB patients and their clinical impact.

7504

EFFECT OF PRIOR ANTIBIOTICS USE ON BLOOD CULTURE POSITIVITY IN CHILDREN UNDER 5 YEARS WITH SUSPECTED INVASIVE PNEUMOCOCCAL DISEASES IN RURAL GAMBIA

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Blood culture plays a crucial role in the diagnosis and treatment of invasive diseases. However, the effect of antibiotics use before blood culture collection among children under 5 years with suspected invasive disease is not well understood. We describe the effect of antibiotic activity on blood culture outcomes in children under 5 years with suspected invasive pneumococcal diseases in rural Gambia. Between September 2019 and December 2021, we collected blood cultures and whole blood at the pediatric outpatient departments of two hospitals from children <5 years old with suspected pneumonia, sepsis, and meningitis who had been enrolled in a pneumococcal vaccine schedule study. Information on antibiotic use in the last week before presentation at the health facilities was collected from parents/caregivers. Blood cultures and pathogen identification were performed using standardized methods. An antimicrobial activity assay was performed on whole blood samples to test for the presence of antibiotics. Descriptive statistics and logistic regression analyses were performed. Of the 1715 samples, the blood culture positivity rate was 77 (4.5%), and 95 (5.5%) had positive antibiotic activity. Blood culture was positive in 9/95 (9.5%) of patients with positive antibiotic activity compared to 68/1620 (4.2%) in those with negative antibiotic activity. Antibiotic activity was detected in 34/420 (8.1%) patients who had reported prior antibiotic use. Blood culture positivity rate was 25/420(6.0%) and 52/1295 (4.0%) among those who reported and those who did not report prior antibiotic use respectively. Those with positive antibiotic activity were 2.4 times more likely to have a positive blood culture compared to those with no antibiotic activity (odds ratio, 2.40; 95% CI, 1.15-4.95; p = 0.02). In contrast to findings from similar studies, we found a positive correlation between positive antibiotic activity and blood culture positivity. Thus, there is still considerable value in performing blood cultures for patients with prior antibiotic use in our setting. Further research is recommended to determine the factors associated with our findings.

7505

RAPID IDENTIFICATION OF NON-TUBERCULOUS MYCOBACTERIAL SPECIES USING FLUOROCYCLER® XT IN SUSPECTED PATIENTS IN BAMAKO, MALI

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Non-tuberculous mycobacteria (NTM) are ubiquitous organisms causing neglected and highlycomplex infections. The lack of epidemiological studies of NTM infections has ultimately led toan underestimation of NTM cases, thus resulting in an increase frequency worldwide. Treatmentof NTM infections is challenging due to their relative resistance to a wide range of antibiotics, andtoxicity of sensitive ones. Therefore, rapid and reliable identification of NTM infected patients isessential to implement specific treatment and preventive measures. To discriminate NTM rapidlyand efficiently from *Mycobacterium tuberculosis complex* (MTBc), we carried out a cross-sectional study in new and previously treated tuberculosis (TB) patients between January 2021 andDecember 2023 at the University Clinical Research Center (UCRC), Bamako in an IRB approvedprotocol. Two separate sputum samples were collected from NTM suspected patients (those withpositive auramine staining microscopy and negative GeneXpert MTB/RIF results). BACTEC™MGIT 960 system was used for the cultivation of mycobacteria, and positive cultures were usedfor molecular identification of the different species using the FluoroCycler® XT (Fluorotype®Mycobacteria V1.0) in accordance with the manufacturer's recommendations. Of the 76 patientsenrolled, 34 (44.7%) were NTM confirmed. The prevalence of HIV/NTM co-infection was 5%.The sex ratio was 4.05 and the age ranged of 31-44 years old was the most represented (17/34).Among the 34 isolates, 25 were from previously treated, and nine from new TB patients.FluoroCycler® XT identified ten different species, and more specifically, *M. avium complex*(N=11), *M. massiliensei* (N=7), *M. fortuitum* (N=5), *M. simiae* (N=4), *M. bolletii*/*M. chimaera*(N=2 each), and *M. interjecum*, *M. mucogenicum*, *M. abscessus* were all identified once. Whilethe pathogenicity of most detected NTM remains uncertain, FluoroCycler® XT was useful indetecting a diverse set of NTM in a relatively

short period of time. NTM is more common onpreviously treated TB patients, and *M. avium* complex is the more common isolated species in oursetting.

7506

EVALUATION OF TRENDS IN PNEUMOCOCCAL ANTIBIOTIC RESISTANCE IN INVASIVE PNEUMOCOCCAL DISEASES IN RURAL GAMBIA

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Management of pneumococcal diseases is complicated by high rates of antimicrobial resistance (AMR) which poses a significant challenge for treating pneumococcal diseases. This study assessed AMR trends of *Streptococcus pneumoniae* in invasive pneumococcal diseases (IPD) in rural Gambia. We evaluated invasive S. pneumoniae, isolated in rural Gambia over a 15-year period between 2008-2022. Standardized, population-based Surveillance for invasive bacterial causes of pneumonia, sepsis, and meningitis was conducted in Basse Health & Demographic Surveillance System from 2008-2017 and 2019-2022, while in Fuladu West Health & Demographic Surveillance System surveillance covered 2011-2014 and 2019-2022. *S pneumoniae* was identified by morphology and optochin sensitivity and ATCC 6583 was used as a reference strain. Antibiotic sensitivity was assessed using Kirby-Bauer disk diffusion method, apply CLSI standards to categorize isolates as resistant, intermediate, or sensitive to antibiotics. We used descriptive statistics to characterize the percentage and the trends of AMR in four time periods, 2008-2010, 2011-2013, 2014-2017, and 2019-2022. Of 450 S. pneumoniae isolates, were isolated in the four time periods, 34% (153/450) of patients were aged <1 year, and 75% were from blood culture. Almost all isolates (94%) were resistant to cotrimoxazole. Proportions resistant to tetracycline were 56%, oxacillin 26%, chloramphenicol 20%, and ciprofloxacin 9%. The resistance to ampicillin was a very little (2.36%). There was limited variation in resistance to individual antibiotics over time. There was a decrease in tetracycline resistance over time (60% to 44%) and also resistance to ≥3 drugs (33% to 16%). There are modest levels of AMR in invasive S. pneumoniae isolates in rural Gambia. Resistance over time was relatively stable with some reductions in the proportion of tetracycline and multi-drug resistance. Amoxicillin and Ceftriaxone, First and second line drugs respectively for for pneumococcal diseases in The Gambia, remain effective.

7507

COMMUNITY PERCEPTION AND IMPACT OF A MOBILE VAN FOR POST-MORTEM SAMPLE COLLECTION IN KARACHI, PAKISTAN: CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS)

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Although post-mortem sampling is essential to mortality surveillance, it can be logistically and culturally challenging to conduct in Muslim societies like Pakistan. Funerary preparations and burial often occur within hours of death, and there is little time in which it is appropriate to collect a sample from the dead. A mobile van, modified for the sterile collection of minimally invasive tissue samples (MITS), allows for sample collection with minimal disruption to community values and funerary logistics. Initially designed to conduct neonatal MITS for a respiratory syncytial virus (RSV) study, the van can navigate narrow streets and densely populated spaces in the catchment area, which includes several peri-urban areas of Karachi. Retrofitted with a sterilizable laboratory interior, the van has an operating table, storage space, ventilation, and sink, with space for a specialist and observer. During the study, the van enabled on-site and immediate MITS collection, eliminated time spent transporting the body, and minimised delays in burial preparations. The van also fulfilled caregivers' desire to observe sample collection and allowed for flexibility in location of sample collection. In preparation for the Child Health and Mortality Prevention Surveillance (CHAMPS) study, we asked the community for their perceptions of the MITS van. Caregivers viewed it as convenient and culturally respectful. They recommended parking strategically to avoid attention from funerary congregations, allowing families to observe sample collection, and using the van to perform *ghusl*, a ritual bath. MITS specialists suggested improvements to van design, including optimising storage, rearranging tables, and increasing ceiling height. New vans were modified and used for CHAMPS MITS according to community and expert feedback. The MITS van has transformed our post-mortem sampling, offering a sterile, efficient, and culturally sensitive solution to mortality surveillance in conservative settings like Pakistan. Its success demonstrates the importance of involving the community in the design of innovative research solutions.

7508

HOW CROSS-BORDER COLLABORATION BETWEEN CAMEROON AND GABON ENHANCED PROMPT RESPONSE TO A DIPHTERIA OUTBREAK, DECEMBER 2023

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In 2023, there was an upsurge of diphtheria cases with epidemics reported in five African countries. In december 2023, a diphtheria case was reported in Ebolowa, South Cameroon, originating from Bitam a border district in North Gabon, raising fears of an epidemic. A joint team from Cameroon and Gabon conducted an investigation in the border districts to describe the case, identify and trace contacts, and assess vaccine coverage. We conducted a cross-sectional descriptive study from december 18-26, 2023. We searched for cases in health facilities registers and in the community. A case was anyone living in the Ebolowa, Ambam, Kye-Ossi, and Bitam districts with pharyngitis, rhinopharyngitis, tonsillitis or laryngitis and adherent pseudomembrane of the throat or nose from november 23, 2023. A contact was anyone who had physical or respiratory contact with a case in the 14 days preceding symptoms onset. Identified contacts were followed up for 14 days by phone. We administered questionnaires to 30 households around each identified case to assess vaccine coverage in children 6 weeks to 9 years. Two suspected cases and one confirmed case of diphtheria were identified in Bitam aged 6, 9 and 10 years, with a M/F sex ratio of 1/2. All three cases were unvaccinated and all three are dead. We identified and traced 69 contacts, none of them developed diphtheria symptoms. Overall, 83% (169/203) of parents were able to present a vaccination record. Estimated diphtheria vaccine coverage was 79% (162/203). The main reasons for non-vaccination were refusal (8/21), difficulty in purchasing a booklet (7/21) and distance from the vaccination site (5/21). Reactive vaccination of 260 unvaccinated children was implemented. This cross-border collaboration led to prompt detection and response to diphteria outbreak in Gabon. Strengthening community and cross-border surveillance, and vaccination in both countries could help to reduce the burden of this deadly disease.

7509

COMPARATIVE MORTALITY ANALYSIS: ERADICATION VS PERSISTENCE OF *PSEUDOMONAS* INFECTIONS

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Chronic obstructive pulmonary disease (COPD) is a significant cause of mortality worldwide. Chronic bronchial infection (CBI) in these patients increases exacerbations and severity. Pathogen isolation is important for treatment, prognosis, and monitoring. Isolation of *Pseudomonas aeruginosa* (PA) is associated with a worse prognosis in CBI, but further studies on treatment and management in COPD patients are needed. We carried out a multicenter observational study of historical cohorts of COPD patients with diagnostic criteria for COPD who had received at least one dose of any inhaled antibiotic between 2013 and 2018. , we only included those with at least one positive culture for PA prior to starting inhaled antibiotic treatment. Mortality was our outcome of interest. Discrete variables are presented as frequencies and percentages. Mantel Haenszel method was applied to estimate the effect of the main exposure (eradication of PA) and our outcome by each variable stratum in order to identify any effect modifier. Next, we determined the relationship between our exposure of interest and our outcome of interest considering as a priori confounder age and sex; logistic regression was performed to investigate the relationship between variables and the outcome. 279 patients eradicated PA infection and 318 didn't. Among those who didn't 122 (38.36%) died compared to 66 (23.66%) that died even when they eradicated the infection ($p<0.001$). Univariate analysis showed that individuals who do not eradicate the infection have 2 times the OR of dying compared to those who eradicate it (CI 95% 1.4-2.8, $p<0.001$). Multivariate analysis showed strong evidence that those who do not eradicate the infection have higher odds of dying compared to those who do, when adjusted by sex, age, extension of bronchiectasis, time of inhaled antibiotic treatment, type of antibiotic and schedule of administration. We finally conclude that individuals who fail to eradicate the PA infection are at significantly higher risk of mortality compared to those who successfully eradicate it; therefore it is important to continue improving treatment in order to have better survival outcomes.

7510

DRIVERS OF COMMON MENTAL HEALTH DISORDERS AMONG TUBERCULOSIS KEY VULNERABLE POPULATIONS IN ASHANTI REGION GHANA

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Tuberculosis (TB) continues to be a significant global health challenge. Despite the global burden of TB and the recognized importance of addressing mental health issues, there remains a gap in understanding the specific drivers of common mental health disorders (CMHD) among TB patients. Therefore, this study aims to investigate the key drivers of CMHD among TB key vulnerable populations (TB-KVPs) in Ashanti region, Ghana. Cross-sectional study design was employed in sampling 302 TB-KVPs at some selected TB treatment centres in Ashanti Region from September to October 2023. CMHD were evaluated using the Self-Reporting Questionnaire, developed by the World Health Organization. In our study, multi-stakeholder of TB engagement was done to prioritized individuals who are at high risk of TB. The TB-KVPs included rural poor individuals, children, informal miners, person living with HIV (PLHIV), inmates and smokers. The lists of TB-KVPs who tested positive for TB were obtained from the selected TB treatment centres. Multiple linear regression analysis was employed to identify the key drivers of CMHD among the TB-KVPs. The prevalence of CMHD was 13 (4.30%). TB-KVPs diagnosed with pulmonary TB *(PTB) (*β*=1.41, CI=0.21, 2.61)* and those reporting fair *(*β*=2.40, CI=0.13, 4.67)* and poor *(*β*=7.06, CI=3.91, 10.20)* health status exhibited higher mental health disorder. Conversely, cohabiting TB-KVPs (β=-1.54, CI=-2.85, -0.23) and those with treatment supporters (β=-0.92, CI=-1.72, -0.12) had lower CMHD scores. Our study found a relatively low prevalence of CMHD among TB-KVPs. Key drivers associated with these disorders included the type of TB diagnosed (PTB), self-reported health status (fair and poor), having a treatment supporter and marital status (cohabiting. Specifically, patients diagnosed with pulmonary TB (PTB), and those reporting fair or poor health statuses exhibited higher scores indicative of mental health disorders. Our study emphasizes the importance of screening for mental health issues among TB-KVPs and addressing key drivers like TB diagnosis and psychosocial factors in intervention strategies.

7511

CARDIOVASCULAR DISEASES ASSOCIATED WITH INFLUENZA INFECTION: SYSTEMATIC REVIEW AND META-ANALYSIS

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Since 1930, a potential association between cardiovascular diseases and influenza virus infection has been posited. Given the substantial burden of cardiovascular diseases in contemporary society, there is a paucity of recent systematic reviews that delineate the risk of cardiovascular diseases following confirmed influenza infection. The aim of this study is to assess the association between prior influenza infection and cardiovascular diseases through systematic review and meta-analysis. A systematic review was conducted following PRISMA guidelines. Electronic searches encompassed databases including EMBASE, PubMed, Global Index Medicus, Google Scholar, and the Cochrane Library. Initially, articles were screened based on titles and abstracts, followed by full-text evaluation. The included studies required laboratory-confirmed influenza cases, excluding those involving pregnant women and children. Quality assessment of studies utilized the standardized tool from the National Heart Lung and Blood Institute, with potential biases evaluated. Additionally, meta-analysis was performed using Cochrane Software Review Manager 5.4.1. Three studies (n=943) were evaluated (one study published twice with the same population, so was considered the more complete publication). A combined odds ratio (OR) was computed for the association between influenza A infection and acute myocardial infarction, yielding 2.52 (95% CI: 1.59 to 4.00). For influenza B infection, an association with acute myocardial infarction was observed with an OR of 4.78 (95% CI: 1.57 to 14.61). One study reported an OR of 5.23 (95% CI: 1.00-27.32) for the association with myocarditis. The evidence indicates a robust and statistically significant positive association between prior influenza infection and acute myocardial infarction. Further studies are warranted to evaluate the long-term effects of influenza on cardiovascular diseases.

7512

TUBERCULOSIS TREATMENT COMPLETION AND CHALLENGES IN RURAL TANZANIA

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Tuberculosis (TB) patients residing in rural settings often encounter difficulties in successfully completing prescribed treatment due to a variety of factors such as geographical distance from healthcare facilities, poverty, limited educational opportunities, and scarce resources. In this report, we

describe the challenges faced by TB patients in a rural setting in Tanzania in an effort to propose strategies to improve TB treatment completion. We used data from a prospectively enrolled cohort of index PWTB in Haydom, Tanzania. We describe TB treatment outcomes for the cohort, explore challenges and solutions as reported by participants, and search for predictors of TB disease treatment completion using a multivariate regression model. 120 index PWTB were enrolled in the study, median was age 35 years (interquartile range [IQR] 23-51) and 45 (38%) were women. 63 of participants (67.7%) completed treatment successfully out of 93 participants whose outcomes were verifiable. 23 participants (19.1%) were lost to follow up and 27 participants (22.5%) transferred TB care to non-participating health facilities and their outcomes were not verifiable. Most participants reported challenges related to cost and missing household activities: 96 (86%) and 89 (80%) respectively. Home visits and health insurance were the most suggested interventions to facilitate care, mentioned by 103 (85.8%) and 102 (85%) participants respectively. None of the evaluated variables significantly predicted TB treatment completion. Many PWTB continue to experience worse treatment outcomes in rural areas with high burden of TB. Additional investment in programmatic support and universal healthcare coverage is needed to help bridge the gap with urban areas.

7513

MATERNAL SARS-COV-2 INFECTION, VACCINATION, AND INFANT STUNTING IN UGANDA

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Gestational SARS-CoV-2 infection may adversely impact infants, particularly males. We evaluated maternal SARS-CoV-2 infection, vaccination, and infant growth in a Ugandan birth cohort. From 3/2021-12/2022, HIV-negative pregnant women between 12-20 weeks gestation enrolled in a malaria chemoprevention trial; their infants were followed longitudinally. In a “pre-vaccine” group of SARS-CoV-2-unvaccinated women delivering 9/2021-2/2022, we tested stored plasma specimens collected at enrollment (12-20 weeks gestation) and delivery for SARS-CoV-2 antibodies to identify maternal infections, and fit linear mixed effects models to examine the association between maternal SARS-CoV-2 infection and infant length-for-age Z (LAZ) scores. SARS-CoV-2 vaccines became locally available late 2021. In a “post-vaccine” cohort delivering 3/2022-5/2023, we examined the association between maternal SARS-CoV-2 vaccination and infant stunting (LAZ-score <-2) with conditional logistic regression stratified by birth month. Of 101 “pre-vaccine” mothers, 82 (81.2%) became SARS-CoV-2 seropositive. At age 12 weeks, 27 (32.9%) infants of infected mothers were stunted, while no infants of uninfected mothers were stunted. In male infants, early pregnancy SARS-CoV-2 infection was associated with lower LAZ scores (Coef= -2.00, 95%CI -3.46 - -0.54) when compared to male infants of uninfected mothers. There was no difference in female infants (Coef=-0.53, 95%CI -3.00-1.95). Of 868 “post-vaccine” mothers, 515 (59.3%) were vaccinated. At 12 weeks, 160 (18.4%) infants were stunted. In males, maternal SARS-CoV-2 vaccination was associated with less stunting (OR 0.52, 95%CI 0.31-0.86, p=0.01) compared to male infants of unvaccinated mothers. No difference was seen in females (OR 1.08, 95%CI 0.62-1.89, p=0.78). In male infants in a malaria-endemic setting, maternal SARS-CoV-2 infection was associated with stunting, while maternal SARS-CoV-2 vaccination was associated with less stunting. More data from larger cohorts should determine if maternal vaccination can prevent developmental sequelae in infants, particularly males.

7514

DISENTANGLING THE SEROCONVERSION AND SEROREVERSION RATES OF SEASONAL CORONAVIRUSES USING AGE-STRATIFIED SEROPREVALENCE DATA

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Despite increased investigation driven by the SARS-CoV-2 pandemic, the dynamics of endemic human coronavirus species are challenging to disentangle. Previous studies have estimated seroconversion and seroreversion rates using serological data but only considered seropositive vs. seronegative, without taking into account heterogeneity due to multiple exposures or variation in individual immune responses. Additionally, previous work has drawn from serological data in different settings, creating challenges in comparing across strains. Using Gaussian mixture models, we classified cross-sectional serological data for four seasonal coronaviruses into seronegative and gradients of seropositivity across the lifespan. These methods identified four (NL63, 229E, OC43) to five (HKU1) distinct seropositive groups, suggesting that among seropositive individuals, there may be varying levels of prior immune history or response to infection. Serocatalytic models are standard to capture disease parameters, and we expanded them to account for varying levels of seropositivity. By fitting these models to the cross-sectional serological data, we found significant differences in the seroconversion rate across strains and serostatus. At lower serostatus, the time to seroconvert was rapid for all strains (0.4-2 years). At the highest level of serostatus, the time to seroconvert was 2.8 years for OC43, but 10.4-11.9 years for the alphacoronaviruses and 34.5 years for HKU1. Additionally, in each pair of alphacoronaviruses and betacoronaviruses, we found that one strain will have a faster rate of seroconversion and reversion, especially at lower levels of serostatus. By parameterizing individual-based models with rates estimated from the serocatalytic models, we compared with cohort studies to validate our findings. Whereas the reported impact of prior seasonal coronavirus immunity on SARS-CoV-2 outcomes is conflicting, understanding patterns in seroconversion at higher levels of immune history can help us contextualize these findings.

7515

PREDICTING TUBERCULOSIS TREATMENT RELAPSE USING STATISTICAL DATA MINING TOOLS. A CASE STUDY OF CAPE COAST TEACHING HOSPITAL, GHANA

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Tuberculosis (TB) continues to be a global public health issue and the leading cause of infectious mortality globally. Despite diagnostic advances and treatment programs, some patients experience relapse after treatment. The study used numerical, analytical, and statistical data mining techniques to develop a predictive treatment relapse model for TB patients in the Central Region of Ghana. A total of 465 records of patients receiving care at the Cape Coast Teaching Hospital from 2017 to 2018, and tested for TB with GeneXpert and sputum smear for acid fast bacilli by microscopy, were used to build a model for predicting the treatment relapse of patients by using R software version 2021.9.1.372.Using addresses, the centroids of geographical position of communities where patients lived were recorded to aid in mapping infections in the study area. Purely Spatial analysis using the Discrete Poisson model was done with software for the Spatial and Space-Time scan statistics (SaTScan version 10.1, Harvard, USA) to explore to identify clusters of the TB burden in the study area.From the study outcome, patients between the ages of 40.5 and 49.5 years were predicted to have

high TB prevalence, TB-HIV co-infections, RIF resistance, PTB, treatment, and test outcomes. However, the burden of TB was significantly high (p< 0.05) within KEEA and CCMA with an incidence of 8.41 and 24.5 cases per 100000 population annually, respectively. Relapse associated with TB treatment was generally low across the study population. Conclusively, a prediction model using GeneXpert and Microscopy test method outcomes, age, and sex predicted unfavourable treatment outcomes of patients. The study highlights the importance of considering age and sex in predicting treatment outcomes of patients. The findings of the study can help improve clinical management and treatment outcomes for TB patients in Ghana.

7516

TIERED MULTIPLEX PCR DETECTION OF RESPIRATORY PATHOGENS IN CAMBODIA'S SEVERE ACUTE RESPIRATORY INFECTION SENTINEL SURVEILLANCE SYSTEM, MAY-DECEMBER 2023

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Surveillance of respiratory pathogens with outbreak potential is key to enhancing global preparedness and response measures. Cambodia recently expanded molecular testing of respiratory pathogens as part of their severe acute respiratory infection (SARI) sentinel surveillance network. Patients hospitalized with SARI, defined as fever within 10 days, cough or sore throat, and dyspnea, were identified at 9 hospital-based SARI sites. Nasopharyngeal and oropharyngeal swabs (NP/OP) were collected and sent to the National Public Health Laboratory. RNA was extracted and tiered testing performed: first PCR of all samples for Influenza A, B, SARS-CoV-2; then PCR of negative samples using the FTD™ Respiratory pathogens 21 assay.From May to December 2023, NP/OP swabs were collected from 3,396 SARI patients. Median age was 7.8 years: 1,572 (46.3%) <5 years, 5, 251 (7.4%) 5-17 years, and 1,573 (46.3%) >18 years. PCR detected respiratory pathogens in 2,086 (61.4%) patients and case fatality was 1.1%. First tier testing identified influenza, 368 (10.1%), SARS-CoV-2, 159 (5.0%), and both pathogens, 11 (0.3%). Second tier testing of the remaining 2,867 patients identified Respiratory Syncytial Virus (RSV), 764 [26.6%], rhinovirus 559 [19.5%], and more than one pathogen, 277 (9.6%). RSV and rhinovirus were the most common pathogens detected among children <5 years (688 [48.6%], and 417 [29.4%], respectively), while Influenza and SARS-CoV-2 were the most frequent among adults (193 [12.2%], and 120 [7.6%], respectively). No pathogens were identified in 1,026 (65.2%) adults and 211 (13.4%) children <5 years. Surveillance trends captured two peaks of influenza transmission in June and November and a peak of RSV in August 2023.Healthcare facilities in low- and middle-income countries may not have diagnostic resources to identify priority pathogens, undermining the rigor of national surveillance. Integrated, expanded respiratory surveillance was feasible using the existing SARI surveillance network, identified important outbreaks, and captured diverse respiratory pathogens among young children.

7517

SUPPORTING INNOVATION IN PNEUMONIA DIAGNOSIS - KEY FINDINGS FROM A RANGE OF STUDIES EVALUATING RESPIRATORY RATE COUNTERS AND PULSE OXIMETERS IN SUB-SAHARAN AFRICA AND ASIA

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Pneumonia is the leading infectious cause of death in under-five children. Community health workers currently count respiratory rate (RR) as a proxy diagnostic sign for pneumonia. Manually counting RR is challenging as it is hard to define a breath, and easy to lose count as the child may be moving, crying, or breathing rapidly. Misdiagnosis of suspected pneumonia is common and can lead to over and under treatment with antibiotics and potential death. New, automated RR counters and pulse oximeters offer a potential solution. To introduce new diagnostic aids their performance must first be validated. Developing a robust reference standard for evaluating the performance of new RR counters and pulse oximeters is challenging and there is currently no gold standard. A series of cross-sectional studies in sub-Saharan Africa (Ethiopia, South Sudan and Uganda) and Asia (Cambodia and Nepal) were conducted to measure the agreement of test devices to several reference standards, including human RR counters, video review panels and automated reference standards. The primary outcome was the agreement between the test device and the reference standard, as measured by intra-class correlation (ICC) coefficient ρ. Secondary outcomes included mean time taken to review a video and the usability and acceptability of the different reference standards by users. There was a low level of agreement found between human counters (ICC=0.3). Better agreement was found between automated reference standards (ICC=0.6), with the highest level of agreement for the video reference panel using an annotation tool (ICC=0.77). Users found video annotation software easy to use and helpful in standardizing RR counting, across a range of ages and situations. Reviewers highlighted the importance of quality video capture. Video annotation has the greatest potential as a reliable reference standard as it better supported reviewers when counting respiratory rate. Visual reference standards have inherent limitations due to human subjectivity, particularly when there is distortion, and can be overcome through adequate training and standardization of panel members.

7518

DESIGN AND VALIDATION OF MULTIPLEXED RESPIRATORY RT-LAMP ASSAYS FOR THE DETECTION OF SARS-COV-2, INFLUENZA A AND RESPIRATORY SYNCYTIAL VIRUS (RSV) IN COVID-19 PANDEMIC SAMPLES FROM WESTERN KENYA.

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The COVID-19 pandemic has highlighted the importance of widespread, accessible and effective viral surveillance to ensure pandemic-preparedness. The quick diagnosis of respiratory infections is crucial not only for effective patient management but also to inform ongoing viral surveillance for the detection of outbreaks. Reverse Transcription Loop-mediated isothermal amplification (RT-LAMP) assays are an attractive alternative to RT-PCR for rapid, point of care testing. Here we present the design and evaluation of two multiplexed probe-based RT-LAMP assays for the simultaneous detection of SARS-CoV-2, Influenza A (H1N1 and H3N2) and Respiratory Syncytial Virus (RSV). Nasopharyngeal swabs collected from 153 participants on the day of enrolment in the MALCOV Cohort study in Kisumu, Kenya were used in the evaluation of two RT-LAMP assays to distinguish between SARS-CoV-2, Influenza A and RSV. Overall 93 SARS-CoV-2, six Influenza A, one Influenza B and zero RSV samples were identified in the cohort by AllPlex SARS-CoV-2/FluA/FluB/RSV RT-PCR kit as well as 53 negative for all targets. Sensitivity and specificity of the SARS-CoV-2/FluA LAMP assay when compared to RT-PCR was 94.85% (CI95%:88.38 - 98.31) and 98.11%(CI95%:89.93-99.95) respectively. Sensitivity and specificity of the SARS-CoV-2/FluA/RSV LAMP assay when compared to RT-PCR was marginally higher at 95.96% (CI95%:94.50-

99.97) and 100%(CI95%:93.40-100.00) respectively. The mean time to a positive result was 10.99minutes, highlighting the speed of this technology compared to the more commonly used RT-PCR.

7519

SENSITIVITY OF CLUSTER, PRACTICAL AND SENTINEL IMPACT ASSESSMENT METHODOLOGIES FOR ADJUSTING PREVENTIVE CHEMOTHERAPY FOR SCHISTOSOMIASIS ELIMINATION IN NIGERIA

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Impact assessment remains a critical step in redefining the endemicity profile necessary for adjusting decisions on preventive chemotherapy (PC), enabling optimized resource allocation, and minimizing implementation costs. Here, we evaluated the sensitivity of three impact assessment methodologies (sentinel, cluster and practical) in adjusting PC decisions in three endemic LGAs (Ese-Odo, Ile-Oluiji and Irele) in Ondo State. Stool and urine samples were collected from 2,093 school-aged children aged 5-14 years across 45 schools. Samples were processed using Kato-Katz and urine filtration techniques to recover *Schistosoma* ova. Findings reveal significant decline in aggregated prevalence estimates in Ese-Odo (0.1% versus 1.2% at baseline, d = -91.7%, p=0.03), and Ile-Oluiji (1.8% versus 58.0% at baseline, d = -97%, p=0.00), respectively. However, in Irele, an increase in prevalence was observed from 3.2% at baseline to 5.3% (d=66%, p=0.13). Sensitivity analysis revealed prevalence was 0.1% (95% CI: 0.01-0.95), 0.3%(95% CI: 0.01-1.7), and 0.0%(95% CI: 0-1.6) for cluster, practical, and sentinel methodologies, respectively in Ese-Odo. In Irele, the prevalence was 5.3% (95% CI: 3.8, 7.3), 5.8% (95% CI: 3.8, 8.8), and 5.4% (95% CI: 3.2, 9.0) respectively. In Ile-Oluji, the prevalence was 1.8% (95% CI: 0.9, 3.3), 2.2% (95% CI: 0.9, 4.7), and 1.5% (95% CI: 0.5, 4.4) respectively. The sentinel approach when compared to the cluster approach had lower sensitivities in Ese-Odo (d= -100%, p=0.554) and Ile-Oluiji (d=-14.5%, p=0.874), but was higher in Irele (d=2.61%, p=0.938). However, the practical assessment had higher sensitivities over cluster approach in Ese-Odo (d=83.1%, p=0.664), Irele (d=10.6%, p=0.715) and Ile-Oluiji (d=21.7%, p=0.687). Findings from the three methodologies adjudged low endemicity in Ese-Odo and Ile-Oluiji, with decision to stop PC. However, the practical approach revealed heterogeneous endemicity in Irele, with 3 schools having prevalence >10%, which requires continuing PC. Our findings suggest that practical assessment is a more sensitive method for refining preventive chemotherapy (PC) decisions.

7520

RAPID VISUAL DETECTION OF *SCHISTOSOMA HAEMATOBIUM* USING RECOMBINASE POLYMERASE AMPLIFICATION FROM SERIALLY DILUTED AND FIELD-COLLECTED HUMAN URINE SAMPLES

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Schistosomiasis, a prevalent waterborne and blood-borne parasitic disease stems from blood parasites classified as Schistosomes. The principal species for human Schistosomiasis include *Schistosoma mansoni* and *S. haematobium*. Presently, an estimated 220 million individuals worldwide are affected by this disease, predominantly in sub-Saharan Africa, South America, East Asia, and the Middle East. However, this is an underestimation. Accurate determination of infection prevalence faces challenges due to the insufficiency of highly sensitive and specific diagnostic tests. Currently, traditional diagnostic testing is contingent on the detection of eggs in urine samples for *S. haematobium*, by techniques such as urine microscopy. Such techniques are often seen as inadequate during different phases of the infection, especially the control phase where the infection level is low. Therefore, the objective of this study is to develop a highly sensitive and specific test for *S. haematobium* by amplifying species-specific cell-free repeat DNA from serially diluted urine samples mixed with genomic DNA and field-collected human urine samples from Zambia utilizing the recombinase polymerase amplification (RPA) technique. Utilizing this technique, 50 filtered urine samples from females and males between the ages of 8 - 16 years were collected in Zambia and filtered with Whatman#3 filter papers. DNA extracted from the filter papers and serially diluted genomic DNA (three each for *S. mansoni*, *S. haematobium*, and *S. japonicum*) were amplified by RPA, followed by column clean-up and gel electrophoresis to visualize and confirm the RPA amplified product. *S. haematobium* DNA was detected at a level of 1ng/µl from serial dilution, while *S. mansoni* and *S. japonicum* serially diluted DNA did not amplify. The study strongly indicated RPA's suitability for diagnostic testing, especially in future use for *S. haematobium* detection with developed probes on lateral flow strips, offering faster, cost-effective, and accurate results compared to other molecular tests.

7521

USING HUMAN-CENTERED DESIGN TO SUPPORT DEVELOPMENT AND IMPROVEMENT OF A MOBILE ENABLED DIAGNOSTICS FOR SCHISTOSOMIASIS CONTROL ANALYTICS (MEDSCAN) SOFTWARE FOR SCHISTOSOMIASIS DIAGNOSIS IN WESTERN KENYA

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WHO has called for development of new tools and diagnostics to help prevent, control and eliminate neglected tropical diseases. In this regard, there has been rapid emergence of mobile health tools but very few studies have been conducted to understand user priorities, acceptability and usability for schistosomiasis. Human-centered design is important in increasing end-user ownership and consistent uptake of mobile phone applications. Therefore, we sought perspectives on functionality of and user experience with a newly developed mobile app, MEDSCAN. In 2023, we conducted 4 focus group discussions (FGDs) with 38 participants purposively selected and usability threshold was determined using System Usability Scale (SUS) 5-point Likert scale. Participants included end users, administrators and experts from schistosomiasis-endemic areas in Siaya and Kisumu Counties. The MEDSCAN App was introduced to the participants who were given time to interact with it in small groups using phones. Qualitative data was transcribed, translated, coded, and analyzed thematically using NVivo version 12 software. Custom Python code was used to analyze the SUS data. All SUS scores passed the usability threshold (>68%). Dashboard was the lowest scoring feature. Overall, participants were comfortable using MEDSCAN's main features and the app was highly acceptable. Participants stated that it was easy to navigate, had a logical flow, and would help accelerate sample collection and analysis processes. They found the screens to be effective and straightforward, with simple and direct language. While participants believed that MEDSCAN app incorporated all components and features necessary for electronic surveillance of schistosomiasis, they raised concern with the app's dependency on internet connectivity and lack of ability to edit some records before submission. They emphasized the need to increase font size, add age and include gender of participants. They also recommended overhauling of the dashboard. Feedback from FGDs will be used to iteratively improve the platform until the application and dashboard meet expectations of the stakeholders.

7522

EXPLORING THE *PARAGOMINUS KELLICOTTI* LIFE CYCLE PROTEOME: IMPLICATIONS FOR THE DISCOVERY OF NEW DIAGNOSTIC TARGETS

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Paragonimiasis is a food-borne trematode infection that affects about 21 million people. More than 30 *Paragonimus* species have been described from Asia, Africa, and the Americas, and about one third of them are confirmed to infect humans. Humans become infected by the consumption of raw or undercooked freshwater crustaceans that contain infective metacercariae. *Paragonimus kellicotti* is the agent of North American paragonimiasis, and an excellent model for other *Paragonimus* infections. To investigate the parasite soluble proteins, we took advantage of the fact that infective stage can be found in crayfish in streams of the Ozark region, near Saint Louis, Missouri and the adult stage can be obtained from experimentally infected gerbils. We performed mass spectrometry analysis of *P. kellicotti* soluble somatic protein of adults (SSPA) and freshly excysted juveniles (SSPJ), metacercarial cyst fluid (MC) after excystation, excretion/secretion products produced by adult worms after in vitro culture (ESP), and lung cyst fluid proteins (CFP) of infected gerbils. We identified more than 2,000 *P. kellicotti* proteins that were found in at least 2 of 3 biological replicates and were supported by at least 2 peptides. Among those were 1,914 proteins found in SSPA samples, 219 proteins in SSPJ, 947 in ESP samples, 37 in CFP samples and 11 in MC samples. The samples that contain excreted or secreted proteins (MC, ESP, CFP) had only one protein in common, a cysteine protease (CP6), that is a well described immunogenic protein. The total soluble fluke extracts SSPA and SSPJ had 171 proteins in common. This extensive proteomic study identified proteins that are not only present in adult flukes but also in freshly excysted juveniles. Furthermore, the protease CP6 was identified as a prominent excreted/secreted protein after in vitro culture of adults and in vivo in the lung cysts with adults and the cyst of the metacerariae. Therefore, CP6 is a promising biomarker candidate for development of an antigen test for paragonimiasis.

7523

MULTI-CONTRAST MACHINE LEARNING IMPROVES SCHISTOSOMIASIS DIAGNOSTIC PERFORMANCE

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Schistosomiasis remains a public health burden despite ongoing global control efforts. Sensitive diagnostic and screening tools are needed to help accelerate these efforts. In this work, we present an artificial intelligence (AI)-based strategy for automated detection of *Schistosoma haematobium* that combines two imaging contrasts, brightfield (BF) and darkfield (DF), to improve diagnostic performance. We used a compact, digital microscope, the LoaScope, to collect BF and DF images of *S. haematobium* eggs in patient samples during two different field visits to Côte d'Ivoire (March 2020, November 2021). We trained AI models (using YOLOv8) to detect parasite eggs in the BF and DF images from March 2020. We evaluated performance of the models on the November 2021 holdout data in four different ways: BF model alone, DF model alone, or both models in combination (with positive diagnosis given by Boolean "AND" or "OR"). We determined the model's patient-level sensitivity at various specificities required by WHO Diagnostic Target Product Profiles (TPP) for schistosomiasis control programs. The Monitoring and Evaluation (M&E) use case has target sensitivity and specificity of 75% and 96.5%, respectively. The AI models, when evaluated at 96.5% specificity, had sensitivities of 76% (BF alone), 83% (DF alone), and 81% (for AND and OR models). The Transmission Interruption and Surveillance (TI&S) use case has target sensitivity and specificity of 88% and 99.5%. The models, when evaluated at 99.5% specificity, had sensitivities of 53% (BF alone), 63% (DF alone and OR model), and 73% (AND model). The Boolean AND sensitivity is the closest to the TI&S target sensitivity of 88%. Our central finding is that using two imaging contrasts, BF and DF, markedly improved diagnostic performance for the high specificity TI&S use case. Capture of the two image contrasts requires minimal changes in microscope optics and no additional sample preparation. Multi-contrast machine learning thus offers a practical means to improve performance of automated diagnostics for *S. haematobium* egg detection and could be applied to other microscopy-based diagnostics.

7524

MAPPING RISKS FOR FEMALE GENITAL SCHISTOSOMIASIS IN URBAN SETTINGS TO GUIDE PUBLIC HEALTH INTERVENTIONS

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Female Genital Schistosomiasis (FGS) is a Neglected Tropical Disease that disproportionately impacts the sexual and reproductive health of women. FGS has been linked with several social and physical impacts. Poor knowledge, attitude, and sociocultural practices also influence behavior of women and girls at risk. Comprehensive examination of women's lived experiences around the risk of FGS are notably scarce in the existing literature. Furthermore, the impact of rapid urbanization, unregulated migration, and environmental changes on the risk of FGS have been largely unexplored. Different levels of urbanicity and rural-urban migration, contributes to increasing risk of FGS among adult females living in such localities. This research seeks to understand how women living in urban endemic areas in Ghana experience risks related to contracting female genital schistosomiasis. Using qualitative approach, investigation will explore how women experience the risk factors for FGS differently in distinct contexts as well as the role of rural-urban migration, and its contribution to expanding urban risk. The study will be conducted in selected endemic areas of the Greater Accra Region in Ghana. Data will be thematically analysed for the risks, including how women in endemic urban areas experience risks related to female genital schistosomiasis. Reports will also provide insights into the challenges and experiences specific to females in urogenital schistosomiasis endemic urban and rural communities of Greater Accra in Ghana. Findings will encapsulate participants' indigenous recommendation to design potential intervention, progressing urogenital schistosomiasis and FGS management guidelines for Ghana and other endemic countries in Sub-Saharan Africa. Data collection will be finalized by July and preliminary findings will be available for dissemination in August 2024.

7525

INTEGRATIVE METABOLOMIC APPROACHES REVEAL TYROSINE METABOLISM AS A POTENTIAL BIOMARKER FOR EARLY *SCHISTOSOMA MANSONI* INFECTION IN CHILDREN LIVING IN POLYPARASITISM SETTINGS IN CAMEROON

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Hepatosplenic schistosomiasis caused by *Schistosoma mansoni* remains a significant public health concern, particularly in areas of persistent transmission. Understanding the metabolic changes induced by *S. mansoni* infection is crucial for discovering host signatures of infection and disease pathogenesis. We conducted LC-MS untargeted metabolomic profiling on plasma samples obtained from school-aged children in areas of low and moderate endemicity for *S. mansoni* in Cameroon, strongholds of parasite persistent transmission. Diagnosis of *S. mansoni* infection was conducted using the Kato Katz thick smear method and complemented by circulating anodic antigen assay. Children were later stratified based on their S. mansoni infection status. Through successive discovery, validation, and polyparasitism runs, we identified significant alterations in multiple metabolic pathways associated with *S. mansoni* infection. Notably, the perturbation of tyrosine metabolism emerged as a robust biomarker candidate across runs, suggesting its potential for complementary diagnostics. The polyparasitism run, wherein we observed the persistence of alterations in tyrosine metabolism in *S. mansoni*-infected hosts even in the presence of coinfections, was used to assess the molecular and biochemical mechanisms underlying these metabolic changes. Initially, we utilized quantitative polymerase chain reaction (qPCR) techniques to quantify the expression levels of key enzymes involved in tyrosine metabolism in cDNA from whole blood samples, obtained from low endemicity *S. mansoni*-infected individuals. These quantitative measurements provided insights into the transcriptional regulation of tyrosine metabolism genes in response to *S. mansoni* infection, further validating the dysregulation observed in our metabolomic analyses, particularly in polyparasitism and low infection burden and settings. This advancement is particularly significant for resource-limited settings where traditional diagnostic methods may be inadequate and further targeted studies on other endemic settings are highly recommended.

7526

ADVANCEMENTS IN SCHISTOSOMIASIS DIAGNOSIS: IS RECOMBINANT ANTIBODY POINT-OF-CARE CIRCULATING CATHODIC ANTIGEN TEST (POC-CCA), MORE RELIABLE?

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Schistosomiasis control programmes have historically relied on Kato-Katz thick smears (KKs) to detect *Schistosoma mansoni* eggs in stool, however, this diagnostic technique has limited sensitivity. An alternative, point-of-care circulating cathodic antigen test (POC-CCA), has been available since 2008 but suffers from batch-to-batch variation and issues surrounding reader variation and trace results, which limits its implementation and interpretation in the field. Here, in *S. mansoni* endemic communities we evaluated the performance of an updated POC-CCA test that was developed using a recombinant antibody-based design (recPOC-CCA). We used the G-score grading system to reduce inter- and intra-reader variability and improve intensity estimates of both the original POC-CCA and new recPOC-CCA. Over 850 individuals were recruited across two endemicity settings in Uganda, with three duplicate KKs carried out across three consecutive days, as well as testing with POC-CCA and recPOC-CCA across and within those 3 days. Through a state-of-the-art Bayesian Latent Class Model, we estimated sensitivity and specificity in the field of these diagnostics and optimal cutoffs to meet the Target Product Profile defined by the World Health Organization. The performance of the recPOC-CCA was comparable with the traditional POC-CCA, with a similar probability of meeting the WHO TPP. Importantly, in contrast to the traditional POC-CCA, within-sample variation across three batches of recPOC-CCA was indistinguishable, suggesting little to no batch-to-batch variation. Therefore, the recPOC-CCA test is a strong alternative to the POC-CCA, with similar performance in the field but a more consistent production cycle and no discernible variation between batches. Programmes should consider lower cutoffs in areas with lower intensity of infection to maximize the performance of the diagnostic. At present neither recPOC-CCA nor POC-CCA achieves the WHO TPP required specificity if only used for one day, however, tests on three urine samples collected on subsequent days would likely meet these requirements.

7527

THE SHORT-TERM IMPACT OF *SCHISTOSOMA MANSONI* INFECTION ON HEALTH-RELATED QUALITY OF LIFE: IMPLICATIONS FOR CURRENT ELIMINATION POLICIES

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The World Health Organisation (WHO) aims to eliminate schistosomiasis as a public-health problem by 2030. However, standard morbidity measures poorly correlate to infection intensities, hindering disease monitoring and evaluation. This is exacerbated by insufficient evidence on *Schistosoma's* impact on health-related quality of life (HRQoL). We conducted community-based cross-sectional surveys and parasitological examinations in moderate-to-high *S. mansoni*-endemic communities in Uganda. We calculated parasitic infections and used EQ-5D instruments to estimate and compare HRQoL utilities in these populations. We employed Tobit/linear regression models to predict HRQoL determinants. Two thirds of the 560 participants were diagnosed with parasitic infection(s) and 49% presented *S. mansoni* infection. Endemic communities reported more health problems and lower HRQoL values than the Ugandan average. High- and moderate-endemicity communities reported similar HRQoL values and health problems, except for the 'pain/discomfort' dimension, where more severe problems were reported in the high-endemicity setting. Importantly, no significant negative association was observed between HRQoL and current *S. mansoni*-infection status/intensity. However, severity of pain urinating (β=-0.106; SE=0.043) and body swelling (β=-0.326; SE=0.005), increasing age (β=-0.016; SE=0.033), reduced socio-economic status (β=0.128; SE=0.032), and being unemployed predicted lower HRQoL. Symptom severity and socio-economic status were better predictors of short-term HRQoL than current *S. mansoni*-infection status/intensity. This is key to disentangling the link between infection(s) and short-term health outcomes, and highlights the complexity of correlating current infection(s) with long-term morbidity. Further evidence is needed on long-term schistosomiasis-associated HRQoL, health and economic outcomes to inform the case for upfront investments in schistosomiasis interventions.

7528

IDENTIFICATION OF SCHISTOSOMICIDAL COMPOUNDS FROM *BALANITES AEGYPTIACA*

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Schistosomiasis remains an important neglected disease that impacts 78 countries globally. The only existing schistosomiasis therapy, Praziquantel, has limited efficacy against juvenile parasites and there is concern of emerging Praziquantel-resistant parasites. *Balanites aegyptiaca* has been

used extensively in various folk medicines as an antibacterial, anticancer, antimalarial, and anthelmintic agent in many developing countries. We aimed to evaluate the schistosomicidal activity of a *B. aegyptiaca* extract against the multiple developmental stages of *Schistosoma mansoni* worms and to identify the active compound(s) therein. Cercariae were mechanically transformed into skin-stage schistosomula (NTS). Mice were infected with *S. mansoni* by tail exposure to cercariae and juvenile and adult worms were obtained by perfusion 21 and 42 days post infection, respectively. Crude extract was screened against these stages and worm viability was assessed by quantitation of ATP. The crude extract was found to be schistosomicidal against all three stages. The crude extract was fractionated by Biotage C18 column fractionation using MeOH:H_20 gradient resulting in 62 fractions that were pooled based on TLC profiling into 8 fractions for bioactivity assessment. The active fractions identified were pooled and fractionated by dichloromethane-MeOH gradient yielding 50 fractions that were combined into 14 fractions based on TLC profile. Active fractions identified underwent tertiary fractionation by acetonitrile:H_20 yielding 40 fractions. Subsequent screening of these 40 fractions identified 4 fractions with 99%, 82%, 73% and 86% killing, respectively, when tested at 20 µg against NTS. Fractionation is ongoing towards identification of the bioactive compound(s). Our preliminary findings show promise against larval, juvenile and adult worms and provide baseline data to further advance our study towards understanding mechanisms of actions of the compounds.

7529

REAL-TIME PCR ASSAY FOR DETECTION OF *PARAGONIMUS KELLICOTTI* IN HUMAN STOOL

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The lung fluke Paragonimus *kellicotti* is found throughout most of eastern and central North America infecting mammals that feed on crayfish such as bobcat, raccoon, coyote, mink, and otters. It is closely related to the human pathogen *P. westermani*, which causes paragonimiasis in eastern Asia. *P. kellicotti* can also cause infections in humans if they consume raw crayfish that are the host species for the metacercaria stage of the parasite. The object of this study was to design a real-time PCR assay for detection of P. *kellicotti* DNA in human stool. Known numbers of eggs from adult *P. kellicotti* were added to stool, and DNA was extracted from the spiked stool samples. Real-time PCR was performed with primers and a probe designed to detect a *P. kellicoti* ITS-2 DNA target. The assay detected the target in DNA isolated from a 200 mg stool sample that had been spiked with a single P. kellicotti egg. This is approximately equivalent to detection of 12 fentograms of parasite genomic DNA. We have previously used conventional PCR to detect the P. kellicotti ITS-2 DNA in lung biopsies, cerebrospinal fluid, and sputum from from *P. kellicotti* patients, and the qRT-PCR assay is more sensitive than conventional PCR. However, additional studies are needed to evaluate the sensitivity of this new assay with different types of clinical samples.

7530

UNDERSTANDING INFECTION VERSUS TRANSMISSION DYNAMICS OF *SCHISTOSOMA MANSONI* PRE- AND POST-TREATMENT, AND THE RELATIONSHIP BETWEEN EGG, ANTIGEN AND DNA BASED DIAGNOSTICS

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Over 240 million people are infected with *Schistosoma*. The World Health Organization has set goals for schistosomiasis elimination as a public health problem by 2030, defined as <1% prevalence of heavy-infections measured by Kato-Katz (KK) in school-aged children. However, KK lack sensitivity, and commonly overestimate drug efficacy. The point-of-care circulating cathodic antigen test (POC-CCA) improves on sensitivity, especially for low intensities and post treatment, but specificity is not 100%. In addition, the relationship between antigens and eggs changes post treatment, resulting in different drug efficacy measures and many individuals who are POC-CCA positive but KK negative. Understanding what proportion of KK negative, POC-CCA positive individuals are true infections, and if they are contributing to transmission, will help inform and guide control programmes. We aimed to estimate the true proportion of school-aged children who are infected with *Schistosoma mansoni* and at risk of morbidity, and what proportion are shedding eggs and contributing to transmission in a high-endemicity Ugandan community. A Bayesian Latent Class Model was developed and fit to data from three days of duplicate KK, miracidia hatching, qPCR of stool and blood spots, and POC-CCA G-scores at pre-treatment, and 3, 9, and 22 weeks post-treatment. Incorporating miracidia hatching data and stool qPCR greatly improved predictions of those shedding eggs, as well as resulting in improved, higher, specificity estimates for POC-CCA. Baseline egg and antigen-based diagnostics were comparable, but at 3 weeks post treatment, egg-based diagnostics lack sensitivity and vastly overestimate clearance, with only a quarter of estimated infections shedding eggs. Miracidial hatching data were the most comparable to model estimates of individuals shedding eggs. In conclusion, after treatment, most infected individuals are not shedding eggs, and therefore not contributing to transmission at that stage. However, egg-based diagnostics overestimate the efficacy of treatment, and more robust diagnostics are needed in order to monitor elimination goal attainment.

7531

COMMUNITY AWARENESS OF FEMALE GENITAL SCHISTOSOMIASIS AND MASS DRUG ADMINISTRATION PARTICIPATION IN THE ABOBO DISTRICT, ETHIOPIA - FINDINGS FROM THE FAST PACKAGE PILOT PROJECT

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Female Genital Schistosomiasis (FGS) is a neglected health issue affecting women and girls in Sub-Saharan Africa. Those with the condition experience physical and social challenges from untreated *Schistosoma haematobium* infections, resulting in urogenital complications. The FGS Accelerated Scale Together (FAST) package is a holistic approach to address FGS by increasing community awareness of FGS preventing new infections by promoting Mass Drug Administration (MDA) and increasing diagnosis and treatment. A baseline cross-sectional study conducted in January 2024 in Abobo District, Ethiopia included 420 participants18 years and above in the community and 400 individuals (15-25 yrs) for urine filtration tests. Baseline-level schistosomiasis prevalence was determined, and mixed-effect logistic regression models were used to assess factors associated with community awareness of schistosomiasis and FGS, and MDA participation. The prevalence of schistosomiasis was 32%, with the disease being more prevalent among males than females (40% vs 30%). Most community participants were aware of schistosomiasis (90%, 378) and have previously participated in an MDA (86%, 361) - however, only 6% (25) of the participants have ever heard about FGS. The mixed-effect logistic regression results highlighted participation in-school MDA was associated with a reduction in the odds of having schistosomiasis [aOR=0.795, P=.044]. As age increases, the likelihood of infection decreases [aOR=.077, P=.034]. Willingness to take Praziquantel preventatively [aOR=2.27, P<.001] and education [aOR=1.25, P=.033] were associated with increased MDA participation. Using risky freshwater sources for domestic purposes [aOR=0.352, P=.025] reduced

odds of hearing about schistosomiasis while higher educational levels [aOR=2.13 P=.01] were linked with schistosomiasis awareness. Effective communication and addressing community perceptions can enhance MDA participation. These baseline findings improve our understanding of community experience and knowledge of schistosomiasis and will shape the FAST Package intervention.

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MOVING FROM DISTRICT TO SUB-DISTRICT SCHISTOSOMIASIS IMPLEMENTATION IN SENEGAL: TIME TO CHANGE AND ADAPT STRATEGIES

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Schistosomiasis is a major waterborne neglected tropical disease (NTD) that remains major public health problem in Senegal, with an 13.5 million people estimated to be currently at risk of infection. In 1999, the Ministry of Health established the National Schistosomiasis Control Programme in implementing mass drug administration (MDA) among school-aged children To eliminate schistosomiasis as public health problem, there has been a shift in strategy to move from district-wide implementation to a more focal strategy by updating the endemicity at the sub-district level to better target those requiring preventive chemotherapy. Here we present historical and recent schistosomiasis mapping results from Senegal, presented at the district and sub-district level. The first schistosomiasis evaluation was conducted between 1996 and 2003 with 29 districts mapped. Between 2009 and 2012, the PNLB continued mapping and commenced MDA in all endemic districts in 2016. After 4-5 years MDA implementation, an impact evaluation was conducted between 2016 and 2019. More recently, a second impact assessment has been conducted in 37 districts between 2022 and 2024. In summary, multiple surveys have been conducted investigating schistosomiasis in Senegal but to date there is no publication on the national schistosomiasis mapping results. The analysis is still underway as we wait for the 2024 survey results (to be finished at the end of April). In brief, endemicity of 1661 sub-districts and 79 districts will be calculated and presented in district and sub-district maps with a descriptive analysis performed, of national schistosomiasis data at baseline (1996-2003), first impact assessment (2016-2019), and second impact assessment (2022-2024). The number of implementation units requiring PC will be summarized at district level compared to sub-district level with the number of school aged children requiring treatment assessed at district-level compared to sub-district level. This study was aimed to analyze data at sub-district level that could be used to update the endemicity review how this change impacts on drug request needs for better targeted MDA.

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PREDICTORS OF SCHISTOSOMIASIS JAPONICUM INFECTION RISK IN SICHUAN, CHINA

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Schistosomiasis japonicum persists in 450 counties in China despite stringent disease control efforts that began in the 1950s. We conducted a study to identify variables that predict schistosomiasis infection risk along with variable levels associated with peak infection risk in regions targeted for elimination using a machine learning approach. Data were retrieved in 2007, 2010, 2016, and 2019 in Sichuan, China, using multiple surveys. This study included data on 5,004 respondents aged 6 to 96 years old across 2 counties. Generalized boosted regression trees were used to evaluate the association between infection risk and environmental, socioeconomic, demographic, and agricultural features across three spatial scales (individual, household, and village-level). We bifurcated the data to evaluate if key predictors changed over time between 2007-2010 and 2016-2019 because the prevalence of infections declined from 8.93% in 2007 to 1.04% in 2019. The predictive performances of the models were high (AUC=0.88 and 0.91 respectively). Our preliminary analyses suggests that village-level factors were the most important predictors of infection risk, with mean night soil use and the percentage of households with improved sanitation as the most important predictors in 2007-2010 and mean night soil use and area of non-rice crops planted in the summer as the most important predictors in 2016-2019. In 2007-2010, infection risk peaked in villages with >300 buckets of night soil used. In 2016-2019, infection risk peaked in villages with >100 buckets of night soil used and >6 Mus (approx.: 4,000 m2) of non-rice crops planted in the winter. These predictors likely influence the emission of schistosome eggs into the environment and the contact rate between individuals and contaminated surfaces. This study contributes to current management practices of endemic schistosomiasis control in rural China by identifying levels of predictors that best predict high infection risk, as well as optimal spatial scales in which interventions may be implemented.

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MORPHOMETRIC TRAITS OF *FASCIOLA HEPATICA'S* INTERMEDIATE HOSTS IN AREAS WITH HUMAN AND ANIMAL FASCIOLIASIS AND STUDY OF PHYSICOCHEMICAL PROPERTIES OF ITS WATER SOURCES

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Trematodiases are transmitted by freshwater snails, mainly limneids distributed worldwide. In the Peruvian Andes, they host trematodes such as *Fasciola hepatica* and some paramphistomids, with the former having the greatest impact on public health. The presence of snails in natural waters used for drinking and irrigation contributes to the transmission of these parasites. This study focuses on the morphometric analysis of Lymnaeidae snail shells and the physicochemical parameters of the water where they dwell. Between March 2023 and March 2024, 656 adult limneid snails and water samples were collected in four rural areas of the province of Cajamarca, Peru. These included Valle Verde/Huayrapongo (VVH) at 2649 m elevation, Otuzco (OTZ) at 2740 m, Chetilla (CHT) at 3055 m and Combayo (CBY) at 3342 m. A quarter of the snails (n = 164) with the best integrity and largest size were selected for evaluation of their shell length (SL), shell width (SW), aperture length (ApL), aperture width (ApW) and aperture area (ApA). Snails from OTZ presented a mean of 8.5 mm in the SL and 4.1 mm in the SW, being significantly larger than those from other areas. The pH of the waters from CHT (7.4) and CBY (7.2) were considerably more neutral than those from VVH (8.7) and OTZ (8.5). The highest turbidity was found in the VVH waters at 329.8 NTU and differed significantly to those of OTZ (16.2 NTU), CHT (1.8 NTU) and CBY (2.6 NTU). No differences were reported for water temperature, which averaged 20.4 °C, and for salinity, which averaged 143.4 ppm. Significance was found in the altitude of CBY with respect to the other study areas, being the highest geographically and influencing the shorter length of the shells. The other traits such as SW, ApL, ApW and ApA suggest a polygenic pattern of inheritance, as they did not show significant differences, while water parameters varied depending on altitude.

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COMPARING STOOL PCR, RECOMBINASE POLYMERASE AMPLIFICATION, AND MICROSCOPY TO DETECT *FASCIOLA HEPATICA* INFECTION IN THE RABBIT MODEL.

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Fascioliasis is an emerging neglected zoonosis worldwide. Communities in the Andean highlands of Peru, where prevalence exceed 10%, are considered hyperendemic. The diversity in transmission patterns and lifecycle complexity of Fasciola pose challenges for early and specific diagnosis the infection. Serology can help in early diagnosis, but limited sensitivity and, particularly, specificity make interpretation difficult. Antigen and DNA detection in stool may identify infection much sooner than microscopy. In this study, we compared real-time qPCR (qPCR) and recombinase-polymerase amplification (RPA) to stool microcopy for the early detection of fascioliasis in the rabbit animal model. Eight *Fasciola* free rabbits at baseline were infected orally with 40 metacercariae of *Fasciola hepatica*. We collected fecal samples before infection and daily starting 15 days post infection (dpi) until the three-day egg count mean was stable in all animals. The stool was tested using quantitative sedimentation microscopy with methylene blue. Stool sedimentation was used to concentrate eggs and DNA extracted from 500ug of fecal sediment using the cetyltrimethylammonium bromide (CETAB). The quantity and quality of the extracted DNA was evaluated by spectrophotometry. We used primers targeting the ITS-1 region of the Fasciola 18s gene. At 49 dpi, 3 rabbit were positive and at 61 dpi all rabbit were positive for Fasciola eggs by microscopy. *F. hepatica* DNA was detected 15 dpi in 3 rabbit using qPCR and in all rabbit at 25 dpi. Using RPA, DNA was detected 15 dpi in 2 rabbit and in all rabbit at 31 dpi. Infection was detected sooner by any of the methods if the number of adult parasites recovered from the animal was higher. Stool qPCR and RPA can detect *Fasciola* infection during the latent phase and several weeks sooner than microscopy.

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DETECTION OF *FASCIOLA HEPATICA* DNA IN DIFFERENT SPECIMENS USING A MINIPCR THERMOCYCLER AND LED LIGHT HANDHELD VIEWER

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Fasciola hepatica is a trematode causing burdens to livestock & human health. Stool microscopy has a poor sensitivity but is the diagnostic test most used. Real-time PCR (q-PCR) can detect *Fasciola* DNA in clinical & environmental samples with high sensitivity and specificity. In this study, we developed a SYBR Green PCR-based test using a portable miniature thermocycler (miniPCR) and LED light P51 mini-viewer to amplify and detect *Fasciola* (Fh) DNA. For these experiments, we used Fh DNA extracted from clinical (stool) and environmental (water and snails) samples. The differentiation between positive and negative samples was based on the fluorescence produced by SYBR Green after amplification of double-stranded DNA. To increase reproducibility, we used a smartphone application (Prismo Mirage) to quantify the fluorescence detected in P51 viewer. The analytic sensitivity was determined by the limit of detection after serial dilutions and the specificity by cross-reactivity with DNA from related organisms. The sensitivity was 100 fg/µl of *F. hepatica* DNA in water samples and 10 fg/µl of *F. hepatica* DNA in stool and snail samples. The Fasciola miniPCR was 100% specific for *F. hepatica* DNA. These results demonstrate that miniPCR is a molecular diagnostic method that can potentially be deployed to laboratories in endemic areas.

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PRE- AND POST-PRAZIQUANTEL TREATMENT ASSOCIATIONS OF *SCHISTOSOMA MANSONI* INFECTION WITH LATENT TUBERCULOSIS AND IMMUNE RESPONSES IN TANZANIA

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Tuberculosis is the second leading cause of death worldwide, with most active TB cases resulting from reactivation of latent tuberculosis infection (LTBI). Emerging evidence suggests that *Schistosoma* infection may decrease the sensitivity of screening tests that detect LTBI due to helminth-induced, altered immune responses. However, data on whether *S. mansoni* infection, and subsequent eradication, alter responses to LTBI are limited. Data from an ongoing cohort study were analyzed among adults aged 18-50 years living in Tanzania from July 2022 through April 2024. LTBI was determined at baseline and 12 months using the QuantiFERON-TB Gold Plus assay, which included: TB1, TB2, Nil and Mitogen. *S. mansoni* infection was confirmed by stool microscopy plus a serum schistosome circulating anodic antigen of ≥30 pg/mL. We used linear and logistic regression to compare *S. mansoni*-infected and uninfected people. Difference in differences of pre- and post-treatment were compared using Wilcoxon matched-pairs signed-rank test. 148 individuals were enrolled, which included 83 men (56.1%) and 65 women with a median age of 32 years [26-40.5]. Sixty-five people (43.9%) had *S. mansoni* infection. At baseline, there was no difference in LTBI between *S. mansoni*-infected and uninfected people, but those with schistosome infection had lower Mitogen concentration (38.5% versus 23% with Mitogen level<10IU/ml, p=0.03). Compared to persistently uninfected people (n=36), those whose *S. mansoni* infection was eradicated (n=14) at 12 months had subsequent increases in responsiveness to TB1 and Mitogen (TB1 +0.87, p=0.06; Mitogen +2.2, p=0.03). Preliminary data from this ongoing study demonstrate that *S. mansoni* may impair host immune responses to TB antigens. Eradication of schistosome infection at 12 months is associated with increased host immune responses to TB1 and Mitogen. Ongoing data collection may further clarify the longitudinal effects of schistosome infection and anthelmintic treatment on the immune responses to TB, which is particularly important in regions where these two diseases overlap, and co-infections are common.

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THE COLONIAL IMPACT ON SCHISTOSOMIASIS RESEARCH, PRESENT DAY INEQUALITIES AND MOVING TOWARDS AN EQUITABLE RESEARCH ENVIRONMENT

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Research into schistosomiasis has been deeply influenced by our shared colonial history, resulting in inequalities that persist to the present day. Despite the burden of this parasitic disease being primarily borne by the Global South, leading research institutions, influential journals, funding bodies, and major players in global health remain concentrated in the Global North. While collaborations between institutions from the Global North and Global South countries are common, issues surrounding power dynamics, longevity, and effectiveness of these collaborations arise. To unravel the complexities of this dynamic, a systematic review delving into the history of schistosomiasis research was undertaken. This review aimed to identify first authors, leading institutions, and the distribution of researchers from the Global North and Global South in published papers related to water, sanitation, and hygiene (WaSH) and schistosomiasis, examining how these dynamics have evolved over time. To further address these inequalities and aid the progression (in both the research environment and wider health

inequalities), it is also imperative to gain crucial insights from researchers in endemic countries as they offer insights into the complexities, barriers, and enablers of these international collaborations. Insights into existing dynamics and challenges were achieved using a mixed-method approach. Surveys, in-depth interviews (IDIs), and focus group discussions (FGD) with researchers from both the Global North and Global South were used to explore researchers' current experiences and help elucidate how research environments can be improved to overcome barriers imposed by colonial legacies. These insights will be presented, and how equitable collaboration between the Global North and South can be contextualized discussed, with tangible actions proposed to close inequality gaps, and improve schistosomiasis research to help control and eliminate this disease.

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QUANTIFYING CHANGES IN THE FORCE OF INFECTION OVER 20 YEARS OF MASS DRUG ADMINISTRATION FOR *SCHISTOSOMA MANSONI*

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Schistosomiasis infects over 240 million people, with the greatest impact on those living in sub-Saharan Africa. Intervention programmes have largely relied on the application of the anthelmintic praziquantel to reduce morbidity and onwards transmission. However, epidemiological evidence indicates that rates of re/infection are as high, and in some locations higher than in previous years despite upwards of 20 years of treatment in some settings. To inform on anthelmintic efficacy and the cost-effectiveness of ongoing control, it is critical to quantify the long-term impact of intervention programmes. To do this, we leverage a longitudinal epidemiological dataset collected over 18 years from school-aged children in three villages with high endemicity of *Schistosoma mansoni* in Uganda. We developed a state-space model that estimates individual-level worm burden from repeated parasite egg counts to investigate whether the mass drug administration programme has reduced the force of infection and what differences exist between these villages, while accounting for challenges such as loss to follow-up and changing cohorts. Our results indicate that the force of infection has marginally reduced over 18 years, with substantial heterogeneity between villages despite their close geographic proximity to one another and Lake Victoria. Owing to the small, though statistically significant, reductions in the force of infection, it is difficult to ascertain whether this is due to repeated mass treatments, or other factors such as i) reduced exposure to infected water sources due to lower fish stocks, ii) education programmes, and/or iii) the implementation of water, sanitation, & hygiene interventions. Future research should aim to quantify the impact of these additional interventions as well as investigate changes to the forceof infection in lower endemicity settings.

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ASSOCIATIONS BETWEEN *SCHISTOSOMA MANSONI* INTENSITY, C-REACTIVE PROTEIN (CRP), AND STUNTING AMONG PRESCHOOL-AGED CHILDREN IN UGANDA

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Schistosomiasis causes linear growth faltering among older children. However, little is known about schistosomiasis-related morbidities in pre-school age children (PSAC). As part of an NIH-funded trial of optimal praziquantel dosing for PSAC in Uganda, we present baseline findings assessing *S. mansoni* infection intensity, systemic inflammatory markers, and risk for stunting. PSAC age 12-47 months with *S. mansoni* infection, diagnosed by Kato Katz in duplicate stool samples, were enrolled from the Lake Albert region. Infection intensity was assessed by eggs per gram of stool (EPG). Plasma C-reactive protein (CRP) was measured by immunoassay. Undernutrition categories of underweight (weight-for-age z score<-2), stunting (length-for-age z score<-2), and wasting (weight-for-length z score<-2) were defined using WHO Anthro. Statistical analyses included multivariate linear and log binomial regression models. A bivariate threshold of $p<0.1$ was used to select covariates and considered age, sex, socio-economic status (SES), non-lake drinking water, malaria coinfection, and HIV coinfection. Among 348 participants, the median *S. mansoni* infection intensity was 72 EPG (IQR 24-258). Sixteen percent of children had malaria and 19.0% were stunted. Fewer than 3% were underweight or wasted. Higher *S. mansoni* infection intensity (EPG) was associated with higher CRP concentrations after adjusting for drinking water, malaria, and HIV (ß=0.08, SE=0.04, p=0.03). Higher CRP concentrations were associated with an increased risk for stunting after adjusting for SES (RR=1.18, 95% CI=1.00-1.40, $p<0.05$). While *S. mansoni* infection intensity was not directly associated with stunting risk, we report that *S. mansoni* may indirectly contribute to stunting via systemic immune activation as captured by CRP. This finding aligns with previously published reports that schistosomiasis contributes to stunting in children via chronic systemic inflammation, which negatively impacts growth factors like insulin-like growth factor 1 (IGF-1). This study offers insight into mechanisms of schistosomiasis-related stunting in children under five years.

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MORBIDITY IN PRE-SCHOOL-AGED CHILDREN AND ADULTS IN A *SCHISTOSOMA MANSONI* ENDEMIC COMMUNITY OF LAKE VICTORIA, UGANDA

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Schistosoma mansoni infection is known to cause damage to the liver, however resource and time constraints limit regular ultrasound screenings in endemic areas. Therefore, the number of eggs in faeces is used as a proxy for morbidity and the high infection intensity (≥ 400 eggs per gram) threshold to inform and evaluate control programs. However, recent evidence has begun to challenge this link between infection intensity and morbidity, urging a revaluation of these control and elimination targets and assumptions. In a cross-sectional survey in Bugoto, Uganda, involving 287 individuals aged 3-74, S. mansoni prevalence and intensity were determined using Kato Katz thick smear microscopy and point-of-care circulating cathodic antigen tests. Ultrasound and the Niamey protocol assessed periportal fibrosis (PPF), portal vein dilation (PVD), and left

parasternal line (PSL) enlargement. Logistic regression models incorporated infection, coinfections, anemia, and symptoms to predict morbidity and infection. PPF prevalence was 9% (B-F) and 4% (C-F), while PVD and PSL prevalence were 34% and 33% respectively. Although 11-14-year-olds had the highest S. mansoni infection intensity, preschool-aged children (PSAC) were more likely to exhibit PVD and PSL morbidities. Current S. mansoni infection showed no association with assessed liver morbidity markers. Our study findings add to the growing evidence indicating a lack of association between current S. mansoni egg count with morbidity markers, which raises significant implications against the use of eggs per gram as a proxy for morbidity within national programs and policy. The age-related distribution of morbidities observed here, with notable burden of PVD and PSL in PSAC, stresses the critical need to both: a) elucidate the impact and progress of apparent 'subtle morbidities' on host health and their interplay with current and past infection status; and b) accommodate and monitor these youngest age classes in treatment and monitoring programmes, if we are to ever truly achieve the revised WHO NTD Roadmap schistosomiasis targets of elimination as a public health problem by 2030.

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EFFECTS OF COMMUNITY-LED TOTAL SANITATION ON IMPROVING HYGIENE AND SANITATION IN THREE VILLAGES OF THE EAST REGION, CAMEROON, APRIL - SEPTEMBER 2023

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Cameroon faces problems in drinking water and sanitation; access rate was estimated at 3.9% and 34% for drinking water and sanitation services respectively in 2010. East Region is among the regions with the lowest sanitation rate, estimated at 16%. To improve hygiene and sanitation in this region, the Ministry of Public Health with its partners implemented the Community-Led Total Sanitation (CLTS) project in 300 villages. The goal was to bring a change in attitudes and hygiene practices. We described the effects of this strategy in 3 villages of the East region. We conducted a comparative study from April to September 2023 in 3 villages purposely selected (Sandae, Sandji 2 and Bazzama villages) after a 2-year CLTS implementation. We estimated the number of households to be interviewed at 278. We used systematic sampling to select households. In each household, the head of household was interviewed. We used a structured questionnaire to collect socio demographics (age, sex, occupation, education), hygiene facilities (latrines and types, handwashing facilities) and hygiene practices (handwashing, use of soap, use of latrines, open defecation) data. We analyzed data using Excel 2016. In total, 278 heads of households were interviewed. Median age was 41 (18-69) years and sex ratio M:F 3:1. In total, 245 (88.1%) did not attend school and 183 (65.9%) were farmers. At endline, 251 (90.3%) households owned a latrine vs 93 (33.5%) at baseline. The full-bottom latrine was most frequent 251 (90.3%) vs 129 (46.4%) at baseline; 241 (86.7%) had a hand-washing facility vs 318 (51.8%). Among those who owned a latrine, 239 (95.2%) used them regularly with 123 (49%) still in good condition. In total, 19 (6.8%) practice open defecation vs 194 (70%) at baseline and 182 (75.5%) systematically washed their hands after leaving the toilet, compared with 34 (12.7%) at baseline but 4 (1.1%) used soap. CLTS brought enormous changes in sanitation and hygiene practices in these villages. However, some practices need to be improved on latrine utilization and handwashing practices. We recommend a close follow-up to ensure the sustainability of these actions.

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HOLISTIC APPROACHES TO WATERBORNE URINARY TRACT INFECTIONS

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Water may be an underrecognized but important route of uropathogen transmission causing urinary tract infections (UTIs). This idea is supported by recent reports of the presence of uropathogens in water supplies from multiple countries, and a report of a decrease in UTIs following installation of a new water treatment plant on San Cristóbal Island in Galápagos, Ecuador. Drinking or bathing in contaminated water may expose people to extraintestinal infections caused by *Escherichia coli*, the most common pathogen associated with UTIs. Studies are needed to investigate uropathogenic *E. coli* in drinking water systems, and the links to infectious disease. The hypothesis for this work is that waterborne exposures to *E. coli* are a causative agent of community-acquired UTIs, driven by environmental factors and household water use. Results from this work have the potential to revolutionize our understanding of the etiology of UTIs and the ecology of uropathogenic *E. coli* to subsequently inform interventions to improve water quality and prevent disease.

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SPATIAL DISTRIBUTIONS & DIVERSITY OF ENTERIC PATHOGENS IN PUBLIC ENVIRONMENT IN LOW-AND MIDDLE-INCOME NEIGHBORHOODS IN NAIROBI, KENYA

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The objective of this study was to evaluate the differences in the detection, species diversity, and contamination level of enteric bacterial pathogens between and within low- and middle-income neighborhoods of Nairobi, Kenya. We also assessed the hygienic infrastructure and sanitation conditions in the two neighborhoods. A TaqMan array card assay was employed to analyze soil samples for 19 enteropathogens alongside Enterobacteriaceae culture assays. An observational assessment was conducted during every site visit to document the hygienic infrastructure and sanitation conditions at the sites. We detected at least one enteric pathogen in 81% (130/160) and two and more than two pathogens in 67.5% (108/160) of the soil samples tested. The four most frequently detected pathogens were EAEC (67.5%), ETEC (59%), EPEC (57.5%), and STEC (31%). The detection rate (93% vs. 69%) and mean (5 vs. 4.7) diversity of enteric pathogens were higher in Kibera than in Jericho. Similarly, a wider spatial distribution of the pathogens was found at Kibera public domain sites. On average, diversity in exposure to different enteric pathogens increased by 0.72 and 0.69 species within-site movements in Jericho and Kibera, respectively and by 1.11 and 0.99 for between-site movements in Jericho and Kibera, respectively. Patterns of pathogen detection in public soil varied seasonally in the middle-class neighborhood but remained consistently high throughout the year in the low-income slum. Our study revealed that several enteric pathogens, notably pathogenic *E. coli,* are prevalent in the public environment across both neighborhoods, with a higher contamination rate and spatial-temporal distribution in low-income Kibera. Future studies should focus on identifying the source of contamination and quantifying the role of contaminated environments in enteric infections in children.

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MENTAL AND ENVIRONMENTAL HEALTH IN URBAN SALVADOR, BRAZIL: LINKS AND OPPORTUNITIES

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Although urban areas have greater access to municipal services such as water and sanitation services, those in densely populated, informal communities experience disparities in distribution, quality, and continuity of services, which can be detrimental to both physical and mental health. For example, densely populated urban favela communities in Brazil often experience high stress related to environmental conditions and exposure to violence. Addressing the association between urban environmental conditions and mental health provides an opportunity to reduce barriers to improved health and quality of life. Mobile health technology (mHealth) has tremendous potential to gather data and may enhance the inclusion of underserved populations in the participatory construction of solutions for these challenging urban environmental problems. Our goal was to examine the association between mental and environmental health in urban communities that are receiving a sanitation intervention in Salvador, Bahia, Brazil. Participants (N=768) in four communities (two sanitation intervention areas and two control communities) completed the SF-12 questionnaire, a standardized questionnaire which examines dimensions of physical and mental health. We found that 60% of participants rated their health as good or better yet 15% responded that they felt discouraged or depressed often. Although there were indicators of strong community cohesion (e.g., 70% of people responded that they felt a desire to help other members of the community), there were also challenges. For example, some cited a lack of trust for others (30%), insufficient presence of community neighborhood associations (20%), concern for violence (28%), and limited infrastructure services (36%) which varied by neighborhood. We also completed focus groups to elucidate the complex links between mental and environmental health in urban areas of Salvador and to assess how the sanitation intervention impacted quality of life. We also looked to identify ways in which mHealth tools could be leveraged to enhance both mental and environmental health in collaboration with these communities.

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ACCEPTABILITY, USAGE AND SATISFACTION OF CHLORINE FOR WATER TREATMENT AFTER DOOR-TO-DOOR MASS DISTRIBUTION IN DISPLACED POPULATION OF CABO DELGADO PROVINCE, MOZAMBIQUE

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Cholera is responsible for high mortality in humanitarian emergencies due to overcrowding, malnutrition, lack of healthcare access, sanitation facilities and treatment of drinking water. The province of Cabo Delgado, Mozambique, has been immersed in a severe humanitarian crisis due to conflict and insecurity since 2017 with declared cholera outbreaks. Hygiene promotion campaigns have been implemented since August 2023 including mass door-to-door distribution of chlorine in resettlement sites and host communities of 7 districts of the province. A total of 52,202 bottles of chlorine were distributed to 245,000 people. The aim of this study was to describe the acceptability, usage, knowledge and satisfaction of the use of chlorine as water treatment method after a mass distribution. A cross-sectional survey was conducted in 6 districts after the distribution. A total of 340 people were randomly selected using proportional population size methodology with the premise they had received chlorine. Overall, 76% of participants were women and the largest age group was between 18 and 35 years old (50%). Eighty-nine per cent of participants confirmed they had used chlorine in the previous two weeks. However, out of the 340 households visited, 199 (59%) tested positive for free residual chlorine in their drinking water. Of the positive ones, 20 households did not have the optimal concentration: 7 of them had less than the required (< 0.2 mg/l) and 13 had more than the recommended one (>5.0 mg/l). Eighty-one per cent of the participants who treated their water showed they knew the recommended dose of chlorine to be used. Most of the participants (98%) said they were satisfied with the use of chlorine and 89% said they would use it again. The study is the first one measuring the uptake of chlorine after mass household distribution in displaced population and it showed a high acceptability, knowledge of use, knowledge on the reason to use and the will of using chlorine again. However, discrepancies between the reported usage rate and the positivity of the free residual chlorine test may indicate issues in the usage or storage after the water treatment.

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EVALUATING FECAL SLUDGE TREATMENT TECHNOLOGIES IN HUMANITARIAN CONTEXT: A COMPREHENSIVE STUDY IN COX'S BAZAR, BANGLADESH

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Efficient treatment of fecal sludge in densely populated settings is essential as it has a direct impact on public health and environment. This study evaluates the performance of selected fecal sludge treatment technologies at the Rohingya camps, Bangladesh. A total of 17 different treatment plants of five different technologies were selected for this study. The treatment technologies were evaluated based on the removal efficiency and standard discharge guideline of different physicochemical and microbiological parameters. Among the treatment technologies, waste stabilization pond (WSP) showed the highest removal efficiency in all parameters except *Escherichia coli*. Upflow filter (UPF) showed good removal efficiency for *E. coli* (99.7%), TSS (95.9%), COD (91.7%), BOD (93.5%) and helminth (93.7%). Decentralized wastewater treatment systems (DEWATS) performed well in the removal of TSS (97.7%), COD (94.4%), BOD (93.9%) and helminth (99.8%). In respect to comparing with the standard discharge guideline, the majority of the treated effluents from WSP were found to be within the guideline values specially for phosphate (61.1 %), TSS (72.2 %) and helminth (66.7 %). In the case of *E. coli* around 43% of treated fecal sludge samples of DEWATS were found within the guidelines, which was higher than all the other technologies. None of the technologies completely follows the national and international guidelines for discharge quality. Therefore, additional treatment options like combining chemical and biological processes to the existing treatment technologies need to be implemented in fecal sludge treatment to effectively ensure safe final discharge into the environment.

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EFFECT OF AN ONSITE SHARED SANITATION INTERVENTION ON MARKERS OF ENVIRONMENTAL ENTERIC DYSFUNCTION IN CHILDREN LIVING IN MAPUTO, MOZAMBIQUE

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The relationship between enteric pathogen exposure and long-term health effects like stunting and cognitive deficiencies may be mediated by environmental enteric dysfunction (EED), a subclinical condition characterized by intestinal inflammation, increased permeability, and malabsorption. Reducing exposure through safe water, sanitation, and hygiene (WASH) may limit or delay the onset of EED. We assessed whether access to a shared onsite sanitation intervention affected the concentration of four fecal biomarkers of intestinal inflammation and permeability among children living in Maputo, Mozambique. The Maputo Sanitation trial was a controlled before-and-after study of an urban sanitation intervention in low-income, unplanned neighborhoods of Maputo, Mozambique. We collected stool at baseline (pre-intervention) and 12- and 24-months post-intervention and measured the concentration alpha-1-antitrypsin (A1AT), neopterin (NEO), myeloperoxidase (MPO), and calprotectin (CAL). We assessed the effect of the intervention at 12- and 24-months post-intervention among all children and in a sub-group of children born into study sites post-intervention. After 12 months, the concentration of NEO was higher among intervention children compared with controls (mean difference 0.39 log nmol/L, 95% CI: 0.15 - 0.62). Concentrations of CAL and NEO, both measures of intestinal inflammation, were also higher among children born into intervention sites by the 24-month follow-up visit (CAL mean difference 0.43 log ng/mL, 95% CI: 0.041 - 0.82; NEO 0.38 nmol/L, 95% CI: 0.0079, 0.76). The intervention did not a have statistically significant effect on the concentration of A1AT, the only marker of intestinal permeability. We found no evidence that the intervention reduced the concentration of EED biomarkers among children up to 24-months after the intervention. The lack of a formal case definition and of representative healthy reference concentrations complicates interpretation of our effect estimates, including their potential clinical significance.

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RISK FACTORS FOR CHILDHOOD DIARRHEAL DISEASES IN PERI-URBAN AREAS OF OUAGADOUGOU, BURKINA FASO: A HOUSEHOLD SURVEY

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AbstractDiarrheal diseases represent a significant global public health challenge, particularly in low or middle-income countries, where access to safe drinking water remains a challenge. In Burkina Faso, diarrheal diseases continue to burden the population, especially in peri-urban areas. This study aims to identify the risk factors associated with diarrheal diseases in two peri-urban areas of Ouagadougou, Burkina Faso. A household survey was conducted from April 7 to 16, 2021, targeting mothers/caregivers of children under five. Data collection utilised a structured questionnaire covering socio-demographic and economic household characteristics, as well as maternal knowledge, attitudes, and practices related to diarrheal diseases, safe water access, sanitation, and hygiene. A total of 660 households were surveyed, with respondents averaging 31.39 years of age, and 58.48% having no formal education. Mothers/caregivers predominantly attributed diarrheal diseases to poor nutrition (70.91%) and inadequate hand hygiene (63.33%), while only 30.61% recognised the role of contaminated water. Despite high reported access to drinkable water (98.64%), primarily sourced from public fountains (70.15%), handwashing facilities with water and soap in the same location were lacking in 25.45% of households. Additionally, a significant association (P<0.001) was observed between household economic status and access to a private tap at home. This study highlights the prevailing misconceptions surrounding the causes of diarrheal diseases among mothers/caregivers of children under five in peri-urban areas of Ouagadougou. It underscores the urgent need for targeted interventions addressing knowledge gaps, and improving access to safe water, sanitation, and hygiene practices, particularly among economically disadvantaged households.

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NOROVIRUS INFECTION RISKS ASSOCIATED WITH CONSUMPTION OF CONTAMINATED TOMATOES - AN APPLICATION OF A NOVEL QUANTITATIVE MICROBIAL RISK ASSESSMENT (QMRA)-LINKED INFECTIOUS DISEASE TRANSMISSION (IDT) MODEL

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Norovirus is a leading cause of foodborne illness in the United States and worldwide. However, the magnitude of disease risk to a population from consuming produce contaminated with norovirus is not known. To estimate the individual- and population-level risks of consuming norovirus-contaminated tomatoes, we developed a quantitative microbial risk assessment (QMRA)-linked infectious disease transmission (IDT) model to 1) characterize individual risk from consumption of empirically sampled, norovirus-contaminated tomatoes, and 2) simulate norovirus cases in a population from a norovirus-tomato seeding event. Sequence-confirmed norovirus GII.6 strains were isolated from tomatoes collected on Mexican farms and quantified using digital RT-PCR. We used a QMRA model to estimate infection risks (10,000 iterations, mc2d package, 1:100 infectious ratio) based on empirically sampled norovirus concentration data and age-stratified tomato consumption rates. Median infection risks varied by age, with the lowest risk (1.9×10^{-4} per day, 95th percentile range [1.8×10^{-6}, 3.1×10^{-2}]) among children (<6 years), and the highest risk ($1 .4 \times 10^{-3}$ per day, 95th percentile range [3.3×10^{-5}, 1.8×10^{-1}]) among adults (21 to <60 years). These risks were integrated into the IDT model (N=100,000; 50% of population exposed to tomatoes) to simulate a one-time norovirus seeding event. Using the IDT model, a single outbreak from tomato consumption alone lasted four days with a cumulative incidence of 16 cases: 11 symptomatic, 5 asymptomatic. When simulating primary cases resulting from tomato consumption and secondary cases from contact with tomato-infected primary cases, the outbreak lasted 17 days with a cumulative incidence of 42 cases: 29 symptomatic; 13 asymptomatic. This study underscores the utility of integrated risk assessments to evaluate norovirus transmission dynamics across scales, the potential to simulate pathogen- and commodity-specific seeding events, and to inform effective surveillance and mitigation strategies.

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PREVALENCE OF ANTIMICROBIAL RESISTANT ENTEROBACTERIA'S IN A COMMUNITY AND IN THE ENVIRONMENT IN SALVADOR, BRAZIL

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We collected 82 community and 77 environment samples between 2023 and 2024, to assess the prevalence of antimicrobial resistant *Escherichia coli*, *Klebisella pneumoniae* and *Enterobacter cloacae* from a neighborhood and a river near the community in Salvador, Brazil. Bacterial isolates were selected based on their characteristics using MacConkey and CHROMagar median culture, and then confirmed with MALDITOF and Vitek. Subsequently, PCR reactions and agarose electrophoresis gel were employed to detect the presence of 13 genes associated with beta-lactamases, particularly those linked to multidrug resistance. We found out that the most prevalent bacteria were *E. coli* (82% in community and 53% in environment) followed by *K. pneumoniae* (18% in community and 37% in environment) and *E. cloacae* (0% in community and 6% in environment). The genes with most frequency in the community and environment was the *bla*TEM with 40% in the community and 37% in the environment. The genes with the least prevalent were *bla*IMP, *bla*VIM and *bla*OXA-48,

both with 0% prevalence. Only 22% of the isolates lacked any resistance associated genes. Furthermore, the antibiotic that showed the most resistance in the analyses was Amoxicillin-clavulanic acid in community and intravenous Cefuroxime in the environment. The most contaminated point with fecal contamination had 6900 CFU/ml in a point closer to mouth of the river. These findings support that antimicrobial resistance is present and increasing worldwide in the environment, needing rapid intervention to slow down this problematic. The prevalence of those bacteria in the environment, besides other associations, is related to the lack of basic sanitation and the traffic between humans and the river. Observing heightened resistance to Amoxicillin-clavulanic acid and intravenous Cefuroxime corresponds with the prevalence of the *bla*TEM gene in the samples, since this gene is related to resistance to cephalosporins and penicillin-like antibiotics.

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PIPED WATER INTERMITTENCY AND ITS IMPACT ON WATER QUALITY AT POINT OF USE

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Intermittent water supply (IWS) systems, characterized by services that are unavailable for hours or days at a time, present a risk for water insecurity. IWS often results in pressure fluctuations and stagnation, leading to increased risk of microbial intrusion and proliferation compared with continuous water supply systems. Households that experience water intermittency often store water to compensate for outages, which can lead to contamination. They also tend to distrust the quality of the water, increasing their likelihood of treating drinking water. To explore the association between household piped water intermittency and piped water microbial contamination at the point of use, we collected 1098 piped water samples from 234 households over four visits spaced six months apart in six communities in northern Ecuador. We assessed *E. coli* concentrations using both Colilert (IDEXX) and Petrifilm (3M) tests, obtaining five contamination levels that correspond to WHO risk levels for safe water. IWS patterns, including frequency (days/week without water supply) and duration (hours/day without water supply) of intermittent periods varied across communities. Households in two community-managed systems reported fewer intermittent periods per week but were more likely to have increased contaminated water samples compared to our study community with a centralized system. We did not observe a significant association between household piped water intermittency and piped water contamination at the point of use. However, households reporting more frequent intermittent periods were more likely to provide samples that were stored before collection (OR: 1.3 [95% CI: 1.1-1.5]), and water storage was associated with higher contamination levels (2.9 [1.7-4.9]). We did not observed associations with household water treatment. These findings suggest that while intermittency itself may not directly influence piped water microbial contamination in our study communities, the coping strategies adopted by households to manage IWS, such as storing water, may contribute to the contamination of their drinking water supplies.

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IMPROVEMENT AND DISPARITY IN WATER, SANITATION, AND HYGIENE (WASH) IN GHANA: COMPARATIVE ANALYSIS OF 2014 AND 2022 GHANA DEMOGRAPHIC AND HEALTH SURVEY DATA

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Provision of safe drinking water, sanitation, and hygiene (WASH) is key in achieving the SDGs by 2030. In achieving this, inequalities are to be considered. In LMICs like Ghana, vulnerable groups disproportionately bear the burden of poor WASH. We assessed Ghana's progress towards provision of WASH and reducing WASH inequalities. We analysed household data from the 2014 and 2022 Ghana DHS. Access to basic WASH intervention was defined using the WHO standard. We estimated the coverage of WASH as a percentage with 95%confidence interval(CI). Concentration index was used to quantify inequality in access to basic WASH interventions. Households in 2014 and 2022 were 11835 and 17933 respectively with a median household size of 3 persons each. Most households were headed by males[2014:66.0%, 2022:63.0%]. From 2014 to 2022, improvements were observed in household access to basic drinking water;84.0%[CI:82.0-86.0] to 87.0%[CI:85.0-89.0], sanitation;21.0%[CI:18.0-23.0] to 23.0%[CI:21.0-26.0] and handwashing facilities; 33.0%[CI:30.0-36.0] to 46.0%[CI:44.0-48.0]. Overall access to basic WASH increased from 6.4%[CI:5.2-7.8] to 15.0%[CI:13.0-17.0] among households. There were significant disparity in household access to basic toilet facilities, drinking water, handwashing facilities, and overall WASH against the poor. Inequality in access to basic WASH interventions was significantly higher in urban households, highest:Greater Accra, lowest:North East region, and increased with educational level, household head gender disparity against female heads was observed in 2014. WASH coverage remains low in Ghana and with high inequality in access to basic WASH facilities across socio-economic status, regions, urban-rural communities, however household head gender disparity was not observed in the current survey. Interventions targeting urban informal settlements need to be considered.

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MOLECULAR DIAGNOSTICS OF PARASITES IN DIFFERENT ENVIRONMENTS AND CLIMATES THROUGHOUT LATIN AMERICA

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Helminths and protozoa are parasites that infect millions of people throughout Latin America. These parasites have part of their life cycle in soil or water; the contaminated environment is a primary source of parasitic infection. Our study involves 5 Latin American Countries, including Argentina, Brazil, Ecuador, Mexico, and Peru, encompassing different ecological areas in rural villages. We employed a filtration and concentration method along with multi-parallel qPCR to test for the helminths *Ascaris lumbricoides, Ancylostoma* species*, Necator americanus, Strongyloides stercoralis, Schistosoma mansoni, Taenia solium, Toxocara canis/cati, Trichuris trichiura* and the protozoan *Acanthamoeba* species*, Blastocystis* species*, Cryptosporidium* species*, Entamoeba histolytica, and Giardia*

intestinalis. There are over 1000 samples from 200 houses dispersed between all sites. The majority of houses had outdoor latrines and were supplied by well water. Preliminary results depended on the surrounding environment for Argentina (Tropical Savana), Brazil (Tropical), Ecuador (Tropical), Mexico (Tropical Savana), and Peru (Sierra, Tropical). The most common helminth/protozoa per area were Argentina (*A. lumbricoides* 16%, *Blastocystis* 4%), Brazil (*T. solium* 30%, *E. histolytica* 30%), Ecuador (*N. americanus* 45%, *Acanthamoeba* 60%), Mexico (*A. lumbricoides* 12%, *Acanthamoeba* 53%), and Peru (*S. stercoralis* 50%, *Blastocystis* 71%). There was a significant increase in the burden of specific helminths DNA when comparing Tropical and Sierra (*A. lumbricoides* 1.34 to 0.099 fg/µl per kg dirt, $p < 0.0001$). A similar burden increase was noted for protozoans in these climates (*Blastocystis* 11.4 to 0.48 fg/µl per kg dirt, $p < 0.0001$). When comparing the different climates, there was a 16.6 (1.83 to 195.7) $p = 0.004$ odds ratio of exposure to *A. lumbricoides* in the Tropical regions. Our study explores the risk factors for people and animals in distinct areas to be exposed to parasites. Future work will examine the cross-sectional and longitudinal impact of climate on these parasites in the environment.

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PREVALENCE OF INTESTINAL PARASITIC INFECTION IN PEOPLE FROM MARGINALIZED COMMUNITIES IN MEXICO CITY AND THE STATE OF PUEBLA, MEXICO

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The prevalence of intestinal parasites in marginalized communities in Mexico City and the state of Puebla, Mexico, was determined. Fecal samples were collected from children and adults without distinction of sex and age. Coproparasitoscopic studies were performed on the samples obtained by the methods of zinc sulfate flotation, sedimentation method and Kinyun staining, the first two for the analysis of protozoa and helminths and the third for the analysis of intestinal coccidia. Risk factors for acquiring parasitic infections were considered, such as the origin of the drinking water (well water, water tanks or basins that are supplied by hoses that take liquid from a water spring), direct coexistence with dogs, cats and poultry, pica disorder, type of diet, intake of between 1 and 3 glasses of water, as well as dirt floors in some homes. The results obtained showed the presence of parasitic protozoa, *Blastocystis hominis* and *Cryptosporidium* spp, as well as commensal organisms, *Chilomastix mesnili* and *Endolimax nana.* So far, a probable endemicity of *Cryptosporidium* spp has been reported in the study area and no presence of geohelminths has been found. The parasites and commensal organisms found are important because they are related to environments where sanitation and hygiene are deficient and their potential adverse and significant impact on health, especially in vulnerable populations. It is important to identify the presence of these parasites and commensal organisms, in order to properly treat infections and assess the patient's health status. Accurate diagnosis and timely treatment are critical to preventing complications and promoting gastrointestinal health.

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COINFECTION OF POWASSAN VIRUS AND *BORRELIA BURGDORFERI* IN A C3H MOUSE MODEL

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Powassan virus (POWV) is a tick-borne flavivirus that can cause an encephalitic disease with high morbidity and mortality. *Ixodes scapularis* ticks that serve as the vectors of Powassan Virus (POWV) also carry Borrelia burgdorferi (*B. burgdorferi*), the causative agent of Lyme disease. Lyme disease can affect many organs, and in the case of neuroborreliosis, this includes the CNS. *B. burgdorferi* is the most common vector-borne disease in the United States and is highly prevalent in the same areas POWV is emerging. In *I. scapularis* ticks, coinfection with *B. burgdorferi* has been shown to increase POWV replication and dissemination to the salivary glands, from which it transmits when the tick feeds. Given the overlapping targets of infection, the high occurrence of *B. burgdorferi* in the regions in which POWV is emerging, and the possibility for a single tick to transmit both pathogens, better understanding how coinfection may impact clinical course is an important question remaining to be addressed. To investigate our hypothesis that coinfection with *B. burgdorferi* alters POWV, this study used C3H mice, an established model for both *B. burgdorferi* and POWV. Mice were injected via footpad with either a media control, *B. burgdorferi*, one of three virus strains—a lab strain or circulating POWV isolates (from field-collected and community-submitted ticks), or one of those same three strains combined with *B. burgdorferi*. All groups included tick salivary gland extract to mimic natural transmission via tick. Mice were monitored daily for clinical symptoms and blood was collected on days 1-5 post infection to monitor bacteremia and viremia. Internal organs were collected from all mice for histology and for RNA extraction. Our results indicate that when delivered simultaneously via footpad, *B. burgdorferi* can alter POWV infection in a strain-dependent manner, leading to an increased POWV titer in the brain in one of the field-collected viral isolates when coinfected with *B. burgdorferi*.

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HOST-SPECIFIC ADAPTATION OF POWASSAN VIRUS TO *AMBLYOMMA AMERICANUM*: ROLE OF PREMEMBRANE (PRM) IN TICK-SPECIFIC VIRAL FITNESS

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Powassan virus (POWV, family *Flaviviridae*) is a reemerging tickborne virus endemic in North America and Russia. POWV was first isolated in 1958 from a fatal encephalitic case in Canada. In 1997, a POWV-like agent was isolated from *Ixodes scapularis* in New England and determined to be genetically distinct. This revealed the existence of two lineages: lineage 1, Powassan virus (POWV-1) and lineage 2, deer tick virus (DTV). Each lineage is maintained in separate enzootic cycles with POWV-1 thought to be primarily maintained between *I. cookei* and woodchucks and *I. marxi* and squirrels, while DTV is maintained between *I. scapularis* and small mammals. POWV-1/DTV, however, have been detected in a range of tick genera. In New York State (NYS) between 2018-2022, POWV-1 was isolated for the first time from *I. scapularis* and detected in *Dermacentor variabilis*, and DTV was isolated from *Amblyomma americanum*. In 2023, two additional DTV-positive *A. americanum* pools were identified. These novel findings suggest POWV-1/DTV circulation in a broader range of tick hosts, which is further supported by the overlapping and expanding geographic and mammalian host ranges of these genera. The propensity for POWV-1/DTV to further adapt to new tick hosts following these rare spillover events is unknown but could facilitate the emergence of increasingly virulent strains. To understand host-specific viral fitness of DTV in novel tick hosts, we conducted genetic and phenotypic characterization of an *Amblyomma*-derived DTV strain from NYS. Genetic results show this strain, DTV NY22-2958, contains a unique substitution in the premembrane (PrM) protein (L268F) and displays a clear fitness advantage in experimentally infected *A. americanum* nymphs. Growth kinetics in *A. americanum* cultures reveal an increased viral burst size associated with DTV NY22-2958. Future work aims to assess contributions of L268F to increased stability and viral release through *in vitro* assays. These data reveal the potential for POWV adaptation to a range of unique tick genera and suggest a role for PrM in species-specific adaptation.

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FIRST EVIDENCE OF NON-VIREMIC TRANSMISSION OF POWASSAN VIRUS BETWEEN CO-FEEDING TICKS

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Powassan virus, a North American tick-borne flavivirus, can cause severe neuroinvasive disease in humans. While *Ixodes scapularis* are the primary vectors of Powassan virus lineage II (POWV II), recent laboratory studies showed that other species of ticks can horizontally and vertically transmit POWV II, such as *Haemaphysalis longicornis*. Originally from East Asia, *H. longicornis* has recently established populations in the eastern United States, coexisting in geographic areas with native vector species such as *I. scapularis*. Reports of *H. longicornis* feeding concurrently with *I. scapularis* on multiple sampled hosts highlight the potential for interspecies co-feeding transmission of POWV II. No vertebrate reservoir host has been clearly defined for POWV II, suggesting that this virus could be sustained in transmission foci via non-viremic transmission between ticks co-feeding on the same vertebrate host. The objective of this study was to evaluate whether uninfected *H. longicornis* co-feeding in close proximity to POWV II-infected *I. scapularis* can acquire POWV independent of host viremia. Using an *in-vivo* tick transmission model, *I. scapularis* females infected with POWV II ("donors") were co-fed on mice with uninfected *H. longicornis* larvae and nymphs ("recipients"). Donor and recipient ticks were infested on mice and screened for POWV II RNA via q-RT-PCR after feeding. Mouse infection status was monitored by temporal screening of blood using the same method. Prevalence of POWV II RNA was highest in recipient *H. longicornis* that fed on viremic mice. However, non-viremic mice were also able to support co-feeding transmission of POWV, as demonstrated by the detection of viral RNA in multiple *H. longicornis* dispersed across different mice. Detection of viral RNA at the skin site of tick feeding but not at distal skin sites indicates that a localized skin infection facilitates transmission of POWV between donor and recipient ticks co-feeding in close proximity. This is the first report examining transmission of POWV between co-feeding ticks. These findings shed some light on possible mechanisms by which POWV could be maintained in nature.

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DEFINING THE KINETICS OF THROMBOCYTOPENIA SYNDROME VIRUS (SFTSV) ACQUISITION AND DISSEMINATION WITHIN FEEDING *HAEMAPHYSALIS LONGICORNIS* NYMPHS

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Severe fever with thrombocytopenia syndrome virus (SFTSV) is an emerging tick-borne bandavirus with a high case fatality rate in humans. This virus is endemic in eastern Asia, and the Asian longhorned tick, *Haemaphysalis longicornis*, is the main vector. Although the presence of SFTSV has been clearly demonstrated in all life stages of *H. longicornis*, the dynamics of virus acquisition, transstadial persistence, and dissemination from midgut to salivary glands remain unexplored. Preliminary data showed that *H. longicornis* nymphs are able to acquire SFTSV during feeding on viremic mice using our *in vivo* tick infection model. Additionally, the virus was transstadially transmitted and disseminated from the midgut to various other organs (hemolymph, salivary glands, and ovaries) by the time nymphs molt into adult ticks. In order to determine the kinetics of SFTSV acquisition by and dissemination within *H. longicornis*, naïve nymphs were fed on viremic mice. Nymphs were collected and processed at defined time points during and after feeding on SFTSV-infected mice: (**i**) partially-fed nymphs were processed after feeding 6, 12, 24, and 48 hours on infected mice; (**ii**) fully-fed (pre-molt) nymphs were processed immediately upon detachment from mice, then every 2 to 3 days over the course of the pre-molt period; (**iii**) molted adults were processed at approximately 2 and 4 weeks post-molting. At every time point, the legs of each tick were collected and used as a proxy to assess virus dissemination from midgut to hemolymph. The nymph body corresponding to each sample of legs was also screened for SFTSV. Molted adult ticks were dissected, and legs, salivary glands, midgut, and ovaries were collected and screened for SFTSV RNA. Analysis of all samples is currently underway. The present study will allow us to determine the temporal pattern of SFTSV acquisition and dissemination within naturally-infected *H. longicornis*. Understanding the fundamental kinetics of intra-tick SFTSV infection biology will ultimately contribute to the development of new strategies to prevent virus transmission.

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NOVEL HYBRID ELISA AS A SINGLE-TIER TEST FOR LYME DISEASE

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Lyme disease (LD), caused by the spirochete *Borrelia burgdorferi* in the United States and also by related genospecies in Europe, is the most prevalent vector-borne disease reported in the United States. Due to the similarity of LD symptoms to numerous other disease conditions, the clinical diagnosis of LD can be challenging. In the original "standard" two-tier testing (STTT) approach, serum specimens are tested first by an ELISA or an IFA, and positive or indeterminate sera are then tested by separate IgG and IgM immunoblot assays; this serial algorithm attains specificity ≥99.5%. More recently, the "modified" two-tier testing (MTTT) protocol substitutes a second ELISA for the immunoblot, improving sensitivity without a significant drop in specificity. However, two separate tests are still needed. We have developed a Hybrid ELISA based on novel immunochemistry, which has demonstrated sensitivity and specificity equal to or better than STTT and MTTT protocols in preliminary studies. The Hybrid Lyme ELISA makes use of the VlsE protein and the C6 peptide derived from it, which are expressed in almost all known Borrelia strains causing Lyme disease. The sensitivity and specificity of the Hybrid ELISA as a single-tier test were compared with the sensitivity and specificity of two-tier testing algorithms using FDA-cleared test kits. Testing a panel of 486 two-tier negative sera from healthy donors in parallel with 112 sera from confirmed LD patients on the Hybrid Lyme ELISA yielded 97.3% sensitivity and 99.8% specificity. Among 61 patients with early stage LD (defined by erythema migrans), the sensitivity of the Hybrid Lyme ELISA was 95.1% vs. 65.6% for STTT or 80.3% for MTTT ($p<0.05$). The Hybrid ELISA also showed 100% specificity on a panel of 57 sera from patients with potentially cross-reactive conditions. A limitation of the Hybrid ELISA is that IgG reactivity is not differentiated from IgM. The Hybrid ELISA offers the potential to reduce two-tier testing to a single tier test, with equal or better sensitivity, while providing equivalent specificity, which would streamline LD testing, improving testing logistics and cost-efficiency.

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ANTIBODIES CONTRIBUTE TO VACCINE-CONFERRED PROTECTION AGAINST FATAL RICKETTSIOSES IN MICE

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Spotted fever rickettsioses (SFRs) continue to pose a significant threat to public health. We recently demonstrated that a single dose immunization with live and attenuated *Rickettsia parkeri* mutant 3A2 confers complete protection against fatal murine SFRs. In the present study, we sought to reveal the immune correlates of protection conferred by *R. parkeri* 3A2 against murine SFRs. Immunization of C3H/HeN wild type (WT) mice with *R. parkeri* 3A2 triggered a significantly elevated IgG antibody titer against *R. parkeri* that lasted for five months without significant decline. In addition, immunization of *R. parkeri* 3A2 induced a significantly greater percentage

of CD19 (+) CD45R (+) IgD (-) splenic plasma cells in WT mice compared to the counterparts of mock-immunized mice. A single intraperitoneal injection of 3A2 immune sera to naïve severe immunocompromised SCID mice resulted in significant protection against intravenous (i.v.) inoculation with a lethal dose of *R. parkeri* as evidenced by significantly reduced concentrations of rickettsiae in tissues, improved illness, and significantly enhanced host survival compared to those receiving mock immune sera. Notably, passive transfer of 3A2 immune sera also provided protection to naïve scid mice from lethal challenge of *R. parkeri* via intradermal (i.d.) inoculation, with or without tick saliva, compared to those passively transferred with control sera. Incubation of 3A2-immunized mouse sera with WT *R. parkeri* resulted in a significantly reduced number of plaques compared to the counterparts of mock-immunized controls. Collectively, our findings underscore the significance of rickettsiae-specific antibodies in conferring vaccine-induced protection against fatal murine SFRs. Antibodies likely play a crucial role in mediating protection in humans against natural rickettsial infections. We suggest that antibodies constitute essential components of vaccine-induced protective immunity and merit evaluation in future studies focusing on vaccines against tick-borne rickettsioses.

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CAPPABLE-SEQ ENABLES ENRICHMENT AND GENOMIC SEQUENCING OF RNA VIRUSES FROM THE DEER TICK *IXODES SCAPULARIS*

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Tick-borne diseases pose an increasing danger to global public health. In addition to bacterial pathogens, ticks also carry a wide variety of viruses, some of which cause severe human diseases and even fatalities. Although the bacterial pathogens and microbiome of ticks has been extensively characterized, the virome of wild ticks is relatively understudied. Some of the challenges include cumbersome protocols for viral particle purification and limited quantities that can be obtained. Here we demonstrate the use of Cappable-Seq technology to directly enrich and sequence the genomes of multiple RNA viruses from the deer tick *Ixodes scapularis* collected in Ipswich, Massachusetts (USA). Cappable-seq method directly enriches any RNA molecules containing 5' triphosphate ends, by using Vaccinia capping enzyme to install a 3'-desthiobiotin-GTP cap at their 5' ends, which are pulled down using streptavidin beads. This method has been used for enrichment and analysis of various bacterial transcriptomes, particularly from complex mixtures of eukaryotic host and endosymbiotic bacteria or microbiomes. Total RNA extracted from such systems can be directly used for sequencing library preparation. Here, we have analyzed total RNA obtained from multiple pools of 8 to 16 individual ticks, as well as RNA from dissected salivary glands from 20 adult female ticks. Taxonomic analysis of sequencing reads revealed around 10-fold enrichment of reads originating from diverse tick-borne viruses including Powassan virus, Blacklegged tick phleboviruses, South Bay virus, Suffolk mivirus and Deer tick mononegavirales-like virus across different samples. The high read coverage enabled assembly of larger, multi-kilobase fragments of viral transcripts, and even complete S and L subunits (6 kb to 15 kb) of some of these viruses. This study therefore provides a protocol for sequencing-based viromics, facilitating unbiased surveillance and discovery of tick-borne viruses. These methods are also expected to be useful for discovery and characterization of arboviruses carried by other arthropod vectors such as other tick species, mosquitoes and biting flies.

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A DECADE OF CHOLERA BURDEN IN AFRICA, A SPATIAL STATISTICAL ANALYSIS FROM 2011-2020

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Cholera is a public health threat in low and middle income countries, and outbreaks with high case fatality ratios have been observed in Africa in the last decade. To support global efforts in monitoring cholera burden and identifying cholera burden hotspots, our study aims to estimate and map the spatial distribution of suspected cholera burden across Africa between 2011-2020. Leveraging a global database of cholera reports and a Bayesian spatial statistical modeling framework, we produced 20 by 20 km maps of suspected cholera incidence for 2011-2015 and 2016-2020 across cholera-affected countries in Africa. We estimated changes in burden, and the population living in high-risk areas, grouped districts into 10-year risk categories, and compared our maps to cholera occurrence reported during the 2022-2023 WHO-declared cholera emergency. Reported suspected cholera incidence increased between 2011-2015 and 2016-2020 to achieve an estimated mean annual incidence of 125,701 (95% CrI: 124,737-126,717) cases across 43 African countries, with a steady mean annual incidence rate of around 11 cases per 100,000 population. Substantial changes in spatial patterns of reported suspected cholera incidence were observed at the regional scale, with a shift of burden from Western to Eastern Africa, and subnational level, where shifts in 16 of 43 countries. We estimated that 296 million people (95% PI: 282-312 million) lived in high-risk districts (> 10 cases per 100,000 per year) in 2020. Districts with sustained high risk over the 2011-2020 period were more likely to report cholera occurrence in 2022-2023, although 2022-2023 cholera was also reported in low- and moderate-risk districts. Although results are limited by reporting challenges and varying case definitions, these estimates present a unified look at cholera in Africa over a 10-year period. The notable sub-national heterogeneity and spatial distribution changes in cholera burden highlight the value of identifying priority areas to stabilize potential OCV demand. Associating risk factors and interventions with historical cholera burden is crucial in monitoring cholera burden globally.

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A 4-YEAR STUDY OF THE CLINICAL AND ENVIRONMENTAL EPIDEMIOLOGY OF *VIBRIO CHOLERAE* AND HOUSEHOLD TRANSMISSION DYNAMICS IN URBAN DEMOCRATIC REPUBLIC OF THE CONGO: PICHA7 PROGRAM

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The Democratic Republic of the Congo (DRC) has one of the highest rates of cholera in Africa. To investigate the community and household-level *Vibrio cholerae* transmission dynamics in an urban cholera endemic setting in DRC, we conducted a 4-year prospective study in urban Bukavu, DRC. We conducted longitudinal surveillance of diarrhea patients for *V. cholerae* at 119 health facilities. A prospective cohort study of household contacts of cholera patients and their water sources was conducted during the 1-week high risk period for *V. cholerae* infections for household contacts after index patient health facility admission. From March 2020 to March 2024, 1148 diarrhea patients were screened for *V. cholerae* by bacterial culture. Thirty percent of diarrhea patients (342/1148) had stool samples positive for *V. cholerae*. Household stored water and source water samples were collected from 176 cholera patient households. Ten percent of households had a stored water sample positive for *V. cholerae* by bacterial culture, and 5% of had a positive source water sample. Four hundred sixty-one household contacts of cholera patients had stool samples analyzed by bacterial culture. Fifty-six percent of cholera patient households had at least one household contact with a *V. cholerae* infection. This is the first

household contact study of cholera patient households in Sub-Saharan Africa. The findings from this study indicate a high risk of cholera among the household contacts of cholera patients in this cholera endemic setting in DRC. These results demonstrate the need for targeted water treatment and hygiene interventions to reduce cholera in transmission hotspots in DRC.

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ENHANCING CHOLERA SURVEILLANCE IN NEPAL: FINDINGS FROM CHOLERA OUTBREAK IN KATHMANDU VALLEY, 2022

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Early detection and rapid responses are essential for controlling cholera outbreaks. However, the accessibility of cholera diagnostics in hospitals across Nepal is frequently limited, which may result in either overreporting or underreporting of cholera cases. Hence, we have conducted sentinel surveillance in Kathmandu Valley from 2021-2024, triaging samples with RDTs from 2022 outbreak for subsequent culture and PCR analysis. In 2022, we collected stool samples from 21 healthcare facilities in Kathmandu Valley, along with clinical and sociodemographic data through case report forms. Meteorological data including weekly precipitation and air temperature, was sourced from the Nepal Ministry of Hydrology and Meteorology. Furthermore, we conducted antimicrobial susceptibility testing and evaluated the diagnostic accuracy of cholera RDT compared to culture and/or PCR. From April to December 2022, 596 stool samples were collected. Out of 596, 66 were RDT positive (11.09%) and 45 were confirmed with culture or PCR. All culture confirmed vibrio cholerae O1 were sensitive to tetracycline but only 2.44% showed resistance to cotrimoxazole. The most common symptoms in lab-confirmed cholera cases were diarrhea (100%), vomiting (88.89%), nausea (77.78%), and abdominal pain (64.44%). Severe dehydration symptoms were observed in less than 20% of lab-confirmed cholera cases, indicating the limitations of relying solely on clinical symptoms for cholera diagnosis. Also, the air temperature was positively associated with cholera (OR 2.41, 95% CI 1.66-3.51). Preliminary results indicate high sensitivity (100%) and specificity (96.19%) of RDT against culture or PCR. This underscores the importance of on-site RDT for cholera surveillance to ensure timely outbreak detection in endemic regions.

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CHOLERA RESURGENCE IN HAITI, 2022. POST-ELIMINATION CHALLENGES

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Despite declaring cholera elimination in February 2022, Haiti witnessed a resurgence in late 2022. We investigated the first cases of suspected cholera reported to the national cholera surveillance system (NCSS) to determine the characteristics and risk factors of this outbreak. We conducted a mixed-methods investigation, analyzing suspected cholera cases reported to NCSS from September to November 2022. Surveillance data were collected and analyzed. Interviews by field teams provided qualitative insights. Quantitative analyses included univariable and multivariable logistic regression. From September 30, 2022, to November 17, 2022, 105 suspected cholera cases were reported to the NCSS database. 98 cases with stool culture results were included in the analysis. The outbreak started in and predominantly affected the Ouest Department (73.5% of cases), particularly the town/city of Cité-Soleil (63%), with a rapid initial surge. Children under 10 years old (55%) and males (60%) were disproportionately represented. Among cases, exposure to prior cholera vaccination (13%) or cholera (7% previously hospitalized for cholera) was low. Univariable analysis identified recent changes in primary water source (OR=7.29, 95% CI: 1.71-39.23) as a significant factor. Notably, risk factors differed by department: recent water source change in Ouest (OR=1.40, 95% CI: 2.11-83.92) and female sex in Centre (OR=7.30, 95% CI: 1.3-43.02). Interviews revealed overcrowded living conditions and gang violence hindering hygiene practices. The outbreak suggests an initial point source in Ouest, followed by secondary transmission primarily in Centre. Children were disproportionately affected likely due to low vaccination and prior infection rates, and/or increased exposure. Socio-economic and political challenges including gang-violence worsened conditions, causing acute on chronic unsafe water access, thus contributing to the resurgence. Resurgence after a declared elimination highlights the need for continued interventions addressing water and sanitation, vaccination, and socio-political stability.

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AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS OF PROTECTION PROVIDED BY KILLED WHOLE-CELL ORAL CHOLERA VACCINES

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Killed whole-cell oral cholera vaccines (kOCVs) are a standard prevention and control tool, used during outbreaks, humanitarian emergencies and in cholera endemic areas. The last review of kOCV protection was published in 2017; subsequently, new evidence has emerged, and both vaccine availability and use policies have changed. We reviewed available evidence on kOCVs to evaluate duration of protection, one dose protection, and protection in young children. We systematically searched for randomized trials and observational studies that reported estimates of protection against confirmed cholera conferred by kOCVs that don't contain the B subunit. Eligible studies published through March 8, 2024, were included. Data on efficacy and effectiveness were extracted as were number of doses, duration of follow-up, and age group. Efficacy and effectiveness estimates were summarized separately using random effects models to produce estimates of protection by time since vaccination; meta-regression models were used to estimate protection, by dose, as a function of time since vaccination. Twenty-three publications from five randomized controlled trials and 10 observational studies met the inclusion criteria. Average two-dose efficacy was 55% (95%CI: 46-62%) one year after vaccination and 48% (95%CI: 36-58%) three years after vaccination. Average two-dose effectiveness was 74% (95% Confidence Interval [95%CI]: 64-81%) one year after vaccination and 48% (95%CI: 7-71%) three years after vaccination. Average one-dose effectiveness was 77% (95%CI: 62-86%) one year after vaccination, and 48% (95%CI: 17-67%) two years after vaccination. By age, pooled two-dose efficacy was 31% (95%CI: 14-45%, I^2 = 0%) for children <5 and 62% (95%CI: 49-71%, I^2 = 60%) for those ≥5 year during an average 37-month follow-up period. Two kOCV doses provide protection against cholera for at least 3 years. One kOCV dose provides protection for at least two years. Children under five are less protected by kOCV, regardless of the number of doses received.

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EVALUATION OF ORAL CHOLERA VACCINE (EUVICHOL-PLUS) EFFECTIVENESS AGAINST *VIBRIO CHOLERAE* IN BANGLADESH AN INTERIM ANALYSIS

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Millions of doses of the oral cholera vaccine (OCV), Euvichol-Plus™, have been deployed from the global OCV stockpile. Here we evaluate the protection provided by a two-dose regimen of Euvichol-Plus™ using the test-negative design in Dhaka, Bangladesh. Two doses of Euvichol-Plus™ vaccine were delivered in response to a large cholera outbreak in Dhaka, Bangladesh, at least 14 days apart, between June and August 2022. Patients aged ≥1 year on the first day of the vaccination campaign, who had resided in the study area since campaign initiation and presented with acute watery diarrhea to designated health facilities, were prospectively enrolled between August 21, 2022, and August 20, 2023. Fecal culture test-positive cholera cases, with up to four test-negative controls, matched to each case according to age, date of presentation, and health facility, were included in the analysis. Vaccination status was ascertained in a blinded manner from a vaccination register created for this study. A conditional logistic regression model was used to estimate the odds ratio for the relationship between vaccination and disease status. Vaccine effectiveness (VE) was calculated as [(1-odds ratio) ×100]. A total of 226 cases and 552 matched controls were included in the analysis. The VE of two doses of Euvichol-Plus™ against cholera was 66% (99.5% Confidence Interval [99.5% CI]: 30% to 83%) for all ages. For children <5 years, no significant protection (12%; 95% CI: -95% to 60%) was observed, whereas protection was 79% (95% CI: 60% to 89%) for those ≥5 years. The VE against cholera with moderate to severe dehydration was 69% (95% CI: 44% to 83%) for all ages, but 6% (95% CI: -206% to 71%) among children <5 years. Two doses of Euvichol-Plus™ provided significant protection against medically attended cholera of any severity as well as cholera with moderate to severe dehydration. However, significant levels of protection were only observed for those ≥5 years.

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VIRULENT BACTERIOPHAGE, ANTIBIOTICS, AND DEHYDRATION SEVERITY NEGATIVELY IMPACT CHOLERA DIAGNOSTIC PERFORMANCE: AN EXTERNAL VALIDATION STUDY

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Early evidence suggests lytic bacteriophage predation on *Vibrio cholerae* influences the performance of cholera diagnostic tests. Patient's antibiotic exposure and antibiotic resistant patterns of both the bacteria and bacteriophage further influence diagnostic test performance. Our goal was to externally validate previous findings and quantify the impact of bacteriophage, antibiotic exposure, antibiotic resistance, and dehydration severity on cholera diagnostic test performance. We used data from a 2018 cluster randomized controlled trial of uncomplicated acute diarrhea in patients ≥2months of age in 10 district hospitals across Bangladesh. Stools samples were immediately preserved to assure integrity of the nucleic acid. We calculated the cholera rapid diagnostic test (RDT) performance against qPCR gold standard for each of the following: no bacteriophage, combinations of V. cholerae-specific lytic bacteriophages (ICP1, ICP2, ICP3), antibiotics, dehydration severity, and antibiotic resistance in both bacteria and bacteriophage. We estimated the odds ratios (ORs) for RDT correctly detecting cholera in the presence/absence of the listed covariates. Among 2,574 patients, RDT sensitivity ranged from 0.27 (95% CI: 0.08, 0.55) to 0.48 (95% CI: 0.42, 0.54) with different bacteriophage present, while specificity was consistently above 0.8. The odds of correctly testing RDT positive was 2.58 (95% CI: 0.87, 9.49) times higher for those without ICP3 compared to those with ICP3 present. RDT sensitivity was higher in the absence of antibiotics (0.83, 95% CI: 0.61, 0.95), whereas specificity tended to be lower (0.59, 95% CI: 0.41, 0.75). Finally, RDT test performance was better in more severely dehydrated patients. Results incorporating antibiotic resistance patterns are forthcoming. Our findings further document factors that influence cholera diagnostic performance, and support the addition of bacteriophage targets into diagnostic testing platforms. These results support ongoing and future efforts to combine additional factors with diagnostic testing results for clinical decision support.

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DOES INSECTICIDE EXPOSURE IMPACT PLASMODIUM TRANSMISSION?

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Resistance to the pyrethroid class of insecticides is now intense and widespread across much of the world. Insecticide resistance is a complex phenomenon, involving changes to the target site, up-regulation of metabolic enzymes and thickening of the cuticle amongst others. Recently, work has demonstrated that insecticide resistant mosquitoes have a higher rate of respiration than susceptible counterparts, which is then depressed upon pyrethroid exposure; this has been shown phenotypically and through -omics work. Furthermore, it is known that pyrethroid exposure causes changes to underlying redox state in multiple organisms. Taken together, these data indicate that insecticide resistance or exposure may result in changes to underlying redox state of *Anopheles* mosquitoes which may change their vectorial capacity. In this work, we show that pyrethroid exposure causes large tissue specific changes to reactive nitrogen species, which when perturbed reduce the capacity of resistant mosquitoes to carry *Plasmodium falciparum*. Our data indicates changes to the haemocyte populations which may impact ookinete invasion. Finally, we generated RNAseq to piece apart the underlying molecular mechanisms. These data indicate that perturbation to underlying reactive nitrogen species in insecticide resistant mosquitoes may change malaria transmission potential.

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A CELL ATLAS OF *ANOPHELES COLUZZII* MALPIGHIAN TUBULES

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Progress in malaria control is threatened by widespread mosquito insecticide resistance. Monitoring the emergence of insecticide resistant mosquitoes using resistance markers is essential to choose effective vector control strategies. Despite the clear role of gene expression in insecticide resistance, current knowledge is derived from a mixture of

mRNA comprising all cell types from either the whole mosquito or dissected tissues. This masks the heterogeneity in gene expression between different specialised cell types; expression in specific cell types that may be pivotal in determining insecticide resistance cannot be assessed. The recently developed technique of single cell RNA sequencing is transforming understanding of gene regulation. Malpighian tubules (MT) are single layered tubes of epithelial cells draining urine to the midgut: hindgut boundary. Comprised mainly of ectodermal principal cells and mesodermal stellate cells, with distinct cell shapes and functions, MT are responsible for excretion of toxins and contribute to their breakdown. MT express genes implicated in insecticide resistance including cytochrome P450s and ABC transporters. Essential for mosquito for survival, they are also a promising new target for insecticides, as currently used ones largely target the nervous system. We present an optimised protocol to isolate nuclei from dissected *Anopheles* tissues and a cell atlas of *A. coluzzii* Malpighian tubule gene expression, including cell type specific marker genes. Furthermore we will show a cell type resolution comparison of gene expression between the susceptible N'Gousso strain and the pyrethroid, organophosphate, organochlorine and carbamate resistant VK7 strain. We investigate how gene expression and stoichiometry (the numbers of cells of each type) may contribute to the resistance function of mosquito MT. The implications for understanding cell type specific insecticide resistance mechanisms and potential target molecules for novel insecticides will be discussed.

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ELUCIDATING THE ROLE OF ARGININOSUCCINATE LYASE IN CONFERRING PYRETHROID RESISTANCE IN THE MAJOR AFRICAN VECTORS *ANOPHELES FUNESTUS*

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Escalating pyrethroid-resistance are emerging in major malaria vectors such as *Anopheles funestus* threatening malaria control and elimination. Unfortunately, the molecular drivers of this super-resistance remain unknown hindering the design of suitable resistance management strategies. Previous RNAseq-based transcription analyses revealed the overexpression of Argininosuccinate lyase (ASL), in pyrethroid-resistant *An. funestus* but the underlying mechanism as well as the genetic factors associated to this overexpression remain unknown. This study aimed to elucidate such factors, detect key DNA markers to design diagnostic tools to track and manage ASL-resistance before it spreads Africa-wide. In this study, after assessing the expression level of this gene in F1 progeny from *An. funestus* populations in Cameroon, Uganda, Ghana, and Malawi, the coding sequence and the 1kb upstream promoter of the ASL were sequenced to detect key allelic variants which were overexpressed in *Drosophila melanogaster* followed by RNAi experiments with field-collected *An.funestus* from Mibellon, Cameroon to validate its role in conferring resistance to pyrethroid. Quantitative PCR confirmed that ASL was upregulated in pyrethroid-resistant populations from Uganda (Fold-change (FC)=33.14±6.34), Ghana (FC=19.92±11.01), Cameroon (FC=9.13±4.8), and Malawi (FC=14.89±3.43). Although this gene was highly polymorphic at both coding and promoter region in resistant mosquitoes. Transgenic expression in *D. melanogaster* demonstrated that overexpression of this gene alone confers resistance to pyrethroids with a significant difference of mortality between ASL transgenic flies compared to the control. Silencing of the gene in the Mibellon population confirmed its implication in pyrethroid resistance with a significant recovery of susceptibility. Higher frequency of the ASL-resistant allele in Uganda compared to all other localities. Our study demonstrates for the first, the roles of ASL in conferring insecticide resistance in *An. funestus* across Africa and provides a DNA-based diagnostic assay for field monitoring of this resistance.

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UNDERSTANDING SELECTION DYNAMICS AND EVALUATING EFFICACY OF INSECTICIDE RESISTANCE MANAGEMENT STRATEGIES USING KNOCK-DOWN RESISTANT *AEDES AEGYPTI*

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Insecticide resistance poses a major challenge for mosquito population control and disease prevention, with knock-down resistance (*kdr*) being one of the most prevalent resistance mechanisms. This study investigates the V1016I and F1534C *kdr* mutations within *Aedes aegypti* to address knowledge gaps in insecticide resistance evolution and management. We investigated both male and female mosquitoes of six different *kdr* genotypes, including heterozygotes. Resistance profiles against deltamethrin and life history traits were quantified, and the efficacy of two insecticide resistance management strategies - low-dose and high-dose-refugee treatments using deltamethrin - were compared to traditional high-dose deltamethrin treatment and no insecticide application across ten generations. We show that male mosquitoes exhibited similar resistance profiles to females when sex and weight differences are considered. This suggests males could be used for resistance surveillance, expanding the sample size of surveillance efforts. Additionally, resistance profiles indicated that the *kdr* mutations were incompletely recessive, which could lead to their persistence within heterozygous individuals even after the removal of insecticides. Life history traits were measured for all mosquito life stages and no fitness costs were observed. This further suggests that these *kdr* mutations are likely to persist in insecticide-free environments, minimizing the possibility of natural reversion of insecticide resistance. Finally, preliminary data suggest that high-dose-refugee treatments may be the best approach for inducing moderate population control (i.e., mortality) with little-to-no increase in insecticide resistance frequency. In line with the no observed fitness costs, no reduction in insecticide resistance frequency was observed for populations with no insecticide exposure. Collectively, this work indicates that *kdr* mutations are likely to persist within mosquito populations, even with reduced selective pressure for insecticide resistance and highlights the need for novel insecticide chemistry and/or other control tools.

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MITIGATING INSECTICIDE RESISTANCE WITH GENERATION MICROBIAL BIOPESTICIDES

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Mosquito insecticide resistance is one of the greatest hurdles for malaria control. Novel environment-friendly insecticides with new modes of actions are therefore required, along with strategies to mitigate insecticide resistance based on synergists that can enhance the potency of current insecticides. We have developed a novel microbial biopesticide from a common soil-dwelling bacterium *Chromobacterium* sp. Panama (Csp_p). Semi-field trials with Csp_p as an attractive toxic sugar bait (ATSB) in Burkina Faso showed high efficacy against local pyrethroid-resistant *Anopheles* mosquitoes. Exposure to no-lethal doses of the Csp_P biopesticide reverted the observed pyrethroid-resistance *Anopheles* mosquitoes. To the best of our knowledge, this is the first demonstration of a biopesticide with both mosquitocidal and insecticide synergistic activity.

7575

URIDINE DIPHOSPHATE (UDP)-GLYCOSYLTRANSFERASES (UGTS) CONFER INSECTICIDE RESISTANCE IN THE MAJOR MALARIA VECTORS *ANOPHELES GAMBIAE S.L* AND *ANOPHELES FUNESTUS*

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Insecticides which target the *Anopheles* mosquito are the primary method to control malaria. The widespread nature of insecticide resistance threatens the control of this disease, exemplified by 249 million cases in 2022, an increase from 247 million in 2021. To reverse the stall in malaria control, there is an urgent need for new vector control tools, which necessitates understanding the molecular basis of insecticide resistance. In this study, we utilised RNAseq, microarray and whole genome sequence data to identify overexpression of uridine-diphosphate (UDP)- glycosyltransferases (UGTs) across multiple *Anopheles* species. Phylogenetic analysis identifies sequence similarities between Anopheline UGTs and those involved in agricultural pesticide resistance to pyrethroids, pyrroles and spinosyns. Expression of five UGTs was investigated with qPCR in *An. gambiae* and *An. coluzzii* to characterise constitutive over expression, induction, and tissue specificity. Furthermore, a UGT inhibitor restored susceptibility to pyrethroids and DDT in *An. gambiae*, *An. coluzzii*, *An. arabiensis* and *An. funestus,* the four major African malaria vectors. This study therefore provides *in vivo* evidence of the role of UGTs in insecticide resistance as well as highlighting the potential use of the inhibitor, sulfinpyrazone, as a novel synergist for malaria vector control.

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DISCOVERY OF KNOCK-DOWN RESISTANCE IN THE MAJOR MALARIA VECTOR *ANOPHELES FUNESTUS* REVEALS THE LEGACY OF PERSISTENT DDT POLLUTION.

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A major mechanism of insecticide resistance in arthropod pests is knock-down resistance (kdr) caused by mutations in the voltage-gated sodium channel (Vgsc) gene. Common in most malaria Anopheles vector species, kdr mutations have never been observed in Anopheles funestus, the principal vector in Eastern and Southern Africa. From whole-genome sequencing of 333 An. funestus samples from a breadth of populations in Tanzania, we found 8 novel amino acid substitutions in the Vgsc gene, including the kdr variant, L1014F (L976F in An. funestus), in tight linkage disequilibrium with another (P1842S). The mutants were found only at high frequency in one region, with a significant decline between 2017 and 2023. When evaluating the resistance phenotype of these samples, we found a strong association between L976F and survivorship to the exposure to DDT insecticide, but no association with a pyrethroid insecticide (deltamethrin). No DDT products are currently prequalified by WHO for vector control, and the chemical is banned in Tanzania. However, widespread DDT contamination and a legacy of extensive stockpiles in the same region where we found the kdr alleles, may have selected for this evolution. Continued monitoring is necessary to confirm the origin of kdr in An. funestus, and how it may threaten the effectiveness of insecticide-based vector control in Africa.

7577

INVESTIGATION OF AN UNEXPLAINED NEUROLOGICAL SYNDROME IN A CLUSTER OF INDIVIDUALS IN BUNDIBUGYO DISTRICT, UGANDA

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In September 2023, Bundibugyo Hospital, located in western Uganda, notified the Viral Hemorrhagic Fever (VHF) laboratory at Uganda Virus Research Institute (UVRI) of an unexplained neurological illness characterized by lower limb weakness and tremors. Samples were submitted for VHF investigations, including metagenomic next-generation sequencing (mNGS). In December 2023, field investigations were conducted by members of the Ugandan Ministry of Health, UVRI VHF program, and the Uganda Field Epidemiology Training Program and found only female individuals were affected. In February 2024, using a hypothesis-generating questionnaire, the investigating team performed comprehensive neurological examinations and collected further clinical and demographical data. A differential diagnosis was formed, prompting additional laboratory tests. Various samples—whole blood, plasma, serum, urine, stool, and nasal swabs—were collected accordingly. As of April 2024, the VHF lab has received 30 unique samples from symptomatic cases. Nucleic acids from these cases tested positive for malaria (12/N) using a TaqMan Array Card assay, while mNGS analysis identified Ekpoma 2 virus infection in 2 out of 8 samples. A real-time reverse transcription polymerase chain reaction (RT-qPCR) assay designed for Ekpoma 2 virus confirmed mNGS findings and detected one more case, bringing the total positive cases to 3/N. The detection of Ekpoma 2 virus, a pathogen with no known association with human disease but with potential pathogenicity, emphasizes the need for extensive epidemiological investigations and advanced laboratory testing in discovering and characterizing new infectious pathogens. More work to better understand the clinical implications of Ekpoma 2 virus in this outbreak, as well as to define other underlying causes of disease for focused public health measures, is being done and will be presented at the conference.

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NIPAH VIRUS IN BREAST MILK: EXPANDING THE HORIZON OF TRANSMISSION DYNAMICS

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Nipah virus (NiV) causes acute encephalitis and/or respiratory illness in humans, with a high case fatality rate ranging from 40-75%. In Bangladesh, there have been 343 reported cases of human NiV infection since its first isolation in 2001. Typically, NiV cases are detected during the winter months of December through April, coinciding with the period

of harvesting and consumption of raw date palm sap (DPS), a popular local delicacy. Consuming DPS contaminated with Pteropus fruit bat (*Pteropus medius*) urine or saliva, as well as exposure to the bodily fluid of an individual infected with NiV, are the primary risk factors for NiV infection in Bangladesh. From December 2022 to February 2023, we detected 14 NiV cases through the National Nipah surveillance platform. During one of the NiV outbreak investigations in 2023, the breast milk of a nursing mother infected with NiV was tested by one-step real-time reverse-transcriptase-polymerase-chain-reaction (rRT-PCR) to detect NiV-RNA. Since the newborn had developed Nipah-like symptoms, they were also tested as a suspected NiV-infected case. We detected NiV, specifically NiV RNA, in the breast milk sample of the mother by rRT-PCR (Ct value 26·45). During the outbreak investigation, it was determined that the mother had consumed raw DPS nine days before her delivery. The newborn was exposed to maternal bodily fluids during delivery and breastfeeding and was in prolonged maternal contact during caregiving. Subsequently, the baby tested positive for anti-Nipah IgM ELISA, which was detected in the serum sample. Additionally, the rRT-PCR assay using nucleic acids extracted from the throat swab of the baby also confirmed the presence of NiV (Ct value 26·88). Our findings signify a crucial step-forward in understanding the transmission dynamics of NiV, especially regarding the risk of vertical transmission through breast milk. We propose the inclusion of breast milk testing in NiV diagnostic protocols for symptomatic mothers. This approach would enhance our understanding of mother-to-child NiV transmission and pave the way for more effective containment strategies.

7579

DENGUE VIREMIA KINETICS AND THE EFFECTS ON PLATELET COUNT AND CLINICAL OUTCOMES

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Dengue, a top 10 global health threat according to the WHO, has been increasing in incidence over the past three decades. Higher peak viral loads have been linked to more severe forms of dengue, but data on kinetics and association with specific clinical outcomes are limited and inconsistent. This pooled analysis investigates viremia kinetics and effects on platelet count, severe dengue, and plasma leakage in 2340 Vietnamese dengue patients enrolled in three studies with daily viremia and platelet count measurements between 2000 and 2016. Viremia kinetics were assessed using a random effects model accounting for left-censored data. To examine the effect of viremia on each specific illness day on subsequent platelet count and clinical outcomes, we respectively used a landmark approach with a random effects model and logistic regression with generalized estimating equations. The model-derived rate of viremia decline was assessed for its effect on clinical outcomes using logistic regression. Results revealed a rapid decline in viremia following symptom onset, with serotype-dependent variations. DENV-1 exhibited the highest and longest detectable viremia, while DENV-4 had the fastest clearance. Higher viremia levels at any illness day correlated with lower subsequent platelet counts from day 6 onwards. Elevated viremia increased the risk of subsequent severe dengue and plasma leakage, with a diminishing effect over illness day. A faster decline in viremia was associated with a reduced risk of these outcomes (odds ratio in each subgroup of serotype and immune status ranged between 0.09 and 0.78 per 0.5 log-10 copies/ml/day increase in the rate of viremia decline). This study provides comprehensive insights into viremia kinetics and its effect on platelet count and clinical outcomes in dengue. Our findings underscore the importance of early-phase viremia measurement in dengue research. Furthermore, the observed association between a faster decline in viremia and a reduced risk of severe outcomes provides a compelling rationale for utilizing the rate of viral clearance as a primary outcome in phase-2 dengue antiviral trials.

7580

CHARACTERIZATION OF ANTIGEN-SPECIFIC HUMORAL IMMUNE RESPONSES IN ACUTE AND PAST DENGUE, ZIKA, AND WEST NILE VIRUS INFECTIONS

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In context of the increasing burden of flavivirus infections caused by the raising case numbers in endemic areas and the spread to up-to-now unaffected geographic regions, the importance of reliable tools for acute diagnostics, evaluation of vaccine responses, and serosurveillance studies is growing. Nevertheless, unambiguous identification of antibodies in samples originating from countries where several flaviviruses are co-circulating is hampered by strong antigenic cross-reactivity. Recently, we developed and validated Fc receptor-based enzyme linked immunosorbent assays (ELISAs) for isotype-specific detection of anti-Dengue virus (DENV), anti-Zika virus (ZIKV), and anti-West Nile virus (WNV) antibodies. In these assay systems, cross-reactive signals are suppressed by addition of an assay-specific Specificity Enhancer reagent, enabling serological differential diagnosis of acute and past flavivirus infections even in samples from probands having experienced multiple consecutive flavivirus infections/vaccinations. Here, we employ these tests for the in-depth characterization of the antigen-specific humoral immune response (IgM, IgG) in acute and past DENV, ZIKV, and WNV infections using comprehensive longitudinal serum panels from returning travelers, West Nile fever patients from Ukraine, and patients from Dengue fever endemic areas in South America (Colombia) and Asia (Lao People's Democratic Republic). In particular, we study the humoral immune responses targeting the Nonstructural Protein 1 (NS1) and the Envelope Protein (EP) of the respective viruses as detected by ELISA in comparison to full virus IgM/IgG indirect immunofluorescence testing (IIFT). Our data show clear differences in the seroconversion patterns detected for the NS1 antigen in comparison to other viral proteins including EP that should be considered when choosing serological assays for a defined intended use (e.g. acute diagnostics of flavivirus infections or flavivirus seroprevalence studies).

7581

A MULTIVARIATE SPATIAL MODELING OF SIMULTANEOUS EPIDEMICS OF DENGUE, CHIKUNGUNYA, AND ZIKA IN COLOMBIA

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Dengue, chikungunya, and Zika are *Aedes*-borne diseases (ABD) that caused large simultaneous epidemics in the 2010s in Latin America and the Caribbean. Evidence suggests that these diseases are temporally and spatially connected, though there is a limited understanding of their co-circulating patterns and contributors at the population level. We modelled registered cases of dengue (n=29,1820), chikungunya (n=75,913), and Zika (n=72,031) by municipality in Colombia from 2014 to 2016 with a Poisson-multinomial multivariate spatial model, which is a novel approach

for analyzing simultaneous epidemics. The model estimated the relative risk of total combined cases and, given the total, the probability of disease presence for each disease, as well as the association with covariates. We found an increased risk of ABDs in regions historically burdened with dengue (valleys and south of the Andes), tourist locations (Caribbean coast), and near borders with other countries. In general, the probability of dengue presence was greater than that of chikungunya and Zika, although chikungunya was more likely present in certain coastal municipalities and Zika on the Caribbean islands. Temperature was found as the main contributor to the total ABD cases (RR 2.32, 95%CrI 2.05-2.64). Compared to dengue, chikungunya and/or Zika was more likely present in municipalities with fewer green spaces (OR 0.75, 95%CrI 0.65-0.86, and 0.85, 95%CrI 0.74-0.99, respectively). Chikungunya's presence tended to occur in more socially vulnerable areas, compared to dengue (1.20, 95%CrI 0.99-1.44) and Zika (1.19, 95%CrI 0.95-1.48). Zika was more likely present in municipalities with higher amounts of rainfall compared to dengue (OR 1.18, 95%CrI 1.01-1.37) and chikungunya (OR 1.20, 95%CrI 1.04-1.37). This is the first study to analyze simultaneously the epidemics of ABDs in Colombia using a multivariate spatial novel model. We found important differences between the diseases that can help guide interventions, such as aimed at preventing the importation of cases in border and tourism locations and reducing the burden of chikungunya in socially vulnerable regions.

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PANDEMIC BURDEN IN LOW-INCOME SETTINGS AND IMPACT OF LIMITED AND DELAYED INTERVENTIONS: A GRANULAR MODELLING ANALYSIS OF COVID-19 IN KABWE, ZAMBIA

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Global discussions, such as WHO's Pandemic and Resilience for Emerging Threats, are taking place to drive binding pandemic preparedness agreements going forward. These call for the formulation of plans and priority actions underpinned by learnings from the COVID-19 pandemic. Yet to date, systematic limitations in epidemiological surveillance data in low-income countries (LICs) have forestalled robust retrospective assessments of the likely true burden of COVID-19 and of limited and delayed access to pandemic mitigation strategies in such settings. We analysed COVID-19 seroprevalence and all-cause excess deaths data from the peri-urban district of Kabwe, Zambia between March 2020 and September 2021 with a novel mathematical model. Data encompassed three consecutive waves caused by the wildtype, Beta and Delta variants. Across all three waves, we estimated a high cumulative attack rate, with 78% (95% credible interval, CrI, 71-85) of the population infected, and a high all-cause excess mortality, at 402 (95%CrI 277-473) deaths per-100,000 people. Ambitiously improving healthcare to similar capacity as in high-income settings, could have averted up to 46% (95%CrI 41-53) of accrued excess deaths, if implemented from June 2020 onward. An early and accelerated vaccination rollout, conversely, could have achieved the highest reductions in deaths. Had vaccination started as in some high-income settings in December 2020 and with the same daily capacity (doses per-100 population), up to 68% (95%CrI 64-71) of accrued excess deaths could have been averted. Slower rollouts would have still averted 62% (95%CrI 58-68), 54% (95%CrI 49-61), or 26% (95%CrI 20-38) of excess deaths if matching the average vaccination capacity of, respectively, upper-middle-, lower-middle-, or LICs. Our study represents the first COVID-19 analysis in an African LIC to break away from relying on official cases and death counts, opening-up new avenues to exploit sparse epidemiological surveillance data typical of LICs. Robust quantitative analyses of pandemic data are of pressing need to inform global pandemic preparedness commitments going forward.

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PREVALENCE OF ASYMPTOMATIC MPOX INFECTION IN THE SAN FRANCISCO BAY AREA, 2022

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Mpox (formerly monkeypox) virus is an enveloped, double stranded DNA virus in the orthopox genus. Historically, mpox has caused isolated infections or small outbreaks with limited human to human transmission in West and Central Africa. However, the 2022 global mpox outbreak was unique in its size and scope, with more than 90,000 cases reported in over 100 non endemic countries. Further, this outbreak is unique in that it disproportionately (though not exclusively) has affected gay, bisexual, and other men who have sex with men, with transmission occurring largely through sexual networks. Outbreaks of emerging pathogens such as mpox virus in non-endemic areas pose several challenges from a public health perspective, including the lack of dedicated public health infrastructure and staff to detect and respond to infections. To address this challenge, our research team implemented a collaborative multifaceted approach to increase the detection of mpox infections in the San Francisco Bay Area, one of the most heavily impacted areas in the United States. First, our team developed an in house mpox virus qPCR assay. This assay was then used to screen all remnant samples gathered for bacterial STI testing from April to September 2022 in the public hospital and clinic system of San Mateo County, a county of 800,000 people in the Bay Area. Further, working with LGBTQ+ community leaders and organizations we implemented an ongoing study in which people at public venues, including City and County Pride events and queer-focused sex positive parties, were offered free mpox PCR and antibody testing. Using these methods we identified several mpox infections which had hitherto been undetected. Additionally, our presence at queer community events allowed us to provide information related to mpox infection and to increase community awareness of continued mpox spread.

7584

FACTORS INFLUENCING SCALE-UP OF COMMUNITY-WIDE MDA FOR SOIL-TRANSMITTED HELMINTHS: A MULTI-SITE QUALITATIVE ANALYSIS

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Soil-transmitted helminth infections (STH) account for an estimated 2.7 million disability-adjusted life years annually. Current World Health Organization (WHO) guidelines recommend controlling STH-associated morbidity through periodic deworming of at-risk populations, including pre-school and school-age children and women of reproductive age (15-49 years). However, there is increasing interest in community-wide mass drug administration (cMDA)—which includes deworming adults who may serve as reservoirs of infection—as a method to improve coverage and possibly to interrupt STH transmission. We investigated determinants of cMDA coverage and opportunities to scale cMDA by collecting and comparing qualitative data from three countries (Benin, India, and Malawi) participating in a large cMDA cluster randomized trial called the DeWorm3 trial. We collected data at study endline, following six rounds of biannual cMDA. We used the Consolidated Framework for Implementation Research (CFIR) to guide design of data collection tools and to inform a primarily deductive codebook. We conducted 56 focus group discussions (FGDs) and 7

individual interviews (20 FGDs in Benin, 18 FGDs in India, and 18 FGDs and 7 IDIs in Malawi) with health center staff, volunteer drug distributors, community drug distributors (CDDs), and community members. We identified six overarching themes describing determinants of future opportunities to scale-up cMDA: (1) community members prefer cMDA to standard-of-care school-based delivery, (2) door-to-door delivery is highly acceptable, although logistically challenging (3) there is strong support to scale-up cMDA, but skepticism about the feasibility, (4) cMDA at scale requires investment in community sensitization, (5) CDD behaviors drive ability to deliver cMDA with high coverage at scale, and (6) programs can expect community resistance initially; with increased acceptance over time as programs build trust. These themes are elaborated upon within twelve subthemes describing specific opportunities and challenges for delivering cMDA at scale across these three heterogenous settings.

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ADDRESSING CHALLENGES IN SOIL TRANSMITTED HELMINTHIASIS CONTROL IN BANGLADESH: LESSONS FROM 15 YEARS OF MASS DRUG ADMINISTRATION

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Bangladesh has been conducting bi-annual school-based mass drug administration (MDA) since 2008 to combat soil-transmitted helminth (STHs) infections. However, despite 15 years of sustained efforts, the government faces persistent challenges in meeting target objectives. This study assessed the current status of STHs prevalence and identified barriers hindering the effectiveness of MDA in hard-to-reach setting of the northeastern region of Bangladesh. A mixed-method study was conducted in the Sylhet divisions of Bangladesh, wherein stool samples from 1800 school-aged children were examined using the Kato–Katz thick smears and Harada-Mori technique. Additionally, 160 questionnaire surveys, 12 in-depth interviews, 8 focus group discussions, and 2 key-informant interviews were conducted among 238 participants, including school-age children, parents, teachers, health workers, community leaders, and MDA program managers. Quantitative data underwent descriptive statistical analysis, while thematic analysis was applied to qualitative data. The prevalence of any STHs infection was 26.83% where *Ascaris lumbricoides* exhibited the highest prevalence (32.29%), followed by hookworm (19.46%), *Trichuris trichiura* (18.01%), and *Strongyloides stercoralis* (12.21%). Participants expressed positive attitudes towards MDA but highlighted difficulties in reaching non-school-going children. MDA coverage was lower than reported by the government, attributed to inadequate drug distribution policies, communication gaps, and misinformation about side effects. A significant number of school-age children did not take any anthelmintics or receive MDA medications. Despite 15 years of MDA, STHs prevalence remains high among school-aged children in Bangladesh. Achieving equitable MDA coverage is facing challenges in the hard-to-reach setting of the northeastern region of Bangladesh, necessitating reevaluation of drug distribution, utilization of local channels for community engagement, establishment of additional distribution points, robust monitoring, and prioritization of health education.

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FACTORS INFLUENCING THE UPTAKE OF MASS DRUG ADMINISTRATION FOR SCHISTOSOMIASIS AMONG PRESCHOOL-AGED CHILDREN: A CROSS-SECTIONAL STUDY FROM MADAGASCAR

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The World Health Organization (WHO) has recently recommended mass drug administration (MDA) with praziquantel (PZQ), the main strategy to control schistosomiasis, for preschool-aged children (PSAC). The availability of the drug alone is not enough to guarantee a successful uptake and experiences from MDAs for other diseases highlight that acceptance of treatment for PSAC may be influenced by several factors, such as fear of adverse events (AE). This study aims at exploring the factors influencing the uptake of PZQ through MDAs in children aged 9-24 months (mo) in the regions of Boeny and Haute Matsiatra of Madagascar.The cross-sectional study was performed from February to December 2023 to enrol 5000 children. A PZQ treatment was offered to the caregivers of children in medical and non-medical settings. Quantitative data were collected to assess factors influencing the uptake, including socio-demographic characteristics, individual awareness, previous experience with PZQ and knowledge of schistosomiasis.A preliminary analysis of the data of 1880 children (925, 51.4% females and 875, 48.6% males) showed that the most of them (614, 34.1%) were in the age group 18-24 mo. Among the caregivers, 1649 (91.5%) were the mother, 542 (30.1%) were accompanied by a relative, and most of the interviewed had secondary education (833, 46.2%), while 126 (7.6%) had no education. Many of them (945, 52.4%) had heard of PZQ, 740 (41.1%) had previous experience with PZQ treatment for other children, 1002 (55.7%) had no concerns about AE. The treatment uptake was 84.7% (95%IC 82.9-86.3). Having heard of PZQ, previous experience with PZQ and being accompanied were positively associated with the uptake, the fear of AE and the level of education showed a negative association. For children, the older age and having siblings presented a positive association. Our preliminary results show an uptake higher than the treatment coverage suggested by WHO, encouraging the promotion of this intervention in Madagascar. This study will contribute to shape the global strategy for the implementation of PZQ treatment among PSAC that is being rolled out in the next years.

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EXPLORING THE RELATIONSHIP BETWEEN WASH (WATER, SANITATION, AND HYGIENE) ACCESS IN SCHOOLS AND SCHISTOSOMIASIS PREVALENCE

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The National Neglected Tropical Disease Program in Sierra Leone conducted schistosomiasis (SCH) baseline mapping in all 16 health districts (HDs) between 2008 and 2009. The results were low (≥1 and <10%) prevalence in five HDs; moderate (≥10 and <50%) in five HDs; and high (≥50%) in four HDs. After over a decade of mass drug administration (MDA) in Sierra Leone, SCH impact assessment surveys were conducted

between 2022-2024 in the nine high/moderate HDs to evaluate the impact of treatment. The results showed that SCH has significantly reduced from an average prevalence of 42.2% at baseline to 19.7%. The World Health Organization (WHO) promotes preventive chemotherapy and water, sanitation and hygiene (WASH) to maintain these gains. A WASH survey using the WHO Joint Monitoring Program indicators was integrated into the SCH impact assessments to understand the relationship between SCH prevalence and the accessibility and utilization of basic WASH services in schools. A total of 8,360 school-aged children were sampled in nine HDs. The results showed gaps in WASH access, with over half (52.6%) of school children lacking water service. There was a significant difference noted for SCH prevalence by access to drinking water with increased prevalence in schools with limited or no access to drinking water (p<0.001). In total 5,030 children (60.2%) of children had no sanitation service in their schools and a significant difference in SCH prevalence was reported among children with no sanitation access (20.8%), limited sanitation service (18.0%), and basic access (18.1%) (p = 0.010). In total, 44.0% of children had no access to handwashing facilities in school. Again, results indicate that children who tested positive for any SCH varied significantly in terms of basic hygiene services (basic, limited and no service) (p = 0.046). The lack of access to basic WASH facilities in schools shows a link with higher rates of SCH infection among school children, highlighting the critical role of WASH infrastructure in disease transmission and control. Improving access to WASH in both schools (and the community) is a key factor for reducing SCH prevalence in Sierra Leone.

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MODELING THE IMPACT OF IMPROVED WATER, SANITATION AND HYGIENE CONDITIONS DUE TO THE CORONAVIRUS DISEASE PREVENTION MEASURES ON SOIL-TRANSMITTED HELMINTHIASIS AND SCHISTOSOMIASIS INFECTIONS IN KENYA: WHAT LESSONS CAN WE LEARN FROM THIS NATURAL EXPERIMENT?

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Kenya has been implementing deworming programme since the year 2012 as the mainstay control approach for soil-transmitted helminthiases (STH) and schistosomiasis (SCH). This study sought to model the effect of improvements in water, sanitation and hygiene (WaSH) and other socio-economic, public health, and infrastructure improvements, as a result of the coronavirus disease (COVID-19), both at school and household levels on the prevalence of STH and SCH infections in Kenya. The study used secondary data collected by the Kenyan National School-Based Deworming programme before (2018) and after (2021) the COVID-19 pandemic in Kenya. Principal component analysis was used to create indices for WaSH and other instituted public health measures. Multivariable, mixed effects, difference-in-difference models were used to establish whether these preventive measures led to statistically significant reductions of STH and SCH prevalence between the 2018 and 2021 surveys and to determine the magnitude of the reductions. The overall average prevalence was 12.9% (95%CI: 10.4-16.1) and 6.4% (95%CI: 3.3-12.6) for any STH and SCH respectively during the 2018 survey. This prevalence dropped to 5.8% (95%CI: 5.7-6.0) and 5.1% (95%CI: 3.8-6.9) for any STH and SCH in the follow-up evaluation survey in 2021. Statistical modeling indicated that mass treatment, improvements in water-related conditions, and individual, school and household levels demographic conditions contributed significantly to the decline in STH prevalence by 4.73% (Coef. -4.73, (95%CI: -5.32; -4.14), p < 0.001), 1.32% (Coef. -1.32, (95%CI: -1.89; -0.77), p < 0.001), and 0.92 % (Coef. -0.92, (95%CI: -1.45; -0.40), p = 0.001) respectively. While improvements in sanitation and individual, school and household levels demographic conditions contributed significantly to the decline in SCH prevalence by 1.98% (Coef. -1.98, (95%CI: -2.39; -1.58), p < 0.001) and 0.95% (Coef. -0.95, (95%CI: -1.37; -0.52), p < 0.001) respectively. This study provides strong evidence that school-based mass treatment and specific WaSH components are needed for sustainable parasite elimination in Kenya.

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IMPACT OF FOUR ROUNDS PER YEAR OF IVERMECTIN TREATMENT IN THE WUDI GEMZU HOTSPOT, METEMA SUB FOCUS, NORTHWEST ETHIOPIA

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Onchocerciasis or “river blindness” is a parasitic disease caused by the filarial worm *Onchocerca volvulus*, transmitted by repeated bites of infected blackflies. The first internationally coordinated interruption of onchocerciasis transmission happened in the Galabat (Sudan)-Metema (Ethiopia) focus in 2017. The focus met the WHO thresholds for transmission interruption in both serological (i.e., upper 95% confidence limit [CL] for children’s Ov16 seroprevalence by ELISA at 0.038% vs. threshold of <0.1%) and entomological evaluations (i.e., upper 95% CL for prevalence of infective flies by O-150 PCR at 0.31 vs. threshold of 1/2000). However, there were 2 positive fly pools in Diviko kebele of the Wudi Gemzu area in Ethiopia, previously indicated as a hotspot by persistent positives in impact assessments. Mass drug administration (MDA) was halted in 2018 in both country sub-foci except for the Wudi Gemzu hotspot (population ~18,000), where the Ethiopia program started enhanced MDA up to four times per year. From 2018 to 2023 we provided 18 rounds of MDA with good coverage (i.e., 85-95%) and geographic coverage of 100%. Education and training was provided to health workers, community members, and blackfly catchers to raise awareness. We evaluated impact by testing blackfly pools with O-150 PCR followed by Ov16 ELISA indicating exposure in children. An interim evaluation conducted in four sites in the hot spot in 2019 found one positive pool of 38 pools (6,453 flies) in Asafekari village in Diviko kebele, 15km from the 2017 positive site. In 2021, all 36 pools (5,955 flies) from the same sites were negative (upper 95% CL=0.64/2000). On the contrary, 15 out of 685 (2.1%) of children aged 5-10 years living near the entomological surveillance sites in 2021 were Ov16 positive. Based on the improved entomology results from 2021, MDA will decrease to a twice per year regimen in the hotspot but continue with further monitoring. However, MDA may restart in the surrounding post-treatment surveillance (PTS) area, where positive fly pools in 2021 and subsequent epidemiologic data have sparked concerns about reintroduction or recrudescence of transmission.

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EVIDENCE OF INTERRUPTION OF ONCHOCERCIASIS TRANSMISSION IN FOUR DISTRICTS OF NORTHERN GHANA: PRELIMINARY RESULTS FROM A LONGITUDINAL SURVEY TO EVALUATE A 2% OV16 SEROPREVALENCE THRESHOLD FOR STOPPING MASS DRUG ADMINISTRATION

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Onchocerciasis is a filarial disease that causes blindness and is transmitted by some *Simulium* blackflies. The World Health Organization (WHO) has targeted onchocerciasis for elimination through mass drug administration (MDA) of ivermectin. Modeling studies suggest that the WHO Ov16 seroprevalence threshold to stop MDA, <0.1% at the upper 95% confidence interval in children <10 years, may be too strict. To evaluate a 2% threshold, we conducted a baseline serosurvey of children 5-9 years and entomological evaluation for infective blackflies in 4 districts in Northern Ghana where MDA has been ongoing for >15 years. If Ov16 seroprevalence by enzyme-linked immunosorbent assay (ELISA) is <2% and O150 qPCR positivity in blackflies meets the WHO stopping threshold, MDA will be stopped and the area monitored for recrudescence. Districts were stratified by endemicity, villages selected by probability proportionate to estimated size methodology, and children randomly selected within villages. A convenience sample of children from first-line villages was additionally selected. Ov16 IgG4 rapid diagnostic tests (RDT) and Ov16m ELISA were run from eluted dried blood spots made from venipuncture specimens. Blackfly collections lasted 6–12 months from 10 catching sites in the study area and analyzed using O150 with confirmatory ND5 qPCR. RDT and ELISA results were available from 2,126 and 2,128 children, respectively, from 66 villages. Overall Ov16 seroprevalence was 1.3% (95% CI 0.7-2.3%) by RDT and 0.09% (95% CI 0.02-0.55%) by ELISA after adjusting for survey design. qPCR results were available from 233 pools with 22,772 blackflies; 3 sites had 1 positive pool each. Poolscreen prevalence was 0.013% (95% CI 0.003-0.038%). The area met the study criteria for stopping MDA suggesting possible interruption of transmission. Yearly serological and entomological monitoring will continue for 3 years in the area to monitor for recrudescence, followed by an intensive reevaluation of transmission. If no evidence of recrudescence is detected, this would provide evidence that the WHO serologic threshold could be modified, allowing programs to stop MDA sooner.

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CROSS BORDER MOBILITY AND THE OCCURRENCE OF PUBLIC HEALTH EMERGENCIES IN REFUGEE HOST DISTRICTS IN UGANDA

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Uganda has an open refugee policy and receives approximately 70,000 refugees annually, which challenges the health infrastructure capacity of host districts. We investigated the association between refugee influxes and public health emergencies (PHEs) in Uganda, as well as the capacity of host districts to respond to them promptly and effectively. We reviewed 1) PHEs from the electronic PHE management system of the National Public Health Emergency Operations Centre (NPHEOC), and 2) refugee population data from the Uganda refugee data portal, that were available from 2020 through 2023. We determined the association between changes in refugee population and the number of PHEs. We also conducted key informant interviews with 8 subject matter experts. There were a total of 13 PHEs across 13 (100%) of 13 refugee host districts, compared to 25 PHEs across 66 (54%) of 122 non-refugee host districts (Fisher exact test, p<0.005). There was a statistically significant but moderate positive association between the number of PHEs and changes in refugee population within a district (r=0.58, 95% CI 0.70-0.85, p=0.03). During the study period, the NPHEOC was activated 29 times related to the 13 PHEs from refugee host districts. The most frequent activations were related to Rift Valley fever (7 [24%] of 29), anthrax (5 [17%] of 29) and Crimean-Congo hemorrhagic fever (3 [10%] of 29). Madi-Okollo district in the West Nile region, which has the highest number of refugees outside of Kampala, prompted the most activations including 3 related to measles, 2 related to anthrax, and 1 each for food poisoning and rabies. Qualitative interviews identified having a regional PHEOC, training in the electronic Integrated Disease Surveillance and Response, and the activation of district disaster management and task force committees during events as factors that contributed to improved capacity to respond to PHEs. Refugee host districts in Uganda face a significant number of PHEs, which prompts frequent activation of the NPHEOC. Targeted preparedness strategies are necessary to manage PHEs linked to cross-border mobility.

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THE DEADLY ASSOCIATIONS BETWEEN CONFLICT, MALARIA AND MALNUTRITION ACROSS WAR TORN COMMUNITIES IN CENTRAL AFRICAN REPUBLIC ONE OF THE WORLDS MOST CHALLENGING HUMANITARIAN CRISES.

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Central African Republic (CAR) has been torn apart by ongoing armed conflict since 2008. Today, 41% of the population is critically food insecure and one in five are living as forced displaced. Insecurity limits access to many communities, functionality of health care facilities and completeness of health data, and limits the value of conventional nutritional survey methods. Consequently, delivery of humanitarian resources and lifesaving services for children, for whom their nutritional status and its associations with geography, malaria, season and conflict are unknown, may miss those most vulnerable. Since 2008 community health workers (CHWs) trained by the international NGO, The MENTOR Initiative, have consistently delivered essential primary healthcare services to <5 years old living in hard-to-reach and conflict-affected areas in eight subprefectures. CHW monthly records (2015-2021), were analysed with conflict and meteorological data. Associations between counts of global acute malnutrition (GAM), malaria, season and conflict were investigated using negative binomial regression. Of the 457,325 consultations with children aged 6-59 months, 6.2% and 0.4% were classified as moderately or severely malnourished, respectively. The negative binomial model demonstrated differences in counts of GAM by subprefecture. Counts of GAM were positively associated with case rate of severe malaria (*IRR*=1.045; 95% CI: 1.04—1.06) and rainy season (*IRR*=1.10; 95% CI: 1.03—1.17). This analysis demonstrates that GAM levels are underestimated in conflict settings, and may be highest in insecure areas not accessed during the standard nutrition surveys used to inform the targeting of nutritional services. The results prove clear associations between malnutrition, season and malaria, and the need for combined nutritional and health services targeted to reach children most at risk of malnutrition and malaria. Lastly, the unique capacity of CHWs in delivering emergency services in insecure areas and gathering the high quality data needed to better target delivery strategies is well demonstrated.

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INTERNALLY DISPLACED PERSONS AND MEASLES EPIDEMIOLOGY IN THE DEMOCRATIC REPUBLIC OF CONGO: INSIGHTS FROM ROUTINE DATA

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The Democratic Republic of the Congo (DRC) is the second country with the highest number of internally displaced persons (IDPs) worldwide. However the health impact of population movements in the DRC is poorly documented. We used routine data to better understand the dynamics of IDPs and how this affects the surveillance and the dynamics of measles.We extracted routine data from the national surveillance system (measles cases, pediatric tuberculosis and HIV infection, stunting in under-5s, and curative services utilization rate in under-16s), the expanded immunization program (measles vaccination coverage), and the humanitarian platforms (IDPs, road density, conflict events). Effect of IDPs on measles surveillance (reporting, testing, and positivity rates) and prevention (vaccination coverage) was assessed using Spearman's correlation. Risk factors of measles attack rate were assessed using generalized estimated equation (GEE). Time-space clusters of IDPs and measles were assessed using scan statistics. A total of 13,137,897 individuals forcibly fled their homes in the DRC between 2018 and 2022, mostly due to armed conflicts (6,685,052), and in North-Kivu province (4,646,954). Bivariate analysis showed significant negative correlation between IDPs and measles weekly reporting rate ($R=-0.19$, $p<0.001$) and positive correlation with the positivity rate of tested samples ($R=0.13$, $p=0.011$). From the GEE, measles attack rate was significantly associated with reporting rate (AOR=2, $p<0.001$), curative service utilization rate in under-16s (AOR=1.3, $p<0.01$), proportion of IDPs (AOR=-3.1,$p<0.05$), road density (AOR=5, $p<0.001$), and stunting rate in under-5s (AOR=1.2, $p<0.01$). A significant positive interaction was observed between IDPs and reporting rate (AOR=5.8, $p<0.05$). Six significant clusters of measles and two of IDPs were found. A total of 40 health districts were found within the overlapping zone of both IDPs and measles clusters. Population movements significantly affect measles surveillance and disease incidence, calling for tailored control strategies, especially in areas within both IDPs and measles hotspots.

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ASSESSING HEALTH DISPARITIES AND ACCESS: AFGHAN REFUGEES HEALTH IN PAKISTAN THROUGH DATA DRIVEN ANALYSIS

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Pakistan continues to be one of the world's largest refugee-hosting countries with 1.3 million registered refugees, 99 % of which are Afghans. It calls for a thorough examination of health disparities and access within this vulnerable demographic segment. Our study employs rigorous data-driven analysis to evaluate health status and healthcare access among Afghan refugees compared to resident Pakistanis, utilizing the Global Reference List 2018 of 100 Core Health Indicators as a framework. We conducted a population-based cross-sectional study in 2023 including 960 registered Afghan refugees and 20,430 resident Pakistanis. Findings reveal significant variations in health and healthcare access, with marked disparities in essential health service coverage indicators, particularly concerning malaria treatment and fundamental healthcare services. Age and sex stratified analyses further highlights disparities across demographic segments, emphasizing the complex nature of health inequalities within refugee and resident populations. Computation of crude odds ratios with 95% confidence intervals quantitatively underscores these inequalities, laying the groundwork for targeted intervention strategies. The observed disconnect between the Refugee Health Information System and the national health information system highlights the urgent need for reliable health data to inform evidence-based decision-making and ensure equitable access to healthcare services among Afghan refugees in Pakistan. These findings underscore the pressing imperative for evidence-based policy interventions aimed at addressing multifaceted healthcare discrepancies experienced by Afghan refugees, emphasizing the necessity of bridging gaps in healthcare access and mitigating health disparities in Pakistan's refugee population. Ultimately, insights gained from our study are call for action for policy development and resource allocation for tangible improvements in health outcomes for Afghan refugees in Pakistan.

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ENVIRONMENTAL AND TOPOGRAPHIC PREDICTORS OF *FASCIOLA HEPATICA* INFECTED HOUSEHOLDS: INSIGHTS FROM CUSCO, PERU

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Fascioliasis is a public health problem affecting 2.4 million people in more than 70 countries. Half of the world's cases occur in South America, particularly in the Andean region. In Peru, 4533 human cases of *Fasciola hepatica* were reported nationally between 2008-2018 with 80% in the Andes Highlands. Sociodemographic and environmental factors are associated with increased exposure to the infection. This study aims to determine the environmental and topographic predictors of *F. hepatica* infected households in Cusco, Peru. In 2023, multispectral and thermal drone surveys were conducted in the Huayllapata community in Cusco. Households were georeferenced and faecal samples were collected from individuals to identify *F. hepatica* infection through modified Lumbreras rapid sedimentation and Kato-Katz microscopy. Drone imagery was used to build orthomosaics and obtain environmental and topographic variables. We used a geographically weighted logistic regression to identify the factors associated with *F. hepatica* infected households and spatially identify clusters of higher (hotspots) or lower (coldspots) coefficient impact. A total of 160 individuals and 61 households were analysed, finding an overall *F. hepatica* prevalence of 10.0% (CI95%: 6.0% - 16.0%), with 21.3% (CI95%: 12.2% - 34.0%) of households with at least one infected individual. Terrain aspect (TA) (OR = 5.52, p = 0.007), valley depth (VD) (OR = 0.03, p = 0.022) and land surface temperature (LST) (OR = 0.31, p = 0.036) were factors associated with *F. hepatica* infected households. Hotspots of LST were located in the northeast area of Huayllapata while coldspots were in the southwest. The clusters of TA and VD are located opposite to those of LST. This information may prove pivotal for informed decision-making in public policies or targeted intervention strategies.

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VISUALIZING EXCESS MORTALITY TRENDS: BURIAL SITE SURVEILLANCE IN KARACHI, PAKISTAN, PRE AND POST-COVID-19 PANDEMIC

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Geographic Information Systems (GIS) offers a powerful toolset for addressing Pakistan's challenges in accurately documenting deaths, particularly during the COVID-19 pandemic. By integrating burial site surveillance with GIS mapping techniques, this study aims to gather precise spatial data on excess fatalities in Karachi, Pakistan. The study conducted geospatial mapping of 177 burial sites across Karachi's seven districts, extracting data for each graveyard both prospective (2022) and

retrospective (2016-2021) data, considering religious beliefs influencing burial practices. Mapping was performed according to districts and further detailed mapping was done for each year quarter-wise to assess mortality trends in major graveyards. Analysis of 203,808 total deaths revealed a distinct pattern, with the highest mortality recorded in 2021 (37,687), followed by 2022, 2020, and 2019. A sub-sample analysis of 67,006 deaths from 21 graveyards during 2016-2018 provided additional insights into historical mortality trends. COVID-19 accounted for 1,606 deaths in Karachi, with 29% of these deaths buried in the EDHI graveyard due to unclaimed burials. Data visualization revealed a surge in fatalities in May-June 2020, reaching its lowest point in July 2020, followed by another peak in August 2021 with a subsequent decrease in September 2021. Karachi Central exhibited the highest proportion of deaths (N = 93,288) among the seven districts with Muhammad Shah graveyard having the highest density of burials (N=32,474). The identification of spatial constraints in 30 graveyards further emphasized the challenges faced in accommodating burials during the pandemic. Overall, GIS played a pivotal role in understanding the spatial dynamics of mortality and guiding targeted interventions during the pandemic. The findings emphasize the critical role of strategic planning in addressing challenges such as burial space constraints during emergencies, enhancing preparedness, and guiding effective interventions to mitigate the impact of pandemics on mortality rates in urban settings like Karachi, Pakistan.

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FEASIBILITY OF DRONE-BASED ENVIRONMENTAL AND TOPOGRAPHIC SURVEILLANCE FOR *FASCIOLA HEPATICA* IN THE PERUVIAN ANDES

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Fascioliasis is the food borne trematode with the greatest distribution worldwide. Human infection is associated with poverty and mainly affects school aged children, making it a public health problem. The Andean countries of South America bear the highest burden of *Fasciola hepatica* infection. In Peru, human *F. hepatica* has been reported from 20 out of the 24 regions. Climate change can alter *F. hepatica* distribution and risk, potentially enabling transmission of the infection in new areas. This study aims to create a drone-based protocol to monitor environmental and topographic factors that may favour *F. hepatica* transmission in the Peruvian highlands. In 2023, high-resolution drone mapping was conducted in four communities in Cusco, Peru. Households and water bodies were georeferenced, with each water body undergoing direct inspection to identify snails. Snails were collected and examined by microscopy to identify *F. hepatica* metacercariae. A total of 211 households and 414 water bodies were included in all communities. Snails were identified in 19.5% (CI95%: 15.9% - 23.7%) of the water bodies. Of these, 12.3% (CI95%: 6.4% - 21.9%) hosted infected snails. Six orthomosaics were obtained for the four communities from visual, thermal, red, red edge, near infrared and green bands. The normalized difference vegetation index, enhanced vegetation index, soil-adjusted vegetation index, slope, aspect and topographic wetness index were computed using the orthomosaics. Overall, the minimum mean distance between households and water bodies was 5.2 (± 11.9) meters revealing accessibility to water bodies. This information will be used to run a statistical model to identify the most suitable set of variables to predict *F. hepatica* cases. This approach will underscore the feasibility of drone technology for environmental and topographic surveillance of *F. hepatica* in endemic regions.

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QUANTIFYING THE IMPACT OF MALARIA IN PREGNANCY ON MATERNAL ANEMIA AND ITS ASSOCIATED BURDEN ACROSS AFRICA

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Malaria is a clear cause of maternal anemia, but there are few quantitative estimates of the malaria-attributable burden of maternal anemia. We aimed to generate estimates of the risk of malaria-attributable anemia faced by pregnant women across Africa, accounting for transmission and gravidity-dependent effects. We model the impact of malaria upon hemoglobin (Hb) concentration throughout gestation using individual-level data collected from women at enrolment into trials investigating malaria in pregnancy encompassing a wide range of endemicity levels across seven countries. We link this model to an existing mathematical model of the relationship between malaria in pregnancy and general population malaria endemicity, and then alongside fine-scale estimates of the spatial distribution of malaria, population density and fertility patterns, to extrapolate how the incremental risk of severe (Hb < 7 g/dL) and severe and moderate (Hb < 9 g/dL) anemia varies across Africa. We develop estimates of each dose of intermittent preventive treatment in pregnancy (IPTp) on increasing Hb concentration throughout gestation, and then estimate the malaria-attributable burden of anemia throughout gestation given current IPTp coverage. We estimate that, in absence of IPTp, approximately 1.8 million women in malaria-endemic countries have malaria-attributable moderate and severe anemia and approximately 690,000 have malaria-attributable severe anemia at the end of the second trimester. Though primigravidae represent only 23% of all pregnancies at risk, over 50% of the burden of malaria-attributable anemia at the end of the second trimester is concentrated in primigravidae. We will present quantitative estimates on how IPTp reduces malaria-attributable maternal anemia throughout gestation. We developed the most up-to-date and high-resolution quantitative estimates of malaria-attributable burden of maternal anemia across Africa. As the malaria-attributable burden increases throughout gestation, strategies focused on clearing malaria infection as early as possible should reduce the burden of malaria-attributable maternal anemia.

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ESTIMATING THE BURDEN OF SEVERE MALARIA IN CHILDREN, SUB-SAHARAN AFRICA 2015 TO 2022

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Plasmodium falciparum malaria is as a key cause of morbidity and mortality in children under five in sub-Saharan Africa (sSA). Malaria infections can be asymptomatic or vary from mild fevers to severe presentations of disease. Uncomplicated malaria can be effectively treated with oral artemisinin combination therapy (ACTs), but a lack of or delay in receiving ACTs can result in progression to severe malaria which requires inpatient care, frequently resulting in long term disability or death. Whilst extensive knowledge and robust models of malaria incidence exist, very little is known about the burden of severe malaria. In this study we use multiple data sources and implement a spatial-temporal modelling framework to

estimate the proportion of malaria cases with severe malaria for children attending health facilities and those in the community separately. Severe malaria prevalence in health facilities is estimated from routine surveillance data, using a Bayesian ST-CAR model in R-INLA. Community severe malaria prevalence is estimated by firstly modelling the prevalence of severe malarial anaemia from DHS surveys, then converting this to severe malaria using a multinomial model of the prevalence of key malaria syndromes, fit using data from published literature. Finally, we use estimates of total clinical malaria cases and treatment seeking proportions from the Malaria Atlas Project (MAP) to calculate the overall numbers of severe malaria cases in children under five in sSA for 2015-2022, at a 5x5 km pixel resolution. Preliminary results indicate 3.07 million (2.03-4.46 million) cases of severe malaria occurred in children in sSA in 2022, equating to an incidence rate of 17.30 (11.42 - 25.12) cases per 1,000 population, and 3.12% (2.73 - 3.61%) of malaria cases progressing to severe malaria. Results vary greatly by location, with the highest incidence rates estimated in Angola, DRC, and Burkina Faso. These estimates may be beneficial for progressing our understanding of malaria mortality and aiding resource allocation and provision of effective severe malaria treatments.

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RISK FACTORS FOR EMERGENT MALARIA CASES IN MUTARE CITY, ZIMBABWE, 2022-2023

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Malaria has diminished in most of Zimbabwe over the past decade following scaled-up vector control and artemisinin-based combination therapy interventions for progressive elimination of the disease. However, the emergence of transmission in former malaria-free zones against a backdrop of climate change, including urban areas with dense non-immune populations threatens to reverse hard-earned gains against the formidable disease. Mutare city was considered free of autochthonous malaria, until 2017, when the Ministry of Health and Child Care formerly confirmed escalating cases of locally transmitted malaria in the city. In the current study, we examined the human-related risk factors for malaria cases in Mutare from 2022 - 2023 to aid in formulation of targeted intervention packages for helping restore malaria-free status to the city. The study was based on de-identified samples and available demographic characteristics of malaria cases presenting at eight health facilities in Mutare. In a multivariate binary logistic model, significant risk factors for malaria cases found in the city included residential locale (OR [95%CI]: 3 [1.1 - 5.8], p = 0.029, N = 7,222), household proximity to still surface water pools or unprotected wells and travel history in the past 2 weeks (OR [95% CI]: 9 [5.2 - 14.4], p lt 0.001, N = 7,222), modal destinations being malaria-endemic adjoining districts of Mutare rural, Mutasa, and Chipinge, within Zimbabwe, as well as areas of neighbouring Mozambique, mainly for trade or work. By far the most predominant risk factor for malaria cases was artisanal mining (OR [95%CI]: 22 [10.7 - 44.1], p lt 0.001), which was 95% dominated by men, and male residents exhibited four-fold higher odds of being malaria cases than females (OR [95% CI]: 4 [2.0 - 6.5]). Environmental management and the deployment and concomitant promotion of ITNs use, found only among 6% of the residents, especially targeting communities exposed to the identified risk factors, to a level of 80% minimum coverage, may be instrumental towards re-establishing malaria elimination in Mutare city.

7601

UTILIZATION OF ANTENATAL CARE SERVICES AMONG WOMEN OF REPRODUCTIVE AGE IN A MALARIA ENDEMIC AREA IN RARIEDA SUBCOUNTY, WESTERN KENYA

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Maternal health care services reduce morbidity and mortality rates for mothers and infants. The World Health Organization recommends 8 antenatal care (ANC) visits during pregnancy. In western Kenya, ANC visits offer malaria preventive services such as intermittent preventive treatment (IPTp). Understanding factors that affect numbers of ANC visits and uptake of malaria services can help optimize maternal and infant health.We used data from a continuous household survey conducted from Aug 2022-Jul 2023 to describe ANC attendance and use of IPTp among women 15-49 years with a pregnancy in the past 2 years. Poisson regression was used to evaluate factors associated with number of ANC visits reported.Overall, 1,652 women of reproductive age (15-49 years) consented from 1,454 compounds. Of these, 348 (21%) had a pregnancy in the past 2 years; 24% were primigravida, 20% secundigravida, and 56% multigravida. Nearly all (99%, 344) attended at least 1 ANC visit, but only 4% (15) attended 8+ ANC visits. On average, women made 4.3 ANC visits (range: 1 - 9). Increasing education (vs no education) was associated with more ANC visits: primary school (aIRR: 1.83, 95%CI: 1.03 – 3.69), secondary school (aIRR: 1.91, 95%CI: 1.08 – 3.83), and higher education (aIRR: 1.75, 95%CI: 0.95 – 3.61). Number of ANC visits was also higher among married vs. unmarried women (aIRR: 1.17, 95%CI: 1.00 – 1.38) and primigravidae vs. multigravidae (aIRR: 1.18, 95%CI: 0.99 – 1.41). Of women attending at least one ANC visit, 250 (72.7%) took any drugs to prevent malaria during pregnancy, of whom 209 (83.6%) reported taking IPTp. Most (63.2%, 132) received the recommended 3+ doses, with an average of 3.0 IPTp doses (range: 1 – 6) among women who received IPTp.In western Kenya, pregnant women attended an average of 4.3 ANC visits, well below the number recommended by WHO. Less-educated, unmarried, or multigravida women are at risk of poor ANC attendance. Despite imperfect ANC attendance, most women received 3 doses of IPTp for malaria prevention. Strategies to promote increased number of ANC visits (e.g., targeted outreach) may help increase access to malaria prevention services.

7602

RISK FACTORS FOR ASYMPTOMATIC *PLASMODIUM FALCIPARUM* INFECTION IN THE DRY SEASON, AND RELATIONSHIP WITH CLINICAL MALARIA RISK IN THESUBSEQUENT TRANSMISSION SEASON AMONG CHILDREN IN WESTERN PROVINCE, ZAMBIA

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Malaria transmission is intense and seasonal in Western Zambia. A cohort study as part of a trial of attractive targeted sugar baits found clinical malaria incidence among children was highly variable geographically. To explore drivers of heterogeneity in transmission, we assessed risk factors for *Plasmodium falciparum* infection among asymptomatic children 1-14 years at the end of the dry season, and the association with clinical malaria during the following transmission season. In 70 clusters, 35 children were randomly selected in November 2021 and 2022, tested by malaria rapid

diagnostic test (RDT) for *P. falciparum* infection and assessed for fever. A questionnaire collected information on demographics, location, vector control use, household construction, and socio-economic indicators. Risk factors for RDT positivity were assessed in generalized linear models with cluster random-effect. Cox proportional hazards models were used to compare time to first clinical case by RDT result among all children and afebriles only. A total of 4492 children were recruited, 1398 (31.1%) being RDT positive. 68.6% of all RDT positive children were asymptomatic (24.9% prevalence overall, 0% to 77.3% by cluster). Asymptomatic RDT positivity was associated with increasing age, not using an ITN the previous night, fever in the prior two weeks, low socioeconomic status, mother's education, and presence of another household member with fever and positive RDT. Household construction, travel time to a health facility, and distance to water bodies had no association with the outcome. While all children received a full course of ACT at enrolment, among asymptomatic children, those with positive RDT at enrolment experienced their first clinical case sooner than RDT negative children (hazard ratio 1.24, 95% CI 1.13-1.36), and had higher clinical incidence over six months of follow-up (incidence rate ratio 1.23, 95% CI 1.15-1.32). These findings highlight the individual- and household-level factors driving risk of asymptomatic parasite carriage prior to the rainy season, and that this risk carries over to having clinical malaria later during the transmission season.

7603

HUMAN MALARIA IN THE ATLANTIC FOREST OF BRAZIL IS MOSTLY CAUSED BY *PLASMODIUM SIMIUM*

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Plasmodium vivax is hypothesized to have arrived with colonizers from Portugal and Spain as vivax malaria was endemic in southern Europe until mid-1900. Once in America, a subpopulation of *P. vivax* underwent anthroponosis, adapting to Neotropical platyrrhine monkeys and originating a sister species, *P. simium. P. simium* infects humans as well, making it unique for studying host-shift in malaria parasites as it went through both anthroponosis and zoonosis. *P. vivax* and P. simium are highly similar at the genome level, differentiating only by large deletions in genes encoding two erythrocyte invasion ligands of P. simium. We have newly obtained leukocyte-depleted samples of P. simium from human and non-human primates from the Atlantic forest in São Paulo region. These samples are expected to yield enough parasite DNA to obtain a high-coverage genome assembly to compare the genomes and identify additional genomic signatures of adaptation. We also obtained *P. vivax* and P. simium sequecing data from public databases from Brazil (n = 215), Peru (n = 46), Colombia (n = 62), Panama (n = 27) and Mexico (n = 20). We mapped the reads to the PvP01 reference genome of *P. vivax* with bwa-mem. The SNP calling was performed with Genome Analysis Toolkit (GATK) version 4.4.0. To assess population structure we performed Principal Components Analysis (PCA) and ADMIXTURE analysis. Preliminary analysis showed that *P. vivax* and P. simium from Brazil form two distinct clades, with *P. vivax* samples from the Amazon clustering with samples from Peru and Colombia. Parasites from humans from the Atlantic Forest of southeast Brazil formerly classified as *P. vivax* cluster together with monkey-derived P. simium samples from the same region. ADMIXTURE results corroborate the subdivision between *P. vivax* and P. simium from Brazil. This result indicates that human malaria in the Atlantic Forest region is mostly caused by P. simium. This parasite is different from *P. vivax* circulating elsewhere in Brazil.

7604

THE IMPACT OF FIRST-TRIMESTER *PLASMODIUM FALCIPARUM* MALARIA INFECTIONS ON MATERNAL, PREGNANCY AND INFANT OUTCOMES IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW AND INDIVIDUAL PARTICIPANT DATA META-ANALYSIS

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Malaria in pregnancy can lead to adverse consequences for pregnant women and their infants, including maternal anaemia, foetal death, and premature birth. Whilst the risks associated with malaria infections in the second and third trimester of pregnancy are well characterised, less is known about infections in early pregnancy. We conducted a systematic review and individual patient data meta-analysis to assess the burden and effects of malaria infection in the first trimester on maternal, pregnancy and infant outcomes in sub-Saharan Africa. The primary outcomes included foetal death, maternal anaemia in the third trimester or at delivery (haemoglobin < 11 g/dl), infant low birth weight, preterm delivery, and a small-for-gestational-age infant (SGA). Additionally, the association with perinatal and neonatal death were examined. Trials and prospective cohort studies were eligible if they reported malaria testing in the first trimester and were conducted in sub-Saharan Africa. A literature search was conducted using the Malaria in Pregnancy Library, PubMed and the WorldWide Sciences databases without time limits, in English (last search January 2024). Two independent reviewers screened the search output. Eligible studies were identified and authors were invited to share data. The data received was reformatted, pooled, and analysed. We approached 38 potentially eligible studies of which 10 responded, and 7 consented and contributed data by the time of the abstract submission. The prevalence of malaria in the first trimester by blood smear ranged from 1.2 to 49.6% in 5 countries (7 studies, total number of participants 1971), whereas low birth weight ranged from 9.2-14.6% (participants N=1554) and SGA ranged from 9.4 to 25.5% (N=1480). The full analysis will be presented at the meeting.

7605

RISK FACTORS FOR SPOTTED FEVER GROUP RICKETTSIOSES IN KILIMANJARO REGION, TANZANIA

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Spotted fever group rickettsioses (SFGR) are a major cause of fever in sub-Saharan Africa, but there are knowledge gaps regarding risk factors. We sought to identify risk factors for each of acute SFGR and SFGR exposure among participants presenting to hospital in Kilimanjaro Region, Tanzania. We recruited febrile patients presenting to two hospitals in Moshi, Tanzania, from February 2012 through May 2014. Standardised clinical and risk factor questionnaires were administered to elicit potential risk factors from within the last 30 days, and geospatial data were collected. SFGR exposure was defined as a *Rickettsia africae* immunofluorescence antibody reciprocal titer of ≥64, and acute SFGR as a ≥4-fold rise in between paired sera. Univariable and multivariable logistic regression was used to identify associations. Of 1,190 participants providing ≥1 serum sample, median (range) age was 21.8 (0.3, 100.2) years, 545 (54.3%) were female, and 650 (54.6%) had SFGR exposure. Of 731 participants with paired sera, 67 (9.2%) had acute SFGR. On multivariable analysis, odds of acute SFGR were higher in age group 0-2 years (adjusted odds ratios [aOR] for all 5 older age groups <0.36, p-values<0.011), rural residence (aOR 4.1, p=0.007), and in areas with a maximum daily temperature <26°C (aORs for all higher temperature groups <0.42, p-values<0.035). Odds of SFGR exposure were higher in those working in the garden (aOR 1.8, p=0.010), and seeing a dog in the village (aOR 1.5, p=0.010). Odds of SFGR exposure were lower in age group 0-2 years (aORs for all 5 older age groups >1.5, p-values<0.026), female sex (aOR 0.62, p<0.001) and being from Chaga tribe (aOR 0.68, p=0.003). Among patients presenting to hospital with fever, those aged <2 years, rural residents, and persons residing in areas with cooler temperatures had increased odds of SFGR. Our results identify groups that warrant further research to understand tick exposure and to target SFGR prevention interventions.

7606

EMERGENCE OF TICK-BORNE SPOTTED FEVER GROUP *RICKETTSIA* IN NORTH, CENTRAL AND SOUTH AMERICA: HIGHLIGHTING THE NEED FOR ATTENTION

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Spotted fever group *Rickettsia* (SFGR) are an important cause of human disease, as evidenced by the US Centers for Disease Control and Prevention (CDC) having an entire branch dedicated to this group of pathogens (Rickettsial Zoonoses Branch). However, less is known about the human impact of these diseases in low- and middle-income countries (LMICs). Our work in South Carolina, USA, El Salvador, and Colombia, between 2018 and 2022 has identified LMICs have 4 to 6 times higher seroprevalence rates than the domestic estimates. The seroprevalence estimates identified were: 3.4% in South Carolina, 13.2% in the Sonsonate department, El Salvador, and 19.4% in the Boyacá department, Colombia. These are the first seroprevalence rates for these regions. This presentation gives an overview of the three study sites and the contrasts and similarities of the epidemiological scenarios that involve this group of diseases. Owning pets exposed to SFGR, being male, older age, and working outdoors were some of the initial risk factors identified. The multisite nature of these studies highlighted the differences in inattention to these infections: despite the high seroprevalence rates, these pathogens are non-reportable conditions in Colombia and El Salvador, yielding lacking adequate surveillance and sufficient public health action. Underreporting of SFGR creates false security, misguiding clinicians, and epidemiologists, which turns into misdiagnosis, delayed treatment, and severe outcomes. Evidence of this unbalanced attention proves the need for increasing capacity and detection in LMICs, and stresses the need to include SFGR in the list of neglected tropical diseases.

7607

TICK-BORNE CRIMEAN-CONGO HEMORRHAGIC FEVER IN WEST CAMEROON: CIRCULATION AND RISK FACTORS AMONG CATTLE BREEDERS

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Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne disease with documented cases in northern Cameroon. However, data on CCHFV exposure prevalence in Cameroon's population, particularly in symptomatic and at-risk individuals, remain limited. This study aimed to assess herder's knowledge attitude and practice, CCHFV circulation in Cameroon's Ndé and Noun, Western Region, and evaluate local cattle tick distribution. A cross-sectional study was conducted from October to December 2021 with 28 male cattle breeders, mostly aged 20-40 years. Knowledge, attitude, and practice (KAP) regarding tick prevention/control were evaluated through questionnaires. Tick specimens were collected, identified, and blood samples from cattle breeders were tested for anti-CCHFV antibodies using ELISA. Majority of participants (94.5%) had adequate tick knowledge, but lacked understanding of disease transmission from ticks. Only 24.7% exhibited favorable attitudes towards tick control, with no one demonstrating sufficient preventive practices. *Rhipicephalus annulatus* (64.1%) and *Amblyoma variegatum* (27.1%) were the predominant tick species. Among 423 tested cattle, 27.4% had anti-CCHFV antibodies, notably higher (17.8%) among cattle breeders and increasing with age (>20 years). Bivariate analysis identified associations between virus seroprevalence and certain behaviors among breeders, like tick removal after animal contact (P=0.007) and post-grazing (P=0.004), underscoring the need for improved preventive measures during animal interactions. This study confirms CCHFV circulation in Cameroon's Western Region, highlighting the importance of active surveillance for circulating strains in ticks to prevent potential outbreaks. Enhanced public awareness and targeted interventions are crucial to reduce CCHFV transmission risk, especially among at-risk populations like cattle breeders.

7608

XENOSURVEILLANCE OF TICKBORNE PATHOGENS VECTORED BY METASTRIATE TICKS ALONGSIDE THE VIRGINIA-NORTH CAROLINA BORDER

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Tickborne disease cases have increased over the past decade across the United States, yet the depth and accuracy of data to inform public health policy remains heterogeneous in quality and resolution. For example, for multiple counties in the Southeastern United States, human tickborne diseases, tickborne pathogen circulation, and tick abundance data are rarely matched, resulting in confusion as to where risk to infectious tick bite exposure occurs. This represents a major health gap and a pressing need for the southeast. To address this need, we launched STEPS (Southeast Tickborne Emergent Pathogen Surveillance), wherein we augmented the tick surveillance activities of several states through the establishment of tick surveillance teams and generated targeted tick sampling data for

counties with a historic dearth of evidence for the presence of ticks and/or tickborne pathogens. We evaluated the infection status of metastriate hard ticks collected through STEPS along the Virginia-North Carolina border, where data for tickborne disease cases and tick abundance are discordant. We conducted repeated cross-sectional sampling in two locations of 10 targeted counties in Virginia throughout June - October of 2021. We then piloted a novel multiplex assay that can categorize tick species, determine bacterial tickborne pathogen infection status, and identify remnant mammalian host bloodmeals among 12,208 flat ticks collected by drag sampling. Tickborne pathogens were found to be widespread in both *Amblyomma americanum* and *Dermacentor variabilis* ticks across the sampled counties that have a dearth of human tickborne disease and tick abundance data, including infections with *Ehrlichia chaffeensis*, *E. ewingii*, Panola Mountain Ehrlichia, and *Rickettsia parkeri*. We discuss the public health implications of our findings in the context of the current suboptimal resolution of both tick abundance and tickborne pathogen infection data for this and other adjacent regions throughout the Southeastern United States.

7609

THE EFFECTS OF IVERMECTIN MASS DRUG ADMINISTRATION DESIGNED FOR MALARIA ON TUNGIASIS IN KWALE, KENYA: A CLUSTER-RANDOMISED CONTROLLED TRIAL

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Tungiasis is an extremely neglected disease, mostly affecting people living in tropical regions, and in extreme poverty. It can cause intense pain, discomfort, and secondary infections, which can lead to school and work absenteeism, and in severe cases deformities of the feet. To date, no formal guidelines exist for the treatment of tungiasis, and affected individuals mostly rely on manual extraction of fleas, which can be very painful and lead to secondary infections. Given the known efficacy of ivermectin against other ectoparasites, we explored the effect of ivermectin on tungiasis during a cluster randomisedcontrolled trial (BOHEMIA), which primarily aimed to assess the effect of ivermectin mass drug administration against malaria in Kwale, Kenya. The intervention consisted of a single dose of 400 mcg/kg ivermectin given monthly to eligible humans in 3 consecutive months during the rainy season. The control group received albendazole. 30 of 84 total clusters were randomly selected and 811 randomly selected participants from within these clusters were monitored for tungiasis among the two study arms. Cross-sectional surveys took place at 1, 2 and 3 months after the first dose. Tungiasis diagnosis was determined by a questionnaire and examination of the feet and hands by non-experts after intense training. Lesions were classified as live, dead or manipulated and counted to indicate the severity of infestations. Preliminary findings have indicated a baseline prevalence of approximately 8%. A full unblinded analysis of the results will be available at the time of the meeting.

7610

DETECTION OF A POTENTIALLY NOVEL TICK-BORNE VIRUS CLOSELY RELATED TO *GUERTU* VIRUS FROM *AMBLYOMMA GEMMA* TICKS AND ITS PREVALENCE IN HUMAN POPULATIONS FROM ISIOLO COUNTY, KENYA

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The unprecedented global reports of novel tick-borne viral agents with public health significance are due to increased interest in pathogen discovery efforts aided by modern sequencing tools. In our study, we collected ticks from different animal hosts in Isiolo county, Kenya. Ticks from individual animals per site were stored in cryogenic tubes, preserved in liquid nitrogen and transported to the laboratory where they were identified, pooled (≤8 ticks) and homogenized. Tick supernatants were inoculated in Vero CCL-81 cells and cultures showing cytopathic effects (CPE) were harvested. In-vitro growth kinetics in cells and mice brain inoculation were determined. High throughput sequencing and phylogenetic analysis of virus isolates were performed. Archived serum samples from a community-based survey in Isiolo, including Kinna, the site of virus detection were analyzed for antibodies to the virus. A virus designated Kinna virus (KV), closely related to Guertu virus (GTV) with nucleotide percent identities of 80.42% in the L segment, 76.54% in the M segment and 81.09% in the S segment, was identified from cultured tick samples of species *Amblyomma gemma*. Sequence analysis revealed a virus with nucleotides lengths of 6403, 3332 and 1752 in the L, M and S segments, consistent with the described genomes of the genus *Dabie bandavirus,* family *Phenuiviridae.* The RdRp amino acid sequence had a 93.3 % identity to that of Guertu virus, an indication of possibly separate strain. The virus was lethal to mice which died 6-9 days post-infection. The virus infected mammalian cell lines (Vero cells) but had reduced infectivity in the mosquito cell line (C636) tested with peak titres reported 3-4 days post-infection. Neutralizing antibodies were detected in 125 (38.6%, 95% CI 33.3–44.1%) of the human sera from the region suggesting exposure to this virus. The isolation of this virus with a potential to cause disease in human and animal populations, necessitates evaluation of its public and veterinary health significance in the region. This also points to the need for continuous monitoring of vector, animal and human populations to establish transmission dynamics.

7611

CROSS-SECTIONAL ANALYSIS OF SEROLOGIC RESPONSE TO ARTHROPOD-BORNE AND HEMORRHAGIC FEVER VIRUSES IN GHANAIAN LIVESTOCK HERDERS IN MILITARY AND CIVILIAN SETTINGS

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Zoonotic diseases account for over sixty percent of emerging infectious diseases and are the leading cause of pandemics. As humans and livestock become increasingly transient and environment and climates continue to change, disease vectors can expand into previously untouched geographical regions, bringing their pathogenic payload along for the ride. In this study, we assessed the seroprevalence of Crimean-Congo Hemorrhagic Fever virus (CCHFV) alongside other viruses of similar clinical presentation and endemicity in high-risk populations in Ghana (livestock

herders, abattoir workers). Total IgG prevalence to neutralizing response against live virus by microneutralization assay was also compared. In total, 300 blood samples were collected from consenting healthy adult volunteers at five military and three civilian sites across Ghana. In this study, we observed a 10.3% seropositivity rate for CCHFV in all blood samples tested. Seroprevalence for other differential diagnostic targets such as Rift Valley Fever virus (RVFV), Ebola virus (EBOV), Marburg virus (MARV), and Lassa virus (LASV) were 14.7%, 2.3%, 0%, and 1%, respectively. Microneutralization data further verified virus specific neutralization positives out of the total IgG positives. Among animal handlers who had recently skinned livestock, 19 (25.3%) of them were exposed to RVFV and 20 (28.6%) in the Coastal Savannah region were likely to be exposed to RVFV compared to those in the other ecological zones (p=0.002). Animal handlers aged <25 years had a high exposure rate to CCHFV than >25 year olds (p<0.001). This data helps us better understand the risk of exposure to CCHFV and other zoonotic and vector-borne diseases in the region and establishes methods for assessing seropositivity in a multiplexed format for higher throughput sample analysis. Surveillance of healthy populations with prior infections to a variety of hemorrhagic fever viruses is of benefit to USAFRICOM leaders planning operations and/or training to West Africa and confirms the need for continued active surveillance regionally.

7612

GENOME-WIDE ASSOCIATION STUDIES UNVEIL SIGNATURES OF SELECTIVE SWEEPS ASSOCIATED TO INSECTICIDE RESISTANCE EVOLUTION IN *ANOPHELES FUNESTUS* IN FOUR ECO-GEOGRAPHICAL SETTINGS ACROSS CAMEROON

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Insecticide resistance is currently threatening to derail efforts to control malaria in Africa. Deciphering the evolutionary dynamics of mosquito populations country-wide is essential for designing effective and sustainable national strategies to manage resistance and accelerate malaria elimination efforts. Here, we employed genome-wide association studies through pooled template sequencing to compare four eco-geographically different populations of *Anopheles funestus* across a South North transect in Cameroon, aiming to identify genomic signatures of adaptive responses to insecticides. Our analysis revealed limited population structure within Northern and Central regions (F_{ST}<0.02), suggesting extensive gene flow, while populations from the Littoral/Coastal region exhibited more distinct genetic patterns (F_{ST}>0.049). Greater genetic differentiation was observed at known resistance-associated loci, rp1 (2R chromosome) and CYP9 (X chromosome), with varying signatures of positive selection across populations. Allelic variation between regions variants underscores the pervasive impact of selection pressures, with rp1 variants more prevalent in Central and Northern populations (F_{ST} >0.3), and the CYP9 associated variant more pronounced in the Littoral/Coastal region (F_{ST} =0.29). Evidence of soft selective sweeps was supported by negative Tajima's D and reduced genetic diversity in all populations, particularly in Central (Elende) and Northern (Tibati) regions. Genomic variant analysis identified missense mutations and complex genomic alterations such as duplications, deletions, mobile element (ME) insertions, and chromosomal inversions, all associated with selective sweeps. A 4.3 kb ME insertion was at higher frequency in Northern and Central populations compared to the Njombe Littoral/Coastal population, where CYP9K1- G454A, a known resistance allele and ME upstream were more prevalent. Our study uncovered regional variations in insecticide resistance candidate variants, emphasizing the need for a streamlined DNA-based diagnostic assay for genomic surveillance across Africa.

7613

DEFINING THE ROLE OF JUVENILE HORMONE III FOR *ANOPHELES GAMBIAE* REPRODUCTION AND *PLASMODIUM* TRANSMISSION

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Targeting *Anopheles* reproduction can serve as a critical tool to reduce vector population and help contribute towards the overall goal of malaria elimination. In the adult female mosquito, the insect hormone Juvenile Hormone (JH) initiates the molecular cascade responsible for tissue maturation in the post-eclosion period, which is required for successful reproduction following acquisition of a blood meal. Methods to block JH are highly effective at preventing egg development in *Aedes aegypti*, and thus have the potential to be used as a mosquito control tool. However, little is known about the role JH in *Anopheles* species in reproduction, and whether this hormone may contribute to parasite development remains completely unknown. We administrated dsRNA targeting the JH receptor Met or its co-receptor Taiman to prevent JH activation, and subsequently measured the effects of gene silencing on Anopheles reproduction and transmission of the human malaria parasite *Plasmodium falciparum*. Following an infectious blood meal, Met and Taiman silencing reduced the number of eggs mosquitoes developed, but also lead to accelerated parasite growth, causing earlier sporozoite formation and invasion of salivary glands. These results suggest that the JH-mediated investment in reproduction limits the availability of nutrients to the *Plasmodium* parasite by yet unknown mechanisms. Finally, we used LC-MS/MS to quantify JH III titers across different time points during the post-eclosion developmental phase and discovered that, unlike in other mosquitoes, JH titers display highly dynamic fluctuations influenced by the time of day. We are currently exploring the connection between the observed periodic fluctuations and JH synthesis by using a CRISPR-Cas9 knockout strategy against key factors in circadian rhythm.

7614

AEDES AEGYPTI POPULATION GENOMICS UNCOVERS EXTENSIVE CONTEMPORARY MIGRATION AND INCREASED DENGUE RISK

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Aedes aegypti is the world's most efficient vector of viral disease and a prodigiously successful invasive species; this enables transmission of arboviruses across the globe. Driven in large part by the ubiquity of this mosquito, 2024 has seen surges in dengue transmission in countries as far apart as Brazil, Thailand, and Burkina Faso. However, the global *Ae. aegypti* population is not homogeneous: mosquitoes on the African continent are of the ancestral 'formosus' subspecies, which has a weak propensity to invade urban habitats and little preference for human hosts; in contrast, the *'aegypti'* subspecies lives outside Africa, and shows a fervent preference for human hosts and a far higher capacity for disease transmission. New population genetics data from the Aedes 1200 genomes project have given us insights into the emergence of human-preferring *Ae. aegypti* in West Africa and its rapid spread around the globe. We have used these data to examine contemporary vector migration, and have uncovered a pattern of extensive secondary contact between the two subspecies within Sub-Saharan Africa. This secondary contact has led to the adaptive introgression of insecticide resistance loci, may have introduced loci involved in human host preference, and frequently occurs in sites that have

seen recent dengue outbreaks within Africa. Left unchecked, the reinvasion of global '*aegypti*' into Africa has the potential to dramatically change the behaviour and vector competence of resident mosquito populations and could impair our ability to control dengue in Sub-Saharan Africa.

7615

SEARCH FOR POSSIBLE LOCI UNDER POSITIVE SELECTION IN EXOMES OF INVASIVE *ANOPHELES STEPHENSI* LARVAE IN ETHIOPIA

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Analysis of exonic regions can elucidate the molecular mechanisms behind adaptations in mosquito vectors. This data is of particular interest when designing novel control methods to combat invasive vectors like *Anopheles stephensi* in East Africa. In this study, the exonic variants in *An. stephensi* larvae in Ethiopia were examined against the UCI whole genome assembly of *An. stephensi* after establishing a protocol for storing, transporting, and extracting RNA from field-collected mosquito larvae for next-generation sequencing (Illumina). RNA from mosquito larvae was stored in ZYMO RESEARCH DNA/RNA shield and extracted using the ZYMO RESEARCH Direct-zol® RNA Miniprep kit. The extracted RNA was stored in DNAase, RNAase-free water, and shipped on dry ice on the same day of the extraction to be sequenced using Illumina NovaSeq PE150 technology. An average of 54,059,221 reads were obtained per sample. Variants were detected using a workflow based on the "bcftools" program. A total of 1,023,276 SNPs with 8,197 multiallelic sites and 121,530 indels were identified against the *An. stephensi* reference genome (UCI_ANSTEP_V1.0). A higher concentration of loci under possible positive selection (Tajima's D < -1) was observed within the region of 60Mbp to 70Mbp in chromosome 2 in the alignment of read sequences to the UCI assembly. This region lies within the 2R*b* inversion region that expands from 55Mbp to 72Mbp in chromosome 2 of the UCI assembly which has important genes associated with insecticide resistance, urbanization, and adaptation to climate. In the next phase of this project, we will evaluate the location of the 2R*b* inversion in *An. stephensi* from Ethiopia with a novel whole genome assembly. The exonic regions with a higher fixation to Ethiopian population compared to Indian *An. stephensi* will be further examined to find the specific genes possibly under positive selection and how they may be impacting the spread of *An. stephensi* in the Horn of Africa.

7616

GENETIC INSIGHTS INTO DIAPAUSE ADAPTATION OF *AEDES ALBOPICTUS* IN TEMPERATE CLIMATES: A GENOME-WIDE ASSOCIATION STUDY

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Aedes albopictus, the Asian tiger mosquito, is a significant vector for transmitting dengue and chikungunya viruses. We investigated the genetic basis of photoperiodic diapause—a critical ecological adaptation that facilitates the mosquito's survival and expansion in temperate regions. We established a breeding colony from the Oak Hill, FL population, which is naturally polymorphic for the diapause response. Under unambiguous short-day conditions that stimulate diapause, we observed a broad range of diapause phenotypes within this population, from 0% to 100%, with an average diapause incidence of 32%. Employing the Aealbo SNP chip, we genotyped 602 females that produced a variable range of diapause incidence phenotypes, from non-diapausing to fully diapausing eggs. Our genome-wide association study (GWAS) identified two significant genomic regions on chromosome 1 associated with diapause adaptation. One genomic region contains a Max-like gene integral to the Mad/Max/Myc transcription machinery, suggesting a possible regulatory role in diapause induction. This result indicates that Max-like genes may influence the transcriptional control mechanisms necessary for diapause preparation and execution, potentially offering new targets for vector control strategies. Our results also suggest a complex genetic architecture of diapause in *Aedes albopictus*, shedding new light on the potential of genetic studies in developing targeted control strategies for this invasive vector and contributing to our understanding of the genetic factors that enable the mosquito's adaptation to colder climates, a pivotal aspect of its global invasiveness.

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POPULATION GENOMICS OF EMERGENT *ANOPHELES STEPHENSI* IN THE HORN OF AFRICA: GENOMIC DIVERSITY, POPULATION STRUCTURE AND INSECTICIDE RESISTANCE.

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The invasion of the malaria vector *Anopheles stephensi* into Africa poses a grave threat to malaria control and elimination efforts, especially in urban areas, to which it is well adapted. First recorded in the Horn of Africa in Djibouti in 2012, An. stephensi was detected in Ethiopia and Sudan in 2016, with widespread distributions in each country. Knowledge of the invasion source, population structure and diversity, and distribution of insecticide resistance alleles in the invasive range, is crucial for effective control but remains limited. Here, we present the results of the first whole-genome population genomic analysis of invasive An. stephensi, having sequenced approximately 500 genomes from Sudan, Ethiopia, Yemen and Djibouti, as well as from the native range in Pakistan and Afghanistan. We reveal insights into *An. stephensi* diversity and population structure across the landscape, as well as evidence for insecticide resistance selection and allele frequencies. These data are the beginning of expanded scale genomic surveillance of An. stephensi across the invasive range in Africa to provide a comprehensive view of invasion source and transport, optimise control efforts, and inform mathematical models of population dynamics and further spread.

7618

DEVELOPMENTAL DYNAMICS OF CHROMOSOME-LEVEL 3D GENOME ARCHITECTURE IN *ANOPHELES COLUZZII*

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Functional interactions between regulatory elements, such as enhancers, and gene promoters play a crucial role in regulating gene transcription during cellular differentiation and in response to stimuli. However, the 3D aspect of gene regulation has not been investigated in insects that transmit human diseases. Here, we examined the dynamic aspects of 3D genome architecture during mosquito development. Genome-wide chromatin conformation capture (Hi-C) was performed on various developmental stages of *Anopheles coluzzii,* including embryonic, larval, and adult stages, as well as on body parts of adult females and males, such as heads,

antennas, proboscises, maxillary palps, thoraxes, and gonads. Comparison of Hi-C maps obtained from adult and embryonic tissues demonstrated the presence of several autosomal and X-chromosomal long-range chromatin interactions across developmental stages of the mosquito. However, some giant multi-megabase chromatin loops are specific to the soma, as they are absent in ovaries or testes but present in the thoraxes and heads of adult mosquitoes. The heads have stronger contacts as well as additional giant loops that are absent in thoraxes, suggesting their possible function in the nervous system. The eyes/brain samples contained the majority of giant chromatin loops, while fewer loops were found in the antennas and even fewer in the maxillary palps. Genes located at the loop anchors have roles in cell-cell signaling, sensory perception, neuron differentiation, signal transduction, and response to stimulus. We also identified a network of smaller head-specific loops (120-2,000 kb) in the intercalary heterochromatin that contains genes encoding for neural-cadherin at their anchors. Our analysis of RNA-seq data has shown that the observed developmental loop dynamics often correlate with transcriptional changes of genes located in the loop anchors. Thus, we discovered that most of the long-range chromatin interactions in An. coluzzii are developmentally regulated. The dynamic nature of the chromatin interactions in different organs points to their functional significance for mosquito biology.

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TOWARDS THE DEVELOPMENT OF A RAPID URINE-BASED DIAGNOSIS OF BURULI ULCER USING COMPUTATIONAL METHODS

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Buruli ulcer (BU) caused by Mycobacterium ulcerans is a necrotizing skin disease that if left untreated may require restorative surgery. The incubation period of the disease is estimated to be 6-8 months during which infections remain undetected until a swelling is observed at the site of previous trauma on the skin. Diagnosing and managing symptomatic BU patients present significant challenges because the current methods are laborious, expertise-dependent and time-consuming and are based on detecting the toxin mycolactone, whose half-life in serum is very short. To enable early diagnosis and to facilitate large-scale epidemiology studies, we hypothesized that mycolactone is hydrolyzed to lactone which is excreted in urine. We therefore utilized computational methods to identify proteins that bind to lactone for use in the development of rapid diagnostic tests (RDTs). Five proteins with affinity to lactone were obtained from literature search. Munc18-b known to bind to mycolactone was included in the analysis. The structures of the six proteins retrieved from the Protein Data Bank were virtual screened against lactone using AutoDock Vina. N-Acyl homoserine lactonases (4G5X), Aryldialkylphosphatase (4G2D) phosphotriesterase (2VC5), Quenching lactonase (6N9I), Gluconolactonase (7RIS), Munc18-b (4CCA) with binding energies of -25.86 kcal/mol, -19.00 kcal/mol, -15.95 kcal/mol, -13.36 kcal/mol, -8.02kcal/mol and -9.59kcal/mol respectively. The stabilities of the proteins-lactone complexes were assessed through molecular dynamics simulation of 300 ns. The Root Mean Square Deviation (RMSD) and The Root Mean square Fluctuation (RMSF) analyses were performed to determine the stability and structural conformational changes of the complexes respectively. Overall, proteins 2VC5, 4G2D and 4G2X exhibited high binding affinity, strong bond interactions, and considerable stability when bound to lactone. These proteins hold promise for use in subsequent experiments aimed at the development of non-invasive RDTs for BU disease

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EVALUATING VECTOR CONTROL STRATEGIES FOR DENGUE: A MODELLING ASSESSMENT OF ALTERNATIVE APPROACHES

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Dengue presents an increasing global public health challenge, particularly in tropical regions. Vector control measures are commonly used to reduce infections, but have varying levels of effectiveness. To optimize resource use, we evaluated the effectiveness of different vector control efforts with different timing, duration, and prioritization strategies in a heterogeneous landscape with varying mobility levels, geographic units, and control efforts. We developed a stochastic, age-structured metapopulation transmission dynamic model using recent seroprevalence and census data from Puerto Rico in 2019-2020. Using varying mobility levels, geographic unit sizes, and interventions, we evaluated the effectiveness of vector control efforts with different timing, duration, and prioritization of management strategies. Vector control interventions included autocidal gravid ovitraps, larvicides, and community source reduction. Implementation options included evaluating different timing of introduction, dynamic versus static intervention implementation (i.e., changing or maintaining intervention locations), and targeting activities by prioritizing specific areas (e.g., based on population density, number of cases, or case incidence). Effectiveness of interventions over a one-year period was measured by the number of dengue cases averted when compared to the scenario of no intervention. Interventions were most efficient when implemented during the low season before dengue cases began to increase and prioritizing intervention locations based on transmission characteristics also substantially reduced overall infections. Further work will integrate additional interventions including Wolbachia replacement and vaccines, which offer additional opportunities to improve vector control. The results of these analyses can be used to better frame the implementation of vector control interventions and help to inform decisions surrounding local and regional dengue control.

7621

EVALUATING A PRACTICAL PERSON-CENTRED HEALTH SYSTEMS INTERVENTION TO ADVANCE JUSTICE AND INCLUSION FOR PERSONS AFFECTED BY SKIN NTDS IN LIBERIA

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For persons affected by skin Neglected Tropical Diseases (NTDs), lack of access to effective serviceprovision results in physical and psycho-social consequences, complex treatment journeys, andcatastrophic socio-economic impacts. Person-centred approaches are a key solution to thesechallenges and Liberia is one of the first countries to develop a national integrated approach. Yet, evidence is limited for quality of services, and how to equitably implement at scale.Using a person-centred participatory action research approach in Liberia we: 1) identified effectivestrategies to detect, refer, treat and support people with skin NTDs; 2) brought health systemsactors and persons affected together to co-design and test new health systems interventions; and 3) conducted a quasi-experimental mixed-methods evaluation of impact guided by the RE-AIM (Reach,Effectiveness, Adoption, Implementation

and Maintenance). We were able to reach 3,245 health system actors including persons affected, community healthworkers, traditional healers, faith healers, and health workers to enhance skills and capabilities inholistic management (biomedical and psychosocial) of NTDs. Increase effectiveness of integratedcase detection across all endemic skin NTDs; significantly decrease experiences of depression,anxiety and suicidal ideation amongst persons affected; and reduce out of pocket (OOP) expenditureby 30USD (50% of national average OOP). Due to high levels of stakeholder buy-in, facilitated by aMinistry of Health Technical Advisory Board, the intervention(s) have now been adopted within national health policy. Mechanisms such as mid-term reviews, supportive supervision andcommunity advisory boards supported appropriate implementation, through local adaptation. An investment case has lobbied funds to ensure ongoing maintenance funding. By taking a person-centred systems wide approach to reforming service delivery for skin NTDs, we catalysed and sustained improvements in service coverage. The versatility and leadership of the Liberian health system was central to this success.

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SPATIOTEMPORAL EVALUATION OF THE 2016-2022 MASS DRUG ADMINISTRATION FOR LYMPHATIC FILARIASIS IN KENYA: TOWARDS IDENTIFYING NEVER TREATED POPULATIONS

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Lymphatic Filariasis (LF) remains a significant public health problem in Kenya despite substantial efforts towards its control and elimination through Mass Drug Administration (MDA). Understanding the effectiveness of MDA interventions requires complementary comprehensive spatiotemporal modeling and demographic analysis to identify low-coverage areas and the never-treated populations who remain potential carriers, risking transmission to those regularly treated. This study integrates spatial modeling and demographic analysis to provide valuable insights into optimizing LF elimination efforts in Kenya. Data aggregation from 2016-2022 MDA records, Pre-transmission and transmission assessment surveys, and the Kenya National Bureau of Statistics were subjected to comprehensive data cleaning, imputation, and analysis using R software and WINBUGS. Bayesian approach was applied to estimate parameters, combining data likelihood with prior distributions to formulate posterior distributions for inference. Descriptive analysis revealed clear variations in reported MDA granular coverage between counties ($p < 0.001$), and within age categories ($p<0.001$). Granular ward-level evaluation models explained higher variation (52.5%) in MDA coverage compared to the standard sub-county-level (44.6%) and county-level (17.8%) models, with 74.1% of the variation in MDA coverage explained by age, sex, and ward-level evaluation. Spatiotemporal modeling unveiled lower coverage (<65%) at the granular level in some wards, with the age category 9-14 years exhibiting the highest coverage across all wards. Those aged 15+ years (adult population) recorded the lowest coverage. There was an association between sub-optimal MDA coverage and positive filarial antigen tests. These findings underscore the need for targeted interventions tailored to address potential LF persistence and recrudescence associated with lower MDA coverage in some wards, which remain potential hotspots. Special attention should be given to the age category 15+ years during health education and awareness campaigns to improve MDA coverage in similar settings.

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USE OF THE COMMUNITY-DIRECTED TREATMENT WITH IVERMECTIN PLATFORM TO ESTIMATE LYMPHATIC FILARIASIS MORBIDITY IN THE CO-ENDEMIC HEALTH DISTRICTS

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In Cameroon, mapping carried out between 2003 and 2016 revealed that 144 out of the 200 health districts (HDs) are endemic for lymphatic filariasis (LF). The country is on track to eliminate the disease by 2027. To date, all 144 health districts (HDs) have reached the criteria for stopping mass drug administration (MDA), 143 have passed the first surveillance survey (TAS2) and 96 have passed the second (TAS3). However, the country requires estimates and location of LF morbidity cases to plan services. The Act to End NTDs | West program in 2023, with the Cameroon MoH, carried out an evaluation of LF morbidity through Community-Directed Treatment with Ivermectin (CDTI) activities in 4 onchocerciasis (OV) co-endemic HDs in the Far North region. Cascading training sessions were organized by experienced staff during the training of nurses for CDTI to explain the steps to identify cases of lymphoedema and hydrocele and to fill in the data collection tools. The health area nurses strengthened the capacity of the community drug distributors (CDDs) to identify and list suspected cases by community. Suspected cases were registered during the census of community members for the CDTI. People with enlarged feet, arms and scrotum were systematically recorded on the suspected case forms. Suspected cases were confirmed after a physical examination by trained health personnel and an interview with the patient. A total of 52 health personnel and 1688 CDD were trained to identify suspected LF morbidity cases. 443,099 people were registered for the MDA by CDDs in the 4 HDs, 40 cases of enlarge feet and 56 cases of enlarge scrotum were recorded. After a physical examination, 33/40 cases were confirmed as lymphoedema, and 33/56 cases confirmed as hydrocele. These results bring the number of HDs with known and confirmed patients in Cameroon to 19 out of 200. The national program plans to scale up the LF burden assessment through CDTI, as used in OV-endemic HDs, in 2023. For the first step in 2024, data collection tools have been revised to include indicators on suspected cases of hydrocoele and lymphoedema at all levels of the health pyramid.

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NTDSCOPE: A MULTIMODAL PORTABLE MICROSCOPE FOR DISEASE DIAGNOSIS

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Efforts to eliminate or control Neglected Tropical Diseases (NTDs) require new diagnostic tools and technologies. Here we introduce the NTDscope, the latest version of the mobile microscope known as the LoaScope, first deployed in 2017 for treating onchocerciasis in *Loa loa*-endemic areas of Cameroon. The NTDscope was designed with upgraded hardware and improved manufacturability to support onchocerciasis elimination efforts. The NTDscope is an integrated device based on mobile phone components, including a Sony IMX586 sensor and touchscreen, but no detachable phone. Sample imaging utilizes the reversed lens system used in the original LoaScope, providing both moderate resolution (~3 µm on center) and a large field of view (5.1 mm x 6.8 mm) in a compact format. The NTDscope features single-axis motion of samples held in optically-transparent, injection-molded, disposable capillaries. For label-free, motion-based quantification of microfilaria such as *L. loa*, rectangular capillaries are loaded with 40 µL of whole blood and imaged across 7 fields-of-view. For filtering parasitic eggs in urine samples such as *Schistosoma haematobium*, we designed a tapered capillary with a Luer connector, such that a 10 mL urine sample can be processed, trapping eggs in a viewing region for imaging. In both cases, data can be processed with on-board algorithms to quantify parasite load at the point-of-care. To provide flexible imaging, the NTDscope can capture images and videos in brightfield, darkfield, and fluorescence contrasts. Recent examples of data collected with the device include videos of *L. loa* and *Mansonella perstans* microfilariae in whole blood, *S. haematobium* eggs filtered from urine, and Soil Transmitted Helminth eggs floated from stool. This portable (<1 kg), Android-based, and user-friendly microscope can image both live and fixed samples and can be used for molecular detection assays based on fluorescence, luminescence, or colorimetric changes. Utilizing this versatility, the NTDscope and future iterations could enable a broad range of assays at the point-of-care, serving as a key element of decentralized healthcare in the future.

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EVALUATING TRACHOMA TRENDS IN THE AMHARA REGION, ETHIOPIA: INSIGHTS FROM THE MOST RECENT 163 POPULATION-BASED SURVEYS, 2015-2023

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The Trachoma Control Program in Ethiopia's Amhara region has shown significant progress towards eliminating trachoma as a public health problem, aligning with the World Health Organization's (WHO) 2030 target, through implementation of the WHO-endorsed SAFE (Surgery, Antibiotics, Facial Cleanliness, and Environmental Improvement) strategy. This report compiles results from the most recent population-based surveys for each of the 163 districts encompassing the entire region, conducted between 2015-2023. All surveys used multi-level sampling to select households within communities. Within all selected households, all individuals ages ≥1 year were examined for signs of trachoma by certified graders. As of 2023, 55 districts had a trachomatous inflammation-follicular (TF) prevalence <5% among children ages 1-9 years, 18 districts were between 5-9.9% TF, 72 were 10-29.9% TF, and 18 were ≥30% TF. Of the 55 districts that have met the elimination threshold of <5% TF, 42 remained <5% at trachoma surveillance survey (TSS), conducted at least 2 years post-threshold achievement at trachoma impact survey (TIS), and 13 were eligible for TSS according to the 2-year timeline. Thirteen (of the 163) districts were recrudescent, having reached the elimination threshold at TIS but with TSS results ≥5%. A total of 95 (of the 163) districts had persistent trachoma, defined as having had a second TIS without reaching the elimination threshold. Of these, 18 districts (19%) could be considered hyper-persistent, with ≥30% TF, meaning they are persistent with hyper-endemic trachoma. Trachomatous inflammation-intense (TI) among children ages 1-9 years was <5% in 154 (94%) districts. Trachomatous trichiasis (TT) unknown to the health system among adults ages ≥15 years was below the elimination threshold of <0.2% in 1 (0.6%) district, between 0.2% and 0.9% in 95 (58.3%) districts, and ≥1% in 67 (41.1%) districts. Despite strides, continued and intensified expansion of SAFE interventions in the Amhara Region is paramount to achieving the WHO 2030 elimination target.

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MULTISTAGE PROTECTIVE ANTI-CELTOS MONOCLONAL ANTIBODIES WITH CROSS-SPECIES STERILE PROTECTION AGAINST MALARIA

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Cell-traversal protein for ookinetes and sporozoites (CelTOS) is a malaria vaccine antigen that is conserved in *Plasmodium* and other apicomplexan parasites, and plays a role in cell-traversal. The structural basis and mechanisms of CelTOS-induced protective immunity to parasites are unknown. Here, we isolated antibodies from mice immunized with PvCelTOS or PfCelTOS and demonstrated their multistage activity in protecting against liver infection and preventing parasite transmission to mosquitoes. These monoclonal antibodies also showed cross-species activity with sterile protection against *in vivo* challenge with transgenic parasites containing either *P. falciparum* or *P. vivax* CelTOS, and with transmission reducing activity against *P. falciparum*. The mAbs inhibited CelTOS-mediated pore formation providing insight into the protective mechanisms. X-ray crystallography and mutant-library epitope mapping revealed two distinct binding epitopes on CelTOS. One antibody bound to a parallel dimer of CelTOS, while the other antibody bound to a novel antiparallel CelTOS dimer architecture. These findings inform the design of antibody therapies and vaccines and raise the prospect of a single intervention to simultaneously combat *P. falciparum* and *P. vivax* malaria.

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EX VIVO RESPONSES OF *PLASMODIUM FALCIPARUM* CLINICAL ISOLATES TO MABS DIRECTED AGAINST PFRH5, PFCYRPA AND PFRIPR

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The global reduction of malaria cases and deaths has stalled, necessitating a highly effective vaccine. The challenge lies in the extensive diversity of *Plasmodium falciparum* antigens, which has been under-prioritized in vaccine candidate evaluation. This study examines the functional contribution of naturally occurring genetic diversity in next-generation malaria vaccine candidate antigens from the RCR-complex: PfRH5, PfCyRPA, and PfRipr, to *P. falciparum* immune evasion and antibody efficacy.Patients were recruited from two clinics in Kedougou, a high malaria endemicity Senegalese region. The phenotypic responses of circulating strains against anti-RCR-complex monoclonal antibodies (mAbs) were assessed using SyBR green flow-based growth inhibition assays (GIA). The percentage inhibition was determined by comparing it to naive IgG at equal concentrations. Anti-basigin (MEM-M6/6) known to inhibit *P. falciparum* invasion was used as a positive control. Twenty clinical isolates were

used to set up the ex vivo GIAs and the assays were done with different concentrations of each mAb. The results showed that Ripr antibodies 5G6 and 1G12 significantly inhibited parasite growth, while 1C4 did not. For PfRH5, only three of the ten antibodies tested were non-inhibitory. The inhibition rates of CyRPA mAbs did not reach 50% when used separately but reached ~80% in combinations. The most potent Ripr antibody was 1G12, resulting in a mean inhibition range of 70% at the highest concentration of 400 µg/ml. For PfRH5, the highest level of inhibition was 75% for c2AC7, c9AD4, R5.016, and was obtained with a concentration of 200 µg/ml. When compared at the same concentration (200µg/ml) mAbs directed against PfRH5 and PfRipr were more inhibitory than those against PfCyRPA. The study found that field isolates from a hyper-endemic site, known to harbor high levels of genetic diversity, are highly susceptible to mAbs targeting PfRH5, PfCyRPA, and PfRipr. These findings confirm these candidates as important and conserved targets for an effective malaria vaccine, highlighting the need to prioritize genetic diversity in vaccine candidate evaluation.

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PROTECTION OF INDONESIAN SOLDIERS AGAINST HIGHLY VARIANT *PLASMODIUM FALCIPARUM* INFECTION IN PAPUA PROVINCE, INDONESIA, BY TWO PFSPZ VACCINES

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Live attenuated *Plasmodium falciparum* (Pf) sporozoite (SPZ) vaccines of West African strain origin (PfSPZ) have achieved 48-86% vaccine efficacy (VE) against naturally transmitted Pf infection in West African adults. Molecular subunit vaccines RTS,S/AS01 and R21/Matrix-M have achieved 45-77% VE against febrile high-grade Pf parasitemia in African infants and small children but only nominal protection against Pf infection, a more stringent endpoint. We conducted a trial of radiation- and chemo-attenuated West African strain PfSPZ vaccines in malaria-naive Indonesian soldiers naturally exposed over 10 months to the Pf parasites in Papua Province, eastern Indonesia, where strains are highly distinct from the vaccine strain. In this randomized, double-blind, placebo-controlled trial, soldiers stationed in a malaria-free area of Riau Province, Sumatra, in western Indonesia were randomly assigned 1:1:1 to 3 doses of normal saline (NS), radiation-attenuated PfSPZ Vaccine ($9x10^5$PfSPZ/dose), or chemo-attenuated PfSPZ-CVac (CQ) ($2x10^5$ PfSPZ/dose). After immunization, the soldiers transited 4400 km to Papua and were followed during a 43.5-week deployment (including under battlefield conditions) for incident Pf infection and Pf infection with clinical manifestations. 334 soldiers received all 3 doses and deployed. There were no differences among groups in rates or severity of adverse events after each immunization. Malaria attack rates were high: after 24 weeks deployment, 42.3% (47/111) of NS controls had a first Pf infection. All but one Pf infection in vaccinees and controls had clinical manifestations, reflecting the malaria-naive status of the soldiers. At 24 weeks, VEs against Pf infection and clinical malaria were 54% (95%CI: 0.26, 0.72) and 56% (0.28, 0.73) for PfSPZ Vaccine and 50% (0.19, 0.69) and 50% (0.19, 0.69) for PfSPZ-CVac (CQ). VE decreased by 15-24% during the next 19.5 weeks. There was no VE against *P. vivax*. PfSPZ Vaccine and PfSPZ-CVac (CQ) had 50-56% VE over 24 weeks in non-immune soldiers against Pf infection and clinical malaria caused by a Pf population that is, globally, the most divergent from the vaccine strain.

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RH5.1/MATRIX-M™: EFFICACY OF A STANDALONE BLOOD-STAGE VACCINE AGAINST CLINICAL *PLASODIUM FALCIPARUM* MALARIA IN 5-17 MONTH OLD CHILDREN: A PHASE 2B RANDOMIZED TRIAL IN BURKINA FASO

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Two pre-erythrocytic vaccines (R21/Matrix-M™ and RTS,S/AS01) are now approved for *P. falciparum* (*Pf*) malaria prevention in children. However, neither vaccine induces blood-stage immunity against parasites that emerge from the liver. The most advanced blood-stage *Pf* vaccine candidate is a full-length protein (RH5.1) that targets the conserved and essential reticulocyte-binding protein homologue 5. RH5.1 induced the highest levels of *in vitro* growth inhibition activity (GIA, a correlate of protection in non-human primates) in 5-17-month-old children when administered with Matrix-M™ in a Phase 1b trial in Tanzania. Here we assess efficacy against clinical malaria in an area of seasonal transmission in Burkina Faso in a Phase 2b, double-blinded, randomised, controlled trial (NCT05790889). Healthy children aged 5-17 months were recruited at the Siglé site and randomised to receive either three intramuscular 10 µg doses of RH5.1 with 50 µg Matrix-M™ (two groups of N=120) or three doses of a rabies control vaccine (two groups of N=60), given as a monthly 0-1-2 or a delayed third dose 0-1-5-month regimen. Primary endpoints were: i) efficacy against clinical malaria at 6 months (starting from 14 days post dose 3), defined as the presence of axillary temperature ≥37.5°C and/or history of fever within the last 24 hours AND *Pf* asexual parasitaemia >5000/µL; and ii) vaccine safety and reactogenicity. Vaccinations started in April 2023 and completed by mid-September 2023. A total of 122, 119 and 120 children were enrolled in the control, delayed and monthly dose RH5.1/Matrix-M™ groups, respectively. RH5.1/Matrix-M™ was well tolerated with no safety concerns or serious adverse events at 12 months of follow-up post first dose. Vaccine efficacy at 6 months as per the primary case definition was 55% (95% CI 20-75, *P*=0.007) in the delayed group and 40% (95% CI -0.03-65, *P*=0.065) in the monthly group. A 0-1-5-month regimen of RH5.1/Matrix-M™ appears safe, highly immunogenic, and shows the first promising efficacy of a RH5-based blood-stage vaccine when used alone, supporting further clinical development within a multi-stage vaccine strategy for *Pf* malaria.

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DEVELOPMENT OF A GLOBAL RESEARCH AGENDA TO GUIDE THE OPERATIONALIZATION AND SCALE-UP OF MALARIA VACCINES

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In 2021, the World Health Organization (WHO) recommended the first malaria vaccine for use, RTS,S/AS01. Two years later, R21/Matrix-M, a second vaccine, was recommended by WHO. Fifteen countries are on track to introduce the approved vaccines in 2024. Given these advances, WHO and Gavi identified the need to develop a research agenda to inform vaccine introduction and scale-up. To develop the agenda, a broad stakeholder consultation process was commissioned by WHO and Gavi with support from the U.S. President's Malaria Initiative. The consultation process was led by Kintampo Health Research Centre and PATH, with inputs by a technical advisory group, to identify priority implementation research topics for the vaccine. In total, 132 stakeholders from national Expanded Program on Immunization (EPI) and malaria programs, research institutions, civil society organizations, and technical partners with vaccine or malaria expertise were consulted from 23 countries, 20 from malaria-endemic countries. Thirty topics covering themes related to vaccine safety, implementation feasibility, acceptability, integration, impact, effectiveness, costing, and cost-effectiveness emerged. Stakeholders evaluated and ranked the topics according to their broad relevance, urgency for informing vaccine rollout, and feasibility. Overall, topics ranked high across the evaluation criteria, illustrating their importance. Topics related to implementation feasibility and vaccine acceptability will provide additional guidance to national programs introducing the vaccine; while topics on impact, effectiveness, costing, and cost-effectiveness will provide national level information to guide long-term planning and scale-up. Several topics address health system issues that extend to delivery of all vaccines and have the potential to provide important learning for national EPI programs more broadly. The agenda intends to serve as a global resource to inform vaccine research investments, with the aim of facilitating a more coordinated and impactful approach to addressing key evidence gaps and information needs of countries taking up the vaccine.

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MALARIA VACCINE IN BURKINA FASO: SUCCESSES AND CHALLENGES OF THE FIRST TWO MONTHS

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The introduction of the malaria vaccine in Burkina Faso marks a significant milestone in the country's ongoing efforts to combat this deadly disease. The introduction of this vaccination took place amidst a context of major insecurity affecting 7 out of the 27 selected health districts. One month after, this article describes the initial trends following the introduction of the RTSS/AS01 vaccine into Burkina Faso's Expanded Program on Immunization (EPI). This is an analysis of data collected from February 5th to March 31st, 2024, from the traditional registers of the Expanded Program on Immunization. Vaccination coverage was calculated based on the monthly targets defined during micro-planning. In the first month of vaccination, 14,550 out of 18,219 children received the first dose of the anti-malarial vaccine, representing a national coverage of 79.9% compared to the operational target of 91% expected by the end of March for a target of 87%. Fifteen out of the 27 health districts, or 55.5%, have a coverage of at least 80%. Gorom-Gorom health district, heavily affected by insecurity, has a coverage of 91.6%. Twelve health districts, six (06) of which are affected by insecurity, have a vaccination coverage ranging from 50% to 80%. The assessment at three (3) weeks into the second month shows that four health districts have vaccinated all the children vaccinated in the first month, and fifteen health districts have vaccinated half of the children who have already received the first dose of the malaria vaccine. Challenges such as social mobilization, interpersonal communication, and the late start of vaccination in localities in insecure zones are constraints and challenges to be overcome in order to improve adherence and reduce dropout rates between doses of the anti-malarial vaccine. The results of the first two months of the malaria vaccine introduction in Burkina Faso are encouraging despite the constraints and challenges encountered. Future challenges will include the monitoring and catch-up of children who have not received the necessary series of doses of the anti-malarial vaccine and scaling up in the country's remaining 43 districts.

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IMPACT OF PREVENTION, DIAGNOSTIC AND TREATMENT OF SIMPLE MALARIA CASES BY COMMUNITY HEALTH WORKERS SUPERVISED BY MOBILE NURSES IN RURAL COMMUNITIES IN BURKINA FASO

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The fight against malaria faces the challenge of the emergence and expansion of the resistance to curative (drugs), preventive (vector control) and diagnostic (HRP2) tools. These evolutions are influenced by the limited access to prevention, diagnostic and treatment, among remote rural and vulnerable communities. In the REACT2 project, we hypothesize that community health workers (CHWs) supervised by a mobile nurse (the tested intervention) could improve access to prevention, diagnostic and treatments against malaria. To evaluate this hypothesis, we conducted a cluster stepped-wedged randomized trial (NCT05535465) in 18 rural areas of Burkina Faso from December 2021 to December 2023, comparing malaria burden between villages with and without the tested intervention. The impact of this intervention was assessed modeling the number of diagnosed and treated cases per epidemiological week per village using a negative binomial regression model. In a population of 5231 individuals across 18 rural villages, our preliminary analyses indicate that a total of 3255 uncomplicated malaria cases were diagnosed and managed by the CHWs. The CHWs facilitated the referral of 27 severe malaria cases for appropriate care in specialized services. Comparative analysis revealed that the intervention led to a threefold increase (RR=3.67 [3.29-4.14]) in the number of malaria cases managed and a 20% reduction (RR=0.08 [0.01-0.96]) in severe malaria cases per epidemiological week compared to control villages. These findings underscore the effectiveness of supervised community-based interventions in malaria elimination. Such results hold great potential for informing and enhancing future national malaria control strategic plans.

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DIFFERENTIAL IMPACT OF INSECTICIDE TREATED NETS AGAINST MALARIA: A META-ANALYSIS AND MODELLING STUDY OF CLUSTER-RANDOMIZED CONTROLLED TRIALS IN AFRICA

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The efficacy of vector control tools against malaria may depend on local factors such as disease prevalence, existing use of control interventions and the population uptake of the tool. Empirical evidence to support this hypothesis, however, is lacking as cluster-randomised controlled trials (CRTs) evaluating vector control tools are not typically powered to explore the impact of these variables. This may complicate the interpretation of future CRTs where the current standard of care cannot be removed. This study aims to assess the impact of local factors on the efficacy of different classes of insecticide treated nets (ITNs), using a meta-analysis and modelling exercise of ITN trials. Using mixed-effects generalised linear models, we analysed data from four CRTs of ITNs in Africa to assess the importance of three key variables - baseline prevalence, baseline ITN use and ITN use throughout the trial - for ITN efficacy. We then simulated each trial using a validated mechanistic model of malaria with parameters determined using different levels of detail for the three key variables (trial arm-level data or cluster-level data) and compared the model fits to trial survey results. Baseline prevalence and ITN use varied substantially between trials and trial clusters. In the meta-analysis, all three variables were important predictors of the efficacy of ITNs, but associations varied by trial and were non-linear. Arm- and cluster-level simulations were broadly able to recreate trial results. Differential results by parameterisation method helped to explain observed differences between clusters and arms. The meta-analysis provides additional information on understanding the effectiveness of different ITNs while the simulations indicate that compiling data without considering important covariates risks generating misleading results. As more interventions are adopted as the standard of care, future CRTs will become increasingly difficult to power and interpret. The use of mechanistic models in future trial design and analysis can support empirical data collection to ensure trials are practically achievable but statistically robust.

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REAL-LIFE *PLASMODIUM VIVAX* MALARIA IN CAMBODIA: A UNIQUE STUDY DESIGN TO CHARACTERIZE IN VIVO RELAPSES

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Plasmodium vivax is characterized by the presence of dormant hypnozoites, which cause relapses upon reactivation. The determinants of relapse periodicity and the molecular processes underlying hypnozoite activation remain largely unknown. Here, we aimed to determine the dynamics of Pv relapses in infected patients from Cambodia and to identify factors associated with Pv relapses. G6PD normal and deficient patients were enrolled and treated with 7-day artesunate without primaquine and then followed for 90 days, while being relocated to a malaria-free area of Cambodia to prevent reinfection. Capillary blood was collected every 2 days and parasite relapses were monitored by qPCR. Upon each microscopically confirmed relapse, patients received another 7-day artesunate course, and follow-up continued until Day 90. A total of 63 patients were enrolled in the study and 82% experienced at least one relapse during the follow-up period, with an average number of relapses of 2.2 (range 1-4). The earliest relapse was detected by PCR 10 days after enrollment, with an average time of 26.5 days (SD: 17.6) from enrollment to first relapse. The interval between the 1st and 2nd relapse was significantly longer, averaging 30.0 days (SD: 10.3, p= 0.013), although the time between the 2nd and 3rd relapses did not significantly differ (mean 25.4 days, SD: 5.3, p= 0.962). The proportion of patients experiencing at least one relapse did not vary significantly between G6PD normal (84%) and deficient (78%) individuals, nor did the average number of relapses (2.1 for deficient vs 2.2 for normal, p= 0.918). This unique cohort enables the calculation of parasite multiplication rates for each relapse using qPCR. Using these data, complemented by the whole genome sequences of every infection, we will evaluate the impact of G6PD deficiency on in vivo parasite growth. Finally, we will present how suspected factors associated with the onset of relapses (i.e., febrile illness) do not align with the results obtained from our cohort and how, notably using RNA-seq in combination with in vitro liver-stage Pv, we investigate other factors associated with hypnozoite reactivation.

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MALARIA CONTROL AND VACCINATION IN THE CONTEXT OF TROPICAL CYCLONES

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Extreme weather events, such as tropical cyclones, can disrupt public health activities and threaten progress towards malaria control goals. A growing body of evidence indicates climate change may modulate malaria risk in areas at the latitudinal or altitudinal margins of transmission suitability. Few studies, however, have focused on the potential impacts of increasingly severe extreme weather events in the high-burden, endemic core areas responsible for the vast majority of global cases. Here, we analyze empirical data from a prospective cohort study in southeast Madagascar with malaria infection observations before and after major tropical cyclones in 2022 and 2023 (n = 20,718). We derive estimates of the force of infection and use mathematical models to characterize the impact of disruptions to public health activities. We then quantify the potential for strategies such as chemoprophylaxis and vaccination to mitigate climate-mediated disruptions. We find delays in interventions as brief as two weeks result in substantial increases in expected infections. Long-lasting prophylactics and vaccination, not currently implemented widely, may mitigate these increases in risk during gaps in coverage. From modeling the deployment of antimalarial vaccination, we find an approximate 49% reduction in the number of symptomatic infections expected in the aftermath of a disruption when high coverage (e.g., 70%) is attained for a vaccine with efficacy similar to that reported for the recently approved R21 vaccine. Together, these data demonstrate the benefit to considering disruptions to malaria control measures when evaluating intervention recommendations in high malaria burden, climate-vulnerable geographies.

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EMPATHY AND SHARED COMPASSION IN MALARIA CARE: A RAPID ETHNOGRAPHIC STUDY OF PROVIDER EMOTIONAL RESPONSE IN UGANDA

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Malaria is a leading cause of morbidity and mortality in Northern Uganda. This study utilizes ethnographic methods to examine the ways provider-client interactions impact malaria care seeking and prevention practices. Surveys comprised 270 health providers (facility-based and Village Health Teams (VHTs)) and 838 caregivers from Karamoja and West Nile. Focus group discussions were conducted with four groups of six community health workers and four groups of six facility-based providers. Eight six-hour ethnographic observations were conducted with facility-based providers and community health workers who routinely provide general clinical care, including malaria care, for children under five years of age. Among caregivers, the odds of practicing all malaria prevention and care-seeking behaviors (ITN use, early treatment seeking, IPTp) were found to be significantly higher among those who reported being satisfied with their provider interactions (OR=5.9, 95% CI: 2.86 - 12.28). Providers and VHTs in surveys and focus groups demonstrated high knowledge of positive counseling practices yet varied emotional responses in interactions with clients. The most common reactions to clients not practicing malaria preventative behaviors or using alternative care for malaria treatment were sadness (62%), support (36%), empathy (19%), anger (17%), and frustration (17%) among surveyed providers. Observational data also showed these emotional responses and illustrated low practice of client confidentiality, considerable client volume, provider fatigue, and minimal supportive supervision for provider relational skills. Given that satisfaction with provider interactions was the highest association with positive malaria prevention and care seeking practices among caregivers, client-provider connections and relationships must be prioritized. Based on these findings, malaria programs would benefit from integrating emotional response awareness into interpersonal communication and counseling training resources to strengthen empathetic, connection-fostering responses and build trust between clients and providers.

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TREATMENT-SEEKING BEHAVIOR FOR FEVER IN KINSHASA, DEMOCRATIC REPUBLIC OF THE CONGO: A LONGITUDINAL STUDY

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The Democratic Republic of the Congo has the second-highest malaria burden in Africa. Despite the adoption of rapid diagnostic tests and treatment with artemisinin-based combination therapy (ACT), implementation challenges, such as access and acceptance of these effective strategies, remain. This descriptive study quantifies treatment-seeking behavior and access to confirmatory diagnosis and treatment with ACT in participants with self-reported fever in the context of a longitudinal study in Kinshasa Province. Data were collected during four active household visits conducted every six months from 2019-2021. Information on recent fever, treatment-seeking practices, and history of testing and treatment was collected. Descriptive analyses determined the proportion of participants seeking and receiving malaria testing and treatment. Weighted multivariate analyses were conducted to identify factors associated with treatment-seeking behaviors. Of the 4,544 interviews, 491(11%) respondents reported having a fever the week before the study visit. Most participants, 78% (383/497), sought treatment for the reported fever, and 93% sought treatment the same or the next day after the fever started. However, two-thirds of those seeking care were self-treated at home, and only 24% (91/383) sought care at the local study clinic. The odds of treatment-seeking were highest for participants less than five years (91%; aOR: 6.52; 95% CI 2.26-18.8; $p < 0.001$). Participants who had a fever >4 days had 3.29 times the adjusted odds of seeking treatment (95% CI 1.58-6.87; $p = 0.0015$). Compared to participants aged 15 years or older, children less than 5 (aOR 2.31; 95% CI 1.18-4.52; $p = 0.0146$) and children 5-14 (OR: 1.82; 95% CI 1.18-2.82; $p=0.007$) had increased odds of seeking treatment promptly (<24 hours). While it is expected that study participants may seek care early, these findings highlight that most participants self-treated fever episodes at home without a confirmatory test. Further research is warranted to understand where fever is treated and why patients do not seek prompt care at their local public health facility, where tests and ACT are free.

7638

MAINTAINING POWER IN MALARIA CLUSTER RANDOMIZED TRIALS USING INNOVATIVE DESIGNS TO MITIGATE THE IMPACT OF HETEROGENEITY

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Cluster randomised trials (CRTs) are the gold-standard for evaluating the community-wide effects of malaria interventions. Results from these trials feed into a body of evidence that the WHO utilises to inform policy recommendations and have been instrumental in the roll out of vital interventions including bed nets and chemoprevention strategies. Nonetheless, CRTs are costly, lengthy and logistically challenging. Moreover, our recent meta-analysis of 21 malaria CRTs revealed many were underpowered to detect their predicted effect size - this is exacerbated in settings where multiple interventions remain in place in the control arm. Notably, many trials underestimated the degree of heterogeneity in prevalence or incidence at the cluster-level, defined as the coefficient of variation or k. This meant that sample size estimations when planning trials were inaccurate which compromised study power. Higher than anticipated cluster heterogeneity in malaria CRTs was more notable in lower endemicity settings where transmission is more spatially and temporally sporadic and among trials that measured incidence over prevalence. In this work, using cluster-level data from 21 trials and statistical simulations, we investigated whether alternate/adaptive trial designs can used to maintain study power, despite high heterogeneity of outcomes. We examined whether re-randomizing clusters using pair matching or stratification at baseline according to outcomes or covariates (such as intervention coverage) minimizes cluster heterogeneity and reduces the level of uncertainty around effect size estimates at the end of trials. Finally, we investigated the impact of different CRT designs on the required size of trials (number of clusters and cluster size) while maintaining adequate power. Results from this work will be used to generate guidelines for future malaria CRTs to help ensure triallists are able to evaluate interventions in a robust and sustainable manner.

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INNOVATING MALARIA PROGRAM COMPLIANCE FOR SCALABILITY USING AUTOMATION AND AI

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Public health interventions that use demand-side financing, product subsidies, and fee-for-service incentives often face challenges preventing fraud and guaranteeing that subsidies reach patients. However, anti-fraud measures risk being slow and cumbersome, which can hinder program adherence and expansion efforts. Maisha Meds' software — used by over 3,200 private pharmacies and clinics across Africa — offers an opt-in reimbursement program that has been shown in an earlier randomized controlled trial to improve the rate of quality-assured malaria case management more than fourfold. This program includes digital

reimbursements to providers who follow testing and treatment guidelines, as well as subsidized out-of-pocket prices for patients. In order to automate compliance and detect fraud during a period of rapid scale-up, Maisha Meds built a novel system called Madai ("claims" in Swahili). This system uses a multi-layered fraud detection strategy that analyzes transaction duration, internal facility compliance scores, and patient identity verification with USSD. Through a partnership with Audere, the system also leverages AI computer vision to verify test results and image quality issues, ensuring that only patients who test positive for malaria get subsidized treatment. From January to August 2023, Madai incorporated partial automation features that still required final approval by human auditors, reducing average processing time from 5.9 to 2.1 days. Between September 2023 and January 2024, Madai introduced fully automated approvals that further reduced average claim review time down to less than a day — 16.4 hours on average. During this period, total malaria claims increased by 170% and about 85% of claims were reviewed automatically. By using automation to accelerate claims and make strategic use of staffing, this approach creates a replicable framework for other reimbursement- and subsidy-driven models.

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STRENGTHENING THE FRONTLINE DURING PUBLIC HEALTH EMERGENCIES: THE ROLE OF INSTITUTIONAL AND SOCIAL SUPPORT FOR HEALTHCARE WORKERS IN LOW-INCOME SETTINGS

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The psychological and social challenges faced by healthcare workers during infectious disease outbreaks such as Ebola and COVID-19 have underscored the importance of institutional and social support. This research aimed to explore the impact of institutional and social support on the professional efficacy of healthcare workers in a low-income setting during the COVID-19 pandemic. This mixed-method study was conducted from February to October 2022 across six districts in Sierra Leone, utilizing in-depth interviews with 24 healthcare workers and a subsequent online survey completed by 1001 participants. Thematic analysis and logistic regression were employed to analyze qualitative and quantitative data, respectively. By utilizing the socio-ecological model as a framework, the study examined the mechanisms through which various levels of support impacted the execution of healthcare roles. The study found substantial variability in the experiences of healthcare workers with respect to support received from families and workplaces. While 83% reported receiving support from family, challenges such as stigma were notable. Workplace support was reported by 78% of participants, but experiences varied greatly in terms of resource availability and institutional policies. National policies and guidelines were generally well-received, with improvements noted since the Ebola outbreak experienced in 2014. Logistic regression analysis highlighted the significant role of workplace support in enhancing professional efficacy during the COVID-19 pandemic, noting that family support was significantly influential only in the absence of institutional support. The findings underscore the critical importance of comprehensive institutional and social support systems for healthcare workers during public health emergencies. Strengthening these support systems can enhance the resilience and professional efficacy of healthcare workers, thereby improving health outcomes during pandemics. Future public health preparedness efforts should include reinforcing these support systems in conjunction with improving disease surveillance

7641

COMPARING IMPLEMENTATION OUTCOMES AFTER AZITHROMYCIN MASS DRUG ADMINISTRATION TO CHILDREN 1-11 VS 1-59 MONTHS OLD FOR CHILD SURVIVAL IN A CLUSTER-RANDOMIZED TRIAL IN NIGER

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Studies have shown that azithromycin mass drug administration (MDA) to children 1-59 months old reduces child mortality. Given the risk of antimicrobial resistance, World Health Organization guidelines recommend limiting azithromycin MDA to children 1-11 months old. This implementation trial was carried out simultaneously with a larger effectiveness trial, and examined differences in costs, coverage, and acceptability between MDA strategies (1-11 months vs 1-59 months). In the Dosso region of Niger, 80 communities were randomized to receive one year of biannual azithromycin MDA to children 1-59 or 1-11 months old. The primary outcome was cost per dose delivered and secondary outcomes included reach (coverage), acceptability, appropriateness, and feasibility. Program costs were estimated using the personnel, training, and supply costs required to distribute azithromycin at the community level. Coverage was defined as the number of doses delivered divided by the estimated number of eligible children. Acceptability, appropriateness, and feasibility were measured for each arm among caregivers, community health workers, and community leaders using a survey conducted after the first distribution. 5,827 doses were delivered in the 1–59-month arm and 1,002 doses were distributed in the 1-11-month arm. The geometric mean community-level cost per dose delivered was $6·5 lower (95% CI -$10·4 to -$3·7, *P*-value < 0·001) in the 1–59-month arm ($1·6, 95% CI $1·0 to $2·3) compared to the 1–11-month arm ($8·2, 95% CI $7·6 to $8·8). Treatment coverage was similarly high (>90%) in both arms, *P*-value 0.05. The intervention was found to be more acceptable (4·2%, 95% CI 0% to 8·4%, *P*-value 0·04) and appropriate (3·4%, 95% CI 0·1% to 6·8%, *P*-value 0·04) by caregivers in the 1–59-month arm compared with the 1–11-month arm. Most respondents in each stakeholder group indicated that including 1–59-month-old children in MDA was more acceptable, appropriate, and feasible than restricting to 1-11-month-olds. Overall, including children 1-59 months vs restricting to 1-11 months resulted in a lower cost per dose, with higher preference among stakeholders.

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IMPROVED ACCESS TO COMMUNITY-LEVEL DATA IN MADAGASCAR'S NATIONAL HEALTH INFORMATION SYSTEM FOLLOWING SUPPORT TO DISTRICT HEALTH TEAMS, 2019 - 2023

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Before 2019, Madagascar's national health information system (HIS) used an offline Microsoft Excel-based system to report community-level data; this system was difficult to access in some areas, and data from volunteer community health workers (CHWs) was often missing or of poor quality. Since 2019, the USAID-funded ACCESS program has supported the Ministry of Public Health (MOPH) to operationalize DHIS2 in Madagascar's 23 regions. Additionally, ACCESS provided human, material, and financial resources to strengthen capacity in community data management among 60 district health teams in 11 intervention regions. The resources supported training, supervision, and data processing and use. We compared the reporting of CHW data (number of reports submitted/number expected) in DHIS2 at baseline and after implementation of the activities in the 11 intervention regions (115,536 reports expected in 2019; 115,608 in 2023) and in the 12 non-intervention regions (129,624 reports expected in 2019; 129,745 in 2023). The CHW reporting rate in intervention regions increased by 75.7 percentage points (95% confidence interval [CI]: 75.4, 75.9; p<0.001)—from 9.9% in 2019 to 85.6% in 2023. In the 12 non-intervention regions, the reporting rate increased from 0.0% in 2019 to 39.2% in 2023, an increase of 39.2 percentage points (95% CI: 39.0, 39.5; p<0.001). Operationalization of DHIS2 may have contributed to improved community data reporting rates nationwide, while the additional HIS interventions potentially contributed to the greater improvement in intervention areas. To foster continuity of reporting after ACCESS ends, in 2023 the MOPH identified 60 officials responsible for entering CHW reports in DHIS2 and managing community health data in the 60 districts of the intervention regions. In addition, ACCESS is supporting the MOPH to ensure these focused district-level HIS strengthening approaches are implemented nationwide, including by developing training materials for those entering community data. Further analyses are recommended to guide implementation and increase effectiveness of these interventions.

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ROUTINE CHILDHOOD IMMUNIZATION COVERAGE AMONGST HOSPITALIZED CHILDREN: A QUALITY IMPROVEMENT INITIATIVE

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Vaccination is the best preventative measure against infectious diseases. However, the COVID-19 pandemic has led to increased gaps in immunization coverage, which are concerning for ongoing circulation of vaccine preventable diseases globally, including measles. Hospitalizations and clinic visits are a missed opportunity to identify and address these gaps. This project used hospital admission to (1) Identify and understand gaps in childhood immunizations; (2) Identify barriers to vaccination amongst unvaccinated or partially vaccinated patients; (3) Implement strategies to improve vaccine access and confidence; and (4) Facilitate increased uptake of immunizations. We implemented a quality improvement initiative on select paediatric wards at The Hospital for Sick Children, Toronto (Ontario, Canada), between December 4, 2023, and February 23, 2024. Demographic information and an enhanced vaccine history, including detailed vaccine records and data on vaccine confidence, were collected by two trained nurses. Participating families received personalized recommendations on vaccination. From 155 families interviewed (of 207 eligible), based on parental report, 106 (68%) were fully vaccinated, 38 (25%) were partially vaccinated, four (3%) were unvaccinated, and seven (5%) were unsure of their vaccination history. Uptake of the measles vaccine, in particular, was suboptimal, with 104/128 (81.3%) of eligible children having received the 12-month dose of the Measles-Mumps-Rubella (MMR) vaccine, and 53/107 (49.5%) of eligible children having received both the recommended MMR and the MMRV doses at 12 months and 4-6 years, respectively. We identified significant gaps in vaccine uptake in hospitalized children that should be urgently addressed in the context of increased global measles circulation. Admission to tertiary care centres is an important opportunity to identify these gaps and implement strategies to improve vaccine uptake.

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REPRODUCIBILITY OF A SMARTPHONE-BASED VISUAL ACUITY TEST (PEEK ACUITY) IN PERUVIAN SCHOOLCHILDREN

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Peek Acuity is a free mobile application that allows for visual acuity assessment with a smartphone. Peek Acuity could be used in community-based or school-based settings by relatively inexperienced personnel to screen for refractive error among children, but the reproducibility of the application among children has not been well characterized. Here, we assessed the reproducibility of Peek Acuity when used with different smartphones and in different lightning conditions in 234 children aged 5 to 9 years from 5 schools in Villa El Salvador (Lima, Peru). Visual acuity of the right eye was assessed with two different smartphones (i.e., Samsung vs Xiaomi) and in two different lighting conditions (i.e., indoors in a very dark room vs outdoors in ambient daytime light) in random order. The reproducibility of visual acuity results was assessed using an intraclass correlation coefficient (ICC). The mean age of the children was 7.0 (SD 1.4), 55% were women, 3% wore glasses during the tests, and the majority attended a public school (61%). The frequency of referral-warranted disease (i.e., visual acuity worse than 20/40) with the Samsung smartphone was 6.0% when used indoors and 11.9% when used outdoors, and with the Xiaomi device was 6.8% when used indoors and 9.8% when used outdoors. The agreement between the Samsung and Xiaomi smartphones was greater when tested indoors (ICC 0.80, 95%CI 0.75-0.84) than outdoors (ICC 0.56, 95%CI 0.41-0.65). Agreement between the indoors vs outdoors measurements was slightly greater for the Samsung smartphone (ICC 0.67, 95%CI 0.60-0.75) than the Xiaomi smartphone (ICC 0.56, 95%CI 0.47-0.64). These results suggest that the Peek acuity app can provide reproducible results when performed with different smartphones, but may provide the most reliable results when done in dark conditions.

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CRITICAL REFLECTIONS ON COSTING PUBLIC HEALTH INTERVENTIONS IN RESOURCE-CONSTRAINED IMPLEMENTATION SETTINGS: CONSIDERATIONS AND RECOMMENDATIONS

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To effectively plan the implementation of public health interventions and efficiently allocate resources, policymakers must understand the associated costs, especially in low-resource settings. However, no unified costing

methodology for public health interventions exists, which has led to a wide variety of costing practices and approaches, often yielding results that are not comparable or generalizable. To enable more standardized and accurate cost estimates, we reviewed the extant costing literature and drew from our own experience costing public health interventions in resource-constrained implementation settings, critically reflecting on the key methodological issues in the costing of public health interventions. Six issues were particularly pervasive: 1) unclear costing parameters, especially the misspecification of studies' analytical perspectives and time horizons; 2) failure to assess the full range of costs required for programmatic implementation, especially indirect costs and costs incurred in the early design stages of an intervention; 3) lack of attention to cost differences stemming from variable participation rates or implementing organizations' differing resource needs to deliver interventions; 4) failure to contextualize studies' cost estimates within the relevant setting contexts; 5) costing conducted retrospectively rather than concurrently with an intervention; and 6) lack of differentiation between implementation and research costs. Building on these considerations, we highlight the necessary steps to produce comparable and generalizable cost estimates and employ case studies to demonstrate how these steps can be applied in practice. Our findings and proposals will better enable researchers to produce accurate and generalizable cost estimates which are necessary for policymakers to determine the affordability, efficiency, scalability, and sustainability of public health interventions.

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FROM MAPPING TO NEAR TRACHOMA ELIMINATION IN UNDER A DECADE: RESULTS FROM TRACHOMA PREVALENCE SURVEYS IN COTE D'IVOIRE FROM 2015-2023

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In the early 2000's, Côte d'Ivoire experienced two civil wars, leading to loss of life, political and economic instability, and disruptions to the health system, including closures of healthcare centers. Due to this situation, it was not until 2015 that large-scale efforts to map trachoma began. This presentation will provide the results of trachoma prevalence surveys from 2015-2023. All trachoma prevalence surveys (baseline mapping, impact (TIS), and surveillance (TSS)) were carried out with WHO-recommended methodology. Briefly, a two-stage cluster random sample design was used for each evaluation unit (EU). An EU was defined as a population of 100,000-250,000, corresponding to a health district (HD), a proportion thereof, or the merger of ≥2 HD. A list of all villages was made; 24-30 villages per EU were randomly selected using probability proportional to size. Then, 30 households per village were selected through simple random selection or compact segmentation. Eyelids of all consenting household members aged ≥1 year were examined. EU-level prevalence for trachomatous inflammation—follicular (TF) was estimated for children aged 1-9 years and trachomatous trichiasis (TT) was estimated for adults aged ≥15 years. Baseline mapping was conducted from 2015-2022 in 78/113 HD (78 EU). 32 EU had TF≥5% (range 5.18 – 28.30%); TT was ≥0.2% in 5 EU (range 0.20-0.8%). TIS were conducted between 2017-2023 in all endemic EU after 1-3 rounds of mass drug administration of azithromycin (Zithromax); TF was <5% and TT <0.2% in all EU (range 0.00% -1.94% and 0.00-0.06%, respectively). From 2019-2023, 13 EU underwent TSS. TF remained <5% (range 0.00-2.80%) and TT <0.2% (range 0.00-0.12%). Côte d'Ivoire has made great strides towards elimination of trachoma as a public health problem in 9 years. At baseline mapping, even where TF was near 30%, TT prevalence was <0.2% in all but 5 EU. We speculate that this may be due, in part, to a secular decline in trachoma that had begun years ago interrupted by recrudescence during civil wars. Côte d'Ivoire plans to conduct TSS in a further 14 EU in 2024 and the rest in 2026.

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CHARACTERIZING THE BURDEN OF SCRUB TYPHUS IN NEPALESE CHILDREN: A NOVEL SCHOOL-BASED SEROSURVEILLANCE APPROACH

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Scrub typhus, an acute bacterial infection caused by *Orientia tsutsugamushi (OT),* is an important, under-recognized etiology of febrile illness in Nepal. Accurate surveillance for scrub typhus is challenging due to non-specific symptoms and limited diagnostics. Outbreaks of scrub typhus have been reported from different parts of Nepal following the devastating earthquake of April 2015. Our aim was to characterize the burden of scrub typhus infections among children in Kavre and Dolakha, Nepal, and to determine if school-based sampling was an efficient but accurate sampling strategy for serosurveillance. We conducted a representative school-based cross-sectional serosurvey by randomly selecting 4 and 9 public schools in Kavre and Dolakha districts respectively, and then randomly selecting up to 100 children in each school. Parents and/or guardians of selected children were contacted for informed consent. From participating children, we collected capillary blood samples and tested for IgG responses to O. tsutsugamushi-derived recombinant 56-kDa antigen using commercially available ELISA kits. We calculated cutoffs using finite mixture models and modeled seroprevalence using mixed-effect binomial logit models adjusting for age with a random effect for school. We enrolled 827 children aged 4 to 18 between 2021 and 2022. The median age was 10.5 years. The overall seroprevalence was 3.5% (29/827). The age-adjusted prevalence was 3.1% (95%CI 1.5-6.8) in Kavre compared to 2.1% (95%CI 1.5-6.6) in Dolakha. There was geographic heterogeneity across schools, with age-adjusted seroprevalences ranging from 0 to 9.0% (95% CI 4.9-16). The overall seroprevalence estimates for Kavre are similar to those obtained from a representative population-based serosurvey in the same ages, where we found a seroprevalence of 3.3% in Kavre among 4 to 18 year-olds. In conclusion, our findings reveal a substantial burden of pediatric scrub typhus in Kavre and Dolokha districts and demonstrate that school-based serosurveys are an efficient sampling frame to assess population-level scrub typhus transmission intensity.

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THE LEPTOSPIRA-SECRETED EXOTOXIN THAT MEDIATES LEPTOSPIROSIS PATHOGENESIS

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Severe human leptospirosis is characterized by pulmonary hemorrhage, shock, acute kidney injury, jaundice and death. We recently discovered the PF07598 gene family-encoded Virulence Modifying Proteins (VMPs), secreted exotoxins found only in pathogenic *Leptospira*. PF07598 gene expression is massively upregulated *in vivo*. VMPs, highly conserved at the amino acid level (>90-95%), are comprised of two tandemly repeated

N-terminal ricin B domains (RBLs) and a C-terminal DNase/toxin domain. Recombinant VMPs cause cytopathic effects on HeLa cells mediated by C-terminal DNase activity, confirmed by comparison of wild-type and active site-mutated recombinant VMPs on HeLa cells. Vaccination with recombinant, VM proteins protects mice and hamsters from lethal challenge infection. We confirmed our hypothesis that VMPs cause dose-dependent human primary pulmonary endothelial cell (HPMEC) dysfunction and cell death *in vitro*, explaining severe human leptospirosis clinical manifestations. The rationale for this hypothesis is that the endothelial cell is a primary target of leptospiral pathogenesis. We used Electric Cell-substrate Impedance Sensing (ECIS) to quantify time-dependent transendothelial electrical resistance (TEER) responses of HPMEC monolayers in response to co-incubation with escalating dose and time of endotoxin-free VMPs. ECIS/TEER and confocal microscopy complementarily confirmed that HPMEC monolayer electrical barrier function and tight junction integrity were disrupted in a dose and time–dependent manner by VMPs. Using our newly developed capture ELISA with anti-VMP monoclonal antibodies, we detected low ng/ml quantities of circulating VMPs in the blood of hamsters infected with *L. interrogans* serovar Copenhageni, further supporting the role of VMPs—the long-sought leptospiral secreted, soluble exotoxin—in leptospirosis pathogenesis. These data are an important foundation for further elucidating the cellular and molecular roles of VMPs in understanding the pathogenesis of human leptospirosis, towards improvement of novel, pan-leptospirosis diagnostic and vaccine strategies.

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MENINGITIS SCREENING IN YOUNG INFANTS BASED ON A NOVEL NON-INVASIVE TRANSFONTANELLAR DEVICE: INITIAL PERFORMANCE RESULTS

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Meningitis is a potentially life-threatening disease if not promptly diagnosed and treated. Clinical presentation is often unspecific, especially among young infants and newborns, justifying the need to perform lumbar punctures (LPs) to obtain cerebrospinal fluid (CSF) for a laboratory-based analysis. In high-income settings, LPs are often part of the protocolized systematic approach to screen for meningitis, but as a result, and given the relatively low incidence of meningitis, most are negative. On the contrary, in low-income settings LPs are seldom performed due to the scarcity of resources, and suspected meningitis are often treated empirically. The aim of this study was to validate a novel non-invasive transfontanellar CSF white blood cell (WBC) level classifier to screen for meningitis, using high-resolution ultrasounds. We prospectively recruited patients under 24 months of age, with suspected meningitis, an open anterior fontanelle and a LP performed within 24h from enrolment, in three Spanish University Hospitals and one Mozambican public teaching hospital (2020-2023). Images showing the backscatter pattern from CSF were obtained using a customized high-resolution ultrasonic (HRUS) probe. A deep-learning model (DL) was trained to classify CSF patterns according to WBC values obtained through the LP, setting a 30 cells/mm^3 threshold to differentiate controls from cases. A total number of 2237 images were obtained from 34 LPs (11 cases and 23 controls) to train the algorithm. The device correctly classified all patients with >30 cells/mm^3, and 21/23 controls (sensitivity 100%, specificity 91.3%). Further research is needed, but these preliminary results suggest that our non-invasive device, based on ultrasound and DL, could be potentially used as a non-invasive meningitis screening method to accurately modulate indications for LPs among neonates and young infants.

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GAPS BETWEEN INFECTIOUS AGENTS DETECTED VS ATTRIBUTED IN THE CAUSAL CHAIN OF MORTALITY AMONG STILLBIRTHS AND NEONATAL DEATHS IN BANGLADESH

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Child Health and Mortality Prevention Surveillance (CHAMPS) network implemented postmortem sampling from multiple organs and a multi-pathogen detection platform to understand infectious etiology of stillbirths and under-5 deaths. We analyzed the gap between detection of an infectious agent and its implication as a cause of stillbirths and neonatal deaths from 2017 to 2023 in Bangladesh. Pathogens are attributed as cause of death by an expert panel reviewing laboratory, pathology, clinical, verbal autopsy and demographic data. We designed a scoring system to categorize the strength of evidence that a detection of infectious agents was likely to be real and representative of a true infection. Strong category indicates the agent was detected either in blood or CSF culture within 48 hours of incubation or where the real-time PCR cycle threshold was < 35 in over 50% repeats for that target. At least one infectious agent was identified from 34% (264/ 769) stillbirths, 15% (115/769) neonates < 1 day, and 24% (182/769) neonates aged 1-28 days. Most frequently detected were *Acinetobacter baumannii 22%* (130/572), *Klebsiella pneumoniae* 16% (93/572), *Enterococcus faecalis* 18% (106/572), *Enterococcus faecium* 19% (112/572), and Coagulase-negative staphylococci 36% (205/572). Among neonates aged 1-28 days, 50% of the pathogens with strong evidence were attributed as a cause of death while for stillbirths only 4% were attributed in the causal chain and 10% in neonates < 1day old. Among infectious agents with strong evidence 97% (31/32) were *A. baumannii* and 94% (15/16) were *K. pneumoniae* attributed as a cause of death. In contrast, *E. feacalis* caused 20% (1/5) of deaths, *E. faecium* 33% (1/3) and staphylococci 3.5% (2/61). A large gap was observed between infectious agents detected vs. those attributed in the causal chain for stillbirths and very early neonatal deaths. The panel lacked confidence in the detections due to limited data on maternal infection/colonization, incubation period to cause death after birth for specific agents, role of multiple pathogens. These should be explored to determine the true infectious burden causing early life deaths.

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IMASOY: A MULTI-CENTRE, RANDOMIZED, CONTROLLED, NON-INFERIORITY TRIAL OF 10-DAY CIPROFLOXACIN ALONE VS. 3-DAY AMINOGLYCOSIDE FOLLOWED BY 7-DAY CIPROFLOXACIN IN MADAGASCAR

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Plague is a high-consequence infectious disease but current treatments are based on weak evidence, with drug registration based on animal and observational data rather than conclusive clinical trials. IMASOY (NCT04110340) is the first Plague is a high-consequence infectiousdisease. Current treatment guidelinesare based on weak evidence, with drug registration based on animal andobservational data. IMASOY (NCT04110340)enrolled individuals of any age andsex (excluding pregnancy) withclinically-suspected bubonic plague over 5 transmission seasons during Aug/2019-Mar/2024at 47 peripheral health centres andhospitals in 12 districts in Madagascar. Randomisationwas 1:1, stratified by site, to either 10-days ciprofloxacin alone (intervention), or three-daysinjectable aminoglycoside followed by seven-day oral ciprofloxacin (controlarm, first-line treatment in Madagascar). The primary endpoint was treatment failure on D11:death, fever, alternative or prolonged plague treatment and/or secondarypneumonic plague. For non-inferiority in the primary ITTI population (laboratoryconfirmed/probable infections), the 2.5% upper bound (UB) of the confidenceinterval around the risk difference (RD) was to be <15%. Of 933suspected bubonic plague patients screened, 450 were enrolled and randomised,with 220 confirmed and 2 probable infections; 53.2% (n=118) male; median(range) age of 14 years (2-72). Ciprofloxacin monotherapy was non-inferior tocontrol; 9.0% (10/111) vs. 8.1% (9/111) treatment failures, 0.9% difference (UB=8.3%).Non-inferiority was also demonstrated in other pre-specified analysispopulations: per-protocol infected (PPI; one patient excluded), ITT and PP (sixpatients excluded) and with adjustment for site. Five and four patients respectively died. Three patients per arm developed secondary pneumonic plague.Similar percentages of patients experienced SAEs, none drug-related(intervention: n=8, 7.2%; control: n=6, 5.4%) and AEs (intervention: n=20,18.0%; control: n=21, 18.9%). The most common AEs were diarrhoea (10/450=2.2%)and vomiting (15/450=3.3%). Ciprofloxacin given for 10 days isnon-inferior to the first-line combination regimen. IMASOY is the firstrandomised controlled trial powered to evaluate the efficacy oftreatments for bubonic plague and can contribute to strengthen theevidence-base for plague treatment guidelines.

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ASSOCIATION OF PARASITIC COINFECTION AND WATER, SANITATION, AND HYGIENE (WASH) WITH CLINICAL CASES OF LEPROSY IN ADDIS ABABA ETHIOPIA

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Leprosy is one of the neglected tropical diseases caused by the slow-growing bacteria called *Mycobacterium leprae* and is marked for elimination by WHO. Recent research has demonstrated the association of poor WASH and helminth infections with leprosy. We assessed the association of parasitic coinfection, water, sanitation and hygiene (WASH) practices and other environmental factors with leprosy in Addis Ababa Ethiopia. A case control study enrolled adults with leprosy from the dermatology clinic at the All Africa Leprosy Rehabilitation and Training Center (ALERT) and anti-PGL-1-negative adult controls were selected from a seroprevalence study. A standardized questionnaire was administered to each participant followed by the collection of stool and blood samples to test for the presence of parasitic infections. A total of 240 participants, consisting of 54 cases and 186 controls, were analyzed. The mean age of the enrollees was 42 years (SD 17) and there were 43% men and 57% women, with men represented 65% of the cases. There were no helminth infections found among participants. Protozoal infections such as *Entamoeba histolytica* and *Giardia lamblia* were identified in 38 participants, but this did not yield a significant association with leprosy [OR= 1.08, 95% CI (0.46, 2.38)]. However, poor WASH practices were found to be associated with leprosy. In multivariable analysis, unimproved sanitation [aOR= 13.1, 95% CI 3.46, 57.2], lack of direct drinking water [aOR= 5.22, 95% CI 1.50, 19.3], exposed dirt flooring [aOR= 6.93, 95% CI 1.94, 31.0], were significantly associated with leprosy, controlling for socioeconomic status. Lack of hand soap did not show a statistically significant association in the multivariate analysis but still maintained a positive directionality [aOR= 4.26, 95% CI 0.30, 54.7].These findings suggest that a complex interplay involving environmental factors may contribute to the transmission of M. leprae. While the insights gained from this study can improve our understanding and inform preventive strategies, it emphasizes the need for a more comprehensive assessment of host factors and environmental influences.

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THE BALANCE BETWEEN GASDERMIN D AND STING SIGNALING SHAPES THE SEVERITY OF SCHISTOSOME IMMUNOPATHOLOGY

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Schistosomes are trematode helminths that infect more than 250 million people, of which 120 million suffer from clinical morbidity. Most schistosome-infected individuals develop a relatively mild form of the disease; however, in 5 to 10% of the patients, the disease is severe and life threatening. Similarly there is significant disease heterogeneity among mouse strains infected with the helminth “Schistosoma mansoni”. Despite the large disease burden, schistosomiasis remains a neglected disease with limited insights into disease pathogenesis and immunopathological heterogeneity. Using in vitro, in vivo and ex vivo assays, we uncovered a unique balance in two critical innate pathways governing the severity of disease. In the low-pathology setting, parasite egg-stimulated dendritic cells (DCs) induced robust IFNβ production, which was dependent on the cyclic GMP-AMP synthase (cGAS)/stimulator of interferon genes (STING) cytosolic DNA sensing pathway and resulted in a Th2 response with suppression of proinflammatory cytokine production and Th17 cell activation. IFNβ induced signal transducer and activator of transcription (STAT)1, which suppressed CD209a, a C-type lectin receptor associated with severe disease. In contrast, in the high-pathology setting, enhanced DC expression of the pore-forming protein Gasdermin D resulted in reduced expression of cGAS/STING, impaired IFNβ, and enhanced pyroptosis. Our findings demonstrate that cGAS/STING signaling represents a unique mechanism inducing protective type I IFN, which is counteracted by Gasdermin D.

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INOS IS NECESSARY FOR GBP-MEDIATED *TOXOPLASMA GONDII* CLEARANCE IN MURINE MACROPHAGES VIA VACUOLE NITRATION AND INTRAVACUOLAR NETWORK COLLAPSE

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Toxoplasma gondii is an obligate intracellular parasite of rodents and humans. Interferon-inducible guanylate binding proteins (GBPs) are mediators of *T. gondii* clearance, however, this mechanism is incomplete. Using automated spatially targeted optical micro proteomics we determined that inducible nitric oxide synthetase (iNOS) was highly enriched at GBP2^{+} parasitophorous vacuole (PV) in murine macrophages. iNOS expression in macrophages was necessary to limit *T. gondii* load in vivo and in vitro. iNOS activity was dispensable for GBP2 recruitment and PV membrane ruffling, however, parasites could replicate, egress and shed GBP2 when iNOS was blocked. *T. gondii* clearance by iNOS required nitric oxide, leading to nitration of the PV and collapse of the intravacuolar network of membranes in a chromosome 3 GBP-dependent manner. We conclude that reactive nitrogen species generated by iNOS cooperate with the GBPs to target distinct biology of the PV that are necessary for optimal parasite clearance in macrophages.

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ACTIVITY OF A FILARIAL ASNRS ON INTERLEUKIN 8 G PROTEIN COUPLED RECEPTORS

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Eukaryotic aminoacyl-tRNA synthetases (AARS) are evolutionarily ancient enzymes that evolved novel secondary and tertiary activities in different species including humans and helminths. The nematodes, Brugia malayi and Wuchereria bancrofti, both overexpress and secrete/excrete asparaginyl-tRNA synthetase (BmAsnRS) at higher levels than any other AARS. In prior research we demonstrated that BmAsnRS chemoattracts human and murine leukocytes that express IL-8 receptors, CXCR1 and CXCR2, both G protein coupled receptors (GPCRs). BmAsnRS did not elicit a calcium transient upon receptor activation as does IL-8 and pretreatment of cells with BmAsnRS blocked the calcium transient of IL-8. These and other data suggest that BmAsnRS and IL-8 bind to the same receptors in different ways. We solved the structure of BmAsnRS and showed that the N terminal 88 residues form significant conformational overlap with IL-8. To study how BmAsnRS acts at GPCRs, we designed G protein dissociation assays using cells expressing either CXCR1 or CXCR2. These data confirm that BmAsnRS acts as an antagonist of IL-8, but in the absence of IL-8, BmAsnRS demonstrated features of an inverse agonist. These observations are consistent with the in vivo effect of BmAsnRS treatments of T cell transfer colitis mice with recombinant, endotoxin free BmAsnRS. Not only is BmAsnRS NOT proinflammatory in this model, but intraperitoneal treatment of dying mice resulted in 100% survival and histological normalization of their colons. Ongoing research focuses on detailed understanding of structure-function relationships in BmAsnRS that are responsible for its anti-inflammatory effects. We anticipate that by better understanding the precise mechanism of GPCR antagonism/inverse agonism by BmAsnRS, its novel anti-inflammatory effects might be recreated using peptibody technology, yielding molecules with similar or improved pharmacological traits. Such novel immunomodulators that evolved in filarial parasites to evade the host immune response, might in the future be applied to treatment of non-infectious human diseases in which IL-8 plays a critical role in pathogenesis.

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MONOCYTE-ASTROCYTE NETWORKS REGULATE CYTOKINE AND MATRIX METALLOPROTEINASE SECRETION INDUCED BY NEUROCYSTICERCOSIS ANTIGENS

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Neurocysticercosis (NCC) is caused by the infection of *Taenia solium* larvae into the central nervous system (CNS) and remains as a public health challenge as the leading cause of acquired epilepsy worldwide. After a silent period of cyst establishment and survival, cyst degeneration triggers an inflammatory response that is poorly understood. We evaluated the effect of the diagnostic antigen mix used to diagnose NCC in the enzyme-linked immunoelectrotransfer blot (EITB) assay (seven lentil-lectin purified parasite glycoproteins) on monocyte-astrocyte networks related to neuroinflammation and tissue remodeling, particularly matrix metalloproteinase (MMP) secretion. We purified the diagnostic antigen and stimulated a primary human monocyte and astrocyte cultures and, in a co-culture, model utilizing conditioned medium from monocytes stimulated after 24 hours with antigens to explore monocyte-astrocyte interactions. Utilizing RT-PCR and ELISA/Luminex, we measured gene expression and secretion of key cytokines (TNF-α, IL-8, IL-6, IFN-γ) and MMPs (MMPs-1, -3, and -9), along with specific tissue inhibitors of MMPs (TIMP-1 and -2). Purified parasite antigen induced pro-inflammatory responses in monocytes, peaking at 48 hours post-stimulation. MMP1 and 9 secretion increased significantly at 24 hours, accompanied by elevated gene expression of inflammatory cytokines and MMPs ($p < 0.02$). Although direct stimulation of astrocytes not demonstrated significant increases; our co-culture model revealed a significant augmentation in IL-8, MMP-1, and MMP-3 secretion in astrocytes stimulated with cysticercal antigens ($p< 0.01$). Purified parasite antigen in stimulates monocyte-astrocyte networks underlying neuroinflammation and tissue remodeling in NCC. Further studies focused on the neuroinflammatory responses triggered by cysticercal antigens are needed for identifying biomarkers for early therapeutic interventions, and timely control of the innate immune response.

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EOSINOPHIL ACTIVATION AND RECRUITMENT IN THE CSF INFLAMMATORY CASCADE IN UNTREATED SUBARACHNOID NEUROCYSTICERCOSIS

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As a consequence of the unyielding inflammation induced by proliferative cysticerci in the subarachnoid space of the central nervous system, subarachnoid neurocysticercosis (SANCC) is the most severe manifestation of neurocysticercosis. Previously, we found elevated levels of certain proinflammatory cytokines and chemokines in untreated SANCC patients, many of which returned to homeostatic levels after successful treatment. The role of eosinophils in driving and/or amplifying inflammation associated with SANCC, however, is one major element of the proinflammatory cascade that has not been studied in depth. To examine the role of eosinophils in the pathogenesis of SANCC, CSF from 25 subjects with untreated SANCC (basilar cistern, sylvian fissure, and/or spinal involvement) was assessed for markers of eosinophil activation and recruitment compared to CSF from 27 uninfected controls. Using a multiplex bead assay, we measured the concentration of eosinophil granular proteins (MBP, ECP, EDN, and EPO) - known markers of eosinophil activation in tissue. We demonstrate that patients with untreated SANCC had significantly higher concentrations of MBP (GM 4.68 vs. 2.55 ng/mL, $p<0.003$), ECP (GM 13.00 vs. 4.60 ng/mL, $p<0.03$), EDN (GM 12.63 vs. 4.88 ng/mL, $p<0.0001$), and EPO (GM 5.53 vs. 3.52 ng/mL, $p<0.001$) compared to

the control subjects. These levels were highly correlated with absolute eosinophil numbers in the peripheral blood (p<0.04 for MBP, EDN, and EPO); in CSF, a similar correlation was found with the non-lymphocyte/non-neutrophil cells (p<0.04 for MBP, ECP, EDN, and EPO). Eosinophil-associated chemokines and cytokines were also measured in these CSF samples by a multiplex bead assay. Of the measured analytes, GROα (p<0.02), MCP-3 (p<0.02), IL-4 (p<0.03), IL-5 (p<0.002), IL-10 (p<0.0001), and IL-13 (p<0.006) were significantly elevated compared to controls whereas eotaxin 1, GM-CSF, and IL-3 were not. Together, these data provide evidence for both eosinophil recruitment to and eosinophil activation in the CNS in patients with SANCC as being significant drivers of the inflammation-induced pathology seen in SANCC.

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SPECTRAL FLOW CYTOMETRY ANALYSIS OF FECAL MICROBIOTA FROM *TRICHURIS TRICHIURA* INFECTED HUMANS AND NON-HUMAN PRIMATES

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Trichuris trichiura infection has been noted to alter gut microbial composition in chronically infected people from endemic regions. However, little is known about the interaction between helminth infection and the human gut microbiota in acute primary infection. This question will be investigated in an upcoming phase 1 clinical trial establishing a *T. trichiura* controlled human infection model (CHTI) in helminth-naïve individuals. A spectral flow cytometry protocol developed using mice in our lab provides a rapid and inexpensive characterization of gut microbiota samples compared to sequencing-based approaches. To allow us to translate this approach towards analyzing human samples, we first analyzed banked stool samples from helminth-infected and uninfected Ecuadorians (n=202) and non-human primates (NHP; n=44). To this end, each stool sample was diluted and analyzed on a spectral flow cytometer (Cytek Aurora) on which we acquired forward scatter, side scatter and spectral autofluorescence data. Then, unsupervised K-means clustering and Principal Component Analysis was used to compare microbial composition in each sample. Preliminary results, show that spectral flow cytometry can differentiate human from NHP gut microbiota samples and can demonstrate spectral differences at an individual level. Differentiation was not noticeable between helminth-infected versus uninfected Ecuadorians. DNA from these same stool samples has been analyzed by 16S sequencing to directly compare bacterial composition from sequencing analyses with spectral flow cytometry. Also, a filter to isolate bacteria from debris via a supervised machine learning algorithm is being trained to improve output quality. In addition to traditional sequencing-based approaches, we will utilize this spectral flow cytometry approach as a rapid and inexpensive way to characterize shifts in gut microbiota composition of longitudinally-collected samples during CHTI.

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ASCARIASIS, TRICHURIASIS AND INTESTINAL HOOKWORM INFECTIONS - CLINICAL PRESENTATION AND ASSOCIATION WITH INTERNATIONAL TRAVEL

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Soil-transmitted helminth (STH) infections are rare in the United States (U.S.) due to public health interventions improving sanitation. However, infections can occur after travel to an endemic region or autochthonous spread. We seek to describe the geographic location (to include known international travel) and clinical presentation of laboratory-confirmed cases of ascariasis, trichuriasis and intestinal hookworm infections (IHI) within the U.S. Military Health System. We performed a retrospective cohort study of active duty service members and their family members who had a diagnosis code of intestinal helminth and/or parasitic infection between October 2012 and September 2018. Chart review was performed for 1,376 individuals who had diagnosis codes of ascariasis (n=278), trichuriasis (n=28), hookworm (n=272), and unspecified intestinal helminth/parasite (n=852); diagnosis was confirmed if a positive laboratory nematode identification or stool ova & parasite was documented. Of the initial cohort, 24 (1.7%) were confirmed to have diagnosis of ascariasis (n=16), trichuriasis (n=6), or IHI (n=2). Patients with ascariasis were more likely to be pediatric (age <18 years) than adult (75% vs 25%). All the patients with trichuriasis and IHI were adults. Only 41.6% reported at least one of 15 commonly-reported symptoms queried: 100% ascariasis, 16.7% trichuriasis, and 50% IHI. Most symptoms were acute with duration <30 days. Of those with bloodwork performed, anemia was present in 66.7% of ascariasis, 50% of trichuriasis, but none of IHI; mild eosinophilia was present in 33.3% of trichuriasis and 100% of IHI. Most patients (62.5%) were located within the U.S. at diagnosis with 60% in West, 26.7% in South, and 13.3% in Hawaii. International travel 1 month prior to diagnosis occurred in 62.5% of patients, with East Asia and Pacific region accounting for 53.3%. One third of patients were born in the East Asia and Pacific region. Notable findings include a low number of confirmed cases, no pediatric patients among those with trichuriasis or IHI, and fewer than anticipated patients with history of preceding travel to STH-endemic areas.

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NOVEL RECOMBINANT ANTIGEN-BASED LATERAL FLOW TESTS FOR THE DETECTION OF *STRONGYLOIDES STERCORALIS* INFECTION AND CONCORDANCE WITH STRONGY *DETECT*™ ELISAS

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The laboratory diagnosis of strongyloidiasis is often serology-based, typically by enzyme linked immunosorbent assays (ELISA). However, the use of these assays at the point of care requires significantly different approaches for serologic measurements. We sought to determine the diagnostic performance of 2 prototype lateral flow tests in comparison with a second generation InBios Internationl Inc. Strongy *Detect*™ IgG and IgG4 ELISAs. Previously, we validated InBios' first generation Strongy *Detect*™ IgG4- and/or IgG- based ELISAs to detect *S. stercoralis* (Ss) infection that uses a cocktail of 2 *Ss*-specific recombinant antigens, *Ss*-NIE and *Ss*-IR (*Plos NTD, 2022 e: 0010126*) which showed sensitivity and specificity of ≥ 96%. Prototype Strongy IgG and IgG4 *Detect*™ Rapid tests (RDTs) were developed at InBios and tested in a laboratory setting using stored serum samples (128) from 77 patients with stool positive *Ss* infection, 14 uninfected healthy individuals and 37 patients with other helminth infections (*Loa loa*, hookworm spp, and *Ascaris lumbricoides*) known to cross-react in some older serologic assays. Parallelly, we also tested the second-generation IgG- and IgG4 ELISAs on the same sera panel. Using ELISA cut-offs determined by Youden J index, the IgG-based ELISA showed 100% sensitivity and 92% specificity, whereas the IgG4-based ELISA showed a 92% sensitivity with 100% specificity. When the same samples were tested using the 2 prototype RDTs, the IgG RDT showed a 95% sensitivity with a specificity of 94%; the IgG4 RDT showed a sensitivity of 84% with 98% specificity. The concordance between the RDT and the ELISA was extremely high, 96% for IgG and 93% for IgG4 assays. Based on these initial evaluations, the higher sensitivity of the IgG assays combined with the higher specificity of IgG4 assays indicate that both immunoassays will be useful in an algorithm for screening individuals for *Ss* infection and monitoring *Ss* seroprevalence in populations.

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PREVALENCE AND INTENSITY OF SOIL-TRANSMITTED HELMINTH INFECTIONS ACROSS RIVERS STATE NIGERIA FOLLOWING SEVEN YEARS OF DEWORMING-EVIDENCE FROM PROGRAM EVALUATION

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Rivers State, Nigeria had one of the country's highest burdens of soil-transmitted helminths (STH) when surveyed in 2014, with prevalence estimated at 43.1%. Since 2017, annual preventive chemotherapy (PC) using Mebendazole has targeted school-age children (5-14 years), consistently reaching above the WHO recommended 75% coverage threshold. Following 7 years of treatment, a prevalence survey was conducted to assess the impact of the program. The cross-sectional, cluster-based survey incorporated the use of Model Based Geostatistics (MBG) to select schools, and analyze data post survey. Survey design was optimized to achieve a high probability of correctly identifying policy relevant endemicity classes across all LGAs. A total of 28 schools were surveyed, collecting fresh stool samples from 1,613 children aged 5-14 years, and examined by Kato Katz for STH infection. Survey results suggest that the overall state prevalence of any STH species sits between 10% to <20% with a probability of >99.9%. All LGAs were individually estimated to sit between 10% to <20% with probabilities ranging from 72.4% to >99.9% with the exception of two LGAs; Omumma and Oyigbo, which sat within the 2% to <10% thresholds. A multivariable analysis found factors such as last deworming round being conducted in 2021 as compared to 2022 (OR: 0.24(P=0.006), 95%CI: 0.08 - 0.66) and 5 rounds (OR:0.50 (p=0.065), 95%CI [0.24-1.04]) of deworming as compared to none, to be statistically significantly associated with lower odds of STH infection; while, unavailability of water or tissue for use after defecating (OR: 2.73(p=0.098), 95% CI: [0.83-8.98]) and non-functional drinking water source (OR: 51.90 (p=0.000), 95% CI: [7.00-384.73]) were statistically significantly associated with increased odds of STH infection. The evidence from program evaluation following 7 years of PC strongly suggests significant rate reduction (70.56%) in STH infections among school-age children. Increased cross-sectoral collaboration to drive improvements in WASH across the state in addition to sustained high quality PC will generate greater gains in STH prevalence and intensity reduction.

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TH1, TH2, AND TH17 CYTOKINE RESPONSE IN IMMUNOSUPPRESSED PATIENTS INFECTED WITH *STRONGYLOIDES STERCORALIS* IN NORTH INDIA

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Human strongyloidiasis is one of the most neglected tropical diseases. Persons with primary or secondary immunodeficiency are at the highest risk of hyperinfection or disseminated strongyloidiasis. This study was conducted to characterize the Th1/Th2/Th17 cytokine responses in immunosuppressed patients infected with *Strongyloides stercoralis*. For this, serum and stool samples of 498 patients with immunosuppressive conditions and/or on steroids/cytotoxic medications from various OPDs and wards of a tertiary care hospital in North India, and 70 apparently healthy controls were obtained. The serum samples were screened by anti-*Strongyloides* IgG antibody ELISA (Bordier Affinity Products), while the stool samples were subjected to *18S rRNA* gene real-time PCR for *Strongyloides*. Of the 498 patients, 67 (13.5%) were positive for IgG antibodies (14 were also RT-PCR positive), while 31 (6.2%) were positive for *Strongyloides* DNA by *18S rRNA* real-time PCR (14 were also serology positive). Of these, 80 serology and/or RT-PCR positive samples, and 54 controls were assessed for Th1/Th2/Th17 cytokines using BD Cytometric Bead Array Human Th1/Th2/Th17 Cytokine Kit as per the manufacturer's instructions; a subgroup analysis was also done on the 80 positive samples (14 ELISA and RT-PCR positive, 53 only ELISA positive, and 13 only RT-PCR positive). Overall, the *Strongyloides* positive patients had significantly higher IL-6 (30.36±75.44 pg/ml, p-value<0.05), IL-4 (0.17±0.58 pg/ml, p-value<0.05), and IFN-γ (0.40±1.57 pg/ml, p-value<0.05) levels compared to healthy controls, while IL-2, IL-10, TNF, and IL-17A were not significantly different. In the subgroup analysis, there was no significant difference in the cytokine levels within the subgroups. In conclusion, a high IgG seropositivity of 13.5% by ELISA and *S. stercoralis* DNA positivity of 6.2% by RT-PCR was observed in immunosuppressed patients from varied clinical specialties. The patients infected with *S. stercoralis* had significant alterations in the levels of IFN-γ, IL-4, and IL-6 cytokines, and a mixed Th1/Th2 type of immune response was observed which needs further elucidation.

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THE IMPACT OF INTEGRATING DEWORMING WITH EYE HEALTH IN SCHOOL TO IMPROVE THE LIVES OF SCHOOL AGE CHILDREN AND TEACHERS: A PILOT PROJECT FOR THE CONTROL OF SOIL TRANSMITTED (STH) HELMINTHIASIS AND VISION IMPROVEMENT IN HIGHLY ENDEMIC COUNTIES FOR STH IN LIBERIA 2018-2022

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Integrating School Health deworming program with eye health focused on improving the health and education outcomes for children and teachers. Integrating deworming and visual screening program into mainstream health and education system in highly endemic counties for soil transmitted helminthiasis (STH) in four counties (Bong, Grand Kru, Maryland and Sinoe that requires twice a year treatment through mass drug administration with Albendazole for STH. The project was implemented in partnership with Ministry of Health (MOH) and Ministry of Education (MOE) with support from Sightsavers. Deworming and vision screening training was conducted for teachers, local MOH and MOE staff at county levels. The project focused on School-based deworming and vision screening, referral of children and teachers with visual impairment, provision of corrective eyeglasses, community awareness and sensitization campaigns in all school in the four counties. To ensure the impact of the project on the control of STH and vision improvement, an independent evaluation was conducted using mixed methods approach that incorporated focus group discussion, key informant interviews and desk review of project documents in 2022. A total of 138 key stakeholders and service users across the four project counties participated in the evaluation. Stakeholders interviewed were teachers, parents, community leaders, eye health professionals, government officials from MOH and MOE and Sightsavers program Staff. The project demonstrated significant results in vision screening and deworming reaching a total of 181,487 school-aged children (SAC) receiving vision screened, 280,373 SAC dewormed and a total of 2,676 teachers trained on vision screening. A Cascade model to train education professionals on vision screening at both national and community levels has the potential for scalability with deworming program in other regions and could help to ensure sustainability and the control of STH and vision improvement through integration deworming and eye health program in Liberia and other endemic countries in the world.

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HELMINTHS, MALARIA CO-INFECTION AND ASSOCIATED INDUCEMENT OF ANAEMIA, IRON AND FOLATE DEFICIENCIES IN CHILDREN

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Hyper-endemicity of malaria in Africa often masks the devastating impact of helminths co-infection as well as associated anaemia and malnutrition. This study aimed at assessing the impact of malaria, helminthiasis co-infection on anaemia and micronutrient deficiencies focusing on iron and folate. We conducted a cross-sectional clinical survey across three hospitals across three ecological areas in Ghana. About 1003 study subjects gave their consent to participate in this study. Venous blood was analysed for malaria parasitaemia and full blood count. Kato katz and formol ether concentration techniques were used to analyse stool samples for intestinal parasites. Indirect ELISA was performed on the serum samples to determine iron and folate levels. Ascaris lumbricoides, Tapeworm spp, Hookworm spp, Trichuris trichiura, Giardia lamblia and Entamoeba histolytica were identified in single or in co-infection. Overall, malaria prevalence was 54.4%, soil transmitted helminths (STH) 15.7%, malaria and STH co-infection 11.4% and intestinal protozoa and STH co-infection 1.5% with significantly higher rates in less urbanised northern study site ($p< 0.0001$) and among younger children ($p< 0.0001$). Malaria ($p< 0.0320$), STH ($p< 0.0001$) and co-infection ($p< 0.0320$) were independent predictors of anaemia. Malaria and STH co-infection significantly exacerbates anaemia ($p< 0.001$), folate deficiency ($p< 0.001$) and iron deficiency ($p< 0.001$) compared to those with malaria and no infection. Malaria and helminthiasis predominantly affect children and are influenced by sociodemographic and housing factors. Co-infection exacerbates the adverse outcomes associated with malaria and helminthiasis.

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EVALUATION OF ACCESSIBILITY TO ELECTRONIC MEDICAL RECORDS FOR CLINICAL RESEARCH IN KAMPHAENG PHET PROVINCE, THAILAND

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Electronic medical records (EMRs) are digital representations of a patient's chart. They constitute patient-centered, real-time records that securely and promptly make information accessible to authorized users within an organization. These records contain information about patients' medical histories, diagnoses, and treatments. For clinical trials such as vaccine studies, these types of records may be important for accessing outcomes related to study participants. However, study enrollment and acute illness forms are not typically developed with this measurement in mind. Kamphaeng Phet provincial hospital (KPPH) first implemented the in-patient department (IPD) EMRs in November 2019 from each section including clinical wards, laboratory, and pharmacy until completion of the full system in January 2020. This retrospective study aimed to assess the enrollment and illness reports forms from an ongoing cohort, the Kamphaeng Phet (KPP) Family Cohort Study in terms of IPD records including history, clinical sign, symptoms, laboratory, diagnosis and discharge status for validity determined by data matching. Investigators selected 24 participant in-patient charts from 2015-2023 to crosscheck with KPPH EMRs. In total, 21 of 24 (87.5%) records were compared, three records were not available. The overall validity was 53.7%. The highest validity items (100%) were date of admission, admission diagnosis, date of discharge, discharge diagnosis of dengue, tourniquet test, discharge status and type followed by symptoms of fever, lung abnormality, blood chemistries (i.e. total protein, albumin, aspartate transaminase and alanine transaminase) in 95.2%. Discrepancies occurred primarily from differences in interview data from different health care professionals, interpretation of unknown and no symptoms in the child age group and count of date of fever onset. These initial findings will be helpful for clinical trial planning as it suggests that further refinement is needed in the reporting and tracking of dengue illness and vaccine outcomes to allow post-licensure evaluation of vaccine safety and effectiveness.

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UNDERSTANDING THE SHORTCOMINGS AND GOOD PRACTICES FROM THE ROUTINE DATA QUALITY ASSESSMENT FOR INFORMED PUBLIC HEALTH DECISION-MAKING IN GUINEA IN 2023

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Ensuring the availability of accurate and reliable data is crucial for effective decision-making in public health. In Guinea, health data is recorded using primary tools and then compiled into paper reports before being entered into the District Health Information Software 2 (DHIS2). A data quality assessment was conducted in March 2024 for the last quarter of 2023 data by national, regional, health district and partners teams. Results of this assessment were analyzed to identify the practices that contributed to improved data quality and areas that require improvement. The evaluation covered 96 health facilities in 24 health districts across 8 regions of the country, focusing on low-performing structures, hospitals, both urban and rural health centers. The Routine Data Quality Assessment tool, configured in Kobotoolkit, was used to assess the accuracy of the data, system management, data use, and functionality of the National Health Information System (NHIS), including the availability and use of NHIS tools. Data accuracy was evaluated by examining six elements from malaria, immunization, and maternal health programs. Verification factors were calculated, with a margin of error of ±10%. Ratios were determined for patients treated with ACTs, BCG administered, and live births. The overall data quality score was 67%, with scores of 93% for overall accuracy, 90% for NHIS functionality, 74% for availability and use of tools, 70% for data management and confidentiality, 63% for data consistency, 54% for data use, and 21% for guideline availability and use. The ratios of ACT consumed to patients treated with ACT were 1.4 and 1.013 between administered doses of BCG and live births. An improvement plan has been drawn up for each structure visited with monthly follow-up by the higher level and 759 providers received training in data quality assurance. While the accuracy of data collected from primary tools and reported in DHIS2 is satisfactory, some areas still need further attention. For instance, the availability and use of NHIS guidelines need to be improved, and the use of data for decision-making at health facilities requires more attention.

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MONITORING THE IMPLEMENTATION OF COMMUNITY HEALTH STRATEGY ACTIVITIES IN FOUR HEALTH REGIONS OF GUINEA THROUGH THE COMMUNITY HEALTH WORKERS TRACKER

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The national community health strategy in Guinea was implemented in Kindia and Telimélé during the pilot phase from 2018 to 2020. Later, it was extended to 15 health districts. During the implementation, the major challenges faced were a lack of control over the number of supervised and active CHWs, their supply of medicines and health commodities, and the quality of care. To overcome these challenges, a tool was developed to monitor the activities of community relays and community health workers. A one-year prospective cohort follow-up was conducted from January to December 2023 in 166 health centers in 15 health districts. The objective was to gather data from all 5541 community relays trained in four regions. The method used was to establish a collection tool that was accessible to the field agents of the sub-recipients. Data were collected monthly during supervision, and health center meetings and targeted CHWs that were active, supervised, and provided with health commodities. Feedback was given to the health centers to correct the shortcomings. The tool implementation has shown impressive results in improving the indicators. The number of supervised CHWs increased from 2381 in the second half of 2022 to 4748 in the second half of 2023, which is a remarkable increase of more than 100%. Additionally, the number of CHWs with no stock-out of commodities increased from 4455 in the first quarter to 4748 in the fourth quarter of 2023. However, in the third quarter, the number of active CHWs decreased from 5184 to 4763 due to non-payment of their bonuses in some districts. Though the CHWs tracker has shown promise in monitoring community activities, efforts must continue to improve it by digitizing it and ensuring the sustainability of support for the national community health strategy.

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UNLOCKING SUPPLY CHAIN EFFICIENCY: DEMONSTRATION OF AN OPEN-SOURCE DYNAMIC ROUTE OPTIMIZATION TOOL

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Ensuring that life-saving and critical public health commodities reach last-mile health facilities and patients in a health system is critical to providing quality of care. As data infrastructure in the international development space improves, decision makers increasingly look to leverage data-driven decision making. Mathematical optimization can leverage such data to provide decision support for complex, multi-factor planning for transportation, logistics networks, diagnostic networks, and more. This educational session will provide an overview of the benefits of using dynamic, optimized routes for last-mile distribution, with a focus on demonstrating how practitioners can use an open-source Dynamic Route Optimization (DRO) tool developed by USAID's Global Health Supply Chain-Procurement and Supply Management project that is used in last-mile distribution in Zambia today. The DRO tool uses a Vehicle Routing Problem (VRP) combinatorial optimization and integer programming approach and geospatial, vehicle fleet, and health commodity and volumetrics data inputs to rapidly plan transportation routes via a user-friendly and low-tech web interface, allowing transportation planners to reconsider the most optimal use of resources based on a specific set of orders and customers each distribution cycle. The session will cover how to: 1. download and install the software from GitHub, 2. deploy the web app in the cloud, 3. prepare the data for the software, and 4. run the optimizations using the web application.

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USING THE SUPPLY CHAIN INFORMATION SYSTEM MATURITY MODEL TO IMPROVE SYSTEM CAPABILITY FOR OPERATION

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Global health supply chains are growing in complexity as they respond to changing patterns of commodity flows and demands for more accurate information in an increasingly digitized world. Information systems, which form the backbone of today's supply chains, must mature in order to manage the growing complexity. As physical commodities move through supply chains, information systems enable the flow of commodity data, ensuring that medicines move from manufacturer to national warehouses to health facilities and, finally, to end users. Weak information systems can hinder effective response to supply chain exceptions, such as stockouts and expiries, as well as efficient procurement and distribution of health commodities. Traditional approaches to improving supply chain information systems, SCIS, tend to have a narrow scope. They might focus on one health area, such as HIV, or a specific operational component, such as warehousing. A holistic approach, on the other hand, enables informed decision making by government, donors and implementing partners to improve overall SCIS functionalities in a coordinated way. The Supply Chain Information System Maturity Model, SCISMM, was developed to help countries analyze their current supply chain systems holistically and plan their SCIS investments. The SCISMM assessment activity helps countries evaluate their supply chain systems' capabilities holistically, enabling informed decision-making. With a more mature SCISs which enhance the interoperability and data exchange across various SCISs it can reduce costs, improve efficiency, and increase the timely delivery and availability of commodities to patients.

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ENHANCING THE QUALITY OF MALARIA SURVEILLANCE THROUGH INTERACTIVE DASHBOARD ACROSS BENUE STATE HEALTH FACILITIES, 2023

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Effective disease surveillance is essential in managing and controlling infectious diseases. The President's Malaria Initiative for States (PMI-S) Project in Benue State, Nigeria, deployed a new data quality improvement strategy, using Power BI software for interactive malaria data visualizations (dashboards) that better explore data trends and gaps. This study aims to evaluate the effectiveness of using Power BI exports to enhance the accuracy and reliability of health data. This application automatically synchronizes relevant malaria data from the National Health Management Information System (NHMIS), performs data queries, and generates detailed reports. These reports include results of built-in queries specifically

designed to flag inconsistent data issues related to fever cases, testing rates, total positivity rates, and treatment rates. Data from over 1300 health facilities (HF) from October 2022 to December 2023 was reviewed monthly. Inconsistent data issues were exported to Microsoft Excel and shared with relevant facility records officers for corrections. Furthermore, data quality consultation meetings with relevant stakeholders helped gather feedback on this strategy. An automatically generated reporting dashboard allowed for identifying gaps in this study, contributing to major reductions in the proportion of HF with inconsistent data. The inconsistency reduced from over 40% in October 2022 to about 1% in December 2023 in Benue State. PMI implementing partners and NMEP appreciated that the short Microsoft Excel reports specified the data elements that required corrections and that these corresponded precisely to what was recorded in the NHMIS, making them recognizable and easy to fix. The findings indicated that when implementing a novel reporting tool, it is beneficial to use familiar data tools, such as Microsoft Excel, and adopt concise reports that clearly define which data elements require attention, by time and HF. This effort supported timely identification and correction of data discrepancies, aiding informed decision-making and improving malaria surveillance at scale.

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ESTABLISHING A VIRUS ECOLOGY DATA HUB FOR MODELING VIRUS DISEASE DYNAMICS

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Viral transmission dynamics in wildlife, domestic animals, and humans are complex systems driven by environmental and biological factors across scales. Advances in computational biology and machine learning have facilitated the integration of increasingly high-resolution temporal and spatial data used in infectious disease dynamics modeling. However, the findability of data sources across various organizations, websites, and published manuscripts is challenging, which limits their reuse by a wider community of researchers and constrains the development of solutions based on the application of virus ecology. Here, we have categorized 64 open-source databases relevant to virus ecology, establishing the Virus Ecology Data Hub, a web-based, searchable tool to help researchers identify data resources for a wide range of relevant features. Each indexed database includes information on data format, scope, and, where applicable, resolution in time and space for each dataset. We classify these databases into seven categories: economic features, health data, social features, environmental and geographic data, pathogen features, and host features. Our findings underscore the extensive range of open datasets available for infectious disease research and advocate for increased collaborative efforts to generate and utilize open datasets, which can inform public health policy and response strategies and ensure that increasingly large quantities of interdisciplinary data can complete their life cycle. Researchers are encouraged to notify us of additional databases for inclusion in the Virus Ecology Data Hub, which will be continuously updated.

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PARENTS' MOTIVATIONS AND EXPECTATIONS SEEKING PEDIATRIC CARE FROM AN INFORMAL PROVIDER ("VILLAGE DOCTOR") IN BANGLADESH

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In low- and middle-income countries, rural populations often look to untrained allopathic practitioners in the informal health sector to address their healthcare needs. In Bangladesh,
informal providers called "village doctors" provide the majority of front-line healthcare to the rural poor and are one of the primary sources of antibiotics throughout the country. Pressure and expectations from patients and patient caregivers, coupled with village doctors' lack of formal medical training and financial incentives for selling antibiotics, likely result in frequent and often unnecessary antibiotic usage, which contributes to community-level antibiotic resistance. The goal of this study was to understand parents' motivations and expectations when taking a child to a village doctor. We conducted in-depth interviews with parents who took their child to a village doctor (n = 18) and village doctors (n = 18). Interviews explored the role of village doctors in the treatment of pediatric diarrhea, and examined motivations and expectations. . The study was conducted in Southeastern Bangladesh in the Sitakunda Upazila (subdistrict) of the Chattogram District. We used thematic analysis to identify themes related to the motivations and expectations of patient caregivers when bringing their child to a village doctor. Motivating factors for seeking care from a village doctor, as opposed to the formal healthcare system, included: geographic proximity, accessibility, familiarity, and trust. Caregivers expressed an expectation of antibiotics to treat their child's diarrhea, and village doctors discussed the important role that parents' expectations play in shaping their treatment practices. In conclusion, village doctors are trusted members of communities and play an important role in meeting local healthcare needs. Understanding the motivations and expectations of parents when taking a child to a village doctor allows us to tailor future initiatives with both communities and village doctors to reduce antibiotic use in children.

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FEASIBILITY AND ACCEPTABILITY OF AN ELECTRONIC DATA CAPTURE SYSTEM FOR A PHASE 2 CLINICAL TRIAL IN RURAL LIBERIA

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Electronic data capture (EDC) systems are increasingly common in clinical research, but many low-and-middle-income countries still rely on paper forms. This survey aimed to highlight strengths and weaknesses of an EDC system for data collection during a clinical trial in rural West Africa. The study site is Bong Mines Hospital in central Liberia which has intermittent electricity and internet connectivity. Four days of EDC training and mock enrollments were conducted prior to the start of a Phase 2 clinical trial of new treatments for onchocerciasis. Clinical trial data (enrollment, treatment, adverse event assessment) were entered on Samsung tablets using the CliniOps Edge application. Data collectors were surveyed to assess their experience and opinions regarding the EDC system. The survey included 10 questions (multiple choice, Likert-scale, and open-ended). Data were analyzed using thematic analysis and descriptive statistics. The survey will be repeated after two months of active enrollment to assess changes in data collectors' attitudes towards the EDC system. Twelve data collectors who completed the EDC survey included nurses, data managers, and study

physicians. 58% of respondents felt that the tablets were very easy to use, 33% felt the tablets were somewhat easy, and one respondent felt neutral. When asked about their preferred data entry method, tablets were preferred by 50% of respondents, paper forms were preferred by 17%, and 33% preferred to have paper forms backup the EDC system. Wifi access and other infrastructure concerns were raised by 67% of respondents regarding use of an EDC system in this setting. These preliminary results suggest that the EDC system is feasible for use in field settings with limited infrastructure. Careful construction and user acceptance testing (UAT) of the CRF plus on-site training likely contributed to these positive results. While the majority of respondents felt that EDC was easy to use and provides important benefits over paper records, some raised concerns whether infrastructure at the study site was sufficient for the system. We think that acceptability of the EDC will increase over time.

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ESTABLISHING AN EVIDENCE STANDARD FOR DETERMINING CAUSE OF DEATHS IN ADULTS USING MINIMALLY INVASIVE TISSUE SAMPLING: EFFORTS OF THE GLOBAL MITS SURVEILLANCE ALLIANCE

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Two-thirds of global deaths go unreported. Understanding who dies and from what are imperative public health questions. Minimally invasive tissue sampling (MITS) offers a potential approach for accurately determining cause of death (CoD) and has been used effectively to-date in ascertaining CoD in those aged under five. Work underway as part of the MITS Surveillance Alliance seeks to understand the feasibility of employing MITS in adult deaths. To establish CoD in adults, an evidence standard combining histopathological, clinical presentation and ancillary studies must be developed. Harnessing the collective knowledge and geographical diversity of the Alliance's member sites, work has focused on HIV and Tuberculosis, cardiac disease and stroke, chosen as initial conditions given their large contribution to the local mortality patterns in the South African, Indian and Ghanian MITS Alliance sites. Regular meetings were convened with a diverse, global group of general practitioners, pathologists, epidemiologists, and public health specialists. Draft guidelines, prepared by individual site investigators, were presented and critically discussed, with final consensus resulting in adoption of the guidelines as a 'final first draft'. Lessons learned in this undertaking, which may have wider relevance include: 1.) appreciation for the value of the undertaking and regularity of engagement; 2.) the importance of representivity within the group and the contexts represented (rural versus urban; facility-based versus community-based); and 3.) previous clinical and pathological experience, particularly in postmortem examination, CoD determination and clinical guidelines. In establishing an evidence standard for determining CoD in adults using MITS, we have sought to develop a resource with global applicability, allowing for use in both higher resourced and lower resourced settings as well as in both facility and non-facility-based (i.e., community) deaths. The continuing efforts will ultimately result in a complete draft of standards to guide CoD determination in adults and the lessons learned contribute to similar undertakings.

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COVID-19 AWARENESS AND BEHAVIOR CHANGE AMONG RECENTLY PREGNANT WOMEN: FINDINGS FROM A HOUSEHOLD SURVEY IN BENIN

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Public health messaging, particularly in the case of a public health emergency such as COVID-19, is critical to alert the population to potential risks and to protective behaviors. However, in public health emergencies, health officials often may not know whether this message is received and understood by the target population. A baseline household survey was conducted from November to December of 2020 in three health zones in Atlantique Department, Benin using questions from the women's module of the malaria behavior survey (MBS) as part of a randomized controlled trial assessing the impact of group antenatal care. Given the ongoing COVID-19 pandemic, questions were included to better understand awareness and behaviors related to the virus and perceived risk of COVID-19, particularly compared to malaria. Questions referred to COVID-19 as the "new disease circulating in Benin." At the time of the survey, national guidelines included staying home, wearing masks, social distancing, and increased handwashing. Among 1259 women surveyed who had given birth in the preceding 12 months, all were aware of COVID-19's presence in Benin. About 92% perceived that COVID-19 posed a greater worry than malaria. The predominant preventive measures reported included frequent handwashing (78%) and going out less (67%). Additionally, 41% practiced social distancing, while 17% used masks. Notably, 7% employed alternative methods to mitigate the risk of disease transmission; of these, environmental sanitation was employed by 22%, hygiene by 13%, and coughing/sneezing into elbows by 11%. Despite disparities in adherence, responses showed that messages about COVID-19 risk from the Benin Ministry of Health reached, were understood by, and instigated behavior change among rural female audiences in Atlantique Department. Further investigation could better identify and analyze which communication channels and messages were most effective at achieving these behavioral changes.

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SYSTEM THINKING IN THE CONTROL AND ELIMINATION OF NEGLECTED TROPICAL DISEASES IN MADAGASCAR

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The World Health Organization (WHO) classifies Neglected Tropical Diseases (NTDs) as a diverse group of conditions caused by a variety of pathogens (including viruses, bacteria, parasites, fungi and toxins) and associated with devastating health, social and economic consequences[1]. NTDs affect an estimated 1 billion people globally, majority living within impoverished communities in tropical countries. Preventive and curative interventions are delivered to affected and at-risk populations through countries' health systems with the support of national governments, non-governmental organizations and civil society groups. The combination of environmental factors that favor NTD pathogens, population characteristics, NTD medicine supply chain, financial resources and technical knowledge to guide effective interventions create a complex system to support successful NTD interventions. The WHO road map for neglected tropical diseases

2021–2030 targets are to reach 90% fewer people requiring interventions against NTDs; ensure 75% fewer NTD-related disability adjusted life years (DALYs); 100 countries achieve elimination of at least 1NTD; and the eradication of dracunculiasis and yaws by 2030. We use Madagascar as a case study and apply a Systems Thinking approach to identify and understand the critical levers that most significantly affect, support or hinder actions towards Madagascar's NTD control and elimination goals. We focus on the context in which interventions for three NTDS - soil transmitted helminths, schistosomiasis and lymphatic filiariasis- are delivered, the role of Madagascar's NTD policy, and their NTD medicine supply chain. We examine changes in NTD outcomes based on these three main levers over a five year period using publicly available data including WHO's ESPEN portal. Findings indicate that systems thinking models can be used to identify critical lever points in health systems and inform prioritization of responses that favor desired outcomes for a country to reach its NTD goals. [1] The World Health Organization, WHO

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MODELLING THE EFFECT OF SEASONAL MALARIA CHEMOPREVENTION ON THE TRANSMISSION DYNAMICS OF MALARIA IN ZAMFARA STATE, NORTHWEST NIGERIA

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Seasonal malaria chemoprevention (SMC) is a highly effective intervention to prevent malaria infections in areas where the malaria burden is high, and transmission is seasonal. The study aimed to investigate the effect of seasonal malaria chemoprevention on the transmission dynamics of malaria in Zamfara state using a mathematical model. Zamfara state, in northwest Nigeria, commenced the implementation of SMC in 2016. Descriptive analysis of uncomplicated malaria cases among under-five children for 2014-2023 from the District Health Information System-2, who were diagnosed by rapid diagnostic tests or microscopy, was done. A deterministic compartmental SVEAIR for human and SEI model for mosquito populations which incorporated SMC, was formulated. Time series analysis was done. Monthly forecasts for 2024-2025 were made against the backdrop of 'business-as-usual' context. Parameter estimation was conducted using the least squares and maximum likelihood fitting techniques. Scenario analysis was done with varying SMC effectiveness levels of 25%, 45%, 65%, 90% and 100%. Between 2014-2021, there was a general upward trend of malaria cases. From 2022, there was a decline in the reported malaria cases, with slight fluctuations. This decrease is forcasted to be continued in the future (2024-2025). However, there is a possibility of increase in malaria cases if SMC effectiveness decreases or due to other factors, such as, non-adherence and drug resistance. With increasing SMC effectiveness, the malaria cases averted increased. This translates to a reduction in the number of exposed children who progress to infected status. SMC is likely to remain effective for some more years but it may take more time to reach the pre-elimination phase. There is need to sustain SMC deployment in the state in the coming years. The estimated parameters may be used for future studies in the state.

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INNOVATIONS IN MALARIA CAMPAIGNS IN MOZAMBIQUE: FROM DIGITALIZATION TO EVALUATION

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Campaigns have long been used by health programs to deliver services at scale. As health campaigns have grown in number, scope, and cost, the resource-constrained global health community has sought innovations to improve efficiency while maintaining effectiveness. In Mozambique this has translated to the digitalization of its insecticide treated net (ITN) campaign in 2022, followed by the seasonal malaria chemoprevention and indoor residual spraying campaigns in 2024. By instituting digitalization, Mozambique aimed to improve campaign coverage, data quality and efficiency. As workers captured data into mobile devices in the field, campaign progress was monitored in real-time, enabling fast decision-making in dedicated forums. Digital records were analyzed to assess campaign results and data quality, and coverages were validated in post-campaign surveys. In addition, 138 qualitative interviews to campaign stakeholders collected their perceptions of the new digital tools, process and their utility. Overall, data accessibility and quality improved substantially over paper-based campaigns, with over 80% of distributed commodities geolocated, and 95% of records becoming available for monitoring within 24h of collection. Data review forums were crucial for campaign management, with over 10% of the population coverage attained in the ITN campaign attributable to them. Coverage assessed in post-distribution surveys was high at 98.1-100% in target districts for ITNs. Across user interviews, 88.6% of campaign workers reported having a positive experience using the digital tools, with a further 97.1% finding them easy to use, despite historical reliance on paper systems. The experience of Mozambique has shown that digitalization has led to improved campaign performance while recording high acceptance across campaign workers. The digitalization of campaigns can strengthen their impact by enabling real-time decision-making, and through improvements in monitoring, data quality and targeting. Moreover, collected digital geolocation data is a useful asset during the planning of upcoming campaigns in targeted geographies.

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FREQUENCY OF HOUSEHOLD VISITS IN DEMOGRAPHIC SURVEILLANCE SYSTEM IN BANGLADESH AFFECTS ESTIMATES OF PERINATAL MORTALITY

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A demographic surveillance system has been established in September 2017 in Baliakandi sub-district of Rajbari district in Bangladesh, as an essential component of the Child Health and Mortality Prevention Surveillance (CHAMPS) project. It covers 57,259 households with a population of 237,170 in 2023, providing data on household location, member characteristics socio-economic status, women's reproductive history and demographic events. Initially, from Sep-2017 data was collected every 4 months intervals, from Oct-2018 it was changed into 2 monthly visits. After 21 months, when PSS full protocol was established and implemented data collection intervals increased to 3 months from Jul-2020. We investigated how household visits at different intervals impact the detection of birth and death events. We compared births and child deaths from Oct-17 to Sep-18 (visits every 4 months), Oct-18 to Sep-19 (visits every 2 months), and Oct-21 to Sep-22 (visits every 3 months); the years between 2019-2021 were excluded due to COVID-19. During the 4-monthly round, 4,698 new pregnancies and 4,737 deliveries were

identified, compared to 5,984 new pregnancies and 5,365 deliveries during 2-month visits, and 6,904 new pregnancies and 5,899 deliveries during 3-month visits. The stillbirth rate (19 /1000 Live birth (LB)+Still Birth (SB)) was observed to be lower with visits every 3 months compared to visits every 4 months (27 /1000 LB+SB) and visits every 2 months (24 /1000 LB+SB). Conversely, neonatal and perinatal mortality rates (NMR and PMR) were higher (32 and 50 /1000 LB and LB+SB) with visits every 2 months compared to visits every 4 months and 3 months (NMR 23 and 20 /1000 LB, PMR 46 and 35 /1000 LB+SB, respectively). Our findings suggest, shorter interval HDSS round captures more events. However, the variation in stillbirth rate may lead to misclassification with abortion and early neonatal death (END). Similarly, increases in NMR and PMR may indicate misclassification of stillbirth and early neonatal deaths in longer visit interval. It has been observed that lower interval of HH data update can capture more SB and END and can minimize misclassification.

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HPV SCREENING IN LOW-RESOURCE SETTINGS: A COMPARISON OF SELF-COLLECTED VAGINAL SWABS TRANSPORTED WITH AND WITHOUT VIRAL TRANSPORT MEDIUM

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Self-collected vaginal samples for high-risk human papillomavirus (hrHPV) DNA testing hold the potential to address cultural barriers and sensitivities around traditional provider-driven cervical cancer screening methods. However, there is limited evidence on effective transportation methods for self-collected samples, particularly in low- and middle-income countries. Samples can either be transported dry (without viral transport media) or wet (with viral transport media). Transportation of self-collected vaginal samples with VTM involves additional costs and difficulties in handling. The clinical study aims to compare the performance of self-collected vaginal swabs transported dry vs wet for the detection of hrHPV DNA to screen for cervical intraepithelial neoplasia (CIN2+) lesions using liquid-based cytology (LBC) as the reference standard. The prospective, multi-centric, comparative diagnostic accuracy study will be conducted in Kenya, South Africa and Bangladesh in 2024. The study will enrol 1306 sexually active adult females ≥30 years (≥25 years if HIV+) presenting for treatment at a facility with an abnormal cervical cancer screening result (abnormal cytology, visual inspection with acetic acid and/or colposcopy), willing to provide all necessary samples (self-collected dry and wet and health care worker collected cervical swabs) with written informed consent. Women who are vaccinated for HPV and/or pregnant will be excluded. All samples will be tested using the Cepheid Xpert and Roche Cobas platforms for hrHPV DNA. Cervical samples will also be assessed using LBC to grade lesions according to NICE guidelines. In addition, surveys will be conducted to assess the acceptability and usability of sample collection methods among participating women and HCWs. Sensitivity and specificity, and Cohen's Kappa statistics will be used to compare self-collected dry vs wet swabs for detection of hrHPV DNA. Survey responses will be assessed using descriptive analysis. The evidence generated through this study will inform country implementation strategies to support the scale-up of HPV screening, using self-sampling.

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UNDERSTANDING CARE SEEKING PATTERNS FOR ANTENATAL CARE IN WESTERN KENYA

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In Kenya, only 58.5% of women attended 4+ antenatal care (ANC) contacts, and only 3.6% attended the WHO recommended 8 contacts (MIS 2020). Only 28.1% attended prior to four months, with a median of 4.8 months at first ANC (ANC1). While there are many barriers to women attending ANC, the desire to conceal an early pregnancy may prompt women to attend ANC late or seek care further from home. Women may avoid facilities where they receive poor care or services are not comprehensive. Understanding patterns of care seeking can help to optimize quality and availability of ANC. To evaluate this, we analyzed data on location of ANC visits from 7 health facilities (HF) participating in a scannable maternal and child health (MCH) handbook feasibility pilot in Siaya County, western Kenya. Women aged 13-49 attending any ANC visit from Oct-Dec 2023 were included, provided with a scannable handbook, and followed for six months. For women enrolled after ANC1, data from previous visits were copied into the scannable book. Data on services provided, including location of each ANC visit, was electronically abstracted. Data on location of care seeking were available from 553 women. Women were a median of 25 years; 28.7% were primigravid, 25.5% were secundigravid, and 45.8% were multigravida. Just over half (52%) were enrolled at the county referral hospital, a level 5 facility. An additional 32% were enrolled from dispensaries (level 2) and 16% from clinics (level 3). Most (86%) women attended the same HF for all ANC visits, 13% attended 2 HF (mean 1.2, range 1-4), with no difference by gravidity. ANC1 occurred at a mean of 17.2 (STD 7.4) weeks gestational age, with no difference between women who attended one vs multiple HF. Among women who sought care for malaria during pregnancy, 92% went to the same HF where they attended ANC and 8% went to a different HF. The majority (88%) gave birth at the same HF where they attended ANC1. While most women sought care from the same HF throughout pregnancy, 14% sought ANC from multiple HF. Understanding the drivers of where women seek care can help with interpretation of routine data as well as target HF for supervision to ensure women receive quality ANC.

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DESIGNING BETTER DENGUE TRIALS: UNDERSTANDING ATTITUDES, EXPERIENCES, AND EXPECTATIONS OF PATIENTS IN THREE ASIAN COUNTRIES

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The unmet need of disease-specific treatment in dengue, a global epidemic affecting >100 countries, calls for an effective antiviral drug besides the currently available medical and nonmedical countermeasures. Understanding patients' journey and their perspective on clinical trials (CTs) is warranted to inform the design of scientifically robust and operationally efficient CTs. In this context, an insight gathering survey was conducted using online community methodology and tele-depth interviews. The study involved 38 patients aged 18-70 years who had experienced mild to moderate dengue within the last 12 months (mo) in Singapore (n=18), 18 mo in Taiwan (n=6), and 3 mo in Vietnam (n=14). The most commonly reported symptoms were fever, persistent/severe headache, muscle and joint pain, rash, and fatigue leading to inability to perform daily activities. All symptoms except fatigue resolved in 1-2 weeks. A second episode of dengue, if reported, was described as more severe. The duration from first symptom to diagnosis was around 72 hours. Most patients self-medicated with over-the-counter medication and home remedies first, highlighting the key barrier to enrolling dengue patients into a CT within 48 hours of fever onset. Additional barriers included safety and efficacy concerns, lack of clarity around CTs, complicated medical assessments, and the impact of trial-related time commitments on jobs and daily responsibilities. The key enablers to CT participation were reassurance through close monitoring of adverse events, health care professional (HCP) endorsement, expected benefits from CT medication, and financial incentives. To address patient expectations, focusing on study benefits and reassurance on safety monitoring are vital. Further solutions include raising disease awareness through education, mass testing for rapid diagnosis, endorsement by

HCPs, sharing clear information about the medication, and smart/flexible study operation to address patient needs. These insights can inform the design and execution of future studies in dengue.

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COMPREHENSIVE REVIEW ON THE USE OF ORAL CHOLERA VACCINE (OCV) IN ETHIOPIA: 2019 TO 2023

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Ethiopia has experienced several cholera epidemics in the past decades and the government has conducted several reactive OCV mass vaccination campaigns to control outbreaks. A comprehensive review of OCV use across the country was needed to assess the impact of vaccination on cholera epidemiology and outbreaks and plan for any future vaccinations with delayed second or booster doses. Data on all OCV requests made by Ethiopian government during 2019-October 2023 and all OCV vaccination campaigns conducted during 2019-December 2023 were extracted from the Ethiopia Public Health Institute database; and a retrospective descriptive analysis conducted. During 2019-October 2023, total 32,044,576 OCV doses (31,899,576 doses to the global stockpile; 145,000 doses to outside of the stockpile) were requested; 66.3% of requested doses to the global stockpile got approved, and 90.4% of approved doses were received in Ethiopia. Using these doses, total 15 OCV mass vaccination campaigns (12 reactive and 3 pre-emptive) were conducted, including five two-dose campaigns with varying dose intervals and single dose campaigns partially in 2019 and entirely in 2021, 2022 and 2023. Overall vaccine administrative coverage was high; except for Tigray region campaign (41.8% in the 1st round; 2nd round didn't occur). No coverage survey data was available. Monitoring and evaluation of OCV use are essential given the current limited vaccine supply. This is the first comprehensive review paper documenting all OCV requests the Ethiopian government has made to the International Coordinating Group on Vaccine Provision and all OCV vaccination campaigns conducted across the country in detail in the recent five years. Our review will contribute to informing future cholera control strategies in Ethiopia, including when and where to conduct future campaigns. Formal coverage surveys beyond administrative data have not been conducted in these campaigns due to resource constraints resulting from the upsurge of cholera outbreaks nationally. The Ethiopian government has developed a protocol for post-campaign coverage surveys which they hope to implement in the future.

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COVERAGE OF TWO-DOSES OF PRE-EMPTIVE ORAL CHOLERA VACCINE (OCV) MASS VACCINATION CAMPAIGN IN CHOLERA HIGH PRIORITY HOTSPOTS IN SHASHEMENE TOWN AND WOREDA, WEST ARSI ZONE, OROMIA REGION, ETHIOPIA

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In context of cholera endemicity with periodic outbreaks in Ethiopia, we conducted a pre-emptive two-dose OCV vaccination campaign in cholera high priority hotspots in Ethiopia under the Ethiopia Cholera Control and Prevention (ECCP) project. The vaccination was conducted in Shashemene Town (ST) and Shashemene Woreda (SW) in Oromia region on May 11-15 (1st round (R1)) and May 27-31 (2nd round (R2)), 2022. A mixed vaccination strategy (fixed posts and mobile teams) was used. Daily monitoring of administrative OCV coverage, and a coverage survey at the end of the campaign was conducted in vaccination target areas. Overall administrative OCV coverage in vaccination target areas was high (ST: 102.0% (R1), 100.5% (R2); SW: 99.1% (R1), 100.0% (R2)). For OCV coverage survey, total 112 and 165 households were surveyed in ST and SW respectively. 78% (73.06-82.94; 95% CI) of household members in ST received two-doses (2D) OCV and 16.82% (12.36-21.28; 95% CI) with no OCV. In SW, 83.06% (79.62-86.50; 95% CI) received 2D OCV and 11.80% (8.84-14.76; 95% CI) with no OCV. In ST, 2D coverage rates were 88.33%, 88.89%, and 71.25% in 1-4 years, 5-14 years, and 15 years and above age groups, respectively. In SW, 2D coverages were 78.23%, 90.96%, and 78.67% in 1-4 years, 5-14 years, and 15 years and above age groups, respectively. In both ST and SW, health workers were the most influential player in community sensitization on OCV vaccination campaign. Only 2.68% (3/112) and 3.64% (6/165) of households in ST and SW respectively answered fear of adverse event as the principal reason for not receiving OCV. Mixed vaccination strategy and daily monitoring of administrative vaccination coverage contributed to promoting the daily uptake of OCV administrations. Vaccine acceptance and confidence on OCV was high as exhibited in high vaccine administrative coverage. A long-term sustainable and systematic cholera surveillance is recommended to further evaluate the impact and effectiveness of this vaccination in ST and SW; and also, in comparison with the other OCV vaccinations conducted by the Ethiopian government with single dose OCV reactive campaigns in recent years.

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HEALTHCARE SEEKING BEHAVIOR AND KNOWLEDGE ASSOCIATED WITH CHOLERA AND DIARRHEAL ILLNESSES AMONG POPULATIONS LIVING IN CHOLERA ENDEMIC AND HOTSPOTS IN SHASHEMENE TOWN AND SHASHEMENE WOREDA, ETHIOPIA

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Healthcare seeking behavior (HSB) and perception on cholera by local populations can influence its management. We conducted a cross-sectional survey to generate evidence on cholera associated HSB and disease perception in populations living in cholera endemic and high priority hotspots in Ethiopia. Total 870 randomly selected households (HHs) in Shashemene Town (ST) and Shashemene Woreda (SW) participated in survey in January 2022. Median HH member size was 5.0 (IQR: 4.0, 6.0). Mean (±SD) age of respondents was 36.81 (±12.26) years. 52.5% (229/440) of HHs in SW showed low wealth index; 41.4% (178/430) in of HHs in ST in high wealth index. For the majority of HHs (91.03%; 792/870), primary health center was the nearest healthcare facility (HCF). Public transportation (75.98%; 661/870) was the main mode of accessing HCFs. Travel time to the nearest HCF was largely less than 30 minutes (57.44%; 247/430) in ST. In SW, 60.23% (265/440) of HHs travelled more than 30 minutes; 25.91% (114/440) over 4km. Two-thirds of all HHs paid less than USD1 travel cost to HCFs, but SW residents had slightly higher travel cost. When experiencing cholera symptoms, predominant respondents preferred to seek healthcare at our study sentinel-HCFs. In ST, 68.03% (83/122) of children under 5 years (y), 75.50% (114/151) of 5-14y, 100% (52/52) of 15-17y, and 100% (426/426) of ≥18y sought healthcare at our sentinel-HCFs. In SW, children and adolescents visited our sentinel-HCFs slightly more (82.56% in 1-4y, 86.67% in 5-14y) than older age groups (74.36% in 15-17y, 75.63% in ≥18y). Relatively more adults in ST (51/426; 11.97%) sought over the counter drugs at pharmacies than in SW (11/435; 2.53%).73.8% (642/870) of HHs were aware of cholera disease. 66.7% (428/642) of HHs

in ST and SW considered eating unclean food as main causes of cholera. Variations in cholera prevention practices between rural and urban residents were shown. Addressing differences in HSB per age groups is needed for community engagement for early case detection and case management; critical in reducing cholera deaths and transmission.

7686

DISSECTING WATER, SANITATION, AND HYGIENE (WASH) RISK FACTORS FOR CHOLERA AND GEOSPATIAL MAPPING OF WASH STATUS AND ITS ASSOCIATION WITH CHOLERA ATTACK RATE IN SHASHEMENE TOWN AND WOREDA, OROMIA REGION, ETHIOPIA

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Understanding water, sanitation, and hygiene (WaSH) risk factors and their association with cholera is crucial for refined interventions and policy development. A cross-sectional household survey was conducted among 870 randomly selected households in Shashemene Town (ST) and Shashemene Woreda (SW) in Ethiopia in 2022. The relationship between WaSH components and sociodemographic/economic levels of households was examined. We used Chi-square test, binary logistic regression, linear regression, LOESS Smoothing Method, Kendal's Correlation, and Moran's I to assess associations between WaSH and cholera attack rate (AR). Approximately 67.5% (95% CI: 64.4, 70.6), 73.4% (95% CI: 70.3, 76.3) and 30.3% (95% CI: 27.3, 33.3) of the households in ST and SW had access to at least basic drinking water, sanitation, and hygiene facilities, respectively; and 53.3% (95% CI: 49.9, 56.6) of the households exhibited better WaSH practice. Better WaSH practices were positively correlated with urban residence (adjusted odds ratio (AOR)=1.70, 95% CI: 1.07, 2.72), household head's tertiary education (AOR=2.68, 95% CI: 1.24, 5.78), and high wealth index (AOR=2.50, 95% CI: 1.58, 3.97). The mean AR of cholera was negatively associated to access to basic WaSH ($p<0.05$). The association between cholera AR and all three WaSH components was not statistically significant (multiple R-squared=0.132; F-statistic=1.127, p-value=0.3599), but Moran's I statistics implied potential localized effects with a borderline significant value for sanitation (I=0.2223, p=0.02398). Rural communities require more public health and development interventions with policy priorities and resources given to all aspects of WaSH. The association between cholera AR and WaSH status at kebele-level (lowest local administrative unit) was not significant, but further analyses including meaningful covariates (e.g., high wealth index) and/or increasing sample numbers (e.g., kebeles) to get more power would be necessary. Additional spatial analysis will be helpful since there was potential spatial autocorrelation between cholera AR and sanitation found using Moran's I.

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FACTORS ASSOCIATED TO GESTATIONAL WEIGHT GAIN TRAJECTORIES OF PREGNANT WOMEN LIVING IN A LIMITED RESOURCES SETTINGS IN SOUTHERN BENIN, WEST AFRICA

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Weight gain during pregnancy is crucial for foetal development and includes factors like foetal growth, placental development, and changes in mother's body. Monitoring weight gain is vital during Antenatal Care (ANC), as deviations from recommended levels can lead to complications for both mother and baby. From June 2014 to March 2017, 1214, women of reproductive age were recruited and followed up monthly at community level until 411 became pregnant. Pregnant women were then followed up monthly from 5-6 weeks of gestation until delivery. During ANC visits pregnant women were weighted and their weight gain was assessed against pre-pregnancy weight measured within 3 months before pregnancy. We used Group Based Trajectory Modelling (GBTM) to identify gestational weight gain (GWG) trajectories. Multinomial regression was used to evaluate factors associated to these GWG trajectories. A total of 294 of the 411 women who became pregnant had three successive weight measurements during pregnancy follow-up and were considered in the analyses. We identified 3 different weight gain trajectories: i) Moderate and Persistent Early Weight Lost (MPE-WL) in 57 of the 294 women (19.4%), ii) Small and Brief Early Weight Lost (SBE-WL) in 166 women (56.5%) and iii) Early and Continuous Weight Gain (EC-WG) in 71 women (24.2%). Of the 294 women, 66 (22.4%) were infected by malaria at least once during pregnancy, with evidence of microscopic infection, and 9 were infected twice consecutively. Having had malaria at least once during pregnancy was not associated with weight gain trajectories (p=0.82). In univariate analysis, pre-pregnancy BMI was associated with GWG (p=0.006)) trajectories. The relative risk ratio of belonging to the MPE-WL trajectory instead of EC-WG trajectory was increased by 80% for women who were overweight or obese at inclusion, compared with women with a normal BMI at inclusion (RRR=1.80, 95%CI: 0.81, 3.98). Other clinical, biological, and gynaecological factors tested were not significant at the 20% level and a multivariate model was not fitted.

7688

CAUSES OF MATERNAL MORTALITY IN RURAL BANGLADESH: ANALYSIS OF VERBAL AUTOPSY DATA OF CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) BANGLADESH

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In Bangladesh, the maternal mortality ratio (MMR) reduced markedly from 322 per 100,000 live births in 2001 to 194 in 2010, but progress has plateaued and MMR remained at 196 in 2016. It has declined to 136 per 100,000 live births by 2023. Women in rural areas with low socioeconomic status face a higher risk. Understanding the major causes of maternal deaths can improve interventions. The study aimed to explore the primary causes of maternal deaths focusing on time and place of death. Verbal autopsies (VAs) were collected for all deceased women of reproductive age in CHAMPS Bangladesh site, rural Baliakandi from 2019 to 2023. A total of 39 deaths were identified during pregnancy, delivery or within 42 days of delivery. Two trained physicians reviewed the VAs to assign a cause of death. The causes were divided into two groups: direct causes which include obstetric complications of pregnancy, labour or puerperium, and indirect causes referring to non-obstetric or pre-existing diseases which deteriorated during pregnancy. A total of 37 deaths were classified as maternal deaths as per WHO definition with an MMR of 136 per 100,000 live births. The other two women died from drowning and homicide. Demographic data showed that 8% (3/37) of women aged 17 years or less while 19% (7/37) were 35 years or older. Caesarean section was the mode of delivery in 49% (18/37). The major direct causes of the 37 maternal deaths were haemorrhage (16%, 6/37) and eclampsia (11%,

4/37). However, indirect causes were predominant (62%, 23/37) and stroke (10/23) was the leading indirect cause. Majority of deaths (76%, 28/37) occurred in the postpartum period. Sixty-two percent (23/37) of women died at hospital, while 22% (8/37) died in transit and 16% (6/37) at home. Before dying, 27% (10/37) of women solely sought healthcare from public facilities and 38% (14/37) from multiple places. Prioritizing high-quality intrapartum and postpartum care can significantly reduce MMR. Moreover, identifying and addressing indirect causes during pregnancy that significantly contributed to maternal deaths, underscore the necessity for comprehensive healthcare strategies beyond obstetric care.

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COMPARISON OF KNOWLEDGE, ATTITUDES AND PERCEPTIONS ON COVID-19 VACCINES HESITANCY BETWEEN RURAL AND URBAN COMMUNITIES IN DEMOCRATIC REPUBLIC OF CONGO

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DR Congo is the third most populous country in Africa. To combat the COVID-19 pandemic, it was among the first to benefit from batches of COVID-19 vaccines through the COVAX, COVID-19 Vaccines Global Access initiative. Since vaccines are given to healthy people, the confidence and safety of the public must be guaranteed. However, a few weeks after the launch of the mass rural area, the government was forced to return vaccines that were in risk of expiring. Extending over 2 million square kilometres, DR Congo has less than 5 km of railways, poorly maintained roads dating back to colonial times and a virtually non-existent electricity network. The aim of this study is to compare the knowledge, attitudes and practices of urban and rural communities regarding immunisation. This is a qualitative study conducted at two sites: at the *Centre Hospitalier du Mont-Amba* in Kinshasa for the urban area and at the health centre of the Community of Baptist Churches in Congo in Kimpese, in the Province of Central Kongo, for the rural area. Data were collected through individual questionnaires administered to medical staff and group interviews with patients' carers. The study included 90 participants, 46 from the Kinshasa site and 44 from the Kimpese site. Around three quarters of Kinshasa respondents (73%) thought that COVID vaccines were safe, compared with only 37% of Kimpese's interviewees. Importance of vaccines in COVID-19 protection was recognised by 87% of city dwellers, versus 57% of villagers. In Kinshasa, overwhelmed by the multiplicity and contradiction of information sources, the public behaviour was affected by several factors around vaccination. In rural areas, on the other hand, without electricity or television, villagers did not benefit from the wide variety of means of communication. Fighting for their survival, they did not understand the benefits of vaccination, especially as the majority of positive cases were found in large towns. There are great disparities in knowledge, attitudes and practices between communities living in urban areas compared to those in villages in the DR Congo. An in-depth analysis of the determining factors is needed.

7690

ASSESSMENT OF AGE-RELATED DISEASE INCIDENCE IN A MISSION CLINIC IN RURAL HAITI, AS A BASIS FOR PLANNING PUBLIC HEALTH PREVENTION PROGRAMS

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The instability in the Haitian political and economic situation makes it difficult to establish proper public health interventions. While infectious diseases continue to be a public health priority, Haiti now faces the "double burden" of both chronic and infectious disease (Fence et all). The Love A Child (LAC) Foundation, a non-profit humanitarian organization, provides medical care for the most vulnerable populations in Haiti, with clinic data recorded in an electronic medical record (EMR). This study sought to assess the incidence and seasonality of age-related diseases in rural Haiti by age groups. De-identified data were analyzed from over 400,000 patient visits from the LAC Foundation Clinic in Haiti from January 2018 until December 2020. It is the first review of the EMR system to assess rates of illness and to assess the impact of age and their seasonality. Data were analyzed descriptively and with standard statistical tests. We selected a subset of 848 patients seen between January 2018 and December 2020 for the initial analysis. The highest proportion of diagnoses for high grade fever (HGF) (32.5%) were in children in the 0 to 4 and 5-to-9-year age groups. For syphilis, cases were most common in the 25-29-year age group (17.45%). The highest proportion of elevated blood pressure (EBP) was seen among persons aged 25-29 years: systolic level 120-129 mm Hg (22.02%); stage 1, 130-139 mm Hg (17.09%); and stage 2, >140 mm Hg (12.79%). Diagnosis of prediabetes (glucose level between 101-125 mg/dl) and diabetes (> 126 mg/dl) was present at the highest proportion in the 25-29 age group, 18.71% and 7.06.% respectively. HGF was most commonly diagnosed between January and March (66.67%). EBP and stage 1 and 2 were most diagnosed between June and September at 29.03%, 28.5%, and 28%, respectively; and prediabetes and diabetes at 32.31% and 28.77%, respectively between June and September. Our observations highlight the utility of EMR in defining groups at increased risk for conditions of public health concern and in development of appropriately targeted interventions.

7691

FACTORS ASSOCIATED WITH THE PERFORMANCE OF MALARIA CASE MANAGEMENT BY COMMUNITY HEALTH WORKERS IN THE DISTRICT OF FRIA, GUINEA

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Malaria continues to represent a substantial health burden in Guinea; the district of Fria has one of the highest malaria case incidences in the country. In 2022, efforts were made by the Ministry of Health and its partners to strengthen community health platforms across the country, including to for malaria prevention and control purposes. To that end, we conducted a study to assess the performance of community health workers (CHWs) in malaria case management. We conducted a cross-sectional survey in Fria district that included 75 CHWs and 375 households (five per CHW). Two study-specific questionnaires were used to assess the performance of CHWs, as well as the quality of the services the CHWs provided to the

community; performance was based on a composite score calculated from the questionnaires' answers on key themes related to CHW performance. Univariate logistic regression analysis was used to determine factors affecting CHW performance. For the 72 CHWs that had performance data available, the overall average score was 81%. Of these, 56% were considered performant, with scores ≥80%. Experience defined as the number of years working as a CHW (Odds ratio [OR] = 4.01; 95% CI = 1.07, 17.30), community support including financial support and support for field work (OR = 4.11; 95% CI = 1.05, 17.80), and access to commodities such as possession of malaria rapid diagnostic tests (OR = 4.03; 95% CI = 1.05, 16.90) were shown to be associated with higher CHW performance. Being a CHW in an urban area was associated with lower performance (OR = 0.17; 95% CI = 0.04-0.64). We show that several factors were associated with CHW performance and should be considered when designing approaches to strengthen CHW performance, supervision, and support. Causes why the performance of CHWs in urban areas is lower than rural areas should be further investigated.

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GRIEVING AND ITS IMPLICATIONS IN A RURAL SOUTH AFRICAN COMMUNITY: A QUALITATIVE EXPLORATIVE STUDY

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Grief occurs across ages without geographical boundaries. Dealing with grief is influenced by one's cultural background, personal beliefs, gender, and the nature of the loss. Despite the psychological toll of grief, rural communities typically have less access to grief counseling and other mental health resources.This qualitative exploratory study involved thematic analysis of 20 interviews with people who experienced death in the past 24 months and six focus group discussions with healthcare, mortuaries, traditional healers, religious leaders, and general community members from Agincourt HDSS. We explored experiences of grief, grieving processes, and their implications on general health. We found that people grieved in diverse ways based on their personality, culture, and support networks. Narratives illustrated the complex emotions experienced prior to acceptance of death. Some families manifest denial by delaying notification of mortuaries, hoping the deceased might return to life; others described being numb. Several described anger and argument particularly when the death was unexpected. Family solidarity in terms of unity, task initiations and financial support, neighborly support through practical tasks such as cooking, and support from churches constituted key coping mechanisms. Those espousing traditional beliefs engaged in ancestral rituals to find closure. Those lacking support described a range of health issues, notably anxiety, chronic stress, and depression, with some becoming isolated or abusing alcohol to numb their emotional pain. Participants described emotions coming in waves, triggering memories that affected their overall health. Healthcare workers corroborated these observations, noting hypertension among grieving patients. Psychological services were not seen to be accessible, due to distance, cost or lack of counsellors.While this rural community described diverse mechanisms to support the grieving process, formal therapeutic psychological support was notably missing, highlighting both the justification and need for accessible grief counselors within rural communities.

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FACTORS ASSOCIATED WITH UTILIZATION OF ANTENATAL SERVICES IN AN URBAN HEALTH CLINIC

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Antenatal care is essential to ensure good health outcomes for the pregnant women and their expected offspring. The objective of this study was to analyze factors associated with the utilization of antenatal services, defined as at least four antenatal visits. A cross-sectional descriptive study, using both quantitative and qualitative methods, was carried out an urban health facility, in Mozambique. The quantitative component was based on a questionnaire administered to postpartum women in the maternity ward and in the postpartum consultation. The qualitative component was based on participatory observation and in-depth interviews with eight health providers. A total of 271 postpartum women responded to the questionnaire. The age of the respondents varied from 16 to 42 years, with a mean of 26 years (standard deviation: ± 5.9). Among the 271 women, 233 (86%) had completed more than four antenatal visits. Antenatal attendance was associated with initiation of antiretroviral treatment at antenatal care. Antenatal attendance was not associated with demographic and socioeconomic variables such as age, marital status, education, occupation, religion, and ownership of property and access to information and communication technologies. Antenatal attendance was also not associated with other variables such as the presence of the partner at antenatal visit, living with a partner, approval of the partner to attend antenatal visits, place where the antenatal was performed and delivery at a health facility. The qualitative data showed that, overall, the health center was ready to provide antenatal services, with the exception of lacking drinking water, for the direct observation of treatment, and an insufficient stock of iron and folic acid supplementation. The utilization of antenatal services in this urban health facility is high. However, additional support should be provided to those women initiating antiretroviral treatment at the antenatal clinic.

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USE OF LOGISTICIAN TRAINEES IN LAST MILE DISTRIBUTION OF EMERGENCY RESTOCKING RESPONSE IN BENIN, APRIL TO MAY 2023

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Benin's central medical warehouse in Cotonou, SoBaps, ships supplies to 34 zonal distribution depots (DRZ) via trucks, but last-mile distribution has not yet scaled up. Most DRZs (75 percent) lack dedicated vehicles for onward distribution. Thus, health facilities (HF) must collect their own supplies from DRZs. From April 1, 2023, to May 15, 2023, public sector HFs experienced shortages of injectable artesunate for treating severe malaria despite adequate supplies at DRZs due delay in delivery by principal donor. To address the shortage, a one-time last-mile intervention was designed. For this effort, Young Professional Logisticians (YPL), a training program for 77 entry-level logisticians based at DRZs, were engaged to use DRZ motorbikes that had been procured by PMI Global Health Supply Chain Program for use in the routine supply chain system. The HFs used standard methods to calculate their medication needs (i.e., consumption rate and stock-on-hand). Over a two-day period, the YPLs delivered 155,070 ampoules of injectable artesunate from 34 DRZs to 115 HFs. This increased stocks at facilities from an average of 0.9 months to 3.5 months. In 2020 the average stock level was 1.21 months and 1.41 in 2021. Observations from the effort revealed that this was a successful distribution

method for one-time response and could serve as a model for emergency response; however, additional analysis is underway to determine if this could also be a more cost-effective method for last-mile distribution than what is currently being planned

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ENHANCING FINANCIAL SUSTAINABILITY OF THE PUBLIC SECTOR SUPPLY CHAIN FOR MALARIA COMMODITIES IN MADAGASCAR THROUGH A TOTAL COST ANALYSIS

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Access to quality medicines in the public sector in Madagascar remains challenging due to insufficient information on costs of peripheral storage and transportation of commodities. Donor funds are used to purchase malaria commodities and cover costs to distribute and store them at district level. However, health facilities (HFs) use their own funds to transport commodities from district pharmacies to HFs. The USAID-funded IMPACT program supported the Ministry of Public Health (MOPH) to conduct a Total Cost Analysis (TCA) of the public sector supply chain in 2020 to enhance financial planning, foster stakeholders' engagement in commodity management, and explore reducing donor dependency. Data were collected on 2017-2019 supply chain costs and revenues at the central warehouse (SALAMA) and in randomly sampled HFs (16 district pharmacies, 17 hospitals, 47 health centers). Findings were used in 2022 to develop a road map for implementing key actions, including revising variable price mark-ups, improving financial management and control, updating contract terms for district and hospital pharmacies, and prioritizing efficiency by reducing supply chain activity costs. IMPACT developed a costing and financial sustainability modeling tool and trained 80 staff from all levels of the health system on its use, including modeling how hospitals can remain financially viable with reductions of price mark-ups applied to essential health commodities of at least 30% of current value and reducing transportation costs to 20% of current value. HFs are asked to support last-mile distribution (LMD) costs of donor-funded products that SALAMA cannot absorb: the TCA showed that HFs have used 14% of their revenues to support LMD costs for vertical programs. The TCA allowed visibility on the costs of storage and transportation of commodities, including those for malaria, at all levels of the supply chain and provided a starting point for donor and MOPH discussions on the sustainability of financing of LMD. Routine use of this tool by the MOPH and SALAMA could lead to further decision making for improved supply chain efficiency and financial resource mobilization.

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CORRELATES OF INTESTINAL FATTY ACID BINDING PROTEIN, A MARKER OF INTESTINAL INJURY, IN A COHORT OF KENYAN CHILDREN UNDER FIVE BEING DISCHARGED FROM HOSPITALS FOR NON-TRAUMATIC CAUSES

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Environmental enteric dysfunction is implicated in substantial morbidity, mortality, and malnutrition among young children living in low- and middle-income countries. Intestinal fatty acid binding protein (I-FABP), a plasma-based biomarker of intestinal injury, has been associated with disease severity and illness recovery in populations living in high-income settings. We therefore sought to characterize I-FABP levels among Kenyan children recently hospitalized for non-traumatic causes and determine correlates of high I-FABP levels. Plasma samples from children under 5 years enrolled in the Toto Bora trial, a randomized controlled trial testing the efficacy of post-discharge azithromycin use on mortality and re-hospitalization during the 6-month follow-up period, were tested for I-FABP concentration using enzyme linked immunoassays. T-tests from linear regression with robust standard errors, adjusting for age and recruitment hospital, were used to find correlates of mean I-FABP levels. Among 1343 enrolled children with samples, the median I-FABP level at discharge, prior to randomization, was 1307 pg/mL (IQR: 902-2017 pg/mL). Children who were underweight (WAZ<-2) had 401 pg/mL (95% CI: 197, 604) higher I-FABP levels than those who were not underweight ($p<0.001$) and those who were stunted (HAZ<-2) had 206 pg/mL higher mean I-FABP compared to those who were not stunted (95% CI: 55, 358, $p<0.01$). However, there was no difference between children with and without wasting (mean difference 238 (95%CI: -92, 568, p-value=0.16). Each month increase in age was associated with a 9.5 pg/mL lower I-FABP level, on average (95% CI: -13, -6, $p<0.001$). Children who received antibiotics during their hospital stay had a 247 pg/mL decrease in I-FABP compared to those who did not (95% CI: -480, -14, $p<0.05$). We did not find evidence of enteric pathogen presence, breastfeeding status, or HIV exposure status to be associated with I-FABP levels at hospital discharge. Further analyses will link I-FABP levels with morbidity and mortality during the 6-month post-discharge period and test whether azithromycin impacts I-FABP levels 3 months later.

7697

VACCINE CONFIDENCE AND WILLINGNESS TO USE A HYPOTHETICAL NEW VACCINE AGAINST LASSA FEVER: RESULTS FROM A POPULATION-BASED SURVEY IN SIERRA LEONE

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Lassa fever (LF) is endemic to West Africa. New vaccines against LF are being developed, thus understanding vaccine confidence in this region is important for the conduct of clinical trials and uptake of a future vaccine. As part of a cohort study to characterize the epidemiology of LASV in Sierra Leone, we administered a validated vaccine hesitancy questionnaire to participating heads of households (HH). Questions included awareness of and concern about LF, and willingness to use a potential new vaccine against LF for themselves, their spouse, or their children. The cohort enrolled 834 households, and 635 (76%) HH were successfully interviewed at the follow up visit. Of these HH, 61% were male, and the average age was 40 (range 17-100). The median household size was 11 residents (range 1-20). Most (80%) participants reported being very or somewhat familiar with LF; 74% considered LF a concern to their household, and 90% felt protecting their household from LF was important. Few (~1%) reported firsthand experience with LF or Ebola virus disease (EVD) in the household. 71% reported receiving a vaccine as an adult, of whom 99% (n=446) reported vaccination for COVID, while 1% reported vaccination for EVD. Interest in a potential LF vaccine was high, with 98% of participants very likely, likely, or somewhat likely to consider receiving a vaccine for themselves and family members. Participants overwhelmingly agreed with elements of the vaccine hesitancy tool suggesting broad confidence in vaccines, however between 5-6% of participants consistently 'strongly disagreed' with statements such as "vaccines are effective," and "being vaccinated is important for the health of others in my community". Despite high enthusiasm for a potential new LF vaccine, more than a third (39%)

strongly agreed or agreed with the statement "New vaccines carry more risks than older vaccines." Over two-thirds (69%) of participants strongly agreed or agreed with the statement "I am concerned about serious adverse events of vaccines." Despite the high willingness to consider taking up a potential new vaccine against LF, a minority of participants report low confidence in vaccines.

7698

FUNGI BIODIVERSITY AND AZOLE RESISTANCE IN DIFFERENT DUMPSITES IN KABALE, SOUTH WEST, UGANDA

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Fungi make up a large portion of Earth's biodiversity and are essential to soil ecosystems because they carry out a range of ecological functions. In agriculture, the usage of fungicides have increased recently which has led to azole-resistant *Aspergillus* strains increasingly reported worldwide. However, there is still limited information available on these strains in Africa. This study aimed to assess fungi diversity in soil samples from fifteen different dumpsites/agricultural farmlands in Kabale, South West, Uganda using an improved culture-dependent approach (culturomics) comprising of five different media (Potato Dextrose Agar, Malt Extract Agar, Chromagar, Fastfungi and Saboraud Dextrose Agar). High-throughput MALDI-TOF MS (matrix assisted laser desorption/ionization mass spectrometry) and 18S rRNA genes sequencing were used for the identification of purified isolates. A total of 42 different isolates were found. *Trichoderma, Fusarium and Aspergillus* spp were the most prevalent fungi found and other pathogenic and opportunistic fungi such as *Simplicillium lamellicola, Mortierella multispora, Torulaspora delbrueckii* were also isolated. All *Aspergillus* isolates were further screened for azole-resistance using E-test method (itraconazole, voriconazole, posaconazole and Amp B) Results showed most Aspergillus species has lower MIC however, *A. clavatus* had MIC of 1.5mg/ml. Cyp 51 gene was also found in some of *Aspergillus* species.

7699

"WARTS AND ALL": THE BIOKO ISLAND MALARIA ELIMINATION PROJECT'S EXPERIENCE EXPANDING BEYOND MALARIA TO COMPREHENSIVE DISEASE SURVEILLANCE

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Since 2004, the Bioko Island Malaria Elimination Project (BIMEP) has supported the National Malaria Control Program within the Ministry of Health and Social Welfare of Equatorial Guinea to reduce the burden of malaria by leading entomological surveillance and vector control campaigns for IRS, larviciding, and LLINs, while providing mentorship, training, and commodity procurement for malaria case management and diagnostics. BIMEP also began supporting the MoHSW and their Health Information System in 2009 to monitor clinically diagnosed health outcomes. In 2015, patient-level data were digitized for select public health services, and in 2018, data collection was expanded to include nearly all public services, and clinical diagnoses were classified using ICD-10 in DHIS2. Here we characterize the spectrum of morbidity beyond malaria affecting the population of Bioko between 2015 and 2024 as recorded within DHIS2. Our findings reveal that noncommunicable diseases, particularly cardiovascular, represent a substantial burden, comprising 27% of all-cause diagnoses since 2015, which poses significant challenges to the MoHSW. These are followed by gastrointestinal infections, constituting 26% of all-cause diagnoses since 2015. The number of malaria cases has remained fairly stable over this period, with an average of 10,000 cases diagnosed each year, mirroring similar trends in parasite prevalence, representing 12% of all-cause morbidity. From the malaria control perspective, this is an important finding given prior to the BIMEP malaria was the leading cause of morbidity on Bioko Island. The expansion of surveillance beyond malaria has allowed to better characterize the main causes of disease as well as to decrease the number of reported ill-defined diseases. This can be attributed to robust health system monitoring and strengthening activities, including on-the-job mentoring and supervision. Crucially, our data also helped unveil the substantial disease burden of non-communicable diseases affecting the people of Bioko and the concerning burden also posed by GII, reflecting pervading challenges in sanitation.

7700

A MULTI-COUNTRY EXAMINATION POLICY AND AGRICULTURAL DETERMINANTS OF SMOKING IN THIRTEEN SUB-SAHARAN COUNTRIES

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Sub-Saharan Africa (SSA) is a focal point of attention for tobacco companies due to its large population & complex socioeconomic landscape. Our study examined associations of tobacco use with demographic predictors, country-level tobacco policies, production, & pricing predictors among 13 countries in SSA. We used Demographic and Health Survey (DHS) data for Angola (2015-16), Cameroon (2018), Democratic Republic of Congo (2013-14), Ethiopia (2016), Kenya (2014), Malawi (2015), Mozambique (2011), Namibia (2013), Nigeria (2018), Tanzania (2015-16), Uganda (2016), Zambia (2018) & Zimbabwe (2015). We matched data on tobacco policies, production, and pricing to consumption data for each country & used multi-level logistic regression to assess the associations between demographic predictor variables (i.e., age, residence, education, literacy, marital status, occupation, wealth index), policy variables (i.e., smoke-free facilities, smoke-free public spaces, smoke-free fines), tobacco production, tobacco pricing and the outcome variables of current tobacco use and heaviness of use. Increasing age, more education, and having a current/previous committed partnership were associated with greater likelihood of tobacco use. Living in a rural area, being literate, more wealth, and being unemployed/working in a non-manual labor job were associated with lower likelihood of tobacco use. Policies, production & pricing did not significantly predict tobacco use. In the final model predicting heaviness of smoking, being divorced, widowed, and having more wealth was associated with a greater likelihood of being a heavy smoker. Living in a country with higher smoke-free fines, more tobacco production, and higher pricing for cigarettes was associated with lower odds of heavy smoking among smokers. Among the countries examined, higher tobacco smoke-free fines, production, and pricing are more likely to be associated with reduced heavy smoking among current smokers, rather than with smoking or not smoking. Tobacco policies are synergistic in other countries, and there is a need to further explore pricing and enforcement policies.

7701

NAVIGATING MATERNAL HEALTH CHALLENGES IN BANGLADESH: AN ANALYSIS OF PREGNANCY COMPLICATIONS AND CARE-SEEKING BEHAVIORS USING NATIONALLY REPRESENTATIVE SURVEYS

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In Bangladesh, approximately 3.3 million annual births result in around 5000 maternal deaths, primarily due to hemorrhage (31%) and eclampsia (24%). Major complications among women aged 15-49 years during pregnancy, delivery or after delivery include pre-eclampsia symptoms, bleeding and convulsion/fit, which may lead to haemorrhage and eclampsia. We explored

the burden and determinants of these complications and care-seeking practices using descriptive and adjusted odds ratios (AOR) with 95% confidence intervals based on data from the 2001 (99202 households), 2010 (168629 HHs), and 2016 (298284 HHs) rounds of nationally representative Bangladesh Maternal Mortality and Health Care Survey. Nearly half (49%) of women aged 15-49 years experienced complications during pregnancy, delivery, or after delivery. Of these, 84% faced any one of major complications: pre-eclampsia (74%), bleeding (16%), or convulsion/fit (13%). The likelihood of developing any one of major three complications declined in 2016 compared to 2001 (AOR=0.6, CI:0.6-0.7), and the care-seeking practice improved from 28% to 41%. Despite this progress, 6 in 10 pregnant women with complications did not seek care from medically trained providers. Twin pregnancies had double the likelihood of developing these complications compared to singleton pregnancies (AOR=2.0, CI:1.4-2.8), and there were greater risks for those with birth intervals of 6 or more years (AOR=1.3, CI:1.1-1.4). Women from the poorest (AOR=1.3, CI:1.1-1.5) and being muslim (AOR=1.4, CI:1.2-1.5) were more likely to face these complications. Mothers with at least primary education (AOR=1.2, CI:1.02-1.44) were more likely to seek healthcare, while non-muslim mothers were less likely to do so (AOR =0.8, CI:0.7-0.9). Factors such as place of death, number of antenatal care visits, and regional disparities also influenced complications and care-seeking practices. Despite progress, many pregnant women with detectable major complications often remain untreated. Targeted interventions considering these factors are crucial for preventing maternal deaths by enhancing timely care-seeking practices.

7702

SOCIOECONOMIC AND DEMOGRAPHIC ASPECTS OF PNEUMONIA AND OTHER RESPIRATORY DISEASES AS CAUSE OF UNDER FIVE MORTALITY IN BANGLADESH, A DECADAL TIME SERIES ANALYSIS FROM NATIONAL SURVEILLANCE

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Bangladesh is committed to reduce the under-five morality rate below 25 per thousand live births by the end of agenda 2030 following the significant achievement in MDGs. To achieve the Sustainable Development Goal for SDG 3.2.1 (reducing child mortality), ending pneumonia and other respiratory disease-related deaths is an imperative preference. Beginning of the journey the baseline rate was 36 which followed by decreasing rates up to Covid-19. During the post Covid years an increasing trend is observed. The National Statistics Office through the Sample Vital Registration System (SVRS), a nationwide surveillance system over 300 thousand households and publishes annual estimates at the national and subnational levels for the under-five morality rates along with other vital statistics. The study follows the primary data analysis of SVRS from 2013 to 2023. According to the SVRS 2023, the deadly tropical disease Pneumonia is the single largest infectious cause of deaths in under-five children over the decades in Bangladesh with more than one-third of the under-five deaths while it is responsible for about half (49 percent) of the under-five deaths along with other respiratory diseases. The burden is 2.5 times higher in Bangladesh than observed globally. The recent estimate shows pneumonia is responsible for more than 38,000 under-five children's deaths every year which was around 31,000 in 2013. This study analysed the socioeconomic and demographic characteristics of the under-five deaths from the deadly pneumonia and other raspatory diseases during 2013-2023 with annual trends. The residence and locality, housing structures, wealth quintile, mother's education, sex, religion, ethnicity, etc. shows significant associations with the under-five mortality from pneumonia and other respiratory diseases. This study also focuses on the geospatial spectrums to identify the association of climate vulnerabilities with pneumonia and other respiratory diseases as cause of under-five deaths. This study also explores the place of deaths to measure the access to health facilities due to pneumonia and other respiratory diseases.

7703

IMPROVING PREP KNOWLEDGE FOR RESIDENT PHYSICIANS IN NEPAL

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Pre-exposure prophylaxis (PrEP) is highly effective for preventing acquisition of HIV. HIV PrEP was initiated in Nepal in November 2020 based on evidence that PrEP was feasible and acceptable among men who have sex with men, male sex workers and transgender people. Current PrEP in Nepal is targeted at these key populations, yet there is need for expansion to other key risk groups and the general population. Gaps in PrEP knowledge among PCPs have been identified in resource-rich countries and education has been shown to increase PrEP prescribing. Engaging primary care provider (PCP) participation is expected to increase PrEP prescribing and uptake in Nepal, as shown in other countries. Our study aimed to assess and optimize PCP PrEP knowledge to support National HIV PrEP expansion in Nepal. We studied Internal Medicine resident physicians at Patan Academy of Health Sciences, a large academic referral hospital in Kathmandu. Residents were surveyed about PrEP knowledge, aptitude and practice surrounding WHO and Nepal Guidelines, before and after a PrEP information session. 87% (27/31) of respondents had never prescribed PrEP, and 42% (13/31) were not familiar with PrEP. 35.5% (11/31) recognized a recent STI as an indication for PrEP, whereas 78% (21/27) answered correctly after education. 29% knew where to refer for PrEP services at baseline, which improved after education to 96% (26/27). 85% (23 of 27) reported seeing themselves as referring patients for PrEP or as a prescriber of PrEP in the future. Our study showed low HIV PrEP familiarity and prescribing among PCPs in Nepal. A single education session greatly increased PrEP knowledge about eligibility and referral location. PrEP education should be emphasized at all levels of physician curriculum to improve access to care for PrEP eligible individuals in Nepal. The next steps to close the gap in HIV PrEP access in Nepal include expanding our intervention at key primary care, gynecology, and harm reduction care sites throughout the country. Provider education is a cost-effective, low effort method that should be utilized in prevention efforts in LMICs in the fight to end HIV.

7704

EFFECTS OF TIMED AND TARGETED COUNSELLING BY COMMUNITY HEALTH WORKERS ON MATERNAL AND HOUSEHOLD PRACTICES AND PREGNANCY AND NEWBORN OUTCOMES IN RURAL UGANDA

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Pregnancy and birth-related complications claim the lives of millions of women and newborns every year. Improving their survival chances remains an urgent global challenge, including in Uganda. Community health workers (CHWs) play a crucial role in bridging the gap between the community and the official health system in Uganda. Timed and targeted Counselling (ttC) is an individual-level behavioral change communication method used by CHWs, aimed at pregnant women and caregivers of children under the age of two. This study examined whether implementation of ttC was associated with improved pregnancy outcomes and newborn survival in rural Uganda. A multi-stage sampling technique was employed with a total of 749 participants in the ttC intervention, and 744 participants in the control group. Data on quality of maternal and household antenatal care (ANC) and essential newborn care (ENC) practices, as well as on pregnancy and newborn outcomes were collected through questionnaires from May 2018 to May 2020. McNemar's Chi-square tests were used to compare outcomes before and after implementation, and between the intervention and control group. Results showed that, compared to baseline, ttC contributed significantly to the demand for quality of service during ANC, ENC and partner involvement in maternal and newborn health. In comparison to the control group, the ttC group showed significantly

higher early ANC attendance rates and higher quality of ANC and ENC. ttC is a comprehensive, goal-driven approach that seems to contribute to the improvement of quality of maternal and household practices, and pregnancy and newborn outcomes in Uganda.

7705

INCREASE OF ANTIMICROBIAL RESISTANCE IN POST-COVID-19 PATIENTS IN BOLIVIA

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The COVID-19 pandemic has exacerbated the use of antibiotics and boosted antimicrobial resistance (AMR), particularly in settings where there is no control over their usage. The aim of this study was to evaluate the distribution of antibiotic resistance and patterns of AMR in Escherichia coli isolates obtained from post-Covid-19 patients in three cities in Bolivia. To this end, a total of 345 fecal samples were collected from post-COVID-19 patients (1-60 years of age) in the period of at least 2-4 weeks following their recovery. E. coli isolates were tested for susceptibility to 19 antimicrobial drugs representing eight antibiotic classes using a disk-diffusion susceptibility test. In addition, a survey was conducted to collect information on COVID-19 severity, gastrointestinal symptoms, WASH conditions, and sociodemographic characteristics. High rates of AMR were detected, with 32% and 55% of the isolates displaying resistance to two and three or more antibiotic classes, respectively. E. coli isolates showed higher levels of resistance to ampicillin (62%), nalidixic acid (60%), sulfamethoxazole/trimethoprim (52%), tetracycline (52%), and azithromycin (48%). Moreover, 62% of isolates were resistant to penicillin and 20% to third-generation cephalosporins (TGC). In general, 87% of the study population was resistant to at least one of the tested antibiotics. The increased resistance to azithromycin, amoxicillin/clavulanic acid, and ceftriaxone in relation to the pre-COVID-19 period may be related to the extensive use of these antibiotics both as part of medical prescriptions and as self-medication. No correlation was found between AMR and sociodemographics, or WASH conditions, or COVID-19 severity. These findings revealed a high prevalence of AMR E. coli circulating in post-COVID-19 patients, which can be potentially considered an important reservoir for AMR.

7706

ENTERIC INFECTIONS, DIARRHEA AND INFLAMMATION IN CHILDREN DURING THE FIRST YEAR OF LIFE IN THE CITY OF EL ALTO IN BOLIVIA

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In developing countries, diarrheal diseases and enteric infections are major health burdens, particularly for children under 5 years of age. The purpose of this study was to evaluate, in a prospective cohort conducted in children during their first year of life, the presence of enteric infection, diarrhea, and indicators of inflammation and nutritional status. From June 2013 to March 2015, a total of 357 enrolled children were considered for the study in two hospitals in the city of El Alto in Bolivia (the NIDI project). Clinical data, feces, and blood samples were collected for further analysis. Pathogens analyzed included norovirus, rotavirus, EAEC, ETEC, and EPEC; indicators of inflammation: C-reactive protein and alpha glycoprotein 1; and nutrition: hemoglobin, ferritin, retinol-binding protein, soluble transferrin receptor, and zinc. The children's population during the first year of life displayed indicators of chronic malnutrition (34,7%) in addition to zinc (83%) and vitamin A (69,5%) deficiencies. The prevalence of diarrhea reached 62.7%, with an incidence of 1.16 episodes per child per year. A significant association between diarrhea and acute inflammation, chronic inflammation, and type of lactation was found. Likewise, diarrhea showed an association with the number and percentage of pathogens and with the co-infections among them. Moreover, viral infections, in contrast to the ones caused by diarrheagenic *E. coli,* displayed a significant association with diarrhea. *Overall, t*hese findings highlight the need for public health interventions to improve child health and avoid long-lasting consequences. impairing childhood development.

7707

NAVIGATING HEALTH ACROSS BORDERS: A JOURNEY THROUGH THE PRACTICE OF TRAVEL MEDICINE AMONG PRIMARY CARE PHYSICIANS IN QATAR

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Travel medicine, an evolving discipline, focuses on preventing and managing health issues among international travelers. With Qatar experiencing a surge in travel, primary care physicians (PCPs) play a crucial role in pre- and post-travel consultations. This study aimed to evaluate PCPs' knowledge and practice of travel medicine in Qatar's primary healthcare centers. We conducted a cross-sectional study using a self-administered questionnaire distributed to all PCPs across 27 primary healthcare centers. Multivariable linear and logistic regression analyses identified factors associated with knowledge and practice of travel medicine. Of 364 participating physicians (response rate: 91%), most (91.1%) provided pretravel consultations, with 72.7% offering fewer than 10 consultations per month. Only 15% had prior travel medicine training. High-frequency pretravel consultations (≥10/month) were associated with multilingual physicians (AOR 2.768, 95% CI: 1.238, 6.189), past travel medicine experience (AOR 2.326, 95% CI: 1.260, 4.293), and experience in tropical medicine or developing countries (AOR 2.526, 95% CI: 1.102, 5.790). The mean knowledge score was 9.54 out of 16.0. Factors predicting higher knowledge scores included age 40-49 years (1.072; 95% CI: 0.230, 1.915), holding a non-Arab medical degree (0.748; 95% CI: 0.065, 1.432), training in travel medicine (1.405; 95% CI: 0.407, 2.403), and providing ≥10 consultations/month (2.585; 95% CI: 1.294, 3.876). Common post-travel illnesses included travelers' diarrhea (79.5%), respiratory diseases (76.6%), and fever (76.2%). Barriers to practice included lack of consultation time (80.4%), lack of training in travel medicine (66.5%), and language difficulties (62%). Overall, PCPs' knowledge and practice of travel medicine were inadequate. Recommendations include integrating travel medicine education and training and developing best practice guidelines.

7708

COLPLEX TECHNOLOGY: AN INNOVATIVE APPROACH FOR THE DEVELOPMENT OF MULTIPLEX POINT OF CARE TESTS

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DNase Colicins are bacteriocins released by bacteria during time of stress. These proteins are secreted in a complex with an immunity protein. The complex is characterized by its high affinity (Kd ≈ 10^{-15} M) as reportd previously. In addition, each immunity protein presents a high selectivity towards its cognate bacteriocin. Taking advantage of the high-affinity interactions between bacteriocins and immunity proteins, BIOASTER has developed the COLPLEX technology [2]. This approach offers an alternative to direct coating of antibodies or the use of streptavidin/biotin as an adaptor molecule in Point of Care Tests. Antibodies are tagged with immunity proteins which subsequently bind to Colicin DNase domains immobilized on a solid support. This results in antibodies being immobilized in an oriented format, rendering the binding site accessible. The sensitivity of the assay is enhanced since the target analyte recognition occurs in solution. Furthermore, the wide variety of bacteriocin/immunity protein pairs can be exploited for multiplexing purposes. The sensitivity and efficiency of the COLPLEX technology were demonstrated in a Biplex format targeting

EBOLA secreted glycoprotein. Our assay can discriminate between Zaire sGP strain and Sudan sGP strain. Tests have been successfully performed in ELISA and LFA systems. Our Biplex LFA demonstrates a sensitivity comparable to Poly-streptavidin/Biotin system. We are currently working towards the development of a Triplex LFA based on COLPLEX technology.

7709

THE PROJECTED IMPACT OF CLIMATE CHANGE ON THE BURDEN OF TROPICAL INFECTIONS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Populations in low- and middle-income countries (LMICs) bear the greatest burden of tropical infectious diseases, several of which are known to be sensitive to climatic hazards. Moreover, there is evidence that LMICs are disproportionately vulnerable to the impact of climate change due to geography, health systems infrastructures, and other factors. The projected long-term impacts of climate change on tropical infections are therefore essential to inform policies and programs focused on climate resiliency in LMICs. Leveraging data from a comprehensive systematic review investigating the projected impact of climate change on human health in LMICs, we extracted and analyzed peer-reviewed studies focused on tropical infections in pediatric and adult populations. We identified 29 studies over a ten-year period that targeted twelve diseases, including World Health Organization-defined neglected tropical diseases (Chagas disease, cutaneous leishmaniasis, dengue, rabies, and schistosomiasis), malaria, and tropical enteric infections (bacillary dysentery, cholera, food poisoning, parasitic worms, trichinosis and typhoid fever). Climate change projection periods ranged from 2030 to 2100. Six studies were conducted in India, and five each in China and sub-Saharan Africa. Dengue and malaria were the most studied infections with eleven studies each, followed by enteric infections with three studies. Nearly all infections studied were projected to experience an exacerbated disease burden and/or a variance in geographic footprint due to climate change. Evidence describing the impact of climate change on malaria was mixed, with some studies projecting an increase in burden, some projecting a decline, and others projecting an epidemiological shift in prevalence or incidence. Temperature was the most studied climate change parameter while humidity, precipitation and rainfall, and atmospheric carbon dioxide were less frequently utilized. The outputs of this study add to the evidence base needed to guide climate mitigation and adaptation initiatives and is expected to inform future studies on climate change and health in LMICs.

7710

CLIMATE CHANGE, ECOSYSTEM SERVICES, AND COLLECTIVE ACTION IN THE ENVIRONMENT IN COSTA RICA: COMMUNITY ENGAGEMENT IN MITIGATION AND ADAPTATION

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Costa Rica's biodiversity is rapidly shifting with climate change, creating environmental hazards among other consequences. We conducted an assessment to better understand environmental attitudes, environmental action, and perception of the environmental hazards communities faced, prior to implementing a mobile application to help organize environmental clean-up and hazard remediation. Costa Ricans age 18+ completed assessments after being mobilized by local organizations and government entities involved in environmental issues. We ascertained a range of environmental attitudes, psychosocial constructs, and ecosystem services. Costa Rican and US IRBs approved this study. Overall, 260 people completed this assessment, with 59.2% (148) between 18 and 25 years old. In total, 94.2% (245) indicated at least one human-induced environmental priority, with 91.2% (237) stating a climate-related challenge, 88.5% (230) a vermin-related challenge, and 76.9% (200) an act of god. In total, 10.5% (27) indicated they would solely discuss environmental problems within their community and resolve, 27.7% (71) would solely report the issue to authorities to resolve, 16.0% (41) would do both (act themselves, and report to authorities), 18.8% (48) would expect someone else to resolve the issue, and 27.0% (69) did not know what to do. Additionally, 64.4% (163) of participants said they would "like to join and actively participate in an environmentalist group." While more positive environmental attitudes were significantly associated with valuing ecosystem services, environmental attitudes overall were not associated with taking action. Education, gender, and age were not associated with action-orientation nor environmental attitudes. Awareness of human-induced and climate change-related environmental problems was common, though participant agency to act on resolving environmental concerns was low. That people with stronger positive environmental attitudes were more likely to reflect aspects of agency and self-determination suggests potential for creating collective action in the environment.

7711

CO-PRODUCING AN EARLY WARNING PLATFORM TO FORECAST OUTBREAKS OF CLIMATE-SENSITIVE INFECTIOUS DISEASES

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El Niño can intensify extreme weather events worldwide, affecting the timing and severity of outbreaks for a range of climate-sensitive infectious diseases. For example, the Latin American and Caribbean (LAC) region is heavily impacted by heterogeneous flooding, drought and warming events which can increase the risk of vector-borne and water-borne diseases. Early warning tools that integrate seasonal climate forecasts into disease prediction models can provide probabilistic predictions of outbreak risk several months in advance. These quantitative forecasts can trigger timely public health interventions that prevent epidemic occurrence or mitigate disease-related morbidity and mortality. Here, we co-created a reproducible framework to forecast outbreaks of climate-sensitive infectious diseases 1 to 6 months ahead and to host predictions on an online early warning platform. Our initial prototype focuses on forecasting the risk of dengue, malaria and leptospirosis outbreaks in El Niño sensitive areas across the LAC region throughout the 2023/24 El Niño. We

harmonised epidemiological and open-access climate data to undertake a comprehensive model fitting, selection and validation process within a Bayesian modelling framework. A locally relevant disease prediction model which incorporates temperature, precipitation and El Niño indicators was identified for each case study. Calibrated climate forecasts from the European Centre for Medium-Range Weather Forecasting (ECMWF) are then used to produce probabilistic predictions of outbreak risk for the next 6 months. These forecasts are hosted and visualised on an operational web platform, co-produced with researchers and decision-makers at multiple administrative levels across the LAC region, to provide useful, timely and relevant information to trigger early action. This reproducible framework could be flexibly deployed to predict endemic climate-sensitive diseases in any location at any administrative level, and be leveraged to make rapid predictions in response to emerging climatic events, which are exacerbated during El Niño or La Niña episodes.

7712

THE BURDEN OF LEPTOSPIROSIS IN PERU, 2006-2022: THE INFLUENCE OF REGION-SPECIFIC METEOROLOGICAL FACTORS AND GENDER-SPECIFIC DISPARITIES IN OUTCOMES

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Leptospirosis imparts a significant disease burden in Peru, which has increased since 2006, as suggested by national surveillance data. Peru has three distinct natural regions (coast, highlands, and jungle) with different climate patterns, but the burden and drivers of leptospirosis in each have not been delineated, which in turn has hampered elaboration of control measures. We aimed to estimate the burden of leptospirosis and evaluate temporal associations with meteorological factors.Leptospirosis case reports for 2006-2022 were obtained from CDC-Peru. Monthly rainfall and Palmer Drought Severity Index (PDSI) by district were extracted from climate datasets. We estimated overall, age-specific, and sex-specific incidence, hospitalization, mortality, and case fatality rates, and tested for differences between demographic groups with chi-squared tests. We plotted rainfall, PDSI and cases in each region to identify potential associations.Incidence was high in the northern coast and jungle regions since 2012, with outbreaks in 2017, 2019-2020, and 2022. Incidence and hospitalization rates were highest among people aged 20-29 years (9.27 and 0.76 per 100 000) and among females (7.62 and 0.58 vs 6.24 and 0.40 per 100 000 in males). However, case fatality was significantly higher among males aged 10-19, 30-39, and 60-69 years than among females of the same age ($p<0.05$). In the arid northern coast, increases in cases were preceded by extreme rainfall during El Niño events. In the jungle region, which has annual wet and dry seasons, outbreaks were preceded by wet conditions unrelated to rainfall, potentially due to high river water levels.Contrary to reports from other countries and settings, our findings indicate that in Peru women have a higher risk of leptospirosis, underscoring the need to identify underlying risk factors which influence this gender disparity in disease burden. Furthermore, variations in disease burden between regions and in the potential underlying drivers highlight the complex interplay between the environment and leptospirosis transmission and the need for setting-specific interventions within the country.

7713

ASSOCIATIONS BETWEEN ENVIRONMENTAL TEMPERATURE, RAINFALL, STILLBIRTH, AND NEONATAL MORTALITY IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Rising temperatures and unpredictable rainfall patterns affect human health. We hypothesized that anomalous high temperature may compromise newborn viability. Understanding the implications of rising temperatures on health outcomes can inform planning for future health promotion and service delivery, including preparations to inform health interventions with tailored understanding of climate-related risks. This spatial-temporal analysis used health program data juxtaposed with publicly available environmental data sources, modeling the impact of anomalous extreme heat on stillbirths and newborn deaths in DRC (2018-2022). Sources included GPCC global monthly rainfall master data, MODIS LST daily temperature data, and aggregated monthly District Health Information System 2 (DHIS2) data from all DRC health zones. Across health zones, the time series analyses highlighted a marked decline between 2018 and 2022 in stillbirth (mean decrease: 41.2%, confidence interval [CI]: 35.2%; 52.3%) and neonatal mortality (mean decrease: 30.4%, 95% CI: 26.2%; 36.1%). Average temperatures have increased (mean overall increase: 0.5C°, 95% CI= 0.4C°; 0.7C°) and were correlated with a decrease of monthly precipitation (mean decrease: 12mm; 95% CI: 9 mm-15 mm). Stillbirth and neonatal mortality rates demonstrate a seasonal pattern with substantial sub-national heterogeneity. Preliminary results indicate association between stillbirth and neonatal death rates and extreme heat and rainfall events in the previous three months. Despite limitations, routinely collected DHIS2 data provide insights into population health trends which can also be extrapolated forward to prepare for further changes. Public health projects and programs can use the identified connections between temperature, rainfall, and newborn outcomes to mitigate population vulnerabilities to the impacts of climate change through tailored messaging and health systems adaptations.

7714

UNDERSTANDING ASSOCIATIONS BETWEEN ENVIRONMENTAL TEMPERATURE, RAINFALL, AND NEWBORN HEALTH OUTCOMES IN SENEGAL

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Increasing temperatures and changes to rainfall patterns threaten human health. This study investigated the effect of temperature and precipitation on newborn health outcomes between 2018 and 2022 in five Senegal regions: Diourbel, Kédougou, Kolda, Sédhiou, and Tambacounda.
Monthly data on population, newborn deaths, and macerated and fresh stillbirths were gathered from Senegal's health management information system. Monthly temperature and precipitation were estimated using remote sensing data from MODIS and from the Global Precipitation Climatology Centre, with anomalous temperature defined as values > 90th percentile. Time series analyses were performed by district to describe the trend of health and weather indicators. The relationship between health and weather indicators was investigated using generalized additive random effect models. Across districts, there was a marked decline between 2018 and 2022 in stillbirths (median -13.9%; interquartile range -8.1%- -32.3%) and neonatal mortality (41.6%; -58.1%-0%). Average temperatures decreased (-4.2%; -2.7%- -5.7%) linked with increased precipitation (10.8%, 1.1%-16.7%) from 2018 to 2021. In 2022, precipitation diminished

(-24.8%; -16.9%- -30.3%) and temperature increased (5.2%; 3.4%-7.6%). Stillbirths and neonatal mortality had seasonality trends with respective peaks in July and in April. Preliminary results indicate significant associations between stillbirths, neonatal mortality, and anomalous heat events and rainfall events.
Understanding climate-health links could help health system adaptation. Public health programs can tailor messaging and health system approaches to mitigate the effects of high temperature on newborn mortality and stillbirth.

7715

ENHANCING BRICK KILN EFFICIENCY IN BANGLADESH: A CRUCIAL STEP TOWARDS AIR POLLUTION REDUCTION IN SOUTH ASIA

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Bricks are a fundamental building material for Bangladesh, However, traditional brick kilns in South Asia employ antiquated, highly polluting methods, contributing significantly to air pollution and public health. In Bangladesh ~7,000 brick kilns annually produce 27 billion bricks, generating 11% of particulate matter, 22% of black carbon, and 17% of total CO_2 emissions. During winter, brick kilns contribute 30 to 60% of PM2.5 in Dhaka city and resulted in 5000 premature deaths yearly. Improving energy efficiency in brick manufacturing presents an opportunity to mitigate environmental damage and reduce emissions. A recent pilot project by icddr,b and Stanford university aimed to enhance combustion efficiency in zigzag brick kilns through low-cost interventions. However, adopting rate was not 100%, and we qualitatively investigate the barriers to adoption. Economic concerns were the primary deterrent to adopting efficiency improvements. Kiln owners, risk-averse to new interventions, awaited proof of success from peers before committing. Although, the efficiency improvement doesn't require additional investment but some kiln owners resisted due to financial risks stemming from high coal prices and reluctance to invest in unskilled labor. Despite training, workers lacked confidence in new practices and demanded higher wages, posing challenges for owners. Additionally, maintenance concerns and a lack of awareness regarding environmental impacts and emission mitigation strategies were identified. The uncertainty in the brick market, compounded by government policy changes, perpetuated reliance on traditional methods. Government support, coupled with proper training and financial incentives for workers is crucial for upgrading to energy-efficient technologies and transforming brick manufacturing. This shift will significantly benefit for the environment by reducing pollution and combating climate change.

7716

TIME SERIES ANALYSIS OF CLIMATE AND ALL-CAUSE MORTALITY PATTERNS IN UGANDA

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The effect of climate change on health outcomes are becoming more apparent across the Sub-Saharan Africa, leading to a notable surge in mortality across all ages. This study investigated the relationship between climate and all-cause mortality in Uganda and also examines the association between mortality by age group, gender, seasons, and causes of death. We analyzed daily mortality data sourced from Iganga Mayuge Health Demographic Surveillance Site (IMHDSS) in Uganda, employing time series model, in particular, the Distributed Lag Non-Linear Model (DLNM) to assess the effect of average temperature on mortality. The study found that the highest mortality occurred among neonates with males exhibiting the highest mortality across all age groups except for the elderly (65+ years) where females had the highest mortality compared to males. We found that there was a statistically significant difference in mortality between the wet and dry seasons ($p < .05$). Malaria was found to be the predominant cause of death for both genders. With regard to the DLNM results, we observed that average temperature, in the lag 0 - 7, and 12 - 29 increases all-cause mortality, but was found to be strongest related to mortality among males (RR = 1.6423). These findings will be invaluable for policymakers in developing responsive strategies that mitigate the effects of climate change in Uganda.

7717

A RETROSPECTIVE ANALYSIS OF CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY (CKDU) AT A SINGLE-CENTER UNIVERSITY HOSPITAL SYSTEM IN THE STATE OF FLORIDA, USA

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Chronic kidney disease of unknown etiology (CKDu) is an emerging public health concern in various regions within the subtropics and tropics. Recognition of CKDu within agricultural communities located in Mexico, Central America, Sri Lanka, India, Tunisia, Egypt, and Taiwan have acknowledged its presence. In Florida, the panhandle, north, and central regions are characterized as subtropical, while the southern part experiences a tropical climate. With approximately 9.7 million acres of land and 47,000 farms contributing to a diverse agricultural workforce, Florida faces concerns about the prevalence of CKDu, a condition relatively unknown in the state. The University of Florida (UF) Health, serving over 2.3 million residents across 23 counties, took initiative in understanding this issue. Examining unique patient data within the electronic medical record system from June 1, 2011, to October 1, 2023, using the UF Health i2b2 data interface system, our team assessed patients diagnosed with CKD based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria. Among 57,514 unique patients (55% Male; 28.5% <65 years) identified with CKD, a computable phenotype algorithm was applied, excluding various comorbidities, infections, and other associated conditions known to cause or contribute to CKD development. Through this analysis, we discovered 5,155 patients living with CKDu, indicating an estimated prevalence of 8.96%. These preliminary findings are the first to provide an estimated prevalence within the state of Florida and correlates with other studies in regions where CKDu is recognized among agricultural regions. More research is needed to better understand CKDu in Florida and within other regions of the United States where farming and agriculture are present.

7718

MIDWIVES: A VITAL CLIMATE SOLUTION

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Research findings show that increases in heat exposure, altered pattern of diseases as a result of climate changes, increased extreme weather events leading to increase exposure to air pollution are resulting in increased risks of preterm birth, premature rupture of membranes, low birthweight, stillbirth, gestational hypertension, gestational diabetes and major birth defects. Investing in midwifery is a key component in strengthening the healthcare workforce. In Sierra Leone, there are fewer than 500 midwives but there is an estimated need for 3,000 midwives. In 2021, Seed Global Health (Seed), partnered with the Ministry of Health (MOH) to support their efforts to decrease preventable maternal and neonatal mortality through strengthening midwifery training. A need assessment to analyze the midwifery landscape in Sierra Leone used a mixed-method approach that included surveys, focus group discussions, interviews, and review of maternal records at four midwifery schools and eight healthcare facilities. Seed placed four midwifery educators at two midwifery institutions and district hospitals to conduct low dose high frequency clinical education for midwifery staff, to teach midwifery students, and to provide supportive mentorships in the clinical setting. Students (n=202) reported insufficient

learning opportunities in operating theater (42%), perineal suturing (32%), completing partographs (27%), and estimation of blood loss (23%). Postpartum hemorrhage (PPH) was diagnosed in 11% women at hospitals and 1% at community health centers. From 2022 to 2023, Seed educators have provided education sessions and clinical mentorship to 857 students and 504 clinical staff. A 60% decline in year-to-year absolute maternal deaths was observed at the Makeni Regional Hospital and a 55% decline at the Bo Government Hospital. The more well-trained, well-supported, and well-resourced midwives that Sierra Leone has, the better the country will be able to withstand and address the health effects of climate change on communities, women, and youth.

7719

NATIONAL AND PROVINCIAL VARIATION IN COVID-19 TRANSMISSION POTENTIAL IN PAKISTAN: AN ECOLOGICAL STUDY

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Time-varying reproduction number (R_t) served as an indicator of epidemic growth and decline. The data was obtained from the publicly available Johns Hopkins COVID-19 Unified Dataset. We assessed and compared the COVID-19 transmission potential in Pakistan, both at the national and provincial levels, including the federal capital. We first employed the Bayesian deconvolution method to estimate the infection dates from the reported dates. A Poisson-distributed multiplier with a mean of four was applied to estimate the daily infection counts accounting for underreporting. We applied the R package EpiEstim to the estimated infection count data to estimate a 7-day sliding-window R_t. Results showed that most cases were reported in Sindh province, followed by Punjab. Gilgit Baltistan (GB) reported the lowest case count. Except for Sindh and GB provinces, all provinces exhibited a similar trend comprising five waves. Notably, at the national level, there was a surge of cases between February and May 2021, with a subsequent 4th wave observed in August 2021. However, this surge in the third and fourth waves combined into a prolonged third wave in Sindh, contrary to corresponding national trends. The R_t estimates stayed persistently between 0.5 and 1.5 across Pakistan and all provinces throughout the five pandemic waves between Jan 2020 and Feb 2023. In comparison to other provinces, Sindh demonstrated a more strategic approach to managing the surge of COVID-19 cases.

7720

CHARACTERIZING LASSA FEVER INCIDENCE IN SOUTHERN NIGERIA

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Lassa fever (LF), a viral hemorrhagic disease caused by Lassa virus (LASV), is endemic across West Africa. Roughly 80% of LASV infections present with mild or asymptomatic disease; hence the true burden of LASV infection in endemic regions is poorly understood. The Walter Reed Army Institute of Research (WRAIR) Emerging Infectious Disease Branch (EIDB), in collaboration with the African Center of Excellence for Genomics of Infectious Diseases (ACEGID) completed a longitudinal cohort study to determine the incidence, prevalence, risk factors for, and transmission dynamics of acute LASV infection at two Lassa-endemic locations in Southern Nigeria: Owo and Abakaliki. Participants were followed regularly and tested for LASV by RT-PCR and serology for up to 18 months. Symptomatic cases were defined based on the WHO case definition criteria. Concurrent zoonotic surveillance of targeted and non-targeted rodent and non-rodent reservoirs was conducted. 380 participants were enrolled (153 male, 227 female) and 7086 follow-up visits completed. 363 (95.52%) were LASV-negative, 6 (1.58%) were LASV-positive asymptomatic and 27 (7.11%) were LASV-positive symptomatic. One death was reported among the symptomatic LASV positive cases. The rate of PCR positive cases was similar between Abakaliki (8.1%, 14/173) and Owo (8.7%, 19/207), but greater for males (12.4%, 19/153) than females (6.2%,14/227) (p=0.041). Participants were recruited both from the community (92.9%, 353/380) and from local hospitals (7.1%, 27/380). Those who tested PCR positive for LASV on their first study visit were considered prevalent cases. Seven participants were lost to follow up after their first visit. Of the 341 participants who were PCR negative at their first study visit, 324 (95.0%) were LASV-negative at the end of follow-up, 15 (4.4%) became LASV-positive asymptomatic and 1 (0.29%) became LASV-positive symptomatic. The prominent difference in proportion of incident asymptomatic vs. symptomatic LASV cases highlight the need to close the knowledge gap of true incidence in Nigeria, which is critical for epidemic preparedness and outbreak response.

7721

DEVELOPMENT OF A NEW PASSIVE SAMPLER USING GRANULAR ACTIVATED CARBON FOR ENTEROVIRUS DETECTION IN WASTEWATER SURVEILLANCE

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Wastewater surveillance (WS) plays a critical role in global polio eradication efforts, complementing the clinical surveillance of acute flaccid paralysis. However, the current gold standard, viral culture from a grab sample (only performed at reference labs), is complex, costly ($150+/sample), and requires approximately a month for results. To overcome these challenges, we developed a passive sampler using granular activated carbon (GAC) for WS. GAC is inexpensive ($1/sample), user-friendly, and directly captures viruses. Since polio virus is an enterovirus, we chose enterovirus as a substitute organism for our experiments. GAC passive sampler performance was compared to positively charged nitrocellulose (NC) filter membranes, often used to capture viruses from wastewater. NC filters and nylon tea bags of various pore-size with 1g GAC in each tea bag were placed in respective bottles of 500 mL wastewater. All samples were incubated for 24hrs on a shaker followed by elution of enterovirus from GAC and NC filters, then RNA was extracted from the eluate using the MagMAX Wastewater Ultra Nucleic Acid Isolation Kit. Due to modest recovery of enterovirus from wastewater, we further explored Nanotrap Microbiome A particles to concentrate viruses prior to extraction using analytical water samples spiked with enterovirus A71. The detection of enterovirus was carried out using a CDC developed pan-enterovirus qPCR assay. In the wastewater samples (n=2), 50% of GAC samples in both 25 µm and 120 µm pore-sized nylon bags tested positive for enterovirus. However, in analytical samples (n=2), 100% positivity was observed for GAC samples in both categories of nylon bags. NC filter membranes were 100% positive for enterovirus in both wastewater and analytical samples. Enterovirus recovery (PFU/µL) was higher for GAC (0.2-1.3%) compared to NC (0.6-0.7%) in analytical samples. These results indicate GAC's potential as an adsorption medium in passive samplers for enterovirus capture in wastewater. However, further optimization to fine-tune the method and materials for higher recovery and extensive field testing are necessary to assess the performance.

7722

NOVEL DNA EXTRACTION METHODS FOR CYTOMEGALOVIRUS PEDIATRIC SAMPLES

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Nucleic Acid (NA) extraction is the process of separating genetic material from cellular components. Currently, the gold standard for DNA extraction is a commercially available kit, for example, the Qiagen DNA Mini kit, which is intended for use with Nucleic Acid Amplification tests (NAAT). Novel isothermal NAAT tests are becoming increasingly available for low-resource settings, but little innovation has been done on NA extraction thus limiting the application of these novel assays. This study aims to evaluate HUDSON (Heating Unextracted Diagnostic Samples to Obliterate Nucleases), a novel NA extraction method, for cytomegalovirus (CMV) DNA in pediatric samples to be used with an isothermal NAAT for CMV developed by the Garry Lab (Chao, K, et al. 2024). Pediatric saliva samples from Innovative Research were spiked with CMV at 1E5 infectious units/mL (N=5). After extracting DNA from samples using the HUDSON and Qiagen protocols, polymerase chain reaction (PCR) was performed at different storage lengths. Statistics were run using GraphPad Prism. HUDSON was effective at extracting DNA from saliva with 4 out of 5 samples having a positive PCR result compared to 5 out of 5 with Qiagen. HUDSON extracted DNA from the saliva similarly to Qiagen (Paired t test: p=0.064). HUDSON extracted DNA was stored without degradation (Repeated Measures: P=0.4477) compared to Qiagen (Repeated Measures: p=0.0820) after 30 days at -20*C. HUDSON successfully extracted CMV serum standards from Bio-Rad. RNAse Alert showed that HUDSON is effective at RNAse inactivation in serum without additional RNAse inhibitors. It is anticipated that we will find optimal RNAse inhibitor concentrations so that RNAseAlert will show effective nuclease inactivation in saliva samples. It is also anticipated that titration assay will show that HUDSON is effective at inactivating CMV virus. We've shown that HUDSON is effective in extracting and storing CMV DNA from saliva. Future work would include clinical validation of this method using congenital CMV patient samples and subsequent compatibility with novel isothermal CRISPR/Cas12a CMV DNA assay.

7723

IMPACT OF HEAT AND HUMIDITY EXPOSURE ON EFFICACY OF SELECTED ANTIBIOTICS

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Global health challenges related to climate change, geopolitical and economic instability, and antimicrobial resistance have led to greater use of both oral and parenteral antibiotics in austere clinical settings; however, the efficacy of these agents' following storage under suboptimal environmental conditions is largely unknown. We investigated the effects of high heat and humidity exposure on the *in vitro* efficacy of five classes of commonly used antibiotics against frequently encountered pathogens (*Streptococcus Pyogenes*, Methicillin-Susceptible *Staphylococcus Aureus*, Methicillin-Resistant *Staphylococcus Aureus*, *Klebsiella Pneumoniae*, and *Pseudomonas Aeruginosa*). Ceftriaxone, ciprofloxacin, clindamycin, meropenem, and vancomycin were each exposed to three different temperature settings (22°C, 36°C, and 42°C) or a combination of 42°C at 80% humidity for varying durations of time (7, 14, and 21 days). Following exposure, antimicrobial susceptibility testing was performed using Kirby-Bauer disk diffusion. For each antibiotic tested, we observed no significant difference in susceptibility testing between all heat and humidity conditions tested. Our findings suggest that these antibiotics may remain effective even after prolonged storage under suboptimal conditions. While further research is needed regarding *in vivo* efficacy, our findings provide reassurance to clinicians practicing in resource-limited settings, where refrigeration and climate-controlled environments may be unreliable or unavailable.

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STRENGTHENING ROUTINE SURVEILLANCE SYSTEMS FOR VACCINE SAFETY IN THE DISTRICTS IN MALAWI: CHALLENGES, MITIGATION MEASURES, AND LESSONS LEARNED FROM ACTIVE HOSPITAL-BASED SENTINEL SITE SURVEILLANCE PROGRAM

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Implementing an active surveillance of adverse events of special interest following immunization (AESI) for vaccine safety in low income countries has its challenges. However, active AESI surveillance may present an opportunity to strengthen systems, address existing challenges and learn lessons to improve the overall routine surveillance. An active hospital-based sentinel site (HBSS) surveillance for COVID-19 vaccines AESIs was implemented in 6 hospitals in 6 districts across Malawi by Malawi Ministry of Health and Kamuzu University of Health Sciences in collaboration with the national Pharmacy and Medicines Regulatory Authority and US Centers for Disease Control and Prevention for the phase one of the surveillance from August 2022 to September 2023. The HBSS surveillance used the existing routine surveillance structures and systems. During the implementation period, the active HBSS surveillance activities contributed towards strengthening and improving the overall routine surveillance in the districts especially for vaccine safety in the areas of: health workers capacity; planning, budgeting and cost-effective investigations; and reporting. The HBSS surveillance encountered challenges such as: logistical, financial and administrative challenges; case classifications using Brighton collaboration case definitions; and untimely reporting. Lessons learned included: the importance of district teams' engagement; sharing of relevant information and guidelines; clear communication; capacity building, and sharing of information and documents with health care workers; and involvement of all key stakeholders. Lessons learned, challenges and their mitigation measures are presented in these categories: operational, administrative and logistics, financial, communication and engagement, and technical. The phase 1 of the active HBSS was able to identify a large number of cases at 1,897 and 118 were investigated despite the encountered challenges. Future similar surveillance work in comparable settings can strengthen routine surveillance and learn from these challenges, mitigation measures and lessons learned.

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COMMUNITY-LED MONITORING: A CATALYST FOR STRENGTHENING AAAQ OF PRIMARY HEALTHCARE AND MALARIA SERVICES

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Community-led monitoring (CLM) has emerged as a promising approach in the fight against malaria, particularly through contribution to enhancing availability, accessibility, acceptability and quality (AAAQ) of primary healthcare. Through CLM, service users carry out routine data collection, leading to data-informed advocacy to improve health services. CLM data is a critical complement to other national monitoring and evaluation efforts. CLM gained traction in the HIV and TB context as a tool to empower local communities in improving the delivery of services. For the malaria response,

CLM has also demonstrated value in responding to gender biases in health service provision in Nigeria, as well as resolving ACT and RDT stockouts in the Democratic Republic of the Congo. In 2023, the Global Fund organized the first-ever global exchange on CLM for malaria. The meeting brought together participants from 15 countries, including representatives of national malaria programs, development partners, civil society, and affected communities. This event led to the development of CLM frameworks for each country, to support the piloting and implementation of malaria-specific CLM models. These results and frameworks have catalyzed greater interest from malaria communities. In the Global Fund's Grant Cycle 7 (2023-2025), at least $US 2.1 million has been budgeted for CLM across at least 10 countries, specifically within malaria grants. Many other investments in multi-disease CLM, or those looking at improving primary health care are additionally budgeted. This is a significant increase from the previous cycle, where few, foundational CLM models were being piloted for malaria. The implementation of CLM into the malaria response offers a promising pathway to reduce malaria incidence and mortality, through advancing AAAQ of primary healthcare. CLM not only improves the delivery of malaria services but also fosters sustainable health systems that are responsive to the needs of populations most vulnerable to malaria infection and poor health outcomes, and signals where populations are underserved by existing interventions.

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ADDRESSING DUAL EMERGENCIES: MASS DRUG ADMINISTRATION FOR EBOLA VIRUS DISEASE OUTBREAK CONTROL AND MALARIA REDUCTION IN UGANDA

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The outbreak of Ebola Virus Disease (EVD) declared in the country on September 20, 2022, quickly escalated, reaching additional districts by October 26, 2022, with Mubende and Kassanda emerging as epicenters. This outbreak, compounded by Uganda's high malaria transmission rates, significantly strained the healthcare system, leading to increased malaria cases and deaths due to delayed treatment-seeking behavior and health worker absenteeism. In response to these challenges, the World Health Organization (WHO) recommended Mass Drug Administration (MDA) to rapidly reduce malaria-related morbidity and mortality during complex emergencies like EVD outbreaks. This study focuses on the implementation of MDA in Kassanda and Mubende districts to control the EVD outbreak and mitigate malaria burden. The intervention targeted three sub-counties and two town councils in Kassanda and Mubende, prioritized based on their epicenter status and malaria incidence rates. Children aged 3 months to 15 years received priority for drug administration due to logistical constraints, with additional groups treated based on available resources. Collaboration between stakeholders such as Malaria Consortium and the National Malaria Control Division (NMCD) facilitated the implementation process, which included district sensitization, cascade trainings, and door-to-door drug distribution by Village Health Teams (VHTs). Data collection was conducted by biostatisticians through DHIS2.The results revealed significant coverage achieved in the targeted population aged 3 months to 15 years, exceeding the set objectives. Specifically, 73.40% of children aged 3 to 23 months and 103.54% of those aged 2 to 15 years were treated, resulting in an overall coverage of 97.79% in this age group. However, adult coverage was lower at 65.70%. The MDA intervention in Kassanda and Mubende districts effectively addressed the dual challenge of EVD outbreak control and malaria reduction. The study underscores the importance of collaborative efforts and targeted interventions in combating infectious diseases during public health emergencies.

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SOCIO-DEMOGRAPHIC, SOCIO-ECONOMIC HEALTH SYSTEM RELATED DETERMINANTS OF MENINGOCOCCAL VACCINATION COVERAGE IN THE SEKYERE KUMAWU DISTRICT OF THE ASHANTI REGION, GHANA

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Achieveing full coverage in third world countries is a challenge. This study assesses the determinants of low meningococcal vaccine coverage in the Sekyere Kumawu District, Ghana. Cross-sectional descriptive study design using quantitative study was adopted. Stratified sampling and simple random sampling techniques were used to sample 596 participants from 9 communities in the district. The study participants were mothers or caregivers with children aged 18 to 59 months. Structured questionnaire was employed for data collection and analyzed using SPSS version 24. The results were presented using frequency distribution tables. Chi-square, Fisher's exact and logistic regression model to establish the strength of association between the dependent and independent variables. Also, there was a significant relationship between care giver's educational status P> 0.001. Mothers with basic (primary and JHS) and secondary/vocational level of education were 10 (OR=10,03: CI=2.156-46.653) and 4 times (4.3:CI=0.755-25.418) respectively. Number of antenatal visits P=0.006, Children who were catered for by their biological parents P=0.014 had a significant relationship with coverage for meningococcal vaccination coverage. Children with their biological parents were almost twice likely to be fully vaccinated (OR=1.8: CI= 0,273-12.250). Socio-economic variables such as occupation P=0.002, estimated monthly income P=0.015, were also significantly associated. Furthermore, health system related factors such as distance to health facilities (P=0.003), responsiveness of health workers P=0.009, receiving education on Meningococcal vaccine P>0.001 were significantly associated with meningococcal vaccine coverage. Vaccination coverage for the meningococcal vaccine was 62.8% within the District which fall short against the 95% recommended by of the World Health Organization. The Ministry of Health, the Ghana Health Service and their partners must continue to adopt innovative strategies to encourage mothers/caregivers to fully immunize their children against the meningococcal infection

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EVALUATION OF LATERAL FLOW DEVICES FOR THE DETECTION OF AVIAN INFLUENZA

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Avian flu is a public health risk with pandemic potential. To facilitate preparedness, laboratory evaluation of lateral flow devices (LFDs) could determine whether they would be suitable to diagnose avian influenza. UK Health Security Agency have performed evaluation of three SARS-CoV-2-Influenza multiplex LFDs to ascertain sensitivity and specificity utilising different approaches to establish the most suitable method for LFD evaluation. Live currently circulating avian influenza strains, and avian influenza inactivated antigens, all produced in clarified egg allantoic fluid, were serially diluted and tested on quantitative PCR and LFDs. Recombinant His Tag nucleocapsid proteins expressed and purified from Escherichia coli were serially diluted and tested on LFDs. Nasal wash samples from ferrets challenged with the H5N1 strain AIV-48 were taken at terminal cull and tested by PCR and LFD. Results were compared with what had been previously found from multiplex LFDs evaluation for the detection of seasonal influenza. There was a marked difference in sensitivity

for the multiplex LFDs between the live seasonal and avian influenza strains, including inactivated H5N1 antigen. This difference in performance was not observed when H5N1 recombinant proteins were used. Furthermore, LFDs showed excellent specificity and excellent clinical sensitivity when tested against clinical samples (where ferret samples were used as surrogates for clinical human samples). Our results suggest recombinant proteins are not a suitable alternative to viruses for LFD evaluation. Whether the devices would be suitable for detecting human infection would need to be evaluated using real-world samples.

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LESSONS LEARNED FROM COMMUNITY-CENTERED EARLY WARNING: EVALUATING THE ACCEPTABILITY OF A COMMUNITY-BASED SURVEILLANCE (CBS) PROGRAM IMPLEMENTED AMONG DISPLACED POPULATIONS IN IRAQ

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While common in sub-Saharan Africa and Asia, community-level disease surveillance does not occur in Iraq, a country with an often-overwhelmed health system. Here, a proven early warning and outbreak response initiative was applied in a new area where not routinely implemented and program acceptability was evaluated among participants. Two CBS programs were piloted in IOM-supported IDP camps in Iraq: COVID-19 CBS (4 camps; May 2021-June 2022) and expanded CBS (7 additional diseases; 6 camps; March-September 2023). Qualified residents were hired as CBS-Health Promoters (CBS HPs). Activities were conducted through heads of household interviews. Selected evaluation indicators included acceptability, flexibility, simplicity, and usefulness. Qualitative assessments were conducted through phone surveys, FGDs, and KIIs with participating heads of households, community leaders, clinic and camp managers. Data were analyzed in SPSS and Microsoft Excel. 284 phone surveys, 9 FGDs (n=60), and 13 KIIs were conducted. Among phone surveys, >98% trusted the field teams with their health information; 92% would seek care if CBS teams referred them for evaluation; >99% stated CBS was beneficial for them, their families, and communities. FDGs and KIIs produced resounding positive feedback on acceptability; flexibility was noted in how CBS incorporated new diseases/concerns; simplicity was noted by participants in all 9 FGDs; usefulness was noted in detecting/reducing disease transmission, promoting health education/awareness, and fostering a sense of community responsibility for health. All FGDs and KIIs wanted CBS to continue and the importance/appreciation of field teams of both genders and the coupon-based referral program connecting community members with information and care were noted. FGD and KII participants requested to include NCDs, childhood diseases, women's health, mental health, and hygiene in future CBS. Findings can help interested parties implement stronger CBS activities, and influence future CBS strategies by contributing to the growing body of evidence and best practices.

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COMPARATIVE ASSESSMENT OF THE OCCURRENCE AND DISTRIBUTION OF ACUTE FEBRILE ILLNESS-CAUSING PATHOGENS IN NORTHERN AND SOUTHERN NIGERIA

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Undifferentiated Acute Febrile Illness (AFI) is a diagnosis that elicits public health concern as it may be the result of an undiagnosed case of a pathogen of epidemic potential. This study compares the hospital-based incidence and distribution of AFI-causing pathogens in Northern and Southern Nigeria, utilizing PCR based surveillance. Patients presenting with AFI at tertiary hospitals in Abuja (North Central) and Irrua (Southern Nigeria) were screened for 25 pathogens using the TaqMan Array Card PCR technology. The analysis focused on comparing the occurrence and distribution of pathogens between these geographical regions, alongside environmental and demographic factors. Of the 463 febrile patients assessed, 266 (57.5%) were from Abuja and 197 (42.5%) from Irrua. Overall, 119 (25.7%) tested positive for *Plasmodium* spp., the causative agent for malaria, with a significant difference between Abuja (29.7%) and Irrua (20.3%; $\chi^2(1) = 5.2310$; $p = 0.02$). Additionally, 92 patients (19.9%) tested positive for non-malarial pathogens. Significant regional differences were observed, particularly for *Rickettsia* spp. (15.8% in Abuja vs. 6.6% in Irrua; $\chi^2(1) = 26.63$, $p < 0.001$). Other pathogens, including *Brucella* spp., Dengue virus, Crimean Congo Hemorrhagic Fever virus, O'nyong nyong virus, Chikungunya virus, Lassa virus and *Neisseria meningitidis* showed no statistically significant differences in occurrence between the regions. The study reveals distinct patterns in the distribution of AFI-causing pathogens across Northern and Southern Nigeria, reflecting the regions' diverse ecological and sociodemographic conditions. These findings emphasize the need for region-specific surveillance strategies and priorities to effectively manage and mitigate AFIs in Nigeria.

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LONG-TERM HUMANITARIAN CRISIS EFFECTS ON HEALTH: A PUBLIC HEALTH SITUATION ANALYSIS, EASTERN SIDE OF THE DEMOCRATIC REPUBLIC OF THE CONGO

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For many years, the Democratic Republic of the Congo has been dealing with intricate humanitarian issues. The protracted, complicated humanitarian crisis has severely hampered the on-people's health. This Public Health Situation Analysis (PHSA) focuses on the humanitarian health risks as a result of violence and conflict in the eastern provinces of Democratic Republic of Congo (DRC). Conducted by a panel of national and international multidisciplinary experts based on the latest secondary health data, as of June 30, 2023. A data validation session prior to the analysis. Using the PHSA short form template for reporting. More than 120 militias and armed groups have been actively operating in the eastern provinces for nearly 30 years. Security situation has continued to deteriorate in recent months despite regional diplomatic efforts. A total of 1.2 million

people has fled conflict since March 2022, creating a major challenge that urgently requires more humanitarian support. The overall health risk is very high including mental health disorders, outbreaks of vaccine-preventable diseases, and the potential resurgence of Ebola. Routine and supplementary immunization has been affected. Communities are facing a lack of safe water, malnutrition, conflict induced displacements, crowded and unsanitary living conditions in temporary shelters, interruption of and lack of access to essential health services. Surveillance for epidemic-prone diseases could also be hampered due to scattered communities in very remote areas in search of life saving resources as well as inadequate human resources. Challenges in responding to the epidemic include limited human resources, diagnostic, laboratory, clinical and vaccination capacities. The above findings strongly suggest that humanitarian crisis in the DRC has had a profound and devastating impact on the health of its population. Addressing these health challenges requires a comprehensive approach that tackles the root causes of the crisis, strengthens healthcare systems, provides psychosocial support, promotes education and empowerment, and works towards a lasting peace.

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SPECIMENS WITH UNKNOWN INFECTIOUS ETIOLOGIES: PATHWAYS TO PATHOGEN DISCOVERY AND IMPROVED DETECTION USING UNBIASED METAGENOMIC SEQUENCING

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Mitigating the impacts of novel, emergent or re-emergent pathogens requires rapid and accurate identification for an early and informed public health response. Identification is often delayed for a number of reasons, including by the local medical community's unfamiliarity of the disease or limited local laboratory capacity to test for the pathogen, resulting in unordered or delayed tests. These factors can contribute to an inability to identify or delay in identifying the causal pathogens in patients with suspected infections even after extensive diagnostic testing. The systematic use of pathogen agnostic metagenomic sequencing (mNGS) for these patients could serve as a surveillance system for emerging pathogens, identify pathogens when traditional differential diagnoses fail, and promote global health security through early detection/identification. We examined domestic and global examples of mNGS use, including those involving foreign travel. Using published case reports where mNGS was used for pathogen detection/discovery, we developed timelines of specimen pathways beginning with the point-of-seeking medical care and all diagnostic testing, until pathogen identification. Among the case reports, between 7-13 targeted diagnostic tests were ordered before mNGS was performed. The timelines revealed significant variance in time to pathogen detection and revealed multiple routes to mNGS. Based on these timelines, we developed a framework to demonstrate existing pathways to mNGS for specimens with unknown infectious etiologies. Components in the framework included specimen collections, type of diagnostic and mNGS laboratory (e.g., public health, research, or commercial laboratory). These pathways could inform design of a surveillance system using mNGS by targeting specimens at key points in their diagnostic pathway. The systematic use of mNGS for patients with inconclusive results, within a representative and population-based surveillance system, could contribute to improved pathogen detection/discovery by including novel, emerging or reemerging pathogens at an unprecedented scale and speed.

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COMMUNITY HEALTH WORKERS' ROLE IN COMBATING AEDES-BORNE DISEASES: INSIGHTS FROM A SCOPING REVIEW AND QUALITATIVE SYNTHESIS

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Aedes-borne diseases (ABDs), including dengue, chikungunya and zika, pose significant global health challenges. There is no "silver bullet" for control of these diseases, and effective approaches such as Integrated Vector Management depend on community context and participation. Community Health Workers (CHWs) are a heterogeneous group of lay health workers and paraprofessionals embedded in the communities they work in. Systematic reviews of CHW programs demonstrate efficacy in cost effective reduction of morbidity and mortality across numerous settings and diseases. While roles and benefits of CHWs in anti-malarial efforts are well established, this is not the case for ABD. A scoping review and qualitative synthesis was conducted to understand the roles CHWs have in preventing, controlling, and treating ABD. Supportive evidence, contextual issues, and how CHW's work connects to vector management infrastructures were also investigated. Pubmed, Scopus and Google Scholar were queried with pre-defined search terms. After eliminating ineligible abstracts, 93 articles underwent full text review, and information was extracted from 82 articles using a standardized extraction protocol. Scoping results of characteristics of programs utilizing CHWs for ABD control, including the settings in which CHWs are utilized, payment or incentive structures, program type (vertical, horizontal or hybrid), work setting (urban, rural, special populations) and evidence supporting CHW involvement in disease control, will be discussed. Our qualitative synthesis focused on benefits and challenges encountered by programs utilizing CHWs. We found issues related to worker safety, exploitation, CHW and vector control worker overlap, and opportunities for CHW retraining in epidemics. CHWs will be important contributors to implementation of future and emerging ABD prevention and treatment strategies, and policy makers should be ready to deploy CHWs in vaccine linkage, improved rapid diagnostic tests, and linkage to treatment.

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BAYESIAN METHODS FOR ATTRIBUTING ETIOLOGY OF ACUTE FEBRILE ILLNESS (AFI) USING AN RT-PCR ARRAY CARD FOR SURVEILLANCE OF 32 PATHOGENS IN THE PERUVIAN AMAZON

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Accurate diagnosis of acute febrile illnesses (AFI) in tropical regions, particularly in the Peruvian Amazon, is notoriously challenging. Prior studies of AFI across Latin America have reported that 40% or more of cases are unable to be attributed to a causal pathogen. A syndromic approach using multiplex PCR panels holds great promise for improving AFI diagnosis and surveillance, but also poses certain interpretive challenges as well. RIVERA, a prospective health facility-based case-control study, employs Taq-Man array cards (TAC) for detection of an entire panel of pathogens simultaneously for patients with acute febrile illness and their matched afebrile controls.

Current multiplex PCR data have been analyzed using the attributable fraction approach, which has multiple limitations that Bayesian methodologies can help address. Firstly, while the attributable fraction approach assumes perfect sensitivity and specificity of the tests used, Bayesian Latent Class Analysis (LCA) incorporates prior knowledge of test performance characteristics of specific PCR primer sequences. Secondly,

while attributable fraction estimates for a given pathogen are based on one test, LCA can integrate results from multiple modalities (e.g. serology, molecular testing, and culture) and sample types (e.g. blood, plasma, tissue). Third, LCA provides not just population-level estimates, but also at the level of individual patients, allowing for direct clinical application of the model.
Here we apply LCA to refine estimates of etiological distribution for AFI cases in the Peruvian Amazon. We compare LCA results with those from the attributable fraction approach to examine the impact of utilizing one method versus the other. Preliminary findings suggest that attributable fraction techniques may be underestimating Dengue virus and overestimating Plasmodium spp. as etiologies of AFI. Ongoing work includes incorporating informative prior parameters into the model, and expansion to include all pathogens tested by TAC.

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STRENGTHENING SUB-NATIONAL SUPPORT TO HEALTHCARE PROFESSIONALS IN PAPUA NEW GUINEA TO PROMOTE EQUITY IN THE USE OF DATA TO INFORM LOCAL RESPONSE TO VECTOR-BORNE DISEASES

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Background: Vector-borne diseases (VBDs) such as malaria pose an intensifying global health threat, especially in the context of resource-constrained healthcare systems such as Papua New Guinea (PNG), accounting for nearly 90% of all malaria cases in the region. A critical need exists for strengthened surveillance and outbreak response capacity that is equitable and effective particularly in decentralized health systems, where sub-national healthcare workers (HCWs) form the backbone of service delivery. The STRIVE project is strengthening the use of digital health information systems (HIS) to support HCWs in using data for decision-making. Methods: Qualitative mixed method assessments have been undertaken across 8 provinces at three time points between 2018 and 2022, including semi-structured interviews with sub-national healthcare providers and HCWs and health facility structured observations. Thematic analysis was guided by the WHO health systems building blocks and adapted health systems strengthening frameworks using Nvivo 14 (QSR). Quantitative data were analysed using MS excel. Results: Strong leadership and governance within sub-national authorities enabled the alignment of data for decision making activities within strategic plans providing a platform for effective monitoring and implementation. Strengthening electronic reporting and use of VBD data increased awareness of local epidemiology, improving the ability to identify local outbreaks. Challenging geographical barriers associated with paper-based reporting were overcome with the transition to electronic HIS, improving equity amongst HCWs in timely, accurate and available use of data. Structural improvements to reporting systems, improved data quality leading to the timely validation and increased confidence in outbreak response capacities. Discussion: Improving equity amongst HCWs to access HIS for data-informed decision making enabled effective monitoring of sub-national performance, improved disease tracking and strengthened activity planning and resource allocation, improving VBD surveillance and response outcomes.

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MANAGEMENT AND MONITORING OF POTENTIAL EBOLA (SUDAN) VIRUS DISEASE CASES IN JINJA DISTRICT DURING THE 2022 OUTBREAK IN UGANDA

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Efficient management and monitoring of potential Ebola cases is crucial for containing outbreaks and ensuring public health safety. Accordingly, we analyzed alert and contact tracing data from Jinja district and surrounding areas in Eastern Uganda to assess the efficacy of control measures during the 2022 Ebola Virus (Sudan Virus) Disease (EVD) outbreak in Uganda. We evaluated data from a Ministry of Health alert and contact database for the period from November 2022 through January 2023. We defined an alert as unstructured data sourced from the media or community members, aimed at early detection of potential health events or risks. A contact referred to an individual who had been exposed to a patient with EVD. There were 239 alerts reported including 184 (77%) related to suspicious deaths and 55 (23%) related to persons still alive of whom 36 (65%) were evacuated to hospital where 1 person died. There were 176 (73%) alerts from Jinja district, 179 (75%) from the community, and 59 (25%) from health facilities. The 239 alerts led to 236 samples being collected of which none were positive for Ebola or Sudan virus. There were 163 individuals with a mean age of 17 years who were identified for contact tracing of whom 109 (67%) were female. Jinja district accounted for 129 (79%) contacts including 75 (58%) from Jinja municipality and 38 (29%) from Buwenge sub-county. Of the 163 contacts, 158 (97%) were exposed to the EVD index case. As evidenced by the absence of confirmed EVD cases among contacts, negative test results from samples, and thorough contact tracing and monitoring efforts, there was effective control and management of potential Ebola cases in Jinja district and surrounding areas.

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CHOLERA AND ACUTE DIARRHEAL DISEASES IN HIGH PRIORITY CHOLERA HOTSPOTS IN ETHIOPIA: PRELIMINARY INTERIM FINDINGS ON AGE-GROUP STRATIFIED CRUDE INCIDENCE, HOSPITALIZATION, AND LEADING CAUSES OF NON-CHOLERA DIARRHEAL DISEASES

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Ethiopia is affected by cholera. Ethiopia Cholera Control and Prevention (ECCP) project supports national cholera control plan. A prospective sentinel healthcare facility-based surveillance of acute diarrheal diseases was set up in Shashemene, Oromia region. Surveillance catchment population was around 351,577, including approx. 100,000 people who received two-doses of oral cholera vaccine during a preemptive vaccination campaign in May 2022. Here we present preliminary interim surveillance results while data cleaning and surveillance are ongoing. Patients with acute diarrheal symptoms were eligible for enrolment. Clinical data and stool/rectal swab samples were collected for cholera rapid diagnostics test (RDT) and culture confirmation. From January 2022 to March 2024, total 6,507

patients were enrolled and 6,505 samples collected. 14.6% (102/701) were cholera RDT positive out of RDT done. 3.1% (204/6,505) of all samples were culture positive; 10.8% (22/204) positive for *V. cholerae* and 89.7% (183/204) for non-cholera isolates out of culture positives. *Shigella* spp. (48.6%; 89/183) and *E. coli* (45.9%; 84/183) were predominant pathogens causing non-cholera diarrheal illnesses. Some *Salmonella* spp. (5.5%; 10/183) were also yield. Populations aged 15+ years accounted for 55.6% (60/108) of cholera cases (either RDT or culture positive), followed by children aged 5-14 years (21.3%; 23/108). Notably, 61.2% (3913/6399) of enrolled patients with non-cholera diarrheal diseases were aged 15+ years, followed by children <5 years old (25.5%; 1,632/6,399). 40.7% (44/108) of cholera patients (either RDT or culture positive) were hospitalized, compared to only 0.2% (15/6,399) in non-cholera diarrheal patients. Overall crude incidence of cholera was 14.0/100,000 person-years (PY). Crude incidence of non-cholera diarrheal disease was 827.3/100,000 PY. Cholera disease severity, household transmission, and seasonality are being analyzed. This interim analysis suggests that despite resurgence of cholera outbreaks in Ethiopia in 2023, limited cases were reported in our study area that may be related to our OCV campaign in 2022.

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ACUTE FEBRILE ILLNESS RESEARCH TO SUPPORT EPIDEMIC PREPAREDNESS AND RESPONSE IN WEST AFRICA

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Fever is one of the most universal and common signs of infectious diseases. Many emerging and re-emerging pathogens of epidemic potential are associated with acute febrile illness (AFI), a concept to guide differential diagnosis. Presumptive diagnosis of AFI cases as malaria or typhoid is common, and can result in improper case management or missed detection of more severe etiologies, hampering timely outbreak identification and response. Such consequences were starkly revealed in 2014, when Ebola virus disease emerged in Guinea and rapidly spread to neighboring countries. Substantial programming efforts have since been made to strengthen health systems in West Africa with respect to surveillance, laboratory and clinical capacities. However, AFI research initiatives, which seek to better characterize and describe circulating fever-associated pathogens in humans and animals, can also support these broader health systems goals, and contribute to compliance with international health security and systems frameworks, such as the International Health Regulations and Performance of Veterinary Services Pathway. Here, we describe how collaborative research projects, engaging diverse and multisectoral stakeholders, are helping to sustain health systems strengthening efforts, build human and animal health surveillance capacities, advance One Health policy coordination and collaboration, and improve diagnostic capabilities across different countries in West Africa, thus contributing to epidemic preparedness and response efforts.

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TRANSCRIPTIONAL AND GENOMIC SIGNATURES ASSOCIATED WITH CHLORFENAPYR RESISTANCE IN THE PRIMARY AFRICAN MALARIA VECTOR *ANOPHELES GAMBIAE*

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The deployment of control tools with new insecticides such as chlorfenapyr has started to exert a selective pressure on field populations of mosquitoes likely to select for resistance. It is vital to monitor these populations regularly to detect molecular basis of such resistance at an early stage when suitable measures could be taken to mitigate their impact. In the present study, after establishing a CFP-resistant strain of *Anopheles gambiae*, RNA-Seq and Whole Genome Sequencing (WGS) were performed to screened for the potential genes/genomic variants associated with CFP resistance. Furthermore, using RNA-interference approach, we silenced the key detoxification-related genes to validate their functions in the CFP tolerance and key allelic variations detected exploited to design simple DNA-based molecular markers for field monitoring of CFP resistance. A total of 6514 differentially expressed genes (DEGs) were identified in chlorfenapyr selected (CFP-R) line versus the unselected CFP-S, in which 3245 genes were upregulated and 3269 downregulated. Strikingly, all metabolic genes commonly found to be associated with pyrethroid resistance (e.g: CYP6P3, CYP9K1, CYP4G16, GSTS1···) were down-regulated in CFP-resistant samples. Very interestingly, two genes from carboxylesterase and Cyclin families were among the predominant over-expressed genes in CFP-resistant mosquitoes (FC= 67.10 and 17.01 respectively) with allelic variation detected after whole genome sequencing. Further knock down of these genes helped to recover the susceptibility in the CFP-resistant mosquitoes. DNA-based assay further supported that a mutation on the Carboxylesterase gene strongly correlates with CFP resistance (χ^2= 26.4; P<0.0001) and combines with that of the Cyclin to additively aggravate the resistance intensity to CFP (OR=608.1; P<0.0001). This study highlights the important role of carboxylesterase in driving CFP resistance and the field-applicable tools designed will help to easily track the spread of CFP resistance and assess its impact on control interventions.

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THE GROWTH INHIBITION OF AN *AEROMONAS* TAXON BY THE ENTERIC MICROBIOME SYNERGIZES DELTAMETHRIN TOXICITY IN *ANOPHELES*

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The bacterial enteric flora of the mosquito vector *Anopheles* has been linked with its vectorial competence, however, its potential influence on insecticide resistance is poorly understood. We found that bacteria microbiome depletion of susceptible *Anopheles* strains through antibiotic (ATB) treatment either from adult emergence in sugar meals or via female blood-feeding led to > 50% insecticide deltamethrin tolerance. We investigated the underlying mechanism of ATB-mediating deltamethrin tolerance by blocking cytochrome P450 activity, known as a metabolic resistance mechanism. We found that blocking P450 activity reverted the tolerance phenotype, indicating that ATB treatment-mediating deltamethrin tolerance is P450-dependent in *Anopheles* susceptible strains. We tested the hypothesis of an ATB-tolerant enteric bacteria becoming major after ATB treatment that could be associated with the deltamethrin tolerance phenotype. We isolated and identified an *Aeromonas* taxon from ATB-treated susceptible mosquitoes, and we show that it is required for the tolerance phenotype observed on deltamethrin-susceptible *Anopheles*. The results presented here illustrate a mechanistic interplay between the enteric dysbiosis promoting a bacteria taxon and the detoxifying P450 enzymes in controlling *Anopheles* insecticide susceptibility, and that these interactions could probably modulate vectorial capacity.

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POPULATION GENOMICS OF *AEDES AEEGYPTI* FROM MERIDA, MEXICO

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Aedes aegypti poses a significant public health threat due to their ability to transmit arbovirus. Understanding the population genetic structure of *Ae. aegypti* both at micro- and macro-geographic scales can help better elucidate gene flow, population selection and response to insecticide-based interventions, and ecological traits. We conducted an unprecedented, in-depth, whole genome sequencing (WGS) analysis to quantify *Ae. aegypti* genetic structure and assess the genome changes to an insecticide-based intervention (Targeted Indoor Residual Spraying, TIRS, with pirimiphos-methyl) occurring in the city of Merida, Mexico. We analyzed 1.4 million SNPs from 198 *Ae. aegypti* samples collected from Merida (a balanced sample from treatment and control areas subjected to TIRS) and locations in Africa and America. Distinct genetic clusters for Merida *Ae. aegypti* compared to global populations were identified, suggesting local adaptation. Interestingly, two genetic clusters were found within Merida with no spatial segregation. Nucleotide diversity analysis supported an African origin of *Ae. aegypti* with subsequent introduction to the Americas. Notably, a decrease in nucleotide diversity was observed in some areas before insecticide interventions, indicating rapid genomic changes in a relatively short timeframe (5 to 6 months). Six non-synonymous mutations associated with insecticide resistance were identified in the kdr gene, including a novel mutation (L925I). Merida populations have a moderate frequency of kdr es alleles, similar to Florida and Caribbean *Ae. aegypti*, with a slight increase observed after 5 to 6 months of intervention. Our findings offer valuable insights into the genetic relatedness of Merida mosquitoes compared to global *Ae. aegypti* populations and identify a set of knockdown resistance mutations circulating within the local mosquito population. The observed rapid changes in mosquito genetics in response to control interventions highlight the importance of monitoring insecticide resistance mutation frequencies over extended periods.

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EFFICACY OF NEXT-GENERATION LONG-LASTING INSECTICIDAL NETS <LLINSGT AGAINST INSECTICIDE RESISTANT *ANOPHELES GAMBIAE* S.L. IN M'BÉ, CENTRAL CÔTE D'IVOIRE: AN EXPERIMENTAL HUT TRIAL AND ANALYSIS OF BASELINE MOLECULAR RESISTANCE MECHANISMS

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Insecticide-treated nets (ITNs) combining synergist and/or partner insecticides, constitute the next generation of interventions to control malaria transmitted by pyrethroid-resistant mosquitoes. This study evaluated three ITNs containing pyrethroid and piperonyl-butoxide (PBO), (PermaNet®3.0; Olyset® Plus; Veeralin®), and an ITN mixture of chlorfenapyr and pyrethroid (Interceptor G2®) *vs.* a pyrethroid-only net (MAGNet®) against free-flying, wild insecticide resistant *Anopheles (An.) gambiae sensu lato* (s.l.), at M'bé field site in central Côte d'Ivoire. To understand the relative performance of ITNs, mainly the PBO based products, a baseline analysis of the insecticide resistance mechanisms in local malaria vector populations at this site was performed on samples collected in the hut containing the control untreated net. Molecular identification was performed using SINE PCR and TaqMan-based qPCR was used to genotype L1014F/S-, V402L- and N1575Y-*Kdr*, G119S-*Ace1*, I114T-*Gste2* and E205D-*CYP6P3* resistance markers. Of the *An. gambiae* s.l. analyzed, only *An. gambiae* s.s (9.4%) and *Anopheles coluzzii* (90.6%) were found. Interceptor G2® mortality rate was the highest against wild free-flying insecticide resistant *An. gambiae* s.l.; the odds of mosquitoes dying in hut with Interceptor G2® was nearly 10 times higher than in the hut with MAGNet® (82% *vs.* 40.1% mortality rates; OR 9.9; CI [6.2–16.2]), whereas the odds of dying in huts with the different PBO-ITNs *vs.* MAGNet® were not significantly different. Six mutations were present and four were found for the first time (V402L-*Kdr* (41.9%), N1575Y-*Kdr* (44.0%), I114T-*Gste* (81.3%) and E205D-*CYP6P3* (22.1%)). Intensive phenotypic resistance and multiple underlying molecular resistance mechanisms are being selected in malaria vector populations in Côte d'Ivoire, leading to reduced mortality of insecticide resistant *An. gambiae* s.l. in the presence of dual active ingredient ITNs, including PBO based nets. Further investigation of the association between mosquito survival, exiting, blood-feeding ability and insecticide resistance markers in the presence of these ITNs is needed.

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THE IMPACT OF INTERCEPTOR G2 AND PERMANET 3.0 INSECTICIDAL TREATED NETS ON ENTOMOLOGICAL TRANSMISSION INDICATORS IN GAYA & GUIDIMOUNI, NIGER, WEST AFRICA

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Entomological surveillance was conducted in Gaya & Guidimouni, Niger, before & after mass distribution of Interceptor G2 (IG2) & PermaNet 3.0 insecticidal treated nets (ITNs) in 2022. The impact of ITNs on vector species composition, human biting rates (HBR) & entomological inoculation rates (EIR) was measured using human landing catches, pyrethrum spray catches, & Centers for Disease Control light traps. Insecticide susceptibility of the main vectors to pyrethroids & chlorfenapyr, as well as the effect of pre-exposure to the PBO synergist were also measured annually. *Anopheles coluzzii*, was the predominant vector before the ITN mass campaign (88%), followed by *An*. *arabiensis* (6%) & *An. gambiae* (6%). The species composition did not change after the campaign in either site, but HBR & EIR were reduced at both sites in 2022 immediately after the campaign. There was some rebound in these indicators in 2023, but not back to pre-campaign values. In Gaya, *An. gambiae* s.l. HBR fell from 1728 bites/person/month (b/p/m) in 2021 to 1098 b/p/m in 2022 & 1298 b/p/m in 2023. In Guidimouni, HBR was reduced from 363 b/p/m in 2021 to 240 b/p/m in 2022 and 228 b/p/m in 2023. The EIR was 23.2 infectious bites/person/month (ib/p/m) in Gaya in 2021 before the campaign but show a reduction of 52.5% (11.0 ib/p/m) in 2022 & rose to19.9 ib/p/m in 2023. In Guidimouni, EIR was 4.8 ib/p/m in 2021 with >70% reduction following the ITN campaign in 2022 (1,2 ib/p/m) but then rose to 1.9 ib/p/m in 2023.

Susceptibility to chlorfenapyr was recorded in Guidimouni before & after the campaign while in Gaya possible resistance was detected before the campaign but full susceptibility was recorded in 2023. Resistance to the three pyrethroids tested (deltamethrin, alpha-cypermethrin, permethrin) was recorded across the years. Pre-exposure to PBO synergist increased mortality of mosquitoes but only fully restored susceptibility to alpha-cypermethrin and deltamethrin in 2023. The overall data suggest that ITN types have an impact on entomological transmission indicators, though monitoring for an additional year is necessary to determine whether efficacy of nets reduces two years after deployment.

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UNRAVELLING METABOLIC RESISTANCE IN *ANOPHELES FUNESTUS* S.S. POPULATION FROM BENGUELA AND CUANZA-SUL PROVINCES, ANGOLA

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The fight against malaria heavily relies on tools based on insecticides to control its vectors, such as treated nets with pyrethroid or indoor residual spraying. The increased resistance to pyrethroid is jeopardising these tools' efficacy. In this study we report the presence of cytochrome P450 Cyp6P9a/b gene variants at high frequency mediating metabolic resistance in Anopheles funestus s.s., a primary vector of malaria in Angola. Mosquitoes were collected from households in one site in Benguela (-12.944755, 14.756086) and two sites in Cuanza-Sul (-10.830917, 14.462028 and -10.735195, 14.995401) provinces, using CDC light traps from July 2022 to March 2023. Mosquitoes collected were morphologically identified to species level. A total of 324 specimens of the An. funestus group were used for this study. DNA was extracted and used to identify members of An. funestus group and genotype the metabolic resistance mechanisms within An. funestus s.s. Species specific molecular identification revealed that the An. funestus group comprised of 88.6% An. funestus s.s., 5.2% An. leesoni and 6.2% did not amplify. Overall, in An. funestus s.s. the Cyp6P9a (87.8%) and Cyp6P9b (98%) resistance alleles were at very high frequency, although the resistant alleles for a Cyp6P9a/b-linked 6.5kb structural variant (SV) and the GSTe2 L119F mutant were absent from the samples. Consequently, the four-locus genotypes (P9a/b/SV/Gste2) are dominated by samples homozygous resistant for the Cyp6P9a and b point mutations (77.2%), with a second most common class being Cyp6P9a susceptible and Cyp6P9b homozygous resistant (14.6%), other 4-locus genotypes were present at <10%. Here we report for the first-time metabolic resistance mechanisms for Angolan An. funestus s.s. The high frequency of the resistance alleles Cyp6P9a and Cyp6Pb, previously associated with pyrethroid resistance, is a warning sign for possible failure of interventions solely based on pyrethroid-treated nets in these sites. The use of complementary strategies such as indoor residual spraying and impregnated nets with different classes of insecticides should be considered.

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WHOLE TRANSCRIPTOME SEQUENCING EXPOSES DISTINCT INSECTICIDE RESISTANCE MECHANISMS IN *ANOPHELES ARABIENSIS*OF VARYING AGES FROM MWAGAGALA, TANZANIA

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Insecticide resistance among *Anopheles* malaria vector species is now widespread. To evaluate the spread and intensity of resistance, World Health Organization guidelines mandate that mosquitoes should be phenotypically tested at 3-to-5 days old, and these samples are usually those used in downstream molecular assays to identify underlying insecticide resistance mechanisms. However, the predominant mechanisms driving resistance in young *Anopheles* vector populations cannot be assumed to be analogous to those in older, malaria transmitting mosquitoes, which are the most epidemiologically important cohort. Differential gene expression in 3-, 6- and 11-day old permethrin resistant, susceptible, and unexposed *An. arabiensis* from Mwagagala, Tanzania was assessed using whole transcriptome sequencing. We identified significant differences in expression of genes encoding detoxification enzymes, cuticular proteins, salivary glands, and gustatory and odorant receptors. In 3-day old mosquitoes, the cytochrome P450 CYP6P3, which metabolises permethrin and deltamethrin, was expressed over 100 times higher in resistant, and almost 50 times higher in unexposed mosquitoes, compared with the susceptible colony strain. Other notable detoxification enzymes included CYP6M2, CYP6Z3, CYP4H19, CYP6Z2 and CYP4H17, the choline-esterase COEJHE2E, and glutathione-S-transferase GSTD7. Expression of these detoxification enzymes was often highest at 3-days, and declined over time, but in some cases remained significant by 11-days. CYP6Z3 was consistently upregulated across all ages, while CYP4H17 only had increased overexpression in 11-day old *An. arabiensis*; this gene may represent a putative marker of ageing in *An. arabiensis,* with the potential to be used for transcriptional age grading. Most cuticular resistance genes were only upregulated in 3-day old mosquitoes, with only CPR86 increasing in expression by 11-days. Dynamic transcriptomic profiles of permethrin resistant *An. arabiensis* of different ages indicates that insecticide resistance is driven by different mechanisms across the mosquito lifespan.

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INSECTICIDE RESISTANCE STATUS OF *AEDES AEGYPTI* IN THE URBAN AREA OF BAMAKO IN THE CONTEXT OF A DENGUE EPIDEMIC

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In recent months, a Dengue epidemic has been observed in several West African countries, including Mali. In Mali, there is no preventive measure in place against arboviral diseases. Interventions are restricted to mitigate outbreaks by spraying insecticides regardless of the resistance status of the vectors to the insecticides. The present study assessed the insecticide resistance status of *Aedes aegypti* populations in the urban environment of Bamako in the context of dengue epidemic. Phenotypic resistance was determined with WHO susceptibility tests using *Ae. aegypti* of generation F_1 aged 3 to 5 days. Synergist assays were performed with piperonyl butoxide (PBO) to investigate the possible involvement of metabolic mechanisms in resistance phenotypes. Using the WHO mortality criteria of equal or greater than 98 percent for susceptibility, *Ae. aegypti* in the urban area of Bamako revealed resistance to all insecticide tested. Resistance to DDT was the highest (0% mortality rate) followed by deltamethrin (4%), permethrin (13.6%), pirimiphos methyl (21%), and bendiocarb (36.8%). Pre-exposure to PBO significantly increased the susceptibility ($P<0.001$) of *Ae. aegypti* to deltamethrin (46.7%) and permethrin (21%). This indicates that metabolic enzymes (monooxygenases) may be involved in the resistance phenotypes observed in the *Ae. aegypti* populations in these sites. *Aedes aegypti,* the vector of many emerging infectious diseases was resistant to all the four

classes of insecticide used in vector control as recommended by WHO. There is a need to set up an appropriate surveillance system to prevent the occurrence of epidemics.

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REDUCED EFFICACY OF PBO-LLINS AGAINST MALARIA VECTORS IN WEBUYE, BUNGOMA COUNTY, WESTERN KENYA.

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Introduction: In response to rising levels of insecticide resistance among malaria vector species and persistent malaria transmission, many countries are turning to next generation ITNs such as those co-formulated with piperonyl butoxide. Although PBO-LLINs are effective for restoring the efficacy of pyrethroid-based nets in several field trials, the effectiveness under scale-up and duration of protection has not been established. Here we evaluate the efficacy of the PBO LLINs in Bungoma County, 2 years after distribution. Materials and methods; Efficacy was evaluated with WHO cone bioassay using wild vectors and the susceptible Kilifi strain. PBO-LLINs used in households were sourced from four villages while an untreated net was used as negative control and a new, unused PBO-LLIN was used as a positive control. Wild *Anopheles* mosquitoes were collected as larvae from villages, reared to adults and five non-blood-fed, 2-5-day old female *Anopheles* were tested per cone in four replicates. Knockdown was recorded at 1-h after exposure while mortality was recorded at 24-h after exposure. Results; Used PBO**-**LLINs from Kinesamo village tested on wild vectors gave a mean of 47% knockdown and 28% mortality whereas LLINs from Nangili had a mean of 53% knockdown and 32% mortality. The highest mortality (46%) in the local vectors was observed in Sitabicha while Maruti nets gave the lowest mortality at only 3%. Untreated net tested on the same wild vectors resulted in 0% knockdown and mortality. The same used PBO-LLINs resulted in at least 94% knockdown and 100% mortality for susceptible Kilifi strain. The new PBO-LLIN resulted in at 95% knockdown and 83% mortality for the wild strain while in the susceptible strain knockdown and mortality was 100%. Over 90% of the mosquitoes tested were *Anopheles gambiae s.l.* Conclusion; PBO-LLINs have very low efficacy against local vector populations after more than a year of use, partly due to age of the net but also to very high levels of resistance in the local vector population. The level of protection against malaria infection is likely greatly attenuated.

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ESCALATING PYRETHROID RESISTANCE IN TWO MAJOR MALARIA VECTORS ANOPHELES FUNESTUS AND ANOPHELES GAMBIAE (S.L.) IN ATATAM, SOUTHERN GHANA

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Aggravation of insecticide resistance in malaria vectors is threatening the efforts to control malaria by reducing the efficacy of insecticide-based interventions hence needs to be closely monitored. This study investigated the intensity of insecticide resistance of two major malaria vectors *An. funestus sensu stricto (s.s.)* and *An. gambiae sensu lato (s.l.)* collected in southern Ghana and assessed the bio-efficacy of several long-lasting insecticidal nets (LLINs) against these mosquito populations. The insecticide susceptibility profles of *Anopheles funestus* s.s. and *Anopheles gambiae* s.l. populations from Obuasi region (Atatam), southern Ghana were characterized and the bio-efficacy of some LLINs was assessed to determine the impact of insecticide resistance on the effectiveness of these tools. Furthermore, molecular markers associated with insecticide resistance in both species were characterized in the F0 and F1 populations using PCR and qPCR methods. *Anopheles funestus s.s*. was the predominant species and was resistant to pyrethroids, organochlorine and carbamate insecticides, but fully susceptible to organophosphates. *An. gambiae s.l.* was resistant to all four insecticide classes. High intensity of resistance to 5×and 10×the discriminating concentration (DC) of pyrethroids was observed in both species inducing a considerable loss of efficacy of long-lasting insecticidal nets (LLINs). Temporal expression analysis revealed a massive 12-fold increase in expression of the CYP6P4a cytochrome P450 gene in *An. funestus s.s*., initially from a fold change of 41 (2014) to 500 (2021). For both species, the expression of candidate genes did not vary according to discriminating doses. *An. gambiae s.l*. exhibited high frequencies of target-site resistance including Vgsc-1014F (90%) and Ace-1 (50%) while these mutations were absent in *An. funestus s.s.* The multiple and high intensity of resistance observed in both malaria vectors highlights the need to implement resistance management strategies and the introduction of new insecticide chemistries.

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WHOLE GENOME SEQUENCE ANALYSIS OF POPULATION DYNAMICS AND INSECTICIDE RESISTANCE MARKERS IN *ANOPHELES MELAS* FROM THE BIJAGÓS ARCHIPELAGO, GUINEA-BISSAU

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Anopheles melas is an understudied malaria vector with a key role in malaria transmission on the Bijagós Archipelago of Guinea-Bissau. This study presents the first whole genome sequencing and population genetic analysis for this species from the Bijagós Archipelago. To our knowledge, this study also represents the largest population genetic analysis using WGS data from non-pooled *An. melas* mosquitoes. WGS was conducted for 30 individual *An. melas* collected during the peak malaria transmission season in 2019 from four different islands on the Bijagós Archipelago. Insecticide resistance mutations associated with pyrethroid resistance in *An. gambiae* s.s. were absent in the *An. melas* population, and no signatures of selective sweeps were identified in insecticide resistance associated genes. Analysis of structural variants identified a large duplication encompassing the cytochrome-P450 gene *cyp9k1.* Phylogenetic analysis using publicly available mitochondrial genomes indicated that *An. melas* from the Bijagós split into two phylogenetic groups due to differentiation on the mitochondrial genome, attributed to the cytochrome C oxidase subunits COX I and COX II, and the NADH dehydrogenase subunits 1, 4, 4L and 5. The absence of selective sweeps in known insecticide resistance genes indicates reduced selection pressure in *An. melas* for insecticide resistance, or alternative mechanisms of insecticide resistance evolution in comparison to *An. gambiae sensu stricto.* Whilst this is one of the largest genomic studies of *An. melas,* further large-scale work could incorporate phenotypic and synergist-insecticide bioassays, and metabolic gene transcriptomics.

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INSECTICIDE RESISTANCE IN *ANOPHELES GAMBIAE* COMPLEX IN ONDO AND ANAMBRA STATES OF NIGERIA

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The spread of insecticide resistance in *Anopheles* vectors poses a significant threat to malaria control. The problem is compounded by a significant dearth of local data on resistance levels in vector species in many Nigerian states. This study sought to determine the resistance of *An. gambiae* s.l. populations to a range of insecticides and unravel the underlying resistance mechanisms in two states lacking such data. Entomological surveys were conducted in Ondo and Anambra states before and after the distribution of insecticide-treated nets (ITNs) containing alpha-cypermethrin and piperonyl butoxide (PBO). The larvae of *An. gambiae* s.l. mosquitoes were collected from six local government areas in each state and reared to the adult stage. The Centre for Disease Control and Prevention (CDC) bottle bioassay method was used to assess resistance against various insecticides. Molecular identification and genotyping of resistance genes were also carried out. Resistance to permethrin and deltamethrin was observed in the savanna zone of Ondo State in February 2022. In a subsequent survey in September 2023, resistance to permethrin and DDT was recorded across all sites tested. *An. gambiae* s.l. was susceptible to alpha-cypermethrin, deltamethrin, lambda-cyhalothrin, bendiocarb, propoxur and chlorfenapyr. In Anambra, the vectors were susceptible to alpha-cypermethrin, deltamethrin, lambda-cyhalothrin, bendiocarb, and chlorfenapyr except in some sites in the northern part of the state where potential resistance to alpha-cypermethrin and deltamethrin was observed but reversed after pre-exposure to PBO. Intensity assays in the second round showed resistance to permethrin at twice the discriminating concentration in Ondo. Pre-exposure to PBO reversed the permethrin resistance except in Ondo's forest zone where it persisted after pre-exposure to PBO indicating mechanisms other than elevated expression of mono-oxygenase enzymes. The study showed resistance to permethrin and DDT in Ondo and Anambra states. The distribution of ITNs containing alpha-cypermethrin and PBO was an appropriate intervention in both states.

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METABOLIC BASIS OF PYRETHROID RESISTANCE IN *AEDES AEGYPTI*

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The absence of cost-effective vaccines against dengue, Zika, or chikungunya emphasizes the crucial role of mitigating the mosquito vector *Aedes aegypti* to prevent arboviral diseases. Vector mitigation primarily relies on outdoor insecticide sprayings, particularly using pyrethroids (PYR) and organophosphates. However, the rapid evolution of PYR resistance mechanisms in mosquitoes, such as knockdown resistance and enhanced insecticide detoxification by enzymes, presents a significant challenge. While genomic and transcriptomic approaches have shed light on metabolic resistance mechanisms, a comprehensive understanding, and biomarkers for PYR metabolic resistance in mosquitoes are still lacking. In this study, we employed untargeted liquid chromatography-mass spectrometry-based metabolomics to uncover metabolic pathways associated with PYR resistance in *Aedes aegypti* mosquitoes. Comparative metabolomic analyses were conducted between PYR-resistant and susceptible mosquitoes. In addition, we assessed the mosquito's metabolic response to sublethal and lethal concentrations of permethrin by performing targeted LC-MS measurements of PYR and metabolites of PYR. This research aims to identify metabolic signatures linked to resistance against one of the most used insecticides for *Ae. aegypti* control and lead to identification of potential biomarkers for pyrethroid metabolism in resistant mosquitoes.

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INSECTICIDE CONTACT EFFECTIVENESS OF ULV FOGGING ACROSS A HETEROGENEOUS PHYSICAL AND FITNESS LANDSCAPE

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Insecticide resistance is a growing issue that plagues mosquito control efforts and hinders vector-borne disease elimination. This issue is especially pertinent in the Americas where about 4 million cases of Dengue Fever were recorded in Q1 of 2024. Insecticides are distributed into the environment via backpack, aerial, or truck-mounted spraying. To manage both the increase in resistance phenotypes in mosquito populations as well as the abundance of mosquito vectors, more targeted methods for dispersal of insecticides are necessary. Insecticides can only effectively kill a mosquito via direct airborne contact or passive contact through residual effect on exposed surfaces. Currently, there is little understanding of the contact effectiveness of airborne or residual insecticides in natural settings. Here, we will present our ongoing research on how heterogeneous landscapes and residual deposition on landscape elements can alter the effectiveness of insecticide droplets during ultra-low volume (ULV) application by a fogging vehicle. We performed detailed dose-response analyses on *Aedes aegypti* in Maricopa county (MC), Arizona, reporting LD_{50} ranging from 0.287–1.303 ng deltamethrin/mg mosquito. To determine the dose to which mosquitoes are likely exposed, we first performed semi-field trials in an unobstructed open field using insecticide capture devices and sentinel cages containing susceptible *Ae. aegypti*. We further demonstrated the residual effectiveness of insecticides deposited on various environmental surfaces in hours and days after fogging. Finally, we assessed droplet distribution and sentinel cage mortality in operational settings with obstructive landscape elements during routine insecticide application with a truck-mounted fogger in MC. Using our resistance profiles, remote sensing data, and geographically weighted regression methods, we aim to demonstrate the waning effectiveness of insecticides across varying landscape types to inform mosquito control agencies where best to deploy insecticides to deter resistance and prevent future outbreaks of emerging tropical diseases in the US and globally.

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EXAMINING THE PROLIFERATION OF *SERRATIA MARCESCENS* IN *ANOPHELES GAMBIAE* MOSQUITOES TOWARDS UNDERSTANDING THEIR ROLE AND MECHANISM IN *PLASMODIUM FALCIPARUM* TRANSMISSION-BLOCKING

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Serratia marcescens is commonly associated with blood-fed *Anopheles gambiae* mosquitoes and has been found to possess anti-plasmodial properties, making it a candidate for bacteria-mediated disease/vector control strategies. However, the experimental approaches used to test their anti-parasitic effects has not considered the natural concentrations of the bacterium in the mosquito midgut. Therefore, the parasite-killing effect of *S. marcescens* may have been exaggerated, could be concentration-dependent and may not hold true under natural conditions. We quantify *S. marcescens* in the midgut of *Anopheles gambiae* mosquitoes after a

blood meal using qPCR and test the effect of these natural concentrations on *Plasmodium falciparum*. The highest concentration ($2.6x10^3$ CFU/mL) of *S. marcescens* in the *Anopheles* midgut occurred at 12 hours post-blood meal representing a 2-fold increase compared to non-blood fed mosquitoes (P=0.02). Introduction of *S. marcescens* cells at 1X (OD_{600}= 2.5) and 10^{-5} to *An. gambiae* adult mosquitoes through sugar meals increased concentration to $0.66x10^3$ CFU/mL (P=0.02) in non-blood fed midgut and $2.7x10^3$ CFU/mL (P=0.0013) 12 hours post-blood meal, compared to the baseline ($0.07 x10^3$ CFU/mL) in those that received the 1X concentration. Mosquitoes that were fed the lower bacteria concentration only showed significant increase ($7.2x10^3$ CFU/mL; P= 0.0005) in *S. marcescens* after a blood meal. These bacteria concentrations will further be evaluated for their effect on the *P. falciparum* parasite in *in vitro* and *in vivo* experiments. This study enhances our understanding of how *S. marcescens* proliferates post blood meal and identifies optimal levels to target for bacteria mediated transmission blocking strategies.

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RETENTION OF ADULT MOSQUITO PHENOTYPE FROM CRYOPRESERVED *ANOPHELES STEPHENSI* EGGS FOR SUCCESSFUL GMP PRODUCTION OF SANARIA® PFSPZ CHALLENGE (NF54)

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Sanaria has produced *Plasmodium falciparum* (Pf) sporozoite (SPZ) vaccines against Pf malaria that are composed of aseptic, purified, cryopreserved PfSPZ attenuated either by radiation, antimalarial drugs, or gene deletion. PfSPZ are produced in a unique aseptic mosquito system, in the absence of any microorganisms that could affect the final product. For the first time, cryopreserved *Anopheles stephensi* eggs from Sanaria`s egg banks were used as starting material for a GMP production campaign to generate PfSPZ Challenge (NF54). Cryopreserved non-aseptic eggs were thawed to establish an *A. stephensi* colony and amplified over three generations. Pupae were used to initiate production of aseptic mosquitoes, adults of which were fed upon Pf stage V gametocytes. In five aseptic mosquito containers, oocyst prevalence was 68%-100%, geometric mean oocyst intensity was 19.5-126.1 oocysts per midgut, and PfSPZ intensities were $0.65 x10^5$ - $1.01x10^5$ PfSPZ/mosquito. PfSPZ Challenge, cryopreserved at $1.5x10^4$ PfSPZ/vial. This lot of PfSPZ Challenge is undergoing all release assays as the final steps for its use in composed of aseptic, purified, infectious PfSPZ, was vialed and controlled human malaria infections (CHMI). These data show that cryopreserved eggs of *A. stephensi* can be used to generate a new colony in just three generations and that the resultant mosquitoes retain the two major required phenotypic characteristics - ability to be used in the aseptic manufacturing process and susceptibility to Pf infection - necessary for Sanaria's GMP production of PfSPZ products. Cryopreservation of mosquito eggs is now established at Sanaria as a GMP process.

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IMMUNOMETABOLIC CROSSTALK IN *AEDES FLUVIATILIS - WOLBACHIA PIPIENTIS* SYMBIOSIS

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Wolbachia pipientis is a maternally transmitted symbiotic bacterium that mainly colonizes arthropods, potentially affecting different aspects of the host's physiology, e.g.reproduction, immunity, and metabolism. It has been shown that Wolbachia modulates glycogen metabolism in mosquito *Aedes fluviatilis*. Glycogen synthesis is controlled by the enzyme GSK3, which is also involved in immune responses in both vertebrate and invertebrate organisms. Here we investigated the mechanisms behind immune changes mediated by GSK3β in the symbiosis between *Ae. fluviatilis* and *Wolbachia pipientis* using a GSK3β inhibitor or RNAi-mediated gene silencing. GSK3β inhibition or knockdown increased glycogen content and Wolbachia population, together with a reduction in Relish2 (REL2) and gambicin transcripts. Furthermore, knockdown of REL2 or Caspar revealed that the Imd pathway acts to control Wolbachia numbers in the host. In conclusion, we describe for the first time the involvement of GSK3β in *Ae. fluviatillis* immune response, acting to control the Wolbachia endosymbiotic population.

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TRANSGENIC OVEREXPRESSING VAGO1 RESTRICTS ARBOVIRUS INFECTION IN *AEDES AEGYPTI*

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Aedes aegypti is the primary vector for numerous arboviral diseases. During viral infection in *Ae. aegypti*, the cytokine-like protein Vago activates the JAK-STAT pathway and may mediate antiviral immune responses. We have generated transgenic mosquitoes overexpressing the Vago1 in midguts and fat bodies using their respective blood-inducible promoter. Overexpression of Vago1 in midguts did not impact dengue virus 2 infection in midguts at 7 days post-infection (dpi), but significantly reduced infection prevalence in the head and thorax at 14 dpi, suggesting Vago1 may inhibit the viral infection in mosquito bodies rather than in midguts. When Vago1 was overexpressed in fat bodies, transgenic mosquitoes exhibited a significant virus titer and infection prevalence in the mosquito carcass at 7 days post Mayaro virus infection. Our data supports that Ae. aegypti Vago1 plays an antiviral role in mosquito bodies.

7757

UNDERSTANDING THE IMPACT OF HOST SPECIES AND SEASONALITY ON THE MOSQUITO MYCOBIOTA AND THE POTENTIAL OF FUNGI AS PARATRANSGENETIC TOOL

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Understanding interactions between mosquitoes and their microbiome is important as mosquito-microbiome-pathogen interactions can modulate pathogen transmission by mosquitoes. Additionally, manipulation of the mosquito microbiome is an increasingly common form of mosquito control, which can be used to target mosquito populations with known insecticide resistance. This includes the use of *Wolbachia* for mosquito population suppression or replacement as well as entomopathogenic fungi. Mosquitoes, are naturally associated with many fungi, and distinct fungal communities are linked to different mosquito tissues. The bacterial microbiome varies because of host species and extrinsic factors like seasonality and landscape. For the mycobiome, the mosquito-associated

fungi, the influence of these environmental variables on fungal abundance and diversity is unclear. For this reason, we profiled the mycobiome of three mosquito species, *Aedes taeniorhynchus, Anopheles atropos,* and *Culex nigripalpus*, collected from Vero Beach, Florida, USA during the dry and wet seasons. We isolated and profiled midgut fungi using ITS 1 and ITS 2-based Illumina Mi-Seq. We observed very high diversity of fungi between mosquito species and only a minor impact of seasonality. However, one fungal isolate belonging to the class Microbotryomycetes, accounted for more than half of the fungal reads in all species. This isolate dominated the *An. atropos* midgut mycobiome, which was less diverse than that of the other two species. Microorganisms that are cultivable and highly prevalent in key mosquito populations have potential for paratransgenetic interventions. This Microbotryomycetes sp. fungus is cultivable, and we are currently exploring possibilities for transformation using antimicrobial peptides such as Scorpine. Our findings suggest the potential of using natural-associated fungus as a tool to control mosquito-borne pathogens via paratransgenesis, exploring interactions between pathogens and the mosquito immune system.

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IMPACT OF INGESTED ANTIMALARIALS IN THE MOSQUITO VECTOR

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In the past year, WHO recommendations regarding acceptable use of antimalarials for the prevention of malaria in endemic areas have greatly expanded, allowing more flexibility in both the demographic groups as well as regions where chemoprevention are acceptable. Expanding temporal and spatial population-level drug exposure raises questions as to whether such exposure may impact the mosquito and/or the parasite following ingestion of drug in a bloodmeal. In particular, drug impact on parasite development and drug resistance selection in the mosquito (sporogony) has often been overlooked. Data suggest infected mosquitoes often re-feed, with potentially ≥4 blood meals in a mosquito lifespan. The downstream drug effects in mosquitoes that feed on people who have taken long-acting antimalarials has largely been unexplored. To address this, we are investigating the impact of exposure to physiologic levels of commonly used long-acting human antimalarials in the mosquito vector via drug-spiked blood feeds. We have not observed any significant differences in lab-reared *Anopheles gambiae* behavior, fertility, or viability after ingestion of piperaquine, amodiaquine, and its active metabolite desethylamodiaquine. We are further performing drug-spiked blood feeds in field-derived F1 *An. gambiae* in Burkina Faso. In order to interrogate drug distribution within the mosquito and the potential for oocyst exposure to drug, we are using LC-MS/MS on both whole mosquitoes as well as midgut and hemolymph samples 24 hours and 5 days post feed to quantity drug levels. These initial studies will lay the foundation for future work to assess the impact of vector-stage antimalarial drug exposure on parasite selection and progression throughout sporogony, which could in turn have important transmission and drug resistance selection implications at a population level.

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EFFECT OF HYDROGEN PEROXIDE ON *AEDES AEGYPTI*: EGG HATCHABILITY AND OVIPOSITION SUBSTRATE PREFERENCE

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Aedes aegypti mosquito is a major vector of several important pathogens such as Dengue virus, Chikungunya virus and Zika virus. Many studies have looked at ecological factors affecting the growth and development of this mosquito species but not much focus has been given to hydrogen peroxide produced in the environment through biological and physico-chemical processes. Recognizing the paucity of knowledge on the effects of environmental factors in aquatic ecosystems on *Ae. aegypti* mosquitoes, we investigated the impact of hydrogen peroxide (H_2O_2) on egg hatchability and oviposition substrate preference. Eggs were subjected to different H_2O_2 concentrations in the laboratory following two scenarios: Firstly, eggs were placed in H_2O_2 at concentrations of 0, 5, 25, 50, and 100 µM and hatching recorded after 48hrs, and secondly, eggs were exposed to the same concentrations as above for of 0, 2, 4, 6 hours and then transferred to water and hatching recorded after 48hrs. To determine oviposition substrate preference in the presence of hydrogen peroxide, heavily gravid *Ae. aegypti* were given a choice of oviposition substrate with various hydrogen peroxide concentrations of 0, 5, 25, 50, and 100 µM and water (control). After 72 hours, the eggs laid at each concentration (oviposition site) were counted and the Oviposition Activity Index scores calculated. Results indicated that H_2O_2 concentration ($p < 0.0001$) and pre-exposure exposure to H_2O_2 for up to ≤ 6hr ($p < 0.004$) influenced egg hatch rates, without any significant interaction between these two variables ($p < 0.8143$). Pre- exposure of eggs to H_2O_2 for a limited time up to ≤ 6hr positively correlated with hatch rates across all H_2O_2 concentrations (5, 25, 50, and 100 µM). The presence of H_2O_2 in the substrate deterred oviposition, with the mosquitoes choosing water over H_2O_2 as indicated by the OAI scores. This study shows that environmental H_2O_2 concentration can affect the reproductive strategies of *Ae. aegypti* and offers valuable insights that could be useful for mosquito management strategies.

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HIGH-THROUGHPUT RNA SEQUENCING REVEALS DIVERSE CLADES OF MOSQUITO-SPECIFIC VIRUSES AND SHEDS LIGHT ON THEIR ECOLOGY

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In recent years, the discovery of new viruses in the environment has significantly increased thanks to advanced high-throughput sequencing techniques. However, interpreting their biology and understanding the key factors that influence their diversity and evolution continue to pose challenges. Mosquitoes, as potential vectors of public health concern, are among the organisms whose viral populations are being extensively studied. Although the identification of new mosquito-specific viruses (MSVs) is growing rapidly, our knowledge of their evolutionary history and ecological role remains limited. Using Illumina sequencing technology alongside a laboratory method to deplete host ribosomal RNA, we studied RNA viruses in pools of three mosquito species: Armigeres subalbatus, Culex nigropunctatus, and Aedes albopictus. Female adult mosquitoes were collected from distinct habitats along a forest-agricultural gradient in central Thailand, specifically forest, fragmented forest, and rice field habitats. We identified and characterized both near-complete and partial genomes of 19 novel and previously known viruses from diverse families or groups

including Birnaviridae, Iflaviridae, Narnaviridae, Negevirus, Nodaviridae, Orthomyxoviridae, Permutotetraviridae, Polycipiviridae, Rhabdoviridae, Sobemovirus-like group, Tombusviridae, Virgaviridae, and Xinmoviridae. Phylogenetic analyses of the conserved RNA-dependent RNA polymerase protein sequences showed that, with only a few exceptions, these viruses clustered with those found in other mosquito species, suggesting a broader clade of mosquito-associated viruses within each of the diverse virus groups. In addition, the presence of a given virus depended more on vector species than collection site or habitat, an observation that has been shown previously. This study underscores the complex dynamics of virus-host interactions and highlights the need for further exploration into how these relationships influence virus evolution and distribution.

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CRYOPRESERVATION OF *ANOPHELES* EGGS AT LARGE AND SMALL SCALE

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Sanaria's original method for cryopreservation of *Anopheles stephensi* eggs [Sci Rep. 2022 12:43] has been modified and scaled up to enable long term cryostorage of lots of >200,000 eggs and also scaled down to facilitate the cryopreservation of small numbers of eggs typically produced by research teams studying genetically-modified *Anopheles* mosquitoes. Both methods follow the same protocol using eggs between 15 to 30 minutes old, a first incubation in 100% methanol as the cryoprotectant additive (CPA) at -6.5 °C for 7 minutes, a second incubation step in CPA at -15 °C for 15 minutes followed by rapid cooling by plunging into liquid nitrogen (LN2). For the large scale method, eggs are gravity-concentrated using a filtration device onto nylon mesh membranes. The eggs are dispersed as a monolayer on the mesh, then transferred through the two incubation steps in CPA and into LN2. To date, five lots of *A. stephensi* eggs have been banked and one lot used in GMP manufacture of *Plasmodium falciparum* (Pf) sporozoite (SPZ) products. The small scale method collects eggs using a brush or pipette and Eppendorf 1.5 mL centrifuge tubes supported in 24-hole aluminum blocks to hold CPA at the two incubation temperatures. At the end of the second incubation step, eggs are pipetted out of the -15 °C CPA onto a rectangle of black card cooled to -15 °C and then plunged into LN2. For both methods, thawing is rapid and eggs are captured in Petri dishes for incubation and hatching assessment. Hatch rates for the large scale method have ranged from ~5% to 18%. Hatch rates for *A. stephensi*transgenic strains are lower and for *A. gambiae* have been ~2% or less. The method for *A. gambiae* needs optimization with collection of large numbers of eggs in a narrow time window and stickiness of the eggs currently the focus of attention.

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DETERMINING THE THERMAL SUITABILITY OF *PLASMODIUM FALCIPARUM* INFECTION IN THE URBAN MALARIA VECTOR *ANOPHELES STEPHENSI* UNDER VARIABLE HUMIDITY

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Malaria causes significant financial and human loss, with billions of dollars spent on control. Despite the recent gains in reducing the overall global burden of malaria, elimination efforts are now being threatened by an invasive South Asian urban malaria vector *Anopheles stephensi*, as well as climate and land use change, two factors rapidly changing the landscape for malaria transmission. Predicting the effects of environmental variation on transmission dynamics will be critical for projecting potential zones of emergence and responses to future environmental change. Temperature and water availability are two of the most important abiotic factors influencing the distribution and abundances of ectothermic organisms, including mosquitoes. While extensive research exists on the effects of temperature on the transmission process, the influence of humidity on mosquito and pathogen parameters affecting disease dynamics are less understood. To investigate the impact of both temperature and humidity on parasite development in this mosquito, we infected *An. stephensi* with *Plasmodium falciparum* NF54 and placed infected mosquitoes under variable temperature (16°C - 32°C) and relative humidity (30-90%) conditions. Midguts and salivary glands of infected mosquitoes were dissected every three days post-infection to quantify the developmental timing of oocysts and sporozoites. We hypothesize that temperature and humidity have compounding effects on parasite development in the mosquito, which is a balance between mosquito immune response to infection and mechanisms of parasite proliferation. We will discuss the infection outcomes under these range of temperatures and previously uninvestigated variation in relative humidity. Understanding the dynamics of malaria infection in *An. stephensi* will help us to better predict and model the environmental suitability for this invasive vector.

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ANOPHELES ARABIENSIS LARVAL DISTRIBUTION IN IRRIGATED RICE FIELDS: SIGNIFICANCE OF WATER CIRCULATION NETWORK AND RICE GROWTH STAGE

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Irrigated agriculture can promote crop production with a managed water regime, yet enhance production of Anopheles vectors of human malaria and increase risk of malaria in farmers. The Bwanje Valley Irrigation Scheme, a 908-ha rice growing cooperative in Dedza District of east-central Malawi with service water from a weir diversion of the Namikokwe River, is part of a long-term, country-wide initiative intended to reduce dependency on rainfall, promote crop production, and enhance rural development. We previously documented increased indoor density of Anopheles arabiensis in villages near the scheme, and high malaria prevalence in villagers. Here, we report results of an empirical analysis of larval An. arabiensis distribution and abundance in the scheme, and model larval density in relationship to scheme architecture, water sources, rice planting stage, and soil properties. There were 9,567 Anopheles larvae collected from 642 sample sites located along 41 transects in three linear water service areas during the first quarter of 2019, when field work was conducted. Larvae were markedly aggregated in the scheme and nonrandomly distributed. Larval density declined with distance of water service area to the diversion. Larvae aggregated within water service areas, and predominated in the first one. An. arabiensis was the sole species encountered and Anopheles funestus was remarkably absent. Regression analysis using larval density permitted inference of best fitting models including both continuous and categorical data. Larval density was strongly associated with distance from headwater (diversion of water from the river source), distance from secondary water supply channel, and early transplanted stage of rice (as opposed to no rice plants present, or to advanced stages of rice growth). These results suggest that populations of An. arabiensis can be modeled as to predominant location within rice irrigation schemes, and that a combination of water service systems and rice cultivation may provide tools for An. arabiensis population management that could be incorporated into the agronomic system.

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COMPARING ENTOMOLOGICAL CHARACTERISTICS DURING INDOOR RESIDUAL SPRAYING WITH DIFFERENT FORMULATIONS IN EASTERN UGANDA

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Malaria incidence among children in the Tororo district of Uganda was reduced from 2.96 to 0.040 episodes/person/year from 2014-2019 with Indoor Residual Spraying (IRS) with Bendiocarb and Actellic. A switch to clothianidin-based IRS in 2020 was associated with malaria resurgence to pre-IRS levels, while returning to Actellic in March 2023 was again associated with reductions. This study uses female *Anopheles* landing and entomological inoculation rates (EIRs) to explore how vectors responded to changes in IRS formulations. Monthly human landing catches (HLCs) were performed from Nov 2020-Nov 2021 in 8 houses and biweekly HLCs from Nov 2022-Sept 2023 in 12 houses. Three main vector species were identified using PCR: *An. funestus s.s.*, *An. gambiae s.s.* and *An. arabiensis.* Sporozoite rates were assessed with ELISA assays. Visual observations were performed from Jun-Sept 2023 to determine whether human inhabitants were outdoors, indoors not using a bednet or indoors using a bednet for each hour from 6pm-6am. Mixed effects negative binomial regression with a log-link was used to compare landing rates and means EIRs were compared with Student's t-test. After adjusting for month, both *An. gambiae s.s.* (RR: 3.3; 95% CI: 2.0 to 5.8) and *An. arabiensis* (RR: 3.1; 95% CI: 2.2 to 4.2) had significantly higher outdoor compared to indoor landing rates following Actellic compared to during clothianidin, but *An. funestus* indoor and outdoor landing rates were not statistically different. After adjusting landing rates for human behaviors, mean nightly EIR during clothianidin was 0.035 (95% CI: 0.027 to 0.043) compared to 0.019 (0.015 to 0.02) during Actellic ($p<0.01$). *An. funestus* contributed 35.5% (95% CI: 29.0% to 41.9%) of the EIR during clothianidin IRS and the malaria surge and 7.4% (95% CI: 3.1% to 11.8%) after Actellic was re-instituted ($p<0.001$) and malaria incidence dropped. These data have important implications for malaria control programs in choosing IRS formulations, as they suggest that clothianidin-based IRS was less effective than Actellic in this district in Uganda and the mechanism may be inadequate reductions in indoor biting of *An. funestus.*

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DIURNAL AND OUTDOOR BITING BY ANOPHELES GAMBIAE COMPLEX MALARIA VECTORS REVEALS RESIDUAL TRANSMISSION ALONG AN URBANIZATION GRADIENT IN BURKINA FASO

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Resistance of vectors to insecticides and changes in vector biting behaviour may lead to malaria transmission persistence, despite insecticide-based control interventions. Malaria is more prevalent in rural than in urban areas. However, adaptation of malaria vectors to urban conditions, coupled with the growth of urban populations may cause an increase in urban malaria. Thus, we investigated biting patterns of malaria vectors along an urbanisation gradient, to gain insights into the emerging issues of urban malaria and vector behaviour in residual transmission.Malaria transmission and vector behaviour were assessed in three localities representing an urban, peri-urban, and rural environment. Human landing catches were conducted over a three-month period during the rainy season of 2023. The collection involved both indoors and outdoors, for 48 consecutive hours. The relative proportions of indoor versus outdoor biting, as well as daytime (06-18 hrs) versus nighttime (18-06 hrs) biting, and the residual transmission force between localities, were compared.In total, 4,428 *Anopheles gambiae s.l.* were caught for 144 days x sites x position x localities. Their distribution across indoor/outdoors, sites and day/night periods varied between localities. In the urban area, outdoor landings accounted for two-thirds of the total, whereas in non-urban settings, this proportion decreased to one-half. Daytime samples represented a mere 0.4-3.4% of the total outdoors, and in the urban locality indoors. In contrast, diurnal samples taken indoors made up 13-19% of biting in non-urban areas. These disparities may be attributed in part to the unequal distribution of members of the Gambiae complex, specifically *A. arabiensis* dominating in the urban locality and *A. coluzzii* prevailing in non-urban settings. Besides insecticide resistance, the strength of diurnal biting indoors and the tendency to bite outdoors can set a ceiling to the effectiveness of insecticide-treated nets. These observations suggest reconsidering vector control strategies for addressing residual transmission in malaria elimination efforts in urban and rural settings.

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USE OF ENVIRONMENTAL DNA (EDNA) FOR MONITORING THE PRESENCE OF *ANOPHELES STEPHENSI* AND ASSOCIATED INSECTICIDE RESISTANCE MECHANISMS IN LABORATORY AND FIELD CONDITIONS

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The invasion and establishment of *Anopheles stephensi* in Africa represents a significant threat, which may jeopardise malaria control, particularly in urban areas which were previously largely malaria-free. Novel, simple-to-implement vector surveillance methods are urgently needed, which require little prior knowledge of mosquito morphology, and are quick and easy to implement at the sampling stage. Entomological surveillance is also vital for control of arboviral diseases, posing a public health threat, as no suitable vaccines or specific drugs are available. As part of the Resilience Against Future Threats (RAFT) research consortium, we evaluated the feasibility of using environmental DNA (eDNA) for entomological surveillance. Phase I of the study assessed the suitability of using eDNA for simultaneous detection of *An. stephensi* and *Aedes aegypti* in laboratory conditions. Using multiplex TaqMan assays targeting *An. stephensi* and *Ae. aegypti*, we validated the use of eDNA for simultaneous vector detection in shared artificial breeding sites and demonstrated that *An. stephensi* and *Ae. aegypti* eDNA deposited by a single larva in 1 L of water was detectable. Characterization of molecular insecticide resistance mechanisms, using novel amplicon-sequencing panels, was possible from eDNA shed by larvae. eDNA was also remarkably stable. Phase II of the study was carried out in Ghana, to validate the feasibility of this technique under field conditions. Results show that methods developed work well in real-world field conditions, and that filtration is better suited to eDNA field work than precipitation method. Once finalised, the methodology will be shared with stakeholders interested in using this surveillance approach. eDNA surveillance has the potential to be implemented in local endemic communities and points of country entry, to monitor the spread and presence of vector species of interest, as collected filter eDNA samples can be easily stored and transported. However, molecular processing of samples is more challenging and may be limited to well-equipped laboratories with sufficient molecular biology expertise.

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CHARTING THE COURSE: ESTABLISHING AN ENTOMOLOGICAL DATABASE IN GHANA, CHALLENGES AND SUCCESSES

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The traditional methods of collecting, storing, and analyzing entomological data have faced challenges related to efficiency, accuracy, and accessibility over the years. Ghana embraced innovations in entomological data management, by the development and implementation of a comprehensive database. This study delves into Ghana's pioneering efforts to revolutionize entomological data management. It explores the country's journey from conventional paper-based systems to the adoption of a modern, technology-driven integrated entomological database for the collection and management of malaria vector data in Ghana. The design and development stage involved a multidisciplinary approach, collaboration, and careful consideration of data requirements. The development was spearheaded by the National Malaria Elimination Program with support from stakeholders including PPME, WHO and USAID-PMI. The steps in the development included defining the database scope and objectives, stakeholder involvement, data model development, user interface design, data collection protocols, and security measures. Before full deployment, a comprehensive training program was developed to build the capacity of end-users, field staff, and database administrators. Also, a pilot testing phase was conducted to identify potential issues and gather user feedback. The design team iteratively refined the database based on user input, ensuring that the final product met the practical needs of those utilizing the system. The database was fully deployed for use after these processes. The development and deployment of the entomological database in Ghana achieved improved data accessibility by the NMEP and all implementing partners, it gave room for partners involved in entomological monitoring to conduct collaborative research. The database has also been designed to adapt to any change in the entomological landscape in Ghana. Despite these achievements, challenges encountered during the design and deployment included data standardization issues, capacity building issues, integration of historical data in the system, security and privacy concerns.

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ISLANDS IN THE STREAM: IMPACT OF FLOOD-INDUCED LANDSCAPE CHANGES ON MOSQUITO COMMUNITY COMPOSITION IN THE BRAZILIAN PANTANAL, WITH IMPLICATIONS FOR ARBOVIRUS TRANSMISSION

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The Brazilian Pantanal is one of the richest areas of biodiversity in the world with over 600 species of vertebrate (host) and mosquito (vector) species that share the same habitat. This region undergoes annual flooding to create capões, which are elevated arboreal patches of herbaceous vegetation which remain dry year-round and provide refuge for land vertebrates. Our study tested the hypothesis that capões serve as concentrated land areas that facilitate unique vector-host interactions that affect mosquito-borne arbovirus transmission. To test this, we sampled mosquitoes and observed vertebrate patterns at 3 study sites in the northern Pantanal. At each site, 3 pairs of sampling points were established, with sampling taking place on both a capõe and on a flat area that floods. Capões were determined using a presence-only modeling framework utilizing occurrence records from the Global Biodiversity Information Facility for plant species intolerant to flooding. Mosquitoes were collected using BG-sentinel traps, CDC light traps, resting shelters, and aspiration of vegetation. Camera traps ran for 3-month-long periods during the dry and flooded seasons. Furthermore, blood-engorged mosquitoes were assessed by PCR to determine host associations. We collected 17,915 individual mosquitoes comprising 35 species. Specimens were pooled by species into 1,172 pools comprising up to 40 mosquitoes each and screened using RT-PCR for flavivirus and alphavirus viral RNA. Finally, we analyzed 300 blood-engorged female mosquitoes to identify vertebrate host species and examined over 20,000 images from wildlife cameras to determine vector/host interactions at each sampling point assess how vector/host density. Although the circulation of several arboviruses has been documented in the Pantanal, very few studies have investigated the more complex host/vector transmission dynamics influenced by the capões. This study seeks to understand the response of vertebrate host and vector communities to annual flooding in the Pantanal, and how these responses can influence the transmission dynamics and spillover risk of vector-borne disease in the area.

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MOLECULAR DETECTION OF THE MALARIA TRANSMISSION-BLOCKING MICROBE *MICROSPORIDIA* SP. MB IN NIGERIAN POPULATIONS OF MALARIA VECTORS

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A few endosymbionts have shown the potential to block malaria parasite transmission in mosquito vectors. These include *Microsporidia* sp. MB recently reported to impair *Plasmodium falciparum* development in Kenyan *Anopheles arabiensis* mosquitoes. Unlike several endosymbionts, *Microsporidia* sp. MB has little or no fitness costs on mosquito hosts. It also has the ability of vertical transmission, which thus enhances its propagation in mosquito populations and prospects of sustainable parasite control. We identified *Microsporidia* sp. MB for the first time in Nigerian mosquito populations. *Anopheles* samples positive for *Microsporidia* sp. MB were collected in field campaigns in southern Nigeria and comprised larval and adult mosquitoes and molecularly identified *An. coluzzii* and *An. gambiae* sensu stricto. Percentage identities of >98.00% were obtained from NCBI-BLAST analysis that compared nucleotide sequences of the Kenyan and Nigerian strains of *Microsporidia* sp. MB. After its discovery in Kenya, *Microsporidia* sp. MB has been detected in Ghana, Niger, and Benin. Our finding of the endosymbiont in Nigeria has further increased its hitherto known spatial distribution range on the African continent. Given the detection in immature mosquitoes in addition to adult mosquitoes, *Microsporidia* sp. MB is apparently undergoing vertical transmission in wild populations of malaria vectors in southern Nigeria.

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MOSQUITO DIVERSITY AND FEEDING HABITS ACROSS VIRGINIA

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To properly manage, identify, and predict the arboviruses that are present and have the potential to become established in a location, it is vital to have an accurate idea of the composition of the vector communities and feeding preferences of these vectors. From May-October 2022, we sampled mosquitoes for three nights each month from four sites across the state of Virginia, USA ranging from high elevation sites within the Blue Ridge Mountains to low elevation sites in the Great Dismal Swamp. To capture the highest diversity of mosquitoes possible we used a combination of CO_2 baited CDC light traps, Gravid traps, BG Sentinel traps, and vacuum aspirators. We captured a total of 7747 mosquitoes composed of 34 species. We also collected 25 blood fed mosquitoes representing 10 species. We then calculated and compared several diversity metrics including Shannon-wiener and Rarefied richness across the four sites.

We found that abundance and richness was highest in the low elevation swamp location, but that evenness and diversity are higher at the Central mid elevation site. We also analyzed mosquito blood meals using a pan-vertebrate PCR followed by amplicon sequencing and found various sources of host bloodmeals including White-tailed deer (*Odocoileus virginianus*), Green frog (*Rana clamitans*), Cottontail rabbits (*Sylvilagus sp.*), and a variety of songbirds. Lastly, we detected two species of human disease relevance recently identified for the first time in Virginia (*Culex coronator and Cx. nigripalpus*). Due to our monitoring efforts we can now create a baseline for the state of Virginia to monitor these vector species.

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ECOLOGY, DISTRIBUTION, AND DISCOVERY OF NOVEL ARBOVIRUSES WITHIN THE STATE OF VIRGINIA

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Arthropod-borne pathogens are among the leading causes of morbidity and mortality worldwide. As we start to experience the effects of climate change and the range expansion of viable disease vectors, establishing a known baseline of vectors and pathogens is integral in developing proper management strategies for disease outbreaks. The state of Virginia has a diverse ecological landscape which, spans from coastal swamps to mountainous ranges. This diverse landscape enables us to test how differences in landscape features may influence vectored pathogen dispersal. We surveyed three sites across Virginia: including the Coastal Plain (swamp), Piedmont (savannah), and Blue Ridge Mountains (primary forest) for one week every month from May until October of 2022. Mosquitoes were collected using CO_2 baited CDC light and gravid traps, and were sorted into pools by trap type, date, and species. A total of 7899 mosquitoes were collected and sorted into 974 pools. Pools were screened for viruses via cytopathic effect assays in three cell lines (Vero-76, BHK-21, and C7/10) at three different incubating temperatures (37° C, 30° C, and 28° C, respectively). We used a diagnostic PCR with pan-Flavi-, pan-Bunya-, pan-Alpha- virus primers to identify virus families, and amplicons were sequenced to identify pathogens. We isolated three vertebrate pathogenic viruses including Jamestown Canyon, and 58 insect-specific viruses including multiple Culex Flaviviruses from 17 different mosquito species representing seven genera, (*Aedes, Anopheles, Coquilletidia, Culex, Culiseta, Psorophora*, and *Uranotaenia*). Several viruses that failed initial identification methods were sequenced and identified using next-generation sequencing. We will report on the phylogenetic characteristics and host-pathogen associations observed during our state-wide vector surveys. This study will shed light on the immense unknown viral diversity across the state and can aid public health officials in developing risk assessments for Virginia and neighboring states.

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EDIBLE MICROCRYSTALS AS A NOVEL MOSQUITO TRACKING STRATEGY FROM LARVA TO ADULT

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Arboviral diseases pose a persistent challenge in today's world. Despite extensive knowledge about these diseases, understanding how their vectors navigate their environment remains a gap. Our group is addressing this gap by developing a novel method to track mosquito movements using DNA barcodes housed within an edible nanoporous crystal protein structure. This structure can be consumed by filter-feeding larval mosquitoes. Our research suggests that these edible trackers minimally impact mosquito survivorship and demonstrate a near 50% marking success rate in laboratory studies. We have also successfully recovered barcodes from field-trapped Culex sp. mosquitoes. Laboratory studies further indicate that our markers do not increase the vector competence of Aedes aegypti when exposed to the Rift Valley Fever virus. Moreover, they can effectively mark Anopheles sp., Culex sp., and Aedes sp. mosquitoes. The crystalline proteins in our system readily absorb DNA when in solution, enabling us to embed a synthesized DNA barcode sequence within. Once ingested by the mosquito, these crystals shield the DNA from harsh environmental conditions, preserving the barcode within the mosquito midgut. Exposure to ATP allows the DNA barcode to be flushed from the crystal structure, facilitating easy detection via PCR. Leveraging the unique capabilities of these trackers, we anticipate being able to trace adult mosquitoes back to their larval origins. This technology holds promise for integration into existing vector surveillance programs, potentially offering enhanced clarity on mosquito movement patterns in their environment.

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ECOLOGICAL CORRELATES OF INVASIVE *AEDES AEGYPTI* MOSQUITOES IN SAN BERNARDINO COUNTY, CALIFORNIA, U.S.A.

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Aedes mosquitoes, particularly *Aedes aegypti* and *Ae. albopictus*, are major vectors of globally significant diseases such as dengue, Zika, and chikungunya, with vaccine development lagging. In California, *Ae. aegypti* populations have rapidly expanded since 2013, posing challenges for control due to their cryptic breeding sites and urban habitat preference. As this is a newly invasive species in this setting, environmental correlates of *Aedes* abundance are not well understood. Here we use earth observation data to investigate associations between environmental factors and counts of trapped adult *Ae. aegypti* mosquitoes in San Bernardino County, California from 2017 - 2023. We used a generalized additive model with a negative binomial distribution to model counts of adult Ae. aegypti mosquitoes using temperature, precipitation, surface water, elevation, and built environment as predictor variables. Our analysis revealed distinct spatial clusters and temporal peaks of high *Aedes* counts. Positive associations were observed between minimum and maximum ambient temperature and counts of *Ae. aegypti*. Precipitation had a negative association, but surface water had a strong positive association. We then stratified the data by time and re-ran our models on data from different time intervals across the time period. In early years we saw little-to-no associations between environmental predictors and counts of *Ae. aegypti* mosquitoes. More recently, temperature and surface water have emerged as consistent predictors. This invasive mosquito species is increasing in abundance and geographic extent in this setting. Surface water had a strong positive association with counts of *Ae. aegypti* while precipitation had a negative association. We hypothesize that this is related to housing developments with gardens that are watered more frequently during dry times, and which create small water bodies that are optimal for larval stages of this mosquito. This information can help with vector control efforts that may be more efficiently targeted at specific places and during specific times of the year.

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COMPREHENSIVE EVALUATION OF INTER-INDIVIDUAL VARIATION IN ANTIBODY RESPONSES TO *ANOPHELES GAMBIAE* EXPOSURE

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Climate change is affecting arthropod ranges, and thus shifting the future landscape of vector-borne diseases (VBDs). To assess the public health

risk of VBDs, the distribution of the vectors that spread them must be elucidated. Antibodies generated in response to arthropod bites can act as natural biomarkers of exposure to VBD-relevant vectors. However, the rate of discovery for these antibodies is low-throughput and antibody levels to individual peptides are known to vary across individuals, which has constrained studies to estimates of population seroprevalence rather than individual exposure. To comprehensively profile antibody repertoires for vector-relevant biomarkers on an individual level, we have created VectorScan, a phage display library containing over 250,000 peptides from the proteomes of vector-borne pathogens and their arthropod hosts. We screened VectorScan against plasma from 14 healthy adults from the Washington, D.C. area who were bitten by uninfected *Anopheles gambiae* mosquitoes. Samples were collected at day 0, prior to exposure, and day 44, after 4 controlled exposures. We observed high baseline rates of seropositivity from mosquito-derived peptides that varied greatly between individuals, indicative of heterogenous antibody profiles from previous exposures. To identify shifts in antibody responses to *An. gambiae*, we used DESeq2 to identify peptides that were differentially enriched in individuals at day 44 vs. day 0. Notably, no single peptide was enriched in more than 3 subjects, indicating persistent heterogeneity in individual antibody responses after nearly identical exposures and highlighting VectorScan's ability to achieve individual level resolution of antibody profiles. However, many enriched peptides share intra-peptide motifs, allowing us to identify potential immunogenic epitopes that could be useful for population-level surveillance. We will continue to develop and test VectorScan to identify novel biomarkers and generate surveillance data that can inform public health measures, train ecological models of climate change, determine new vaccine targets for VBDs, and more.

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DISTRIBUTION OF *AEDES AEGYPTI* LARVAE IN CHACHAPOYAS AND LUYA PROVINCES, AMAZONAS REGION, PERU

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In 2023, the *Aedes aegypti* mosquito was responsible for approximately 274,246 dengue cases in Peru, with the Amazonas region being one of the most affected. Although these mosquitoes are usually found in low-altitude tropical and subtropical areas, recent studies have located them up to 2,500 meters above sea level (masl). Climate change and various socioeconomic factors have modified the distribution patterns of the vector, taking them to cooler and higher cities. In March 2024, a "bi-stage" sampling study was carried out in four districts of Chachapoyas and two of Luya to evaluate the presence of the vector larvae. The specimens were subjected to morphological identification using the taxonomic key of Rueda, 2004. Likewise, a surveillance and control record form was completed for *Ae. aegypti* to calculate entomological indices. In this study, a total of 175 households were evaluated, revealing that, approximately 10% of the households inspected, tested positive for the presence of larvae, mainly in buckets, tubs, and pots, followed by vases, tires, unusable tanks and, water tanks. After morphological identification, it was confirmed that one town in Yerba Buena (Chachapoyas) and two in Ubilón (Luya) tested positive for *Ae. aegypti*. In Yerbabuena, the Breteau, Aedico (IA) and Container indices were 1.69, 1.69, and 0.22, respectively. While in Ubilon, these indices were 18.18, 18.18 and 1.74. The IA was classified as high risk when it exceeded 2%, due to the low number of homes. These towns are located at 1925 and 1981 masl, respectively, with temperatures ranging between 29 and 31°C and a relative humidity of approximately 70%. The results suggest the rapid adaptation of this vector to new environmental conditions, expanding its range to new areas. In conclusion, it is crucial to continue surveillance and monitoring of these areas to prevent dengue outbreaks, considering that cases of this disease are reported in nearby districts.

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EARLY DETECTION OF DENGUE OUTBREAKS: TRANSMISSION MODEL ANALYSIS OF A DENGUE OUTBREAK IN A REMOTE SETTING IN ECUADOR

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Transmission of an infectious disease outbreak generally begins well before it is identified by a surveillance system. Therefore, an outbreak investigation typically determines the timing of the *primary* case (the first case of the outbreak, whether detected or not) retrospectively. However, details on the initial onset of the outbreak are often hard to obtain, especially for pathogens like dengue virus (DENV) where infection has a high asymptomatic rate. In these cases, the outbreak investigation is conducted based on knowledge of the *index* case, or the first detected case. In first dengue infections close to 80% are asymptomatic, making it unlikely that the primary case is detected. Therefore, infected individuals can begin a chain of transmission that goes undetected until the outbreak is intractable. We use a 2019 dengue outbreak that occurred in a riverine town part of a longitudinal active surveillance and cohort study in Northwestern Ecuador to investigate potential undetected transmission dynamics prior to the outbreak detected by the Ministry of Health mid-May. Based on epidemiologic data shared by the Ministry of Health, the outbreak was preceded by 4 candidate *index* cases occurring on February 9th, February 13th, March 28th, and May 2nd. Using a hidden Markov model, we estimate the most likely date of the primary case. We found that the most likely date was highly dependent on the assumed case reporting fraction. For higher reporting fractions, the most likely primary case was the candidate index case that occurred the closest to the outbreak (May 2nd for the 15%, 20%, 30%, and 40% reporting fractions) and for the 7.5% and 10% reporting fractions, the most likely candidate index was March 28th. However, individual simulations suggest that earlier primary cases are possible. Surveillance systems that can detect low-level transmission events in the early stages of an outbreak can significantly reduce disease burden in both endemic and immunologically naïve settings.

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DISTRIBUTION AND DYNAMICS OF *ANOPHELES GAMBIAE* S.L. LARVAL HABITATS IN THREE SENEGALESE CITIES WITH HIGH URBAN MALARIA INCIDENCE

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Urban malaria became an important public health challenge for most African countries due to high urbanization and increasing citizen populations with issues of water dragging coupled with flooding during every year rainy season. These conditions in the highly populated cities, now threaten the progress made so far toward the malaria elimination goal of several sub-Saharan countries. To understand the case of Senegal, we assessed the distribution of larval habitats and vector population dynamics in three cities of the country where high malaria burden is often reported to identify the main malaria transmission drivers in the areas. The study was conducted between 2019 and 2020 in the health districts of Diourbel, Touba, and

Kaolack, the three most populated areas after the capital city of Dakar. Larval surveys were carried out in each of the city to locate and characterize larval habitats of malaria vectors, generate a map and assess monthly larval density until the habitat was dry. Of the 56 permanent larval habitats monitored during the rainy and the dry seasons, 80% (8/10) in Diourbel, 67% (12/18) in Kaolack and 43% (12/28) in Touba were productive throughout both seasons. Most of the larval habitats in Touba were recorded in the immediate environment of the human population; either in the used house water basins or the abandoned reservoirs, while Kaolack reported a particularity of flooded areas within the city. The data generated was meant to support the control stakeholders for evidence-based decision making and implementation of appropriate, cost-effective, and sustainable larval source management where possible to accelerate malaria elimination in eligible areas of the three cities.

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EVALUATING THE CONTRIBUTION OF *AEDES ALBOPICTUS* ON DENGUE INFECTIONS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Although *Aedes aegypti* is routinely cited as the principal mosquito vector of dengue virus, there is limited evidence base around its contribution relative to *A. albopictus*. We performed a systematic review and meta-analysis to compare the prevalence of dengue virus in *A. albopictus* and *A. aegypti* among studies simultaneously evaluating both species. We searched EMBASE, PubMed, SCIELO and Global Index Medicus databases. We performed meta-analyses using the inverse variance heterogeneity model and separated studies reporting individual and pooled mosquito data. We reported prevalence ratio (PR) to estimate the relation between *A. albopictus* and *aegypti* positivity for dengue virus. Subgroup analyses were conducted by WHO region, income level, urbanization level, and whether mosquitoes caught indoors/outdoors. The MASTER scale was used to assess risk of bias. We conducted sensitivity analyses utilising the leave-one-out technique. We included 48 studies (n=12, n=32, and n=4 among individual, pooled, and artificially-infected mosquito data). The prevalence ratio using individual (PR=0.95, 95%CI=0.40, 2.27) and pooled (PR=1.01, 95%CI=0.59, 1.73) mosquito data indicated that there was no difference in the prevalence of dengue virus between species. Subgroup analyses revealed higher prevalence of infected *A. albopictus* in upper-middle income countries (PR=1.92, 95% CI=1.03-3.58). Overall, we found substantial heterogeneity (I^2>65%) and a relative change in estimates between -14% and 16% compared to the main meta-analysis results when applying the leave-one-out technique. The risk assessment confirmed the absence of accommodating confounding variables in the evaluated studies, limiting their generalisability. Findings showed there is no clear dominance in *Aedes* species for dengue. Prevalence of infection among vectors is only one aspect in determining the relative role that these species have on dengue transmission, and our findings urge more discriminatory future studies. Disentangling their contributions will improve current and future risk assessments, and have important implications for control strategies.

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THE FEASIBILITY AND IMPACT OF INDOOR RESIDUAL SPRAYING AND LARVICIDE FOR MALARIA CONTROL IN REFUGEE CAMPS - A 10 YEAR OBSERVATIONAL STUDY IN SOUTH SUDAN

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In 2023, over 360 million people were affected by humanitarian crises, and the total forced displaced population rose to 110 million. Of these, over 75% were living in or fled to, places endemic for malaria or other vector borne diseases. South Sudan and its neighbours have experienced more than a decade of conflict, but malaria is the overwhelming cause of morbidity and mortality. Over 2.3 million South Sudanese fled and are refugees, 2 million are internally displaced, and it hosts some 330,000 Sudanese and Ethiopian refugees largely in camps managed by UNHCR. The MENTOR Initiative, has since late 2013, undertaken malaria prevention in these camps. Upper Nile State, Maban County houses Doro, Kaya, Yusuf Batil and Gendrassa - camps for 200,000 refugees. Most live in temporary shelters constructed with plastic sheeting or local materials. In response to an epidemic in 2013, despite over 95% coverage and utilization of recently distributed LLINs, MENTOR commenced annual larvicide treatment of open surface water across camps, and indoor residual spraying (IRS) of all temporary shelters to align with the wet (malaria) season (June to late November). This study presents the monthly incidence of malaria from 2013 to 2022 in the camps in direct correlation to the annual vector control activities, the timing of IRS and larvicide campaigns and the active ingredients of each. It documents increasing mosquito resistance to pyrethroid insecticides on plastic sheeting through to 2015, and the switch to IRS AI rotation using four non-pyrethroid insecticides from 2016 onwards. The results demonstrate a reduction in annual malaria incidence from peaks of 40 per 1000 with LLIN alone, to not less than 20 per 1000 with Lambda-cyhalothrin CS, and between 10-17 per 1000 population when using IRS on plastic sheeting with bendiocarb (FICAM), pirimiphos methyl (Actelic®), deltamethrin & clothianidin (Fludora® Fusion) and clothianidin (SumiShield™). IRS, with larvicide, has proven feasible
and effective for control of malaria when applied to temporary shelters made with plastic sheeting. Insecticide AI vary in level of effectiveness when used for IRS.

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KNOCKDOWN OF RIBOSOMAL PROTEIN P1 ARRESTS EGG DEVELOPMENT IN THE YELLOW FEVER MOSQUITO, *AEDES AEGYPTI*

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After taking a blood meal, the fat body of the adult female yellow fever mosquito, *Aedes aegypti*, switches from a previtellogenic state of arrest to an active state of synthesizing large quantities of yolk protein precursors (YPPs) that are crucial for egg development. The synthesis of YPPs is regulated at both the transcriptional and translational levels. Previously, we identified the cytoplasmic protein general control nonderepressible 1 (GCN1) as a part of the translational regulatory pathway for YPP synthesis. In the current study, we used the C-terminal end of GCN1 to screen for protein-protein interactions and identified 60S acidic ribosomal protein P1 (P1). An expression analysis and RNAi-mediated knockdown of P1 was performed to further investigate the role of P1 in mosquito reproduction. We show that the RNAi-mediated knockdown of P1 in adult female mosquitoes resulted in a strong, transient knockdown with observable phenotypic changes in ovary length and egg deposition. Our results suggest that 60S acidic ribosomal protein P1 is necessary for mosquito reproduction and is a promising target for mosquito population control.

7781

THE IMPORTANCE OF SCHOOLS FOR COMMUNITY EDUCATION AND ENGAGEMENT: A MEXICAN EXPERIENCE INCORPORATING IIT-SIT INTO INTEGRATED AEDES MANAGEMENT PROGRAMS

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Incorporation of IIT-SIT (combined Incompatible and the Sterile Insect techniques) as part of Integrated Aedes Management (IAM) programs is in the process of scaling-up in South-Mexico. Over the next two years, controlled mass-releases of male Aedes aegypti mosquitoes with Wolbachia will be carried out at Dengue urban hotspots in combination with activities regularly carried out (ULV, LSM) by the dengue vector control program of the Ministry of Health of Yucatan, Mexico. A strong socio-community education component is essential for the introduction, acceptance and public support of these innovations based on rear and release of mosquitoes. We describe our experience incorporating IIT-SIT into Integrated Aedes management programs in Yucatan. The initial involvement and engagement of schools was a fundamental approach that outlined further strategies to communicate to the overall community the goals and benefits of IAM with IIT-SIT. As part the activities with the school's communities - teachers, children, and parents- we developed workshops, demonstrative fairs and scientific tours. "Hand in cage" to demonstrate, interactively, that male mosquitoes do not bite and, therefore, do not transmit diseases, and scientific tours to the facilities where the mass production of male mosquitoes is carried out were very important to facilitate the education and trust of the community. The identity of the project "good mosquitoes" ("mosquitos buenos"/"uts k'oxol" in Spanish and Mayan language as a cultural-sensitive brand considering the sociocultural context) and a mascot were very important educational and promotional elements. Initial acceptance was also obtained from this specific community, who afterwards played a crucial role in the dissemination of information and awareness raising to a wider community.

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OPTIMIZING THE BLOODMEAL ALTERNATIVE, SKITOSNACK, FOR *ANOPHELES* MOSQUITOES

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Mosquitoes are reared in research laboratories to study their physiology and vector-borne disease transmission. Blood meals are necessary to maintain laboratory-raised mosquito cultures of anautogenous species. Blood is often sourced from live animals which can be costly and have a short shelf life. In addition, there are ethical, economic, and safety challenges for using blood in laboratory settings. Hence, there is a demand for alternatives to bloodmeals that are easy to use, have long shelf lives, and can effectively support mosquito culture. SkitoSnack is a blood meal replacement that has been previously developed to rear *Aedes* mosquitoes. SkitoSnack's nutritional content is analogous to that of vertebrate blood and can stimulate physiological processes in *Aedes* mosquitoes such as engorgement, oogenesis, and egg deposition. However, *Anopheles* mosquitoes do not engorge on this SkitoSnack recipe. Therefore, in this study, we modified SkitoSnack for the rearing of *Anopheles* mosquitoes. By changing single components of the original recipe, we developed several variations of this diet that are suitable for *An. stephensi* culture. We measured engorgement rates, egg numbers, and hatch rates to identify an optimized version of SkitoSnack for *Anopheles*. We present a modified SkitoSnack as a cruelty-free, sustainable, effective, and affordable blood meal alternative that can support laboratory-reared *Anopheles* mosquitoes.

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FIELD DEPLOYABLE MOLECULAR SURVEILLANCE OF MALARIA

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We present the developed a novel *Anopheles* insecticide resistance surveillance system, for deployment and use in low-income malaria endemic countries, providing an unprecedented speed, and logistics- and cost-effectiveness. Our field-deployable surveillance system is based on a battery-powered portable compact qPCR machine and a reagents preloaded cartridge with 6-month stability at ambient temperature, thereby abolishing the need for a cold-chain and electric grid. Our pilot testing has demonstrated a mosquito collection - to - insecticide resistance marker data retrieval time of 3-4 hours at rural malaria endemic conditions. Our preliminary studies have also demonstrated a promising potential for adapting our molecular surveillance system to assay other markers such as mosquito species specificity, infection status, pathogen species, and blood meal source - thereby enabling the creation of a general malaria surveillance kit where all these markers can be assayed on one, or a pool of, mosquitoes in one single cartridge in only 2-3 hours.

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IMPROVING THE USE OF MOSQUITO SCREENS AND DENGUE PREVENTION IN PONCE, PUERTO RICO

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Puerto Rico is currently experiencing a dengue epidemic with over 724 accumulated cases reported as of March 2024. The epidemic underscores the importance of implementing effective preventive measures. A collaborative project initiated by the Puerto Rico Vector Control Unit (PRVCU), in partnership with the Ponce Health Science University (PHSU), the Puerto Rico Department of Health (PRDH), and funded by the US Department of Housing and Urban Development (HUD), aims to mitigate dengue transmission by improved use of house screens to combat *Aedes aegypti* mosquitoes in Ponce, Puerto Rico. The study began in August 2023 and is slated to span over two years. The study site, facilitated through the Communities Organized for the Prevention of Arboviruses (COPA) project, comprises a cohort study of 38 clusters in Ponce, encompassing over 5,000 participants. The recruitment target of 500 households consists of 250 intervention homes with screen installations in doors and windows, and 250 unscreened homes as untreated controls. The home eligibility was first assessed by inspecting for existing doors and windows. Over 1,000 calls were made, resulting in contact with 720 participants. Of the 380 households evaluated for eligibility across 19 selected clusters, 340 were deemed eligible, with n=167 (40%) assigned to the treatment group (screening installed) and n=173 (51%) to the control group. A total of 83 households have been installed with screens, showing promising progress in the intervention implementation. Initial data suggests a notable reduction in female *Ae. aegypti* mosquito populations in screened homes compared to unscreened ones, with approximately one-third as many mosquitoes observed. Screened houses exhibited about 1/3 as many mosquitoes compared to unscreened homes (1.0 female *Ae. aegypti*/home vs 2.89 female *Ae. aegypti*/home), highlighting significantly lower dengue transmission risk in screened homes. As the dengue season progresses into late summer/early fall, we expect this difference in vector population to result in a measurable reduction in dengue cases.

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CITIZEN-DRIVEN ACTIONS FOR DENGUE VECTOR CONTROL IN ABIDJAN, CÔTE D'IVOIRE: KEY STEPS TOWARDS A MULTISECTORAL AND COMMUNITY MOBILIZATION

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In Côte d'Ivoire, the governmental dengue outbreak responses based on a top-down approach have often failed to sustain *Aedes* vector control. We describe key steps towards initiating and implementing a bottom-up citizen action for a sustainable control of *Aedes aegypti* in Anono and Gbagba in Abidjan, Côte d'Ivoire. We held multisectoral workshops coupled with entomological, environmental and social data collections to inform the citizen-led clustered-randomized controlled trial (cRCT) based on larval source management (LSM) and Biogents Gravid *Aedes* Traps (BG-GATs). This trial has four study arms: 1) LSM, 2) BG-GAT, 3) LSM + BG-GAT and 4) Control arms. It has 40 clusters, with 10 clusters per study arm. We held an initial kick-off workshop together with scientists, stakeholders and community leaders to present the study objectives and collect their feedbacks and a second workshop with the same participants in the study areas to identify enabling factors and barriers to an effective control of *Aedes* and dengue. We carried out workshops including 30 community members divided into three groups of 10 people in each study area and invited them to identify and classify any problems and solutions related to mosquitoes, dengue, sanitation and water management and indicate local priorities, needs, contributions and expectations. In parallel, we sampled *Aedes* mosquitoes and breeding sites and community knowledge, attitudes and practices regarding *Aedes*, dengue, water and solid waste risk and management. Data showed that *Ae. aegypti* was the most abundant vector, and discarded cans, tires and water storage containers were key breeding sites. Dengue risk was very high and associated with a poor management of water and solid waste. We co-designed and amended the trial protocol according to the workshop feedbacks and collected-field data. We allocated treatments to the study arms and trained community supervisors who, in turn, mobilized and trained the residents to enable them to control *Aedes* larvae and adults. This stepwise and inclusive model can build up local capacities, improve community adherence and sustain dengue vector control in Anono and Gbagba.

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SILENCING *ANOPHELES STEPHENSI*

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Anopheles stephensi, a highly competent vector of malaria parasites, is rapidly spreading across the globe. The ecological plasticity of this highly invasive mosquito allows it to thrive in urban as well as rural habitats, making it a significant threat to millions of people who live in cities, and the discovery and implementation of novel strategies to support existing vector control interventions is therefore critical. RNA interference (RNAi)-based gene silencing using *Saccharomyces cerevisiae* (baker's yeast) as the RNA expression and delivery system facilitates the custom design and use of environmentally safe pesticides that specifically target essential genes for mosquito development and survival. This study investigates the hypothesis that RNAi yeast insecticides designed to silence essential genes in *A. stephensi* can kill both larvae and adult mosquitoes without harming non-target arthropods. In this investigation, we evaluate the Sh.463 RNAi yeast insecticide, which recognizes a conserved site in mosquito *Shaker* genes that is not found in non-target organisms. Consumption of heat-inactivated and dried RNAi yeast by *A. stephensi* larvae resulted in significant larval mortality in laboratory trials conducted in small containers. We are now optimizing formulations and strategies for the use of this yeast insecticide in large barrel-sized containers, the most productive *A. stephensi* habitats in urban locations. Additionally, the delivery of Sh.463 yeast to *A. stephensi* adults in the form of attractive targeted sugar baits (ATSBs) resulted in highly significant mortality in laboratory trials. We are presently evaluating the potential for delivering this yeast to mosquitoes in a highly attractive soda-based ATSB system. The next steps include the pursuit of outdoor semi-field and field trials at multiple field sites with the long-term goal of incorporating these new vector control interventions into mosquito control programs worldwide.

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HIERARCHICAL BOOSTED REGRESSION MODELS FOR PREDICTING EASTERN EQUINE ENCEPHALITIS VIRUS PRESENCE/ABSENCE IN MOSQUITOES IN UNSAMPLED AREAS

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Using mosquito and arbovirus data from the Connecticut Agricultural Experiment Station's (CAES) statewide mosquito and arbovirus surveillance program (2001 – 2020), we modified a state-wide risk projection pipeline originally developed for West Nile virus (WNV) to project risk of detecting Eastern Equine Encephalitis virus (EEEV) in mosquitoes. We used boosted regression tree (BRT) methodologies to first develop predictive algorithms of *Culiseta melanura* collections in light traps based on climate data (including lagged values for prior fall), land cover variables, and hydrology data indicative of ground wetness; these algorithms were then nested within a BRT algorithm of EEEV detection probabilities. Results of the EEEV prediction models were averaged to within 5 km of a currently operational surveillance site and then successfully validated against observed EEEV detection rates in mosquitoes sampled in 2021 – 2023. Overall, our EEEV detection predictions explained a significant amount of variance in our mosquito surveillance data. The over-arching goal of this research was to develop more targeted risk maps of EEEV that will allow CAES' public health partners to estimate arbovirus risk at locations not explicitly sampled by the surveillance network. The utility of these risk maps was evaluated during the 2024 surveillance season using qualitative surveys and improvements to these risk communication strategies are discussed.

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POPULATION GROWTH AND MALARIA TEST POSITIVITY RATE IN NIGERIAN'S URBAN SETTLEMENTS

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Rapid urbanization in Nigeria, fueled by population growth, has led to an increase in informal and slum settlements. Although urban areas still present lower transmission relative to rural regions, the scale of urban population expansion means that even low prevalence can translate into a substantial malaria burden. This study analyzes wet season data from Ibadan to understand the dynamics of malaria prevalence in the context of urban growth and highlights the factors that facilitate malaria transmission across different urban settlements. Settlements in selected Ibadan wards were classified into formal, informal, and slum categories. We used data from the field study and secondary sources to compute the weighted Test Positivity Rate (TPR) of malaria by settlement type. Selected variables from the field study were employed in principal component analysis (PCA) to derive proxies for household wealth (WI) and the Water, Sanitation, and

Health (WASH) performance index. Variables such as WI, WASH, net use and presence, insecticide-treated bed nets (ITNs), and age were used to estimate unadjusted and adjusted odds ratios using logistic regression models. Findings reveal that the highest TPR was in slum areas, at approximately 12%, compared to formal and informal settlements. The age group with the highest TPR varied by settlement type, with children aged 10-17 in formal (17.2%) and slum (25.9%) settlements exhibiting high rates, while those aged 5-10 had high rates in informal settlements (12%). Multivariable logistic regression highlighted a strong negative association between WI and malaria burden across all settlement types, with the odds ratio being 0.8 (0.72-0.9) in informal and slum settlements and 0.7 (0.6-0.9) in formal settlements. The TPR in informal and formal settlements was the same, suggesting that factors beyond simple urban categorization influence malaria transmission. This research emphasizes the importance of addressing malaria with a multifaceted approach that considers the specific needs and characteristics of various urban settlement types in Nigeria, as the country continues to urbanize at a high rate.

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EXAMINING THE IMPACT OF TRANSFLUTHRIN-TREATED EAVE RIBBONS IN A HOLOENDEMIC MALARIA SETTING IN ZAMBIA

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Despite a decade of intensive indoor residual spray and insecticide-treated net campaigns, malaria remains holoendemic in Nchelenge District, Zambia. Insecticide resistance and outdoor biting among the major vectors, *Anopheles funestus* and *An. gambiae*, present challenges for malaria control in this region. This study was designed to test the efficacy of a spatial repellent tool in this high transmission setting with entomological outcomes including indoor and outdoor anopheline abundance, resting blooded rates, and human biting rates. Two clusters of 50 households were identified, and one was selected to have ribbons impregnated with transfluthrin hung the eaves outside of their homes, while the other received no intervention beyond national programmatic control efforts. Twenty households from each cluster were selected to receive entomological surveillance for 3 months prior to installation and were followed for 9 months post-installation. At baseline, control and intervention households did not differ significantly in anopheline abundance indoors or outdoors from any collection method. We hypothesize that these ribbons will reduce overall indoor and peri-domestic abundance in treated households, leading to reduced contact with humans and pathogen transmission.

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FACTORS ASSOCIATED WITH INSECTICIDE-TREATED NET OWNERSHIP BEFORE A MASS DISTRIBUTION CAMPAIGN IN ANAMBRA STATE, NIGERIA

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Until recently, the coverage of insecticide-treated nets (ITNs) in Anambra State, Nigeria, has not achieved recommended levels. In 2015, a year after an ITN campaign, 75% of households in the State had one or more ITNs. However, in 2021 this had declined to 27%. Understanding where people get their nets in the absence of campaigns and factors associated with access to ITNs is important for designing appropriate strategies to sustain coverage. In 2022, prior to the ITN campaign, we conducted surveys to investigate the relationship between source of nets and ITN access rates. A multi-stage stratified cluster sampling design was used to select households in 48 wards in Anambra State, in southeastern Nigeria. Stratification was by rural-urban residence and level of security risk (high and low). Data were gathered through household interviews. The data were analysed using Stata version 16, confidence interval and chi square statistics were employed. ITN ownership in Anambra State was low, with only 13.2% of households owning one or more ITNs before the campaign. Only 9.5% of the de facto population had access to ITNs within their households. Several factors were significantly associated with household ownership of one or more ITN ($p<0.05$): educational level of household head (none 8.5% vs higher 23.7%), rural-urban residence (rural 22.9% vs urban 11.2%), security risk profile (low 21.3% vs high 10.3%), and socio-economic status (SES) (low 9.6% vs high 26.5%). The majority of existing nets were obtained from antenatal care clinics or health facilities and schools. This study showed that alternative ITN distribution channels could play a vital role in maintaining high levels of ITN ownership between campaigns, but may not be sufficient to sustain high levels of ITN coverage without campaigns. Educational level, rural-urban residence, and SES are important factors associated with household ownership of nets. These factors should be considered when planning and implementing continuous distribution strategies to ensure equity in ITN ownership.

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IMPROVING LLIN DISTRIBUTION STRATEGIES IN THE DOMINICAN REPUBLIC TO ACHIEVE ELIMINATION: INSIGHTS FROM LLIN POST-DISTRIBUTION MONITORING

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In pursuit of malaria elimination, the Dominican Republic has implemented targeted LLIN distributions in recent years. However, the absence of post-distribution monitoring for the past decade has hindered intervention optimization. In 2023, the Ministry of Health, with support from CHAI, conducted a cross-sectional household survey in the country's two primary malaria foci, which collectively account for 95% of cases. Results reveal significant gaps in LLIN coverage and utilization, evident as early as 5 months post-distribution, and suggest that the low coverage can be due to inadequate LLIN quantification. Moreover, suboptimal LLIN washing and storage practices were observed in both foci, indicating that bioefficacy could be compromised. This session will unveil the survey findings and explain how they are being used to improve LLIN quantification and distribution strategies in the country. By addressing identified deficiencies, this initiative aims to bolster LLIN effectiveness and contribute to help the Dominican Republic achieve malaria elimination.

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NAVIGATING UNCERTAINTY - FORECASTING GLOBAL TRENDS IN MALARIA VECTOR CONTROL COMMODITIES

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In the global strive towards the elimination of malaria, vector control commodities are the cornerstone of control, yet find themselves at a critical juncture. With emerging guidelines shaping the evaluation and implementation of vector control tools and market dynamics poised for continued rapid change over the next five years, uncertainty exists over the future of insecticide-treated nets and insecticides for indoor residual spraying. The challenge of predicting market trends is also exacerbated by the current global funding constraints, at a time when the population at risk

of malaria is continuing to grow rapidly. The Global Malaria Commodities Forecasting Project, led by the Clinton Health Access Initiative and informed by a global consortium of partners, aims to generate consensus on market trends and predict the impact of external factors on the procurement of commodities for malaria control. In this work, the new iteration of the short-term forecast for ITNs and IRS is presented for 2023-2025. Budgets were allocated according to available data shared by procurement partners and between the three types of ITNs on the market: Standard pyrethroid bed nets, piperonyl butoxide (PBO) and dual active ingredient bed nets. Remaining budgets and ITN volumes were allocated according to insight from partners into country-level decision making which underpin assumptions that drive the uptake of dual AI ITNs. Outputs will show forecasted global vector control commodity volumes under baseline and assumption-based scenarios. Outputs will incorporate available budgets and sub-national tailoring strategies. Both ITN and IRS volumes will be presented by product type and class and any ITN coverage gaps will be presented, according to historical volumes. Despite the global vector control market and elimination efforts being under threat from several factors, the use of forecasting methodologies and global partnerships can help to identify potential funding and resource allocation gaps and assist in navigating the uncertainties in the future. This coordination will be essential as new commodities enter a rapidly evolving and uncertain market.

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LQAS: A METHOD TO MONITOR LLINS AFTER HIGHLY TARGETED DISTRIBUTIONS IN ELIMINATION SETTINGS

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LLINs are widely used in countries approaching malaria elimination, sometimes as the main or sole vector control intervention, however little is known in many of them about their performance among local at-risk populations. This is because commonly used methods to understand LLINs performance post distribution (e.g. MIS, DHS, MICS, durability monitoring) are rarely implemented in these settings due to their high cost compared to the budgets and capacities of most of these countries. Understanding LLIN performance is, however, critical to improve and optimize vector control programs, ensuring that effective vector control is implemented to achieve malaria elimination. With the aim to provide countries in the Americas with an unexpensive practical method to understand LLIN performance post distribution, PAHO developed an LQAS-based monitoring methodology. With CHAI and CDC support, the Honduras Ministry of Health and the Panama Ministry of Health piloted the methodology in the country's main malaria foci where no or little LLIN monitoring data had previously been collected. In this session we will present the method, the results and lessons learned from implementing it in Honduras and Panama, as well as progress and prospects for the implementation of this methodology in other countries. Beyond supporting countries in the Americas, this method can support any resource-constrained countries to obtain valuable information on LLINs to guide their vector control programs.

7794

MALARIA VECTOR POPULATION DYNAMICS <AND> *PLASMODIUM* TRANSMISSION IN PENKA-MICHEL, WESTERN HIGHLANDS OF CAMEROON

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Malaria remains a major public health concern in Cameroon. Understanding vector distribution and disease transmission dynamics is critical to evaluate the performance of control strategies. We performed a longitudinal study from September 2023 to March 2024 in Penka-Michel, a highland site in Western Cameroon. Human landing catches (HLC) were performed monthly from 6pm-9am indoors and outdoors, during 3 consecutive nights in randomly selected houses using 12 collectors per sampling period. All collected *Anopheles* were identified to species and tested for sporozoites. Spearman's correlation and canonical correspondence (CCA) analyses were used to explore associations between species abundance, rainfall, temperature, humidity and mosquitos' infection rate. Shannon-Weiner index and Simpson's dominance indices were calculated for all collected mosquito species. Overall, 3171 *Anopheles* representing 5 distinct species were identified as *An. gambiae*, *An. coluzzii*, *An. funestus*, *An. leesoni* and *An. ziemanni*). Members of *An. gambiae sl* and *An. funestus sl* were predominant throughout the collection period with a peak in September (relative density: 68.05% and 27.38% respectively). The population density decreased significantly between December and February, coinciding with peak temperature (28.5°C) and relative humidity (61%). Rainfall (r=0.931; p-value<0.05) and relative humidity (r=0.761; p-value=0.024) were the most significant factors influencing mosquito density. *An. gambiae sl* exhibited the highest species diversity (Shannon-Wiever: 0.103) and dominance (Simpson's index: 0.491). *Anopheline* biting behavior increased rapidly from 3 b/h/n in February to 48 b/h/n in September. Only *An. gambiae, An. funestus* and *An. ziemanni* were found infected with sporozoites. Infection rates were respectively 5.3% (39/729), 2.8% (20/729) and 1.09% (8/729) for *Plasmodium falciparum, P. malariae* and *P. ovale.* Our study revealed changes in mosquito composition and density due to climatic conditions, along with a fluctuation in mosquito infection rate by season. Effective vector control in the region will require continuous surveillance

7795

THE ROCKIES AND HIGH PLAINS VECTOR-BORNE DISEASES CENTER (RAHP VEC)

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The Rockies and High Plains Vector-borne Diseases Center (RaHP VEC) was formed in 2023, funded under a 5-year cooperative agreement with the U.S. Centers for Disease Control and Prevention to form regional training and evaluation centers (TECs). RaHP VEC encompasses a region including the states of CO, NM, UT, WY, and the TX panhandle. The primary goals of the center are to contribute to training of future and potential vector control and public health personnel in this region, evaluate the capacity and needs of vector control and public health operations, evaluate mosquito and vector control measures implemented regionally, and form partnerships to facilitate the above goals build frameworks for cooperation and collaboration moving forward. Here, we will report on our operations from the first year, with the first active season to take place during the summer of 2024. This includes training workshops and webinars, training internships placed in our region, efforts to coordinate surveillance mapping

and communication, promote integrated pest management practices/ action threshold-based vector control, and provide technical and laboratory assistance for insecticide resistance and pathogen testing. We will also describe upcoming graduate and undergraduate degree certificates that will soon be available from two institutions in our region, the potential for expanding to additional institutions, and efforts to evaluate how our program is meeting and achieving educational and training goals.

7796

RETHINKING LLIN QUANTIFICATION METHODS FOR ENHANCED MALARIA CONTROL: INSIGHTS FROM CENTRAL AMERICA

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WHO recommends using a ratio of 1.8 people per net to quantify the LLINs needed for mass campaigns, unless data to inform a different quantification ratio are available. This 1.8 ratio has been widely adopted to plan mass campaigns, including in Central America. However, an analysis of extensive data from Central American countries has revealed a varied reality where the average number of individuals per sleeping space ranges from 1.2 to 1.8. This discrepancy underscores the potential for substantial coverage gaps if the 1.8 ratio is applied. Drawing upon data from Guatemala, Honduras, Panama, Haiti, and the Dominican Republic, we demonstrate the diverse rates of individuals per sleeping space prevalent in the region. Considering the paramount importance of maintaining high vector control coverage for effective malaria control and elimination, standard LLIN quantification practices should be revised to draw on available data, or rapid household surveys should be conducted, to calculate the right ratio of people per net. This proactive approach not only addresses the specific needs of Central America but also serves as a model for enhancing LLIN coverage globally.

7797

REGIONAL VARIABILITY IN THE RELATIONSHIP BETWEEN PRECIPITATION AND DENGUE INCIDENCE IN BRAZIL: INSIGHTS FROM BIWEEKLY TIME SERIES ANALYSIS

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Dengue fever presents a complex public health challenge influenced by various environmental factors, with precipitation being a key component in vector breeding and transmission dynamics. This study aims to elucidate the temporal relationship between precipitation and dengue incidence across different Brazilian regions.Utilizing biweekly data from 1999 to 2014, we conducted a time series analysis incorporating STL decomposition and cross-correlation functions (CCF) to explore seasonal patterns and lagged relationships between precipitation and dengue incidence. The analysis was stratified by region to capture local variations.Our analysis revealed significant regional variability in the timing and strength of the relationship between precipitation and dengue incidence. The Centro-Oeste region showed a peak correlation at an 8-biweek lag, while the Nordeste region exhibited a longer lag of 30 biweeks. The Norte region presented the strongest correlation at a 27-biweek lag, suggesting a substantial delay in the impact of precipitation on dengue cases. The Sudeste and Sul regions demonstrated moderate correlations with 11 and 37 biweek lags, respectively. These findings indicate potential shifts in dengue seasonality and underscore the influence of regional climatic patterns on disease transmission.The study highlights the importance of regional climate variations in predicting dengue incidence and suggests that precipitation is a significant but variably timed predictor across regions. The observed shifts in correlation lags may reflect changes in dengue seasonality, with implications for enhancing surveillance and targeted intervention strategies. Future research should integrate additional environmental and socio-economic factors to develop a more comprehensive predictive model for dengue outbreaks.

7798

SPATIALLY REFINED ESTIMATES OF THE RISK OF WEST NILE VIRUS

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Since its introduction in 1999, West Nile virus (WNV) has established itself as the leading domestically acquired arbovirus in the United States. Transmission is driven by *Culex spp.* mosquitoes who predominantly feed on birds but also on mammals in the late summer, resulting in West Nile virus spillover events in humans. In 2022, New York City experienced its worst recorded human WNV spillover event. Mosquito abatement districts attempt to prevent these spillover events by disrupting WNV transmission patterns through larvicide and adulticide applications; thus, it is essential to understand the spatial risk of WNV for more targeted interventions. This presentation will report the results of a Bayesian model that combines global and local data together to understand infection rates more accurately at the local scale. Here, we combine the global, city-wide prevalence of infected mosquitoes, along with the local, United Hospital Fund (UHF) zone's prevalence of infected mosquitoes, to improve our estimates of mosquito infection rates at the local spatial scale, defined as UHF zones. We validate our model performance by examining the correlation between the mosquito infection rates and the reported annual number of human cases. Overall, the city-wide prevalence of infected mosquitoes to human cases has a strong positive correlation of infected mosquitoes to reported human cases r=0.74 (p=0.0001). However, as the spatial scale is finer the correlation of infected mosquitoes to reported human cases decreases where the UHF zone is weakly correlated r= 0.29 (P = 0.00001). Combining the local UHF zone mosquito infection data, which has high uncertainty, with the city-wide prevalence data to calculate the UHF zone infection rate, the algorithm is able to improve the correlation of infectious mosquitoes to human cases to moderate, r=0.35 (p=0.00001). This work provides a foundation for implementing a statistically rigorous system to maximize mosquito monitoring data for real-time spatial risk of arboviruses.

7799

HIGH-THROUGHPUT SCREENING OF BIO-INSECTICIDES AGAINST MOSQUITO VECTORS

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The increasing use of chemical insecticides always leads to resistance. Bio-insecticides, as eco-friendly, cost-effective alternatives, are not likely to encounter resistance. In this study, we extracted and grew bacteria from 48 different soil samples collected in Puerto Rico, obtaining 510 different colonies and performing high throughput larval bioassays. We have identified 15 colonies exhibiting mortality rates ranging from 80% to 100% against mosquito larvae after 24 hours of incubation (*Aedes aegypti Liverpool*, *Culex quinquefasciatus*, and *Anopheles stephensi*). We further conducted experiments to determine the growth conditions for these 15 selected bacteria to boost their optimizing toxicity against mosquito larvae. So far, we found that for *Serratia.marcescens* when they are grown on YPD

medium at 28 degrees Celsius aerobically for 2 days, they show the highest mortality rate towards Aedes Liverpool larvae. *Citrobacter.freundii* grown aerobically for one day followed by anaerobically for 3 days on LB medium at 28 degrees show the highest killing ability towards Aedes Liverpool larvae. Interestingly, for *Acinetobacter*, the optimal conditions would be on LB medium at 28 degrees Celsius no matter whether they are grown aerobically or anaerobically. In the future, we will continue experimenting with the remaining selected bacteria to develop a formula suitable for large-scale industrial production.

7800

DEVELOPMENT AND EVALUATION OF PCR-BASED DETECTION OF *W*MEL IN *AEDES AEGYPTI* EGGS FOR USE IN LARGE SCALE MONITORING OF *WOLBACHIA*-BASED INTERVENTIONS FOR ARBOVIRAL DISEASES

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Wolbachia-based vector control interventions have shown to be effective in reducing the risk of arboviral infection and are being evaluated for WHO prequalification. However, release of *Wolbachia* (*w*Mel)-positive *Aedes aegypti* requires labor- and cost-intensive monitoring of adults with BG-Sentinel traps or less costly monitoring of hatched larvae with oviposition traps to evaluate long-term introgression into local populations. Performing *Wolbachia* detection assays directly on eggs collected from oviposition traps poses a more efficient, timely method of monitoring to increase the scalability of the intervention. We aimed to develop a single egg-based DNA extraction and qPCR method for *w*Mel *Wolbachia* detection and *Aedes* species differentiation. We developed and optimized our method by testing several qPCR assays and variations of DNA extraction methods assays in single *Aedes* eggs. We then validated our method in three steps: in defined mosquito populations, in artificially-pooled mosquito populations, and by comparing results from eggs to those from larvae. Our single egg-based DNA extraction and qPCR protocol showed high sensitivity in identifying *w*Mel-positive *Ae. aegypti* (98.43%), *w*Mel-negative *Ae. aegypti* (99.20%), and *Ae. albopictus* (96.97%) eggs, and 100% specificity. Accuracy was high at levels of *w*Mel *Wolbachia* prevalence varying from 0 to 100%, which is crucial for detection in a real-world *Wolbachia* release setting. When comparing our egg-based method to results obtained from larvae collected in trapping sites from Belo Horizonte, Brazil, we found a high correlation in prevalence estimates of *w*Mel-positive *Ae. aegypti* (Spearman rank $r = 0.87$, $p<0.001$) and *w*Mel-negative *Ae. aegypti* (Spearman rank $r = 0.87$, $p <0.001$). These findings indicate that the method of PCR detection of *w*Mel *Wolbachia* detection and *Aedes* species differentiation in a single egg presents a highly accurate, faster, and less resource-intensive method of monitoring *Wolbachia* in areas where oviposition traps are being used.

7801

EFFECTS OF BIOLOGICAL CONTROL OF MOSQUITO LARVAE: A META-ANALYSIS

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Control of vector-borne diseases such as malaria is threatened by the emergence and spread of insecticide resistance and other aspects of anthropogenic global change. There is an urgent need to expand the vector control toolbox beyond the current major interventions that are largely insecticide based. Biological control of mosquitoes using predators, parasites and pathogens is an age-old method whose use for large-scale mosquito control is underutilized. Empirical research and reviews have largely focused on single natural enemy species and their impact on larval mosquito populations rather than examining the efficacy of multiple control agents or effective communities of antagonistic species. We conducted a meta-analysis of published research to comprehensively quantify the effect of antagonistic species including predators, competitors, parasites and pathogens on mosquito larvae across all habitats. Our literature search resulted in a total of 474 effect sizes that were included from 50 studies that met the inclusion criteria: 43 competitor, 13 fungal pathogen, 2 parasite, 410 predator, and 6 viral pathogen effects. Based on Bayesian hierarchical meta-analysis models, all interactions (predator, competitors and pathogens) showed negative effects on mosquito larvae with the highest effects under field and natural conditions compared to laboratory conditions. Posterior mean beta (β) and credibility interval: predators ($\beta = -0.556$, CI = -0.855 to -0.26), natural habitats ($\beta = -2.422$, CI = -2.905 to -1.932), field studies ($\beta = -1.143$, CI = -1.54 to -0.766) and laboratory studies ($\beta = -0.413$, CI = -0.712 to -0.11). The strong negative effects in natural and field studies could be due to the increased structural complexity they offer which previous studies have found to affect direct and indirect community interactions with a resultant effect on mosquito larvae. Diversity in community interactions involving predators, competitors and parasites is essential for effective mosquito control using biological approaches.

7802

STAKEHOLDER-INFORMED DEVELOPMENT OF MICROSPORIDIA MBITA BASED MALARIA CONTROL INTERVENTION

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Sub-Saharan Africa accounts for 93% of global malaria deaths. The main preventive strategies for malaria control include the use of insecticide-treated nets (ITNs) and indoor residual spraying (IRS). However, even a complete implementation of these strategies cannot entirely halt malaria parasite transmission due to insecticide resistance and the increasing tendency of Anopheles to feed early and outdoor. A novel and improved strategy is the Microsporidia MB-based control which impairs the development of plasmodium in Anopheles and would potentially involve the release of Microsporidia MB spores or Microsporidia MB-positive males or both sexes in the environment. Although Microsporidia MB is naturally occurring a generally low acceptance from the public is anticipated unless communities are involved earlier. The study explored perspectives on malaria risks, current malaria prevention strategies and possible concerns, opportunities towards the implementation of *Microsporidia MB*-based control strategy in five Counties in Kenya with diverse cultures and malaria epidemiology. We conducted 12 Key informants' interviews with purposively sampled malaria control implementers. Data was digitally recorded, transcribed verbatim and coded using thematic framework analysis. Malaria was identified as a leading public health problem. Local Malaria related problems were found to be inaccessibility to health facilities, inadequate Health Care workers and commodities , unaffordability of medicine and prevailing cultural practices & behaviors and low literacy levels which delayed treatment seeking. The aspects of current malaria control methods that need strengthening were revamping surveillance and domestication of national strategic plan for malaria eradication. Majority were unaware of the MB strategy with their concerns of environmental and human safety, release site criteria and community willingness to adapt. There is an opportunity to co-develop the communication strategy that can inform institutional and community trust to promote acceptability of the potentially new strategy for malaria eradication.

7803

IDENTIFICATION OF DENGUE HOTSPOTS IN ENDEMIC REGIONS OF PERU. A SPATIAL ANALYSIS

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Dengue transmission risk exhibits heterogeneity in both spatial and temporal dimensions. To identify areas that significantly contribute to transmission and serve as potential outbreak origins, our objective is to examine the temporal persistence of dengue transmission hotspots in endemic regions of Peru spanning from 2011 to 2023. Moreover, we aim to characterize the spatial distribution of these hotspots during the 2023 epidemic. We analyzed symptomatic dengue cases from regions with a high disease burden (i.e., the top upper quartile) in Peru from 2011 to 2023. In this spatial analysis, cases were aggregated at the district level. The Getis-Ord Gi* statistics were used to show dengue disease patterns, including areas of high prevalence (hot spots) and lower prevalence (cold spots). We estimated transmission persistence, using the sum of the years that each district was considered a hotspot per month. Furthermore, we evaluated the monthly distribution of hotspots throughout 2023, prompted by a significant upsurge in dengue cases, precipitating an epidemic. A total of 428,090 clinically apparent dengue cases in endemic regions were reported to the Peruvian health system during the study period. Evidence of transmission heterogeneity was present across all regions. We identified districts within each region with persistent DENV transmission for up to 11 years, concentrated primarily in their central areas. Altogether, the hotspot areas contained 49,95% (213,814) of all cases within 32,78% of the region's 302 districts. During the 2023 epidemic, 196,193 dengue cases were documented in the regions with the highest burden. With different zones becoming active at different times of the year.

7804

ASSESSING THE RESIDUAL EFFICACY OF PYRIPROXYFEN-BASED LARVICIDES FOR THE CONTROL OF THE INVASIVE MALARIA VECTOR *ANOPHELES STEPHENSI* IN ETHIOPIA

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The application of larvicides is a vital component of larval source management (LSM) for the control of *Anopheles stephensi,* an invasive malaria vector in Ethiopia. A key consideration for LSM implementation includes assessing the residual efficacy of larvicides, as this data may be used to inform operational feasibility and costs. The residual efficacy of two pyriproxyfen-based insect growth regulator larvicide formulations, SumiLarv® 2MR and SumiLarv® 0.5G, and one bacterial larvicide, VectoBac® WG, were evaluated against the aquatic stages of *An. stephensi* under field and experimental settings in Dire Dawa, Ethiopia for one year. Larvicides were directly applied to water-containing drums (capacity of 230 liters) and community cisterns (capacity ranging from 262,5-11,261 liters) at manufacturer-recommended doses: one 2-gram disc of SumiLarv® 2MR per 200 liters, 0.4 g SumiLarv® 0.5G per 200 liters and 0.5 g VectoBac® WG per 200 liters of water. A total of 50 third instar *An. stephensi* larvae were placed in two floating cages and exposed every 7 days for the VectoBac® WG and every 30 days for SumiLarv 0.5G, and SumiLarv® 2MR. Additionally, larvae were exposed on Days 1, 2 and 4 for VectoBac® WG due to the short residual efficacy, and the number of dead larvae and pupae were monitored for four to six days. For the two pyriproxyfen-based products, adult emergence inhibition was assessed with live pupae transferred from floating cages to glass cups and adult emergence monitored in mosquito cages every 24 hours until no alive pupae remained. Product and operational costs were also estimated. The results show that SumiLarv® 2MR inhibited 96-100% *An. stephensi* adult emergence for 11 months in both drums and cisterns but reduced to 79-86% after the 12th month. SumiLarv® 0.5G inhibited the emergence of adult *An. stephensi* for six weeks. On the other hand, VectoBac® WG showed very short residual efficacy with mortality of 31% after 48 hours. The findings showed promising larvicide products that are shown to control *An. stephensi* longitudinally in certain settings, creating potential response opportunities to invasive *An. stephensi* in Africa.

7805

TREND MALARIA PREVALENCE AND ASSOCIATED RISK FACTORS AMONG SCHOOL CHILDREN IN MAINLAND TANZANIA, BETWEEN 2015 AND 2023; A MULTILEVEL ANALYSIS OF SCHOOL MALARIA AND PARASITE SURVEYS

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Abstract Schoolchildren play an important role in malaria transmission. Malaria infections can be asymptomatic or present with symptoms which may contribute to anaemia, severe illness and fatal malaria. This analysis provides trends of malaria prevalence and associated risk factors among school children in mainland Tanzania. Data for this analysis were obtained from nationwide school malaria surveillance conducted every other year from 2015 to 2023. A total of 307,999 school children aged 5 - 16 years old from 876 public primary schools were tested for malaria infection using rapid diagnostic tests, assessed for malaria control intervention coverage and other malaria-related parameters. A multilevel mixed-effects logistic regression model was used to assess associated risk factors. Overall malaria prevalence was 21.6% (95%CI: 21.3 - 22.0) in 2015 which progressively decreased to 11.8% (95%CI: 11.5 - 12.0 p <0.001) in 2021 with no significant change in the overall malaria risk between 2021 and 2023 (AOR 1.32, CI: 0.92 - 1.81, p=0.08). School children aged between 9-12 years and 13-16 years had 20% higher risk of malaria (95% CI: 1.15 - 1.25) and 21% higher risk of malaria (95% CI: 1.16 - 1.27), respectively, compared to those aged between 5-8 years. Geographically, children from the Lake zone had the highest odds of prevalence (AOR: 18.75; 95% CI: 12.91 - 27.23) compared to the Central zone, and sleeping under an insecticide-treated net demonstrated a protective effect (AOR=0.68, 95%CI: 0.64-0.72, p < 0.001). There was a significant decline in the prevalence of malaria infection across the study period. We presented a countrywide active surveillance data, collected over time and in different settings which are unique and seldom presented. We believe various stakeholders will use our findings and join force to combat malaria not just in Tanzania but, in all malaria endemic countries.

7806

THE IMPACT OF INSECTICIDE TREATED NET USE ON MALARIA PREVALENCE AMONG SCHOOL-AGED CHILDREN IN MAINLAND TANZANIA

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Tanzania aims to achieve an ITN coverage of above 85% by 2025 through mass and continuous distributions including the school net program (SNP) and reproductive child health (RCH). Despite these efforts, there is a paucity of data on the impact of ITN use, particularly among school-age children (SAC). This analysis used data from the School Malaria Parasitological Surveys (SMPS) of 2017 and 2021 to assess the impact of mosquito bed net use on malaria infection in SAC in Mainland Tanzania. SMPS is a biennial school-based surveillance involving children aged 5-16 years in public primary schools, covering a sample of representatives 650 schools selected from all 26 regions and 184 councils of mainland Tanzania. A multilevel mixed-effect logistic regression model adjusted for individual and household factors was constructed to determine the impact. The overall malaria prevalence decreased from 15.8% (2017) to 11.8% in the 2021 SMPS. The proportion of mosquito bed net users among malaria-infected children was higher at 83.9% in 2017 compared to 69.1% in 2021. Among mosquito bed nets users, female children were less likely to have malaria infection compared to males (AOR=0.80(0.77-0.84), p.<0.001) in 2017, and the odds decreased further (AOR=0.78(0.71-0.85), p.<0.001) in 2021. Using mosquito bed nets showed an almost two-fold lower risk of infection in young children (5-8 years) compared to older children (13-16 years) in both surveys (AOR=1.51(1.40-1.63), p.<0.001 in 2017 and (AOR=1.80(1.58-2.05), p.<0.001 in 2021). Also, the risk of malaria infection was higher among bed net users within large family sizes (AOR=1.91(1.79-2.05), p.<0.001) in 2017 and (AOR=1.56(1.37-1.78), p.<0.001 in 2021) compared to those within the family size of fewer than 7 members. Using bed net showed a significant protection against malaria infection. However, the risk of malaria increased with increasing age of SAC and family size. Thus, efforts to maintain the availability of mosquito bed nets in large families and improved use among older SAC are crucial.

7807

POPULATION GENOMICS OF AN INVASIVE MOSQUITO VECTOR, *AEDES AEGYPTI,* IN SOUTHERN NEVADA

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Aedes aegypti mosquitoes, known vectors for dengue, Zika, and chikungunya viruses, have rapidly spread across Clark County, Nevada since 2017, prompting a need for a robust public health response. Within a short period, this mosquito species has established itself across over 30 zip codes in Clark County. Recent cases of dengue in California (188 in 2023) and Arizona (32 in 2023), as confirmed by the CDC, as well as dengue virus positive *Ae. aegypti* specimens in Arizona, demonstrate the importance of this invasive vector species in Nevada. Strong capacity for ecological adaptation in *Ae. aegypti* could significantly expand its regional geographical distribution and disease outbreak potential. Population structure analysis can identify introduction sources and be used to guide prevention and mitigation efforts. Fifty-two *Ae. aegypti* mosquito samples were collected across 18 zip codes in Clark County by the Southern Nevada Health District. Whole genome sequencing analysis was performed using an optimized pipeline based on FastQC, Trimmomatic, Bowtie2, IGV, Samtools and GATK programs. Unsupervised hierarchical clustering was performed to group individuals based on their genetic similarity using Python and R. Population structure and adaptation potential were investigated using a multi-pronged statistical approach. Principal Component Analysis (PCA) identified major axes of genetic variation. Additionally, Bayesian analyses pinpointed loci under selection, potentially associated with adaptation to the subtropical hot desert climate of southern Nevada. Preliminary analysis of *Ae. aegypti* samples identified 86 genes implicated in environmental adaptation with one or more local topo-climatic variables. Two genetic clusters were evident among 52 individuals, indicating two separate introductions into Southern Nevada from genetically distinct populations. Study findings provide a comprehensive baseline of *Ae. aegypti* genetic diversity for prospective longitudinal monitoring of changing vector-borne disease dispersal dynamics in the US Southwest.

7808

CHARACTERIZING EPITOPE SEQUENCE-INDEPENDENT DISRUPTION OF IMMUNOGENICITY IN NOVEL *PLASMODIUM FALCIPARUM* ANTIGENS IDENTIFIED THROUGH WHOLE GENOME SIEVE ANALYSIS

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The development of malaria vaccines with high efficacy has eluded the scientific community for decades. A major obstacle to improving vaccine efficacy lies with allele-specific efficacy, the phenomenon by which vaccines are most efficacious against pathogen strains encoding variants of target antigens that are sufficiently similar immunogenically to the vaccine strain's. Though this process may be mediated by changes in epitope sequence, it is also possible that structural changes cause epitope-independent changes in immunogenicity. We hypothesize that, in pre-erythrocytic antigens, SNPs occurring outside of epitopes may result in structural changes that modify the accessibility or shape of protective $CD8^+$ *T-cell epitopes*. Our lab has conducted whole genome sieve analysis (wgSA) using *Plasmodium falciparum* (Pf) isolates collected from vaccine and placebo recipients in Pf sporozoite (SPZ)-based efficacy field trials. The wgSA identified several novel putative Pf antigens from which 12 were down-selected for characteristics important to vaccine antigens. These targets contain a number of SNPs found to be significantly differentiated between the Pf strains from vaccinee and control recipients of the PfSPZ-based vaccine field trials. Currently, all antigens from 64 individuals in both trial arms from two studies have been reconstructed. Additionally, using NetMHCPan, all $CD8^+$ T-cell epitopes have been predicted for the 26 HLAs most prevalent globally. For each of the 12 antigens of interest, we will use DALI to perform distance-matrix alignment, and UCSF Chimera to perform root-mean-squared-deviation analysis and quantify changes in tertiary structure between the vaccine strain and the breakthrough Pf infection variants. These methods will be applied both on the entire antigen sequences and using a sliding window approach, to assess the impact of structural changes with greater granularity. Potential impacts on immunogenicity will be assessed by examining changes in surface accessibility and T-cell receptor binding at identified $CD8^+$ T-cell epitopes.

7809

PREDICTING THE AGE OF FIELD *ANOPHELES* MOSQUITOES USING MASS SPECTROMETRY AND DEEP LEARNING

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Mosquito-borne diseases like malaria are rising globally, and improved mosquito vector surveillance is needed. Survival of *Anopheles* mosquitoes is key for epidemiological monitoring of malaria transmission and evaluation of vector control strategies targeting mosquito longevity, as the risk of pathogen transmission increases with mosquito age. However, the available tools to estimate field mosquito age are often approximate and time-consuming. In this study, we show a rapid method that combines matrix-assisted laser desorption and ionization time-of-flight (MALDI-TOF) mass spectrometry with deep learning for mosquito age prediction. This approach was validated using techniques such as convolutional neural networks, conventional classification, rank-consistent classification, and regression. Using 2,763 mass spectra from the head, legs, and thorax of 251 field-collected Anopheles arabiensis mosquitoes, we developed deep learning models that achieved a best mean absolute error of 1.74 days. We also demonstrate consistent performance at two ecological sites in Senegal, supported by age-related protein biomarkers changes. Our approach is promising for malaria control and the field of vector biology, benefiting other disease vectors like Aedes mosquitoes.

7810

CRYOPRESERVATION OF *ANOPHELES STEPHENSI* EGGS: GENOTYPIC CONSERVATION AFTER LONG TERM CRYOSTORAGE AND GENERATION OF A STRAIN-SPECIFIC MARKERS

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Sanaria manufactures *Plasmodium falciparum* (Pf) sporozoite (SPZ) vaccines against Pf malaria that are composed of cryopreserved PfSPZ attenuated either by radiation, antimalarial drugs, or gene deletion. PfSPZ are produced in a unique aseptic mosquito system. Sanaria has successfully cryopreserved *Anopheles stephensi* eggs to quickly recover from catastrophic loss of the mosquito colony. The genotypic and phenotypic characteristics of any new colony should match those of the *A. stephensi* used currently in manufacturing, and to incorporate the offspring of these eggs into PfSPZ production. Therefore, we have performed whole genome sequence analysis (depth coverage of 438-485X) on pools of hundreds of mosquitoes from our current colony and from mosquitoes derived from cryopreserved eggs. The analysis revealed no differences in SNP profiles of mosquitoes in the current colony with those reared from eggs cryopreserved and stored for up to 32 months in vapor phase liquid nitrogen. An important consideration for using the mosquitoes in GMP processes is strain identity. Sanaria uses *A. stephensi* SDA500 9800 in manufacturing its PfSPZ products. This strain is derived from the original SDA500 strain selected in Wageningen, the Netherlands, for high susceptibility to Pf infection. The deep sequencing and genome-wide SNP analysis mentioned above revealed highly specific *A. stephensi* 9800 alleles that can distinguish it from other *A. stephensi* strains such as *A. stephensi* India. Moreover, these markers (including odorant binding protein gene, AsteObp1) were discriminatory between *A. stephensi* SDA500 9800 and other closely related SDA500 sub-strains such as from the NIH, as well as the sub-strain that was used for the reference SDA500 genome database. We have used these data to develop PCR and RFLP assays to confirm *A. stephensi* SDA500 9800 identity against other very closely related SDA500 strains. Cryopreservation of *A. stephensi* eggs does not result in any genetic bottleneck of the mosquitoes that hatch and are used to generate a colony. These are critical data for establishing mosquito egg cryopreservation as a GMP process at Sanaria.

7811

GENE DRIVE PERFORMANCE IN SMALL CAGE POPULATIONS OF THE YELLOW FEVER MOSQUITO, *AEDES AEGYPTI*

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The mosquito, *Aedes aegypti* is ubiquitous throughout the tropical regions of the world and the principal vector for arboviruses such as dengue, Zika and chikungunya viruses. Novel control strategies for arboviruses include population replacement in which pathogen susceptible mosquitoes in the wild are replaced by engineered pathogen-resistant mosquitoes within a target region. This genetic approach requires the designs of synthetic antiviral effectors and a gene drive system spreading an effector throughout the target population via super-Mendelian inheritance. Here, we compare two CRISPR/Cas9 based single-component gene drives, which express Cas9 in the germline at an ideal locus for antiviral effector delivery using either *nanos*- or *zpg*- promoter sequences. Gene drive performance was measured in small non-overlapping cage populations of *Ae. aegypti* over 12 discrete generations. Starting with an initial release of 1:9 male gene drive carriers : wild-type males for each gene drive into populations of 300 total mosquitoes with equal sex ratios, we tracked the gene drive carrier and allele frequencies. Using deep-sequencing, the formation and retention of gene drive blocking indels was measured. We observed a substantial increase in gene drive carrier frequency from 5% in the initial release up to over 65% of the population for both gene drives. The *nanos*- gene drive spread more quickly, invading 50% of the mosquito populations by generation G5. It has been suggested that specific features of the DNA repair mechanism in *Ae. aegypti* during gametogenesis are impacting gene drive function due to high rates of gene-drive blocking indel formation. We observed that the promoter choice for Cas9 expression had a large effect on the accumulation of gene drive resistant alleles. The *nanos*-promoter controlled gene drive exhibited a greater rate of drive, but imposed a higher fitness cost, leading to a high accumulation of gene drive blocking indels. By comparison, the *zpg*-promoter controlled gene drive had a lower fitness cost and was predicted to achieve greater rates of fixation and stability in gene drive carrying populations.

7812

EFFECT OF ANTICOAGULANT TREATED BLOOD ON GENE EXPRESSION OF *AEDES AEGYPTI* MOSQUITOES

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Ingestion of blood is vital to the survival of anautogenous mosquito species, particularly those of public health importance. Previous studies have established the ability of unique bloodmeal characteristics to influence gene expression in various mosquito tissues that impact fecundity, host-seeking behavior, and vectorial capacity. To study the biology of mosquitoes it is necessary to rear them in laboratory colonies with a controlled blood supply. However, the effect of anticoagulants already present in vertebrate blood on arthropod gene expression has not been evaluated. To determine the effects of bloodmeals containing exogenous anticoagulants, we tested gene expression using whole mosquito abdomens by RNA-seq analysis among four experimental groups of *Aedes aegypti* mosquitoes at two time points (24 and 72 hours post blood-feeding). Our experimental groups included mosquitoes fed either blood containing ethylenediaminetetraacetic acid (EDTA), blood containing sodium citrate, blood containing heparin, and one group fed only a 10% sucrose diet. Our preliminary data found a total of 193 upregulated and 12 downregulated genes across all treatment groups at 72 hours post-feeding compared to the 10% sucrose only mosquitoes. When comparing EDTA fed mosquitoes against those given blood containing heparin at 72 hours, 8 genes were upregulated and only 1 gene was downregulated. Comparison of the EDTA fed group with the sodium citrate fed group at 72 hours, resulted in 18 upregulated genes

and 4 downregulated genes. The same analysis comparing the sodium citrate fed group against the heparin fed group at 72 hours, showed only 3 upregulated genes and 4 downregulated genes (3 corresponding to uncharacterized proteins). Future in-depth analyses will examine these differentially regulated genes for possible biological associations with fecundity, host-seeking behavior, and vectorial capacity.

7813

EXPLORING THE VIROME OF THE WEST NILE VIRUS VECTOR *CULEX TARSALIS*

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Culex tarsalis is a mosquito species broadly distributed across North America, where it is an important vector of zoonotic arboviruses such as West Nile virus (WNV), Western equine encephalitis virus, and St. Louis encephalitis virus. Various factors affect the interactions between vectors and pathogens, including the microbiome. It has been previously shown that simultaneous infection with insect-specific viruses (ISV; unable to infect non-insect animals) can alter arbovirus titers in diverse mosquitoes. Here, we show that ISV's can alter the competence for WNV both in vitro and in vivo in *C. tarsalis*. Using sequencing, we also characterized the *C. tarsalis* virome and its distribution in 17 populations across the Midwestern USA. Our study enhances the understanding of the ISVs associated with *C. tarsalis*, offering valuable insights for further microbiome, host-pathogen interactions, and disease ecology studies.

7814

TOTAL RNA SEQUENCING TO IDENTIFY MOLECULAR MARKERS OF BACTERIA AND FUNGI IN *ANOPHELES DARLINGI*

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Microbiota is commonly identified via amplicon sequencing targeting universal taxonomic markers, such as 16S rRNA or ITS. However, the RNA sequencing approach has potential for the successful detection of bacterial and fungal sequences in complex samples. This study aimed to detect molecular taxonomic markers in bacteria (16S, 23S rRNA) and fungi (ITS sequences) in *Anopheles darlingi* mosquitoes using a metatranscriptomic approach. The mosquitoes were collected from different natural populations in Colombia. Total RNA was extracted from pooled mosquitoes and used to prepare cDNA libraries. Illumina NovaSeq 6000 was used for total RNA sequencing. The bioinformatics workflow included read quality check, followed by filtering/trimming. Mosquito reads were mapped to the *An. darlingi* reference genome using Bowtie2 to exclude host sequences from the analysis. After de novo contigs assembly using MetaSPAdes, the taxonomic assignment was performed using BLAST against SSU/LSU SILVA and UNITE databases. Bacterial and fungal contigs were confirmed in a second BLAST query against the NCBI non-redundant database. A total of 153 bacterial and 12 fungal contigs were identified. Complete 16S and 23S rRNA sequences of *Asaia sp. a*nd partial ITS region of various fungal genera, were recovered. The metatranscriptomic approach identified 17 bacterial and 7 fungal genera. The most common bacteria were *Klebsiella, Acinetobacter* and *Thorselia*, while the predominant fungi were *Aspergillus, Alternaria* and *Nigrospora.* The results indicate that RNA-Seq analysis is a valuable approach for identifying bacteria and fungi metabolically active in the mosquito; furthermore, this approach is useful for recovering complete microbial taxonomic markers. Future studies will focus on the evaluation of the *Anopheles* microbiome, including taxonomic and functional profiling based on metatranscriptomics.

7815

HI-C PROXIMITY LIGATION APPROACH IDENTIFIED CHROMOSOMAL REARRANGEMENTS IN *CULEX PIPIENS* MOSQUITOES

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Mosquitoes of the *Culex pipiens* complex serve as primary vectors for lymphatic filariasis worms and encephalitis viruses. They represent a geographically widespread, taxonomically, and ecologically diverse group of insects. The complex consists of four species, including *Cx. pipiens*, *Cx. quinquefasciatus*, one subspecies, and two so-called physiological forms, *Cx. p. pipiens* and *Cx. p. molestus*, which exhibit important physiological and ecological differences. Genetic divergence between closely related taxa is often associated with chromosomal rearrangements, but few chromosomal rearrangements have been documented in *Culex* mosquitoes due to the challenges posed by the poor quality of their polytene chromosomes. In this study, we used a recently developed chromosome-scale genome assembly for *Cx. quinquefasciatus* and the Hi-C proximity ligation technique to visualize chromosomal rearrangements in mosquitoes from the *Cx. pipiens* complex. A total of 11 strains were included in our study: 5 strains of *Cx. p. pipiens*, 3 strains of *Cx. p. molestus*, and 3 strains of *Cx. quinquefasciatus*. Most of the strains were represented by recently colonized mosquitoes. A total of 10 chromosomal inversions were identified. Inversions varied in size from 7 to 21 Mb and were unevenly distributed along the chromosomes. Based on taxa/strain specificity, two inversions in the 2p arm were classified as common, present in all three species/forms, two overlapping inversions in the 1p arm were identified as pipiens-specific, and one inversion in the 1p arm was considered molestus-specific. Based on the structure of the Hi-C heat map analyses, we considered all chromosomal inversions as polymorphic. Interestingly, we found more chromosomal inversions in the 1p and 3q arms, which are homologous to the inversion-rich 2R arm in the *An. gambiae* complex. Thus, our study confirmed that the Hi-C proximity ligation method can reliably identify chromosomal rearrangements in mosquitoes from the *Cx. pipiens* complex. Our study revealed a large pool of structural variation in the genomes of *Cx. pipiens* mosquitoes and provides new insights into mosquito genome evolution.

7816

THE MICROBIOTA OF *ANOPHELES* AND *AEDES* MOSQUITOES IN FRENCH GUIANA: INVESTIGATING MICROBIAL COMMUNITIES AND THEIR RELATIONSHIP WITH ENVIRONMENTAL FACTORS

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Mosquitoes host microbial communities that influence various aspects of their life, from development to fecundity and lifespan. Additionally, the microbiota can impact the vectorial competence of mosquitoes for diseases such as malaria or dengue fever. The diverse microbial actors within the intestine can interact with pathogens in different ways, either facilitating or hindering the establishment of pathogens within the mosquito's body. Therefore, understanding the effects of the various microbial communities present in mosquitoes is crucial. While sequencing-based studies have analyzed microbial compositions in mosquitoes, it remains unclear whether variations in the microbiota are random or influenced by bacterial interactions or environmental factors, favoring specific compositions. In our study, we focused on a broad range of Aedes and Anopheles mosquitoes from various locations in French Guiana, sampled across several months and years. Using 16S sequencing and MiSeq technology, we analyzed the bacterial composition of individual mosquito midguts. Our findings revealed

a varied microbiota, however predominantly dominated by core bacteria, rather than various typical compositions. Furthermore, we gained insights into the influence of capture location, month, and mosquito species on the microbiota and correlated our results with an analysis of mosquito metabolism from two different study locations. These findings enable the identification of typical and dominant bacteria within the mosquito microbiota, which could serve as targets for future functional studies or be utilized in studies involving manipulation of the mosquito microbiota.

7817

CHROMOSOMAL DIMORPHISM OF THE LEFT ARM OF CHROMOSOME IN *ANOPHELES QUADRIMACULATUS* IS ASSOCIATED WITH MULTIPLE OVERLAPPING CHROMOSOMAL INVERSIONS

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The most dangerous malaria vectors in the Northern Hemisphere belong to the Maculipennis group of mosquitoes. Among them, *Anopheles quadrimaculatus* has wide distributions in the Eastern United States and has been reported to transmit both *Plasmodium falciparum* and *P. vivax* malaria. This mosquito is a type species of the *An. quadrimaculatus* complex, the group of species with uncertain taxonomic status. Previous studies have observed dimorphism in the 3L chromosomal arm of *An. quadrimaculatus*, designated as 3L1 and 3L2, but the details of rearrangements have not been identified based on chromosomal banding patterns. Although a draft genome assembly was developed for the Orlando colony of *An. quadrimaculatus*, but the Hi-C scaffolding approach could not completely assemble the different arrangements of the 3L arms. In this study, we developed a preliminary cytogenetic map for the polytene chromosomes from ovarian nurse cells, for 3L arm. Cytogenetic analysis confirmed the presence of only two homologous regions of 3L arms that were paired in the polytene chromosomes. In contrast to previous observations, our study identified only heterozygous arrangements of 3L1 and 3L2 arms present together in all individuals from the Orlando colony, suggesting that all homozygous individuals died at the embryonic or larval stages. We used the draft genome assembly to develop a physical map for this species based on fluorescence in situ hybridization of PCR-amplified DNA probes. We designed 16 probes for both sides of the 8 largest scaffolds from the assembly and simultaneously hybridized two probes from the same scaffold to the chromosomes. Physical mapping revealed the presence of at least 4 large overlapping chromosomal inversions that distinguish the 3L1 and 3L2 arms. Some of the probes hybridized to only one arrangement of the 3L arm, suggesting the presence of the deletions in both 3L1 and 3L2 arm arrangements, which can potentially explain the absence of homozygous arrangements of the 3L arm in the Orlando colony. Our study provides new insights into the evolution of the 3L arm that can be linked to the evolution of the *An. quadrimaculatus* complex.

7818

EPIDEMIOLOGICAL, ENTOMOLOGICAL, AND CLIMATOLOGICAL INVESTIGATION OF THE 2019 DENGUE FEVER OUTBREAK IN GEWANE, AFAR REGION, NORTHEAST ETHIOPIA

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Dengue Fever (DF) is an important arthropod-borne viral infection that has repeatedly occurred as outbreaks in eastern and northeastern Ethiopia since 2013. A cross-sectional epidemiological outbreak investigation was carried out from September to November 2019 on febrile patients (confirmed malaria negative) who presented with suspected and confirmed DF at both public and private health facilities in Gewane District, Afar Region, northeastern Ethiopia. Entomological investigation of containers found in randomly selected houses belonging to DF-positive patients was undertaken to survey for the presence of *Aedes* larvae/pupae. A total of 1185 DF cases were recorded from six health facilities during the 3-month study period. The mean age of DF cases was 27.2 years, and 42.7% of cases were female. The most affected age group was 15–49 years old (78.98%). The total case proportions differed significantly across age groups when compared to the population distribution; there were approximately 15% and 5% higher case proportions among those aged 15–49 years and 49+ years, respectively. A total of 162 artificial containers were inspected from 62 houses, with 49.4% found positive for *Ae. aegypti* larva/pupae. Aedes mosquitoes were most commonly observed breeding in plastic tanks, tires, and plastic or metal buckets/bowls. World Health Organization entomological indices classified the study site as high risk for dengue virus outbreaks (House Index = 45.2%, Container Index = 49.4%, and Breteau Index = 129). Time series climate data, specifically rainfall, were found to be significantly predictive of AR (p = 0.035). Study findings highlight the importance of vector control to prevent future DF outbreaks in the region. The scarcity of drinking water and microclimatic conditions may have also contributed to the occurrence of this outbreak.

7819

SEROPREVALENCE OF DENGUE IN SENEGAL

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Senegal is recognized to be an endemic country for dengue. Despite this, little is known about theage-stratified immunity profile of the Senegalese population against dengue, which is crucial forguiding effective public health responses to outbreaks.To assess the extent of dengue circulation across Senegal, we conducted a dengue seroprevalencesurvey across 14 regions, leveraging blood samples collected from a previous SARS-CoV-2serosurvey of individuals aged 0 to 94 years using a commercial IgG ELISA test. We used catalyticmodels to estimate dengue force of infection from the observed age-dependent seroprevalence,testing alternative assumptions on the temporal variation of the transmission intensity and durationof immunity. We used the Wantanabe-Akaike Information Criterion for model selection.Our results suggest constant, endemic dengue transmission across most of the regions, withincreasing transmission in Saint-Louis and Thies. We observe significant heterogeneity in the per-capita risk of dengue infection across regions, ranging from 0.2% (95% CrI: 0.1, 0.3) in Dakar to2.6% (95% CrI: 1.9, 3.6) in Fatick, corresponding to overall seroprevalence estimates of 5% (95%CrI: 3, 8) and 39% (95% CrI: 32, 47), respectively.Given the large heterogeneity in population immunity, these findings highlight the importance ofidentifying underlying risk factors and strengthening dengue surveillance across the country tomonitor its transmission and respond to future outbreaks.

7820

PRECLINICAL EVALUATION OF LIVE-ATTENUATED, REARRANGED V4020 VACCINE FOR VENEZUELAN EQUINE ENCEPHALITIS

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Venezuelan equine encephalitis (VEE) is a naturally occurring viral infection, primarily in endemic areas in South America. It is highly infectious, easily aerosolized, and capable of causing significant, debilitating symptoms within 24-48 hours of infection. There are no FDA-approved countermeasures available. Live, attenuated virus vaccines offer the potential for long-term immunity with a single dose. A live, attenuated vaccine may be a particularly advantageous VEE countermeasure. We are currently developing a novel VEE vaccine, V4020, which is intended to improve on the safety and efficacy profile of the historic TC83 live, attenuated VEE vaccine developed by the US Army. The V4020 experimental vaccine includes attenuating mutations from VEEV TC83 vaccine, as well as structural gene rearrangement to provide additional attenuation and resistance to reversion. V4020 was designed using an infectious clone manufactured using a serum-free process. In preclinical studies, BALB/c mice were vaccinated subcutaneously with a single 10^4-10^5 PFU dose of V4020 virus, or with 0.5-5.0 ug of pMG4020 plasmid expressing V4020 virus intramuscularly (by electroporation). Mice had no adverse reactions to vaccinations and developed high titers of neutralizing antibodies (PRNT80 up to 1:2560). Following challenge with the wild type VEEV, all vaccinated mice survived with no morbidity, while unvaccinated controls succumbed to infection. Safety was demonstrated by intracerebral passages in mice with no evidence of reversion. The safety and immunogenicity of V4020 vaccine was further confirmed in New Zealand rabbits vaccinated transdermally using hollow microneedles with either 10^4 PFU of V4020, or with 20 ug of pMG4020. Finally, cynomolgus macaques were vaccinated subcutaneously with 10^4 PFU of the V4020 vaccine resulting in protection from aerosol challenge. No adverse reactions to vaccination were noted. Currently, neurovirulence and neuroinvasion of the V4020 vaccine virus is being compared with the TC83 vaccine in preclinical toxicology studies in anticipation of Phase 1 clinical trials.

7821

EVALUATING THE EFFICACY AND CORRELATES OF PROTECTION OF AN INSECT-SPECIFIC FLAVIVIRUS VECTORED ZIKA VACCINE

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Flaviviruses continue to emerge worldwide, causing significant morbidity and mortality. ZIKV recently caused immense economic and health impacts throughout the Americas, and re-emergence poses a significant threat. Novel vaccine strategies for flaviviruses and Zika virus remain urgently needed. Here, we created a chimeric virus expressing ZIKV prM and E proteins on an Aripo virus (ARPV; an ISFV) backbone and assessed this vaccine candidate's safety, immunogenicity, efficacy and correlates of protection using a variety of *in vitro* and *in vivo* models. Our *in vitro* safety studies showed that after infection of mammalian cells with ARPV/ZIKV, the virus did not replicate nor cause cytopathic effects. ARPV/ZIKV also did not produce ZIKV E protein in mammalian cells. ARPV/ZIKV also demonstrated exceptional safety when administered at high doses intracranially to suckling mice. Protective efficacy was next evaluated in immune -competent (C57BL/6J) and -compromised (IFN-$\alpha\beta R^{-/-}$) murine models. ARPV/ZIKV-vaccinated mice were completely protected from viremia, weight loss, and mortality after being challenged with ZIKV. ARPV/ZIKV immunization also prevented *in utero* ZIKV transmission in gravid IFN-$\alpha\beta R^{-/-}$ mice. Vaccinated dams and their embryos exhibited no morbidity post-challenge, and no detectable ZIKV was present in placental, spleen, or brain tissues. Vaccine efficacy studies in $Rag1^{-/-}$, $Tcra^{-/-}$, and $muMt^{-/-}$ mice, and T-cell depletion, adoptive transfer, and passive transfer studies in IFN-$\alpha\beta R^{-/-}$ mice, show both humoral and cell-mediated responses are important contributors to ARPV/ZIKV-induced protection. ARPV/ZIKV vaccination shows single-dose efficacy, and both neutralizing antibodies (nAbs) and T-cell responses mediate the robust protection observed, with nAbs playing a larger role at the time of challenge but T-cells playing a significant role in the development of protective immunity after ARPV/ZIKV vaccination in mice. ISFV vaccine platforms are being continually refined, and it seems plausible that they may be an important tool for reducing the global burden of flavivirus disease.

7822

BIOLOGICAL AND MOLECULAR PROPERTIES OF A SYLVATIC YELLOW FEVER PLAQUE SIZES VARIANTS ISOLATED FROM A HUMAN PATIENT IN BRAZIL DURING THE 2017-18 OUTBREAK

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Yellow fever (YF) is a febrile and hemorrhagic infectious disease caused by Yellow fever virus (YFV) YF is considered one of the most lethal viral infections and is endemic in tropical areas including the Amazon basin. In 2017-18, a major YF outbreak occurred in Brazil causing almost 800 deaths and over 2000 human cases reported. This study aimed to perform a molecular and biological characterization of the sylvatic YFV strain that circulated during the 2018 outbreak. For that, a serum sample collected from a Yellow Fever acute phase patient was used for viral isolation in the C636 cell line. The isolated sample presented plaque-size variants and required purification, which was performed through limiting dilution and plaque purification protocols. After two rounds of each purification protocol, we were successful in generating purified plaque size variants, a small plaque-size (B2) and a large plaque-size (P3). To gain further insights about the molecular characterization of those variants a next-generation sequencing was then performed, using a pool of primers that cover the entire YFV genome. After alignment, we observed that these variants have genomic differences mainly distributed in non-structural proteins, except for one mutation that we detected in the envelope gene of B2 (451nt position), which resulted in an isoleucine-valine substitution. Growth kinetics of both B2 and P3 variants were performed in Vero, HepG2 and C636 cells (MOI 0.01). In general, P3 presented higher viral titers compared to B2 in all cell lines tested. In Vero and HepG2 cells the multiplication peak (MP) of P3 coincided with the beginning of cytopathic effect (CE) and that occurred 3 days post infection (DPI). Interestingly, in HepG2 cells, the MP of B2 was very early (1DPI) with no evident CE and, in Vero cells, the MP and CE occurred at 5DPI. In C636 cells a similar behavior for both variants were observed. The MP occurred at 5DPI, and the CE was visualized at 7DPI. Other genomic analyses were conducted to better understand the wild-type YFV variants isolated, demonstrating the importance of this type of study in understanding the biology of YFV.

7823

A COMMERCIAL SEROLOGIC ASSAY (ELISA) FOR DETECTION OF ZIKA VIRUS IGG ANTIBODIES WITH MINIMAL CROSS-REACTIVITY

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The Zika virus (ZIKV) outbreak of 2015-2016 underscored the causal link between ZIKV infection and neurological complications including congenital Zika syndrome and Guillain-Barré syndrome. While several FDA-approved molecular tests are available for diagnosis, their utility is limited as viral RNA is typically detectable in serum only ≤10 days post onset (DPO) of symptoms. Detection of ZIKV antibodies could be a preferable means to determine exposure to ZIKV, due to the transient nature of the virus and the fact that most infections are asymptomatic. IgM detection is useful during acute infection but may be subject to low assay specificity. Considering the potential for clinical complications, especially the risk of fetal anomalies, reliable diagnostics are crucial beyond the limited RNA and IgM detectability windows. Here, IgG detection emerges as a valuable tool for assessing past infections and associated risks. However, structural similarities between ZIKV and other flaviviruses, particularly dengue (DENV), pose cross-reactivity challenges for serological assays. To address this problem, we developed a ZIKV IgG ELISA using a recombinant ZIKV envelope protein engineered to excise cross-reactive epitopes, combined with a competition step using DENV envelope. The ZIKV IgG ELISA was formatted as a kit with ready-to-use reagents and internal controls, with turnaround time less than 3 hours. The test's performance was evaluated using blinded, well-characterized serum samples (n=130). Sensitivity for detection of ZIKV IgG was 18% in RNA-positive individuals collected at DPO <14 (n=22), while for DPO ≥14 (n=43) was 93%. The same samples yielded sensitivities of 14% and 88%, respectively, on another commercial ZIKV IgG test (BioTechne). Specificity among ZIKV negative healthy individuals (pre-2015; n=33) was 100% and among individuals with recent DENV (n=21), chikungunya (n=2) or West Nile virus (n=9) infections was 72% overall. In conclusion, Kephera's ZIKV IgG ELISA demonstrates high sensitivity and specificity, making it a valuable tool for ZIKV IgG detection, especially in regions with other circulating flaviviruses.

7824

DEVELOPMENT OF A LATERAL FLOW DEVICE FOR DETECTING ANTI-MPXV SPECIFIC ANTIBODIES AS A MECHANISM TO CONDUCT SEROSURVEILLANCE AND TARGET AT-RISK INDIVIDUALS FOR VACCINATION

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In early 2022, a cluster of Monkeypox virus (MPXV) cases was identified within the UK in gay, bisexual, & other men who have sex with men, with no previous travel history to endemic regions. This subsequently led to the identification of a global Mpox outbreak of 94,000 cases, with ongoing transmission within countries including the UK, USA, & new outbreaks in Southeast Asia. Vaccination with Smallpox vaccines (IMVANEX/JYNNEOS) was offered as a public health measure in identified risk groups to reduce infection & limit transmission. However, cases of Mpox are thought to be considerably higher than reported, due to under-recognition during mild disease & asymptomatic transmission. Serosurveillance studies can aid in our ability to detect the true extent of Mpox transmission in specific communities & target at-risk individuals for vaccination. Mpox serology is confounded by previous historical vaccinations & the need for complicated serological testing methods. Existing commercial antibody Mpox lateral flow devices (LFD) were found to perform poorly, detecting <30% of vaccinated or convalescent samples. Here, we detail the development of a simple, cost-effective, & sensitive antibody LFD for detecting anti-MPXV specific antibodies. Using our knowledge gained from understanding both Mpox & Smallpox-vaccination immunology, we have generated several candidate LFDs. Using individual & pools of antigens, we have been able to generate LFDs with sensitivities as high as 93% when compared to gold-standard ELISAs. Furthermore, we have been able to generate candidate LFDs that are able to discriminate between Smallpox vaccinated- & Mpox convalescent-induced antibodies.
These candidate LFDs provide an alternative to the serological tests currently on the market, with high sensitivity & specificity in detecting Mpox-/Orthopox vaccination-specific antibodies. We are now looking to assess the optimal components of the LFD to generate second-generation Mpox-specific LFDs, aiding in our ability to conduct remote serosurveillance studies & target at-risk individuals for protective vaccination, both in countries with high and low incidence.

7825

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF AIRCREW INFECTIOUS WITH MPOX DURING TRAVEL, UNITED STATES, MAY 10 - SEPTEMBER 30, 2022

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Prior to 2022, mpox cases in the U.S. were limited to travelers from endemic countries or exposures associated with imported animals. Human-to-human transmission during the global 2022 outbreak was largely associated with sexual contact. Early in the outbreak, US Centers for Disease Control and Prevention (CDC) initiated aircraft contact investigations (CIs) for mpox when a passenger or aircrew was infectious during travel. Published data are limited on aircrew who traveled while infectious with mpox. This analysis characterized aircrew who traveled on commercial aircraft while infectious with mpox and the outcomes of resulting CIs from May 10 through September 30, 2022. Clinical and epidemiological data and mitigation measures taken by aircrew with mpox were reported by health departments (HDs) to CDC and entered into CDC's Port Health Activity Reporting System. Deidentified data were analyzed using SQL and Excel. HDs notified CDC of 44 aircrew who flew while infectious, resulting in 173 aircraft CIs. Among the 44 aircrew with mpox, 93% (41/44) were male; median age was 35 years (range = 23-59 years). Of those with available information, 58% (22/38) reported fever, 21% (8/38) reported respiratory symptoms, and 95% (38/40) reported rash, most commonly in the genital/perianal area or limbs. Additionally, 63% (15/24) reported masking, and 78% (21/27) reported covering their lesions while traveling. Seven hundred and ninety aircraft contacts were identified (defined as aircrew who flew with an infected aircrew for cumulative flight time of >3 hours). No contacts were reported as developing mpox following their exposure, based on aggregate HD outcome reporting. Aircrew with mpox worked on multiple flights during their infectious period, but most followed recommended precautions to mask and cover lesions. No secondary cases were reported. These data suggest risk of transmission from infectious aircrew is low. In general, persons with mpox are recommended to isolate; if travel is necessary, they should take precautions to prevent transmission.

7826

COMPARISON OF EBOV GP IGG ANTIBODY REACTIVITY; RESULTS FROM TWO ASSAYS: FANG AND A MAGPIX-BASED MULTIPLEX ASSAY IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Ebola virus (EBOV) is a highly infectious pathogen, and its long-term consequences are slowly being investigated as the cohort of EBOV survivors continues to grow. With its high fatality rate reported during outbreaks in West and Central Africa, and potential for reinfection or latent infection, continued investigation and development of research tools are of utmost importance. Using a randomly sampled "artificial cohort" (n = 503) of existing bio-banked samples from the Democratic Republic of the Congo (DRC) two EBOV glycoprotein (GP) immunoglobulin G (IgG) antibody (Ab)-detection assays were compared: the gold-standard FANG and a custom Magpix Multiplex bead-based Immunoassay (MIA) containing EBOV GP as an antigen target. As not all Ab detection assays have been shown to detect vaccine-induced immune responses, and previous serosurveillance of EBOV has been primarily conducted with single-plex technology, this MIA was assessed as an additional resource. Among the cohort, as sample seroreactivity increases, assay correlation increases ($r^2 = 0.80$). This correlation is sustained between the two assays among sub-populations of the selected cohort - both in detecting natural immunity among known EBOV survivors and vaccine-derived immune responses. Additionally, when results are binarized as by seroreactivity, there is high correlation between the two assays on a categorical scale (Cohen's kappa = 0.71) with 71 sero-discordant samples. These data indicate that the MIA is an apt alternative to the single-plex FANG in detecting relative seroreactivity and can be used as a potential tool for widespread pan-filovirus serosurveillance in the DRC and similar contexts, especially when reactivity to multiple viral antigens is of interest to achieve study objectives.

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EXPLORING THE IMPACT OF RANDOMIZED CONTROLLED TRIALS EVALUATING COVID-19 THERAPEUTICS ON CLINICAL PRACTICE GUIDELINES

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There was an unprecedented response from the scientific community to the COVID-19 pandemic with many randomised therapeutic trials registered within a short time. However, many trials were too small or poorly conducted and thus did not contribute to evidence generation. We aim to quantify the overall policy impact of COVID-19 related clinical research by assessing the proportion and characteristics of randomised controlled trials (RCTs) used as evidence for developing the WHO COVID-19 treatment guideline (WHO guideline). All RCTs that enrolled SARS-CoV-2 positive patients and evaluated therapeutic agents listed in the WHO guideline (version 13, Jan 2023) were eligible for inclusion. Registration information for these RCTs was obtained from the Infectious Diseases Data Observatory's living systematic review of COVID-19 clinical trial registries. Pre-print and peer-reviewed publications were obtained through a systematic search of the Europe PMC database. Each trial registration was linked with a resulting publication through its registry ID. Between Jan 2020 and Nov 2023, 332 registered and/or published RCTs were considered eligible for use as evidence in the WHO guideline. Of the 332 RCTs, 3 (0.9%) were published but never registered, 172 (51.8%) were registered and published, and 157 (47.3%) were registered but not yet published. Only 63 out of 332 RCTs (19.0%) were used as evidence in the WHO guideline. The sample size of RCTs that were incorporated as evidence into the guidelines was larger (median: 432, interquartile range (IQR): 145-2,330) than RCTs that were not used (median: 145, IQR: 82-382). Of the 269 studies not used in the WHO guideline, 40 (15%) were registered after the first recommendation for the drug the study was evaluating had already been made. For published studies, the median time to publication was 14 months (95% confidence interval: 12-17). These findings demonstrate that a large proportion of RCTs had no impact on clinical guidelines. The pandemic response was marked by a delay in initiating trials and their subsequent publication, which hindered their prompt utilisation as evidence in clinical guidelines.

7828

BEYOND EBOLA VIRUS AND LASSA VIRUS IN GUINEA: MNGS UNMASKS A SPECTRUM OF VIRAL PATHOGENS IN SAMPLES OF PATIENTS WITH HEMORRHAGIC FEVER COLLECTED DURING EPIDEMICS AND SURVEILLANCE ACTIVITIES

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Metagenomic next-generation sequencing (mNGS) allows pathogens identification in a sequence-agnosticmanner, and opens a yet under-explored opportunity of broadened pathogen detection within viralhemorrhagic fever (VHF) surveillance programmes. This study explored mNGS diagnostic accuracy to detectEbola virus (EBOV) and Lassa virus (LASV) in stored blood samples of patients with VHF available from theGuinean national VHF laboratory biobank. Samples that had tested positive (n=9 for EBOV and 16 for LASV) ornegative (n=37) using qPCR were selected to represent established outbreaks (2021 & 2022) or surveillanceactivities (2023) in different regions. Samples were extracted at the national VHF laboratory and preserved inthe Zymo DNA/RNA Shield kit before shipment to the Chan Zuckerberg (CZ) Biohub (SF, USA) for mNGS analysisusing FastSelect-based (Qiagen) host background depletion with miniaturized dual-indexed Illumina librarypreparation and pathogen identification using the CZ ID cloud-based platform. 81.3% (13/16) of LASV and 44.4%(4/9) EBOV-positive samples were confirmed by mNGS. Importantly, LASV and EBOV was detected inrespectively two (out of 46; 4.3%) and one (out of 53; 1.9%) initial qPCR test-negative samples. Additionalviruses were identified usually not associated with VHF: Enterovirus B, human mastadenovirus C, bubaline-associated gemykrogvirus, Primate erythroparvovirus 1 and Gila monster-associated gemycircularvirus 1; aswell HIV (n=1), HBV & HAV (n=2 each) and Pegivirus A & C (n=2 and 5 respectively). Interestingly, Dengue virus(DENV) was detected in two samples, which marks the first ever molecular confirmation of Guineanautochthonous DENV infections. Our study highlights mNGS's capability to detect known VHF and circulation ofyet undescribed pathogens in GuineaHowever, with a 1.9-+4.3% rate of non-specific results, mNGS should becomplemented by confirmatory qPCR. The utility of mNGS to broaden pathogen detection in early-warningsystems and complement targeted testing in VHF surveillance warrants further prospective evaluation.

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VARIABILITY OF REPORTABLE DATA BASED ON CALCULATION OF CHIKUNGUNYA VIRUS NEUTRALIZING ANTIBODY TITERS

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Chikungunya is a recognized global health concern and an important travel-related disease due to its rapid geographical expansion and potential for prolonged morbidity. It is estimated that over three quarters of the world's population live in areas at risk for transmission. Additionally, travel from North America and Europe to Chikungunya virus (CHIKV) at-risk areas is predicted to exceed pre-pandemic levels. Neutralizing antibodies are of interest because they are generated within weeks of immunization or infection and can provide protective immunity. Given the many types of serological assays for quantifying neutralizing antibodies, a comparison of different assay results can be challenging. Furthermore, there is limited standardization of neutralization titer endpoints and although an international standard for Chikungunya is available, it has not been used productively to harmonize interlaboratory data from clinical trials. Here, we demonstrate the difference between reporting NT50 versus NT80 antibody titers, which are the concentrations of serum to reduce maximal *in vitro* virus infectivity by 50% or 80%, respectively, compared to virus without serum. This provides a measurement of how much neutralizing antibody is present and how effective it is and when taken together, these data can inform a surrogate threshold likely to confer clinical benefit. Additionally, we show data from a collaborative study conducted with the Paul Ehrlich Institute on generation of an international standard for Chikungunya and how harmonization can be achieved between laboratories offering a feasible way to better compare results from different CHIKV neutralization assay methodologies.

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FOUR YEARS LATER: STABILITY OF THE COVID-19 SEROLOGY CONTROL PANEL DRIED TUBE SPECIMENS

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We report here the stability of human plasma stored as dried tube specimen (DTS). Previously we described the COVID-19 Serology Control Panel (CSCP kit, 2020, doi:10.4269/ajtmh.21-1036) and its evaluation as WHO secondary standard (doi.org/10.3389/fmicb.2022.893801). We maintain continuous monitoring of the CSCP reactivity with SARS-CoV-2 variants to ensure its relevance. For evaluating its stability, multiple CSCP kits, stored for 4 years at -20ºC, were placed at -20°C, 4°C, 25°C, 35°C, and 45°C for 1, 2, and 4 weeks then reconstituted with 0.2 ml PBS-Tween. Samples were serially titrated for IgG using the Luminex Magpix platform as singleplex (Sx) and all antigens together in the multiplex (Mx) format. Antigen-coupled beads included: SARS-CoV-2 *Wuhan* N, RBD and S1+S2; *B.1.1.7*, S1+S2; *B1.351*, S1+S2; *B1617.2*, RBD; *BA.4/BA.5/BA5.2*, RBD; *BA.5*, RBD; *B1.1.529*, RBD; *XBB1.1*, S+S2 and tetanus toxoid (+) and BSA (-). Results are expressed as median fluorescence intensities (MFI) and plotted by area under the curve, $\log_{10}$. There was concordance between Sx and Mx MFI results for all the variants. Samples placed at -20ºC through 25°C retained reactivity through day 7 ($>10^8_{log}$) but diminished at 1 week in samples conditioned at 35°C and 45°C (loss of 0.5_{log} to 1_{log} compared to 4ºC sample) against Wuhan and variants, and total loss of reactivity with BA.4/BA.5 RBD, a short-lived Omicron sub-variant. In conclusion, CSCP kits, after 4 years, retain reactivity consistent with our 1-year stability results. This suggests that CSCP or any same set of DTS plasma can be calibrated as secondary WHO standards for targets like vaccine preventable diseases. The DTS format was first used in 2010 as HIV reference samples and adopted for other antibody, antigen and nucleic acid materials. Our study adds to the evidentiary utility of the DTS format. This is the first time that the DTS stability has been evaluated after 4 years and is the first time it has been used in a Mx format. A set of DTS samples can be calibrated for multiple targets, the protocol is simple and low-cost so that this can be prepared in low resource settings and shipped without cold storage.

7831

IMPACT OF VACCINATION STRATEGIES FOR HEALTH-CARE WORKERS AGAINST MERS-COV: REACTIVE STRATEGIES OUTPERFORM PROACTIVE STRATEGIES

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Several vaccines candidates are in development against Middle East respiratory syndrome-related coronavirus (MERS-CoV), which remains a major public health concern. Using data from the 2013-2014 Kingdom of Saudi Arabia epidemic, we employ a novel Bayesian analysis on inferred transmission trees ("who-infected-whom"). We assess the potential impact of healthcare worker vaccination on MERS-CoV mortality. We investigate the conditions under which proactive campaigns outperform reactive campaigns (i.e. vaccinating in anticipation of the next outbreak, or in response to an unfolding outbreak). Finally, we examine the relative efficiency (cases averted per thousand doses) of different strategies. Substantial and disproportionate reduction of MERS-CoV morbidity and mortality is possible. The spatial scale of reactive campaigns is crucial. Proactive campaigns outperform vaccinating healthcare workers in response to outbreaks at their hospital unless efficacy has waned significantly. However, reactive campaigns at regional or national level consistently outperform proactive campaigns. When considering the number of cases averted per vaccine doses administered, the rank order is reversed: hospital level reactive campaigns are most efficient, followed by regional level reactive campaigns with national level and proactive campaigns last. Our results are robust to values of vaccine efficacy and duration of protection, as well as effectiveness of animal reservoir control measures. The sporadic nature and low prevalence of MERS outbreaks will render vaccine efficacy and duration of protection difficult to measure using traditional clinical trials. Therefore, the consistent policy recommendations that emerge from our analysis are of practical use in preparation against future MERS outbreaks. Our work underlines the need for at-risk countries to stockpile vaccines when available. The methodology underlying this work is currently being used to estimate the efficacy of "universal" sarbecovirus vaccines against transmission.

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TYPE OF VACCINE RECEIVED AND CLINICAL SEVERITY IN PATIENTS WITH TWO DOSES OF COVID-19 IMMUNIZATION

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Peru has been one of the Latin American countries with the highest COVID-19 global mortality rates. A key point to control and reduce mortality worldwide was the start of immunizations. In Peru, the first vaccine against COVID-19 was BBIBP-CorV (Sinopharm) based on inactivated virus; but shortly after, arrived batches of the BNT162b2 vaccine (Pfizer) based on messenger RNA. During the he initial stages of the immunization campaign in Peru, many people believed that one type of vaccine was more effective than the other, even refusing to be vaccinated and delaying nationwide vaccination coverage. The aim of the study was to evaluate the association between vaccine type and COVID-19 disease severity. Based on electronic health records from four epidemiological surveillance systems (HIS MINSA, SISCOVID, NETLABV2 and NOTIWEB), a retrospective cohort of 368

individuals from Jaen (Peru) was conducted. The participants had received two doses of Sinopharm or Pfizer vaccine, including only participants whose second vaccine dose was of the same type as the first vaccine received. The median follow-up period was 9 months. Ethical approval and authorization for accessing the information was obtained from the regional authority and participant confidentiality was ensured. During the follow-up, 118 moderate cases (32.1%) and 14 severe cases (3.8%) were identified. The probability of having a moderate or severe case was 50% and 94% lower, respectively, compared to the probability of a mild case after receiving two doses of vaccine ($p<0.01$). In patients who received Sinopharm, 41 moderate cases (30.8%) and 4 severe cases (3.1%) were identified, while in those who received Pfizer, 11 moderate cases (32.8%) and 10 severe cases (4.3%) were identified. Multinomial models adjusted for age, sex, and comorbidities did not report significant differences between the two types of vaccine, regarding the probability of having a severe or moderate case ($p>0.05$). It is concluded that vaccination with two doses significantly reduces the probability of having a moderate or severe COVID-19 case, and that both types of vaccine have equivalent effectiveness.

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ZIKA VIRUS IN PERU: EPIDEMIOLOGY, CLINICAL PRESENTATION AND GEOGRAPHIC DISTRIBUTION

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Zika virus (ZIKV) is an arthropod-borne virus of public health importance in Latin America and Peru, often considered as a cause of acute febrile illness (AFI) in tropical regions. However, its epidemiology remains unclear due to challenges like limited resources and passive surveillance, especially in remote areas of Peru. To address this, we conducted a study in the Peruvian jungle, aiming to determine ZIKV prevalence and describe its clinical features among the local population. This study was conducted alongside the epidemiological surveillance of acute febrile illness (AFI). Patients were included if they presented with AFI, defined as an axillary temperature greater than or equal to 38°C within at least 7 days prior to consultation without an identifiable source of infection. The signs and symptoms were assessed by the attending physician using a standardized questionnaire. Blood samples were collected and IgM detection for ZIKV was performed by ELISA-based assays. A total of 227 ZIKV cases were identified from 4204 patients with acute febrile illness, with a prevalence of 5.40%. Most of the infected patients were adults aged between 18-39 years (53.97%) and 40-59 years (15.90%). 34.31% were male, and 65.69% were female. The main clinical characteristics identified in ZIKV-positive patients were headache (89.43%), arthralgias (81.50%), myalgias (75.33%), and hand polyarthralgia (65.20%). When comparing ZIKV-positive patients with ZIKV-negative patients, the following symptoms showed significant differences: polyarthralgia in hands (65.20% vs 51.20%, $p <0.001$), nausea (54.63% vs 39.97%, $p <0.001$) and vomiting (53.30% vs 37.98%, $p <0.001$). Zika virus remains an ongoing emerging disease in the high jungle of Peru. It is an important cause of AFI, presenting nonspecific clinical symptoms; however, some symptoms such as polyarthralgia in hands, nausea and vomiting may aid guiding the diagnosis. Infections by this virus may go unnoticed in the national surveillance system, therefore precise and point-of-care diagnostics are required to establish its clinical impact in high-risk areas.

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CHARACTERIZING THE IMPACT OF COVID-19 ON OTHER RESPIRATORY INFECTIONS IN CHILE

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Many countries implemented a series of non-pharmaceutical interventions (NPIs) in response to the COVID-19 pandemic to reduce the spread of SARS-CoV-2. Despite the differences in timing and stringency in the implementation of NPIs during 2020, they led to a reduction in population contact patterns. Consequently, these NPIs not only lowered the transmission of SARS-CoV-2 worldwide but also slowed down the spread of other respiratory diseases. Still, it remains unclear how long it would take for each of these respiratory viruses to return to their pre-pandemic seasonality, and how these dynamics might vary across pathogens. Here, we analyzed several publicly available datasets from Chile to quantify the changes in respiratory viral transmission observed since the emergence of SARS-CoV-2 in 2020. Our results show that the resurgence of respiratory viruses in 2022 and 2023 displayed a high prevalence in the incidence. For instance, the annual Influenza A laboratory-confirmed cases (normalized by total population) were 4.58 times higher in 2022 and 2.80 times higher in 2023 compared to previous years, while RSV cases were 1.13 and 1.59 times higher in 2022 and 2023, respectively. However, when we analyzed the ER visits, we observed a decrease of 40% and 12% in Influenza (J09-J11), and a reduction of 28% in 2022, as well as an increase of only 1% in 2023 in acute bronchitis and bronchiolitis. Similar trends were observed in hospital discharge and mortality data, suggesting a discrepancy between the incidence and other datasets analyzed. While media and public health authorities have emphasized the rise in the number of laboratory-confirmed cases in the past two years, we suggest that changes in access to laboratory-confirmed tests and hospital availability post-emergence of SARS-CoV-2 explain the discrepancy across different datasets and, therefore, cautious conclusions should be made when interpreting these datasets in isolation.

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QUANTIFYING THE POTENTIAL OF CHIKUNGUNYA VACCINES USING THE 2022-2023 OUTBREAK IN PARAGUAY

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With Chikungunya vaccines finally available, we now have tools to battle outbreaks, although it remains unclear if vaccines deployed during an ongoing epidemic could be used to effectively reduce disease burden. Here we used a large outbreak in Paraguay in 2022-2023 (123,781 reported cases and 298 deaths during the study period) to understand how a vaccine could be used in the future. To understand the underlying burden of infection from the outbreak, we first conducted a seroprevalence study in four of the five subregions of Paraguay to estimate age-specific case detection probabilities and infection fatality ratios. We then used mathematical models to quantify the impact of a vaccine had it been available at the time. We estimate that 34% of the population was seropositive following the outbreak (340/1001 samples), compared to

<5% prior to the outbreak, with seropositivity greatest in the Centro Este subregion (47%). We estimate that the surveillance system detected 5.4% of infected individuals and the average IFR was 0.013%. Had a chikungunya vaccine been available at the time, we estimate a reactive campaign would have prevented 570,000 infections (2,500 per 10,000 doses used) and 74 deaths (0.32 per 10,000 doses used) and required 2.3 million doses for 40% coverage. However, delays in initiating a campaign would significantly reduce the impact of the vaccine. These findings provide a robust understanding of the underlying epidemiology and suggest the new vaccine can be effective in a reactive campaign if the outbreak is detected in a timely manner.

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THE EPIDEMIOLOGY OF CHIKUNGUNYA VIRUS IN BRAZIL AND POTENTIAL VACCINE IMPACT

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Chikungunya virus (CHIKV) is an *Aedes*-borne alphavirus that can cause chronic arthralgia and death. The first chikungunya vaccine was licensed in 2023, providing an opportunity to tackle the substantial public health threat the virus poses. However, its epidemiology is poorly understood, which means it is unclear how best to use the vaccine. Here we focus on Brazil, where high-quality surveillance data can help provide a robust description of the epidemiology across the country. We pooled information from confirmed cases (N=353,252), probable cases (N=1,058,403), and confirmed deaths (N=853) from 2013 to 2022, and public data from serological surveys (N=10), to inform a sero-catalytic model to track CHIKV circulation in each of the 27 federal units of Brazil since 2013. Using outputs from our model, we then estimated the impact of various potential vaccination strategies. We found high spatiotemporal heterogeneity in CHIKV circulation across Brazil. We estimate that Ceará and Rio Grande do Norte, in the Northeastern region, had the highest attack rates, with an average of 8.8% (95%CrI: 8 - 9.3) and 7% (95%CrI: 6.2 - 7.9) of the susceptible population getting infected annually. We found females were 1.79 (95%CrI: 1.74 - 1.84) more likely to develop severe symptoms than males and an overall infection fatality ratio of 0.003% (95%CrI: 0.003 - 0.004), with mortality being 17 times more likely in over 60 year olds than in 1-30 year olds. The size of a CHIKV outbreak in a state was not significantly correlated with dengue infection risk, *A. aegypti* or *A. albopictus* occurrence estimates (correlations: 0.29, 0.52, and -0.5, respectively). We estimate that if a disease blocking vaccine with 75% efficacy had been deployed in Ceará and Rio Grande do Norte prior to 2018, targeting 20% of the population over the age of 15, 10% of confirmed cases (95%CrI: 2 - 16) could have been averted between 2018 and 2022. Our findings are consistent with greater disease severity risk in females and older age groups. They suggest that CHIKV has not yet reached all regions where it could circulate and highlight the potential impact of vaccination for disease burden.

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OCCURRENCE OF VIRAL HEMORRHAGIC FEVERS IN GHANA DURING COVID-19 PANDEMIC, 2019-2022

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Amid the backdrop of the COVID-19 pandemic, the occurrence of viral hemorrhagic fevers (VHFs) such as Marburg Virus (MARV) and Yellow Fever in Ghana presents critical challenges to public health. VHFs, renowned for their severe morbidity and high mortality rates, represent a group of pathogens that continue to pose significant threats to the global fight against emerging infectious diseases. This study sought to describe the occurrence of VHFs in Ghana from 2019 to 2022. Clinical samples were collected from VHF-suspected patients in health facilities nationwide and sent to the Noguchi Memorial Institute for Medical Research for testing. Using standard molecular testing assays, samples were tested for VHFs such as Lassa fever (LF), Yellow fever (YF), Dengue, Chikungunya, Zika, Ebola, and Marburg. Laboratory results and demographic data were analysed for the period under review. Out of 358 clinical specimens tested, 69 (19%) were positive for yellow fever and 3(1%) for Marburg. The recorded mortality for Marburg was 2 out of 3. No Lassa fever, Dengue, Chikungunya, Zika, or Ebola cases were identified. Yellow fever cases were predominantly detected in individuals under 16 years 14%, (49/358). Geographically, yellow fever cases were concentrated in the Savannah region (52), Upper West region (8), Northern region (8), and Oti region (1). Marburg positive (3) cases were confined to the Ashanti region. There were no laboratory-confirmed VHFs for 2019 and 2020. Most yellow fever cases occurred in late 2021, with fewer cases in 2022. All confirmed cases of Marburg were recorded in 2022. Sequence analysis of the two cases who died indicates a close relationship to the 2021 Guinea MARV sequence. The notable surge in yellow fever cases in 2021 reaffirms its 5-year cyclical pattern, with concurrent Marburg cases, underscores the urgency of heightened surveillance and preventive measures in endemic areas to combat VHFs effectively.

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THE GLOBAL BURDEN OF CHIKUNGUNYA VIRUS AND THE POTENTIAL BENEFIT OF VACCINES

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With the first licensed chikungunya virus vaccine becoming available, organisations such as CEPI, Gavi and WHO need to assess the potential impact of alternative vaccination strategies to guide implementation. However, due to limited chikungunya surveillance, especially in low and middle income countries, the underlying burden is poorly understood, hampering the development of vaccine investment cases. We conducted a literature review to identify countries that have experienced chikungunya transmission. We used case data, serological and mosquito suitability measures to categorise each country as having endemic, epidemic or no evidence of transmission. We used data from 40 age-structured seroprevalence studies across 26 countries to estimate the frequency and size of outbreaks in epidemic countries and the force of infection in endemic areas. Finally, we estimated the impact of different vaccine roll-out scenarios on morbidity and mortality. We identified 103 countries with epidemic transmission and a further 10 with endemic transmission, with a total population at risk of 4.4 billion people. In epidemic settings, the mean duration between outbreaks was 7 years with an average of 9.4% of the susceptible population infected per outbreak. In endemic locations the mean force of infection was 2.9%. We estimate that there are 37.1 million annual infections and 26,900 deaths globally . The most affected regions are Africa, followed by Southeast Asia and the Americas. In epidemic areas, achieving 50% vaccination coverage in response to outbreaks would require 128 million doses per year. Endemic areas would require a further 486 million annual doses. On average the vaccination of at-risk individuals

would result in 22.1 infections averted, 0.016 deaths averted and 0.81 disability-adjusted life years gained per 1,000 doses administered. This work represents the first quantification of the global burden of chikungunya and provides key evidence to support the targeted use of vaccines in both epidemic and endemic locations. Improved outbreak surveillance will be needed to fully maximise the impact of vaccination.

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CIRCULATING NOROVIRUS STRAINS IN CHILDREN UNDER FIVE YEARS OLD MEDICALLY TREATED FOR ACUTE GASTROENTERITIS IN THREE HOSPITALS IN LIMA, PERU, 2022-2023

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Norovirus is a leading cause of acute gastroenteritis (AGE) worldwide, affecting approximately 20% of children under 5 years old. These highly genetic diverse viruses are classified in more than 10 genogroups, 48 genotypes, and 60 P-types. Surveillance of norovirus strains is crucial to evaluate the effectiveness of candidate vaccines against the agent, which are currently under investigation. From April 2022 to March 2023, we enrolled children under 5 years with AGE needing oral or intravenous rehydration in three public hospitals in Lima, Peru. After obtaining informed consent from the legal guardian, a stool specimen was collected and tested for norovirus by real time RT-PCR. Positive samples were sequenced based on dual typing (genotype and P-type) and using an online human calicivirus typing tool. Norovirus was detected in 342 (40.7%) of 840 stool specimens, with GII viruses associated with 91.5% of the cases. The predominant strain was GII.4 Sydney[P16] (41.3%), followed by GII.4 San Francisco[P31] (13.6%), a novel GII.4 variant detected since September 2022 in our study. Norovirus was present throughout the year with lower prevalence (19-36%) from April to July, when rare genotypes GII.27[PNA9], GII.6[P7], and GII.17[P31] predominated; a median prevalence (around 40%) from August to January, when GII.4 Sydney[P16] strains were predominant; and a high prevalence in March reaching a peak of 55% with the emergence of the novel GII.4 San Francisco[P31]. In summary, norovirus infections are a major cause of moderate/severe AGE in infants in Lima, Peru, a country with high coverage of rotavirus vaccine, with a prevalence higher than has been reported to date in the literature. Our data highlight the genetic diversity of noroviruses and the need for ongoing surveillance of norovirus strains in children with AGE to detect the emergence of rare and novel strains, that may be relevant for the development of effective norovirus vaccines.

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A SYSTEMATIC REVIEW OF FINE SCALE ESTIMATES FOR CHIKUNGUNYA MODELING IN THE CARIBBEAN: THE MISSING IMPACT OF HUMAN MOVEMENT ON TRANSMISSION RISK

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Ten years after its 2013 introduction into the Western Hemisphere, chikungunya virus (CHIKV) outbreaks continue across Latin America and the Caribbean (LAC). The decline of investigations into CHIKV transmission dynamics has led to its underdiagnosis, misdiagnosis as dengue (DENV) or Zika (ZIKV) viruses, and incomplete granular level data that does not accurately detail the risk of CHIKV infection in particular regions. Human movement is considered a modifying component of arbovirus transmission dynamics; however, characterizing its complexities has resulted in simplistic models and a lack of integration into traditional infectious disease models. The return to normal travel patterns and resulting influx of tourists to LAC following the lift of COVID-19 travel restrictions, the unknown level and duration of immunity amongst local populations, and the climate suitability for *Aedes* spp. make LAC an appropriate region of focus. A systematic literature review was conducted to assess sources of geographically linked epidemiological and entomological data, human movement data, and mathematical modeling efforts throughout LAC. The search extracted 195 LAC-focused studies published between 2014 and 2023 from PubMed, Scopus, and Web of Science, and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data from the included studies can be parameterized within potential mathematical models in three categories: *Ae. aegypti* ecological factors; CHIKV, DENV, and ZIKV human case data; and human movement dynamics. Examination of CHIKV transmission risk at subnational scales revealed rich entomological data and adequate epidemiological data that could incorporate human mobility factors more comprehensively into future modeling efforts. Assessing existing epidemiological, entomological, and human mobility data at a granular level is necessary to quantify human mobility factors for local and traveler populations and to inform transmission risk for immune local and naïve traveler populations moving throughout endemic regions.

7841

EPIDEMIOLOGY OF SARS-COV-2 NEUTRALIZING ANTIBODIES IN A RURAL COMMUNITY IN WESTERN KENYA DURING THE FIRST 24 MONTHS OF THE COVID19 PANDEMIC

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Sero-reactivity to SARS-CoV2 antigens was commonly reported in African settings in the early phases of the Covid19 pandemic, though many assays suffered from poor specificity owing to cross-reacting responses to *Plasmodium falciparum*. SARS-CoV2 neutralizing antibodies (nAbs) are not only correlated with functional protection from disease but also highly-specific for virus-specific responses. We used these responses to investigate the evolution of virus exposure and its interaction with *P. falciparum* infection in a community-based, longitudinal cohort of over 500 people in rural villages in Western Kenya. We previously reported an absence of SARS-CoV2 nAbs in cohort participants just prior to the introduction of Covid19 in Kenya in early 2020. Here, we report the results of interval testing of cohort participants for nAbs during through the end of 2021 for contemporary circulating viral variants. We tested participants every 3 months for sero-conversion to SARS-CoV2 using the GenScript surrogate virus neutralization test on serum eluates from dried blood spots. Additionally, we tested preceding and subsequent monthly samples from any participant who tested positive, and we tested all monthly samples for *P. falciparum* using PCR. For over 800 people sampled between May 2020-December 2021, we tested over 2,800 samples for nAbs by ELISA and over 9,000 for *P. falciparum* by real-time PCR. We recorded only 13 sero-positive nAb tests in 10 people, indicating 10 cases of seroconversion, all of which were clustered in December 2020 (wildtype virus) and September 2021 (delta variant). Following sero-conversion, people positive for nAbs sero-reverted within two months. *P. falciparum* prevalence was high as expected, with nearly 20% of monthly asymptomatic samples testing positive for parasites. The limited sero-conversions to SARS-CoV2 prevented analysis of the interaction between parasites and viral acquisition. In this rural community in Western Kenya with endemic *P. falciparum* transmission, development of nAbs directed against SARS-CoV2 was rare in the first 24 months of the Covid19 pandemic.

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EVIDENCE FOR THE DRIVERS OF INFANT DENGUE RISK FROM SURVEILLANCE DATA IN BRAZIL

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Maternally acquired antibodies to dengue virus (DENV) contribute to increased risk of severe disease, including dengue hemorrhagic fever (DHF) through antibody-dependent enhancement (ADE), leading to a peak in DHF risk between six and nine months in infants in Southeast Asia. In Brazil, the burden of DHF is lower in infants and there is an additional peak in severe disease at <1 month. To understand future trends in infant dengue in Brazil, and the potential effect of DENV vaccination on infant dengue, it is necessary to determine the role of maternal serostatus, ADE, and age on risk of DENV infection and severe disease. In this project we fit a mechanistic model of infant DENV and severe DENV risk to surveillance data in Brazil from 2000-2014 to explain the spatiotemporal and age distribution of infant dengue. From Brazil's national notifiable disease surveillance system (SINAN), we extracted data on reported dengue and severe dengue cases by age and state. We developed two mechanistic models. The first model estimated annual DENV risk for DENV-naïve individuals using the age distribution of reported cases. The second model constructed age-specific hazard of infection and severe disease risk, incorporating maternally derived protection against infection, maternally derived ADE, and age-specific changes in infection risk, severity, and reporting. By comparing models with and without key mechanisms, we find strong support for ADE driving the second peak in severe cases. In addition, we find strong support for varying force of infection over the first year of life; models with the strongest support included higher infection and reporting probability among children aged <1 month together with protection at birth that declined to age one, possibly representing changes in exposure. Limitations in surveillance data mean that key questions remain unanswered, including the interaction between maternal Zika and dengue antibodies, and the true extent of under-reporting.

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MODELING THE ECOLOGICAL AND PUBLIC HEALTH IMPACT OF DENGUE VACCINATION IN AN ENDEMIC SETTING

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Global dengue fever burden remains high, and novel interventions will be vital to disease control in the face of ongoing climate change and vector range expansion. While vaccination against dengue virus is one such promising intervention, dengue's unique four serotype structure and resultant eco-evolutionary dynamics pose complex challenges for the development and implementation of a dengue vaccine. Through a process called antibody-dependent enhancement, secondary infections with a heterologous serotype to the primary infection can result in more severe disease and possibly enhanced transmission; a vaccine without pan-serotype protection risks priming a seronegative recipient for a more severe secondary infection. Here, we present a transmission dynamic model to predict how new vaccines, with differential efficacy by serotype and recipient serostatus, are likely to impact the serotype dynamics of dengue and resultant epidemiologic patterns. We investigate the potential ecological and public health implications of widespread vaccine introduction in a dengue-endemic setting, including changes in serotype prevalence; impact on annual and multi-annual cycles; reductions in hospitalizations; and risk of enhanced disease in seronegative recipients. In the absence of vaccination, our findings show complex, non-linear relationships between multiple co-circulating serotypes, as the number secondary infections with one serotype is closely tied the previous transmission intensity and number of primary infections with other serotypes. We find vaccine introduction may lead to multi-annual cycles of outbreaks among seronegative vaccinated individuals, which may lead to an increase in severe infections if vaccination does not provide pan-serotype protection. Our model gives theoretical insights into the potential effect of vaccination on dengue dynamics and can be extended to predict vaccine impacts in specific contexts, such as routine immunization in endemic countries.

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RELATIONSHIP BETWEEN ROTAVIRUS IGA SEROCONVERSION FOLLOWING FULL VACCINATION AGAINST G1P[8] ROTAVIRUS AND ROTAVIRUS GASTROENTERITIS IN A NICARAGUAN POPULATION

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Rotavirus is the leading cause of diarrhea-related deaths globally. Despite the roll-out of live-attenuated oral rotavirus vaccines (ORV), ORV efficacy in children from low-and-middle-income countries (LMICs) trails high-income countries. Low IgA seroconversion, waning immunity, and non-secretor histo-blood group antigen phenotype may contribute to ORV underperformance. IgA titers ≤ 1:90 also predict lower efficacy. We asked if IgA seroconversion (4-fold IgA increase between pre-and post-vaccine titers) predicted rotavirus acute gastroenteritis (AGE) risk in a vaccinated Nicaraguan birth cohort followed weekly for 3 years. Rotavirus was detected in stool with RT-qPCR. Serum IgA titers were measured by ELISA in pre- and post-vaccine serum and at 1 year. Seropositive was defined as titers ≥ 1:80. Secretor phenotype was detected in saliva with ELISA. We analyzed pre- and post-vaccine titers in 276 of 444 children. 88 (32%) of the children, (34% of secretors and 19% of non-secretors) seroconverted after the second dose. 34 children (13%) were seropositive at baseline; only 3 of them (9%) seroconverted. 1-month post-vaccination, 117 children (43%) had IgA titers ≥ 1:80, including 76% of children seropositive at baseline. At 1 year, 84% of 73 children with available titers remained seropositive. Of 255 children with non-missing AGE, 41 (16%) experienced ≥1 rotavirus AGE episode from 1-month post-vaccination to 36 months of age. Among those seronegative at baseline, seroconversion predicted higher rotavirus AGE risk (RR=1.29, 95% CI 1.28, 1.30), even after excluding non-secretors (RR=1.17, 95% CI 1.16, 1.18). Five-month IgA titers ≥ 1:80 was associated with greater AGE risk (RR=1.24, 95% CI 1.23, 1.24), even after excluding non-secretors (RR=1.14, 95% CI 1.13, 1.15). Seroconversion and post-vaccine titers may not associate with reduced rotavirus risk in all settings, and community exposure to wild-type and vaccine-derived rotavirus is common. Future work should explore other immune correlates of protection, novel vaccines, and other strategies to reduce rotavirus burden in LMICs.

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DEVELOPMENT OF A MULTIPLEX MICROSPHERE IMMUNOASSAY TO DETECT PATHOGENIC ARBOVIRUSES IN BRAZIL

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Several mosquito-borne arboviruses including dengue (DENV), Zika (ZIKV), West Nile (WNV), yellow fever (YFV), and chikungunya (CHIKV) viruses have resulted in disease outbreaks of public health concern in the tropics and subtropics. Knowing the seroprevalence of these medically important arboviruses is critical to our understanding of the epidemiology and development of intervention strategies. The overlap distribution of these arboviruses and cross-reactivities of antibodies to flavivirus envelope protein underscore the need of a reliable and convenient serological test to distinguish these arboviruses in countries such as Brazil. We developed a multiplex IgG microsphere immunoassay (MIA) using the non-structural protein 1 (NS1) of DENV1–4, ZIKV, WNV, YFV, and CHIKV, and virus-like particles (VLP) of CHIKV and DENV to test serum panels (n=374 in total) of primary DENV (pDENV), ZIKV (pZIKV) and WNV infections, secondary DENV infection, ZIKV with previous DENV infection, and CHIKV infection that had been confirmed by reverse-transcription-polymerase-chain reaction or neutralization assay, as well as YF-17D vaccinees and negative samples reported previously. The sensitivity/specificity of combined DENV (DENV1–4) NS1, ZIKV NS1, WNV NS1, YFV NS1, and CHIKV VLP IgG MIAs were 90.0%/97.8%, 100%/98.1%, 94.4%/96.5%, 39.1%/94.1%, and 100%/99.6% for pDENV, pZIKV, WNV, YF-17D, and CHIKV panels, respectively. We further tested serum samples (n=200) collected from Saude, a town in the state of Bahia, Brazil and found seropositivities for DENV, ZIKV, YFV and CHIKV as well as multiple arbovirus infections; the results were compared with those based on a recently reported Western blot assay, which distinguished 4 flavivirus serocomplexes using anti-premembrane antibodies (Chen et al. 2024 Emerg Microbe Infect. 13:2301666). In summary, the multiplex and high-throughput MIA assay can be applied to serodiagnosis and serosurveillance of DENV, ZIKV, WNV, CHIKV and YFV infections/exposure in countries where multiple arboviruses co-circulate.

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A NOVEL MODELLING FRAMEWORK TO SIMULATE THE EFFECTS OF HIV STIGMA ON HIV TRANSMISSION DYNAMICS

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HIV stigma significantly shapes both individual behavior and community responses to HIV. However, modeling approaches have rarely represented the highly complex role of stigma in HIV epidemics. Our study introduces an innovative modeling framework designed to disentangle the intricate interplay between HIV stigma and HIV transmission dynamics.We built an individual-based model representing the HIV epidemic (referred to as HIV-IBM) in a USA-like population of 3 million individuals. The HIV-IBM accounted for community demography, same-sex and heterosexual encounters among simulated individuals, healthcare-seeking patterns, drug injection behaviors, healthcare accessibility, and treatment. Stigma parameters were based on a scoping review focused on the prevalence and effects of stigma in people living with and without HIV. The HIV-IBM was used to assess effects of interventions targeting different types of simulated stigma. We tested reductions of stigma by 50% and 100% across the simulated population and performed a sensitivity analysis to identify the effect of each type of stigma on the simulated HIV epidemic. The HIV-IBM without reduced stigma had an annual incidence of 12.6 (95% CI: 9.2-14.4) new cases per 100,000 people. Reducing the overall level of stigma in the population by 50% resulted in an annual incidence of 8.3 (95% CI: 6.3-10.1) new infections per 100,000 people. A 100% reduction in stigma resulted in an annual incidence of just 5.3 (95% CI: 2.3-7.1) new infections per 100,000 people. The result of this study showed that reducing HIV stigma could have a large impact on HIV incidence. Our model framework provides a dynamic approach to understanding the role of stigma in HIV transmission. This novel approach could facilitate the exploration of stigma reduction strategies and offer insights to inform evidence-based policies and interventions for reducing stigma and curtailing HIV.

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IMPACT OF CHRONIC CHIKUNGUNYA ARTHRALGIA ON QUALITY OF LIFE AND MENTAL HEALTH: A PROSPECTIVE COMMUNITY-BASED COHORT STUDY

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Few community-based cohort studies have detected incident chikungunya virus (CHIKV) infection to investigate the risk of chronic arthralgia (CA) and its health impact. This study aimed to identify risk factors for CA and the effect of CA on self-rated quality of life, physical and mental health, and activity level. In 2019, 606 residents ≥6 months old from a neighborhood in Salvador, Brazil were enrolled in a cohort study through a baseline serum survey and were followed up in 2020 to detect the development of anti-CHIKV antibodies using ELISA. During the period, biweekly contact with the participants was maintained to identify symptoms compatible with acute chikungunya. Participants with CHIKV antibody seroconversion who reported acute onset arthralgia for ≥90 days were classified as having CA. During the 2020 survey, participants aged ≥15 self-rated their quality of life, physical and mental health, and activity level through validated questionnaires (SF-12, SRQ-20 and WPAI-GH, respectively). Multivariable Poisson regression with robust variance was used to identify risk factors for CA and the effect of CA on quality of life, physical and mental health, and activity impairment. Of the 456 participants who were negative for anti-CHIKV antibodies at enrollment and completed follow-up, 227 (49.8%) had antibodies in 2020; 49 (21.6%) of which developed CA. The risk of CA was higher in women (RR: 1.5, 95% CI: 0.9-2.4) and among those aged 30-44 years (6.8, 2.5-18.7), 45-59 years (9.5, 3.4-26.0) and ≥60 years (8.0, 2.7-23.6), compared to those <30 years. Age- and sex-adjusted analysis found that among participants ≥15 years of age, those with CA had worse quality of life in the physical component (2.2, 1.3-3.9), worse health status (1.6, 1.1-2.3), and greater activity impairment (1.7, 1.1-2.6) than infected participants without CA. CA participants also had a non-significant increased risk of mental distress (1.7, 1.0-3.0) and worse quality of life in the mental component (2.0, 0.9-4.3). Until vaccines are available to prevent CHIKV infection, ensuring medical care and rehabilitation is critical to reducing the health impact of CA.

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MOLECULAR TYPING OF NON-POLIO ENTEROVIRUS ISOLATED FROM STOOL SAMPLES AS PART OF THE EPIDEMIOLOGICAL SURVEILLANCE OF ACUTE FLACCID PARALYSIS IN DEMOCRATIC REPUBLIC OF THE CONGO

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Although the majority of non-polio enterovirus (EV) infections are asymptomatic, some serotypes can cause paralysis and other serious

clinical conditions. However, non-polio EVs isolated from stool samples collected as part of acute flaccid paralysis (AFP) surveillance are not routinely typed in DR Congo. We typed 141 cell culture NPEV samples from stools collected from AFP cases in DR Congo between January 2021 and September 2022 by RT-PCR followed by Nanopore sequencing of the entire capsid coding region which allowed us to classify isolates in different serotypes. 157 different NPEV strains belonging to 36 different serotypes were detected from 141 cell culture samples from AFP cases. Species B EV (EV-B) strains were the most prevalent at 80.9% followed by species C EV (EV-C) strains at 17.8% and species A (EV-A) strains at 1.3%. E-11 (15/157), E-3 (11/157), CV-A15 (9/157), CV-B5 (9/150), E-7 (9/157), E-6 (8/157), CV-A19 (8/157), E-24 (how many?), E-13 and CV-A20 (7/157) were among the most commonly identified serotypes. Eight serotypes were sequenced for the first time in DR Congo: CV-A19, CV-A11, CV-A10, CV-A9, E-5, E-18, EV-B84, and EV-A119. EV-C99 sequences from two samples were genetically distant from previously sequenced EV-C99 isolates including the only previously known EV-C99 isolate from DR Congo, suggesting a high diversity of circulating EV-C99 strains. Overall, our sequencing data show a high variety of non-polio EV serotypes circulating in D.R. Congo associated with AFP cases and the need for further work to better understand the morbidity of these viruses

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IMPROVING DIAGNOSIS AND MANAGEMENT OF VIRAL INFECTIONS AMONG UGANDAN CHILDREN UNDERGOING CANCER CHEMOTHERAPY THROUGH USE OF NEXT-GENERATION METAGENOMIC SEQUENCING

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Febrile neutropenia (FN) is a life-threatening and presumed infectious condition in immunocompromised patients. Identification of the causative pathogen is crucial for appropriate and timely treatment. Globally, community-acquired viral pathogens cause illness in neutropenic children but data from Sub-Saharan Africa is limited. To describe the epidemiology of viral pathogens among neutropenic children in Uganda, we prospectively enrolled a cohort of children receiving cancer chemotherapy at the Uganda Cancer Institute with fever (N=33) and without fever (N=140) at the time of initial presentation for care. Demographics, clinical parameters and baseline laboratory data were recorded in a standard case report form. A flocked nasopharyngeal swab was collected and stored for batch analysis. Short-read next generation sequencing was performed on nucleic acid extracts from these swabs at Makerere University with enrichment for viral sequences using a hybrid-capture panel targeting >400 common human respiratory pathogens (Respiratory Pathogen ID/AMR Panel, Illumina). 173 children were enrolled from Oct.2022-Oct.2023. To date, we have completed sequencing on 59 patients, 24 (41%) with measured fever at presentation and 35 (59%) without measured fever. Among those who were afebrile at presentation, 24 had a history of reported fever. ≥1 virus was detected in 54% of febrile patients compared to 35% of afebrile patients, most commonly Epstein-Barr virus (N=6), rhinovirus A (N=5) and parvovirus (N=3). Six viruses were found only in febrile patients (parainfluenza 1, rhinovirus B, influenza A, SARS-CoV-2, enterovirus D68, and respiratory syncytial virus B), while cytomegalovirus, parainfluenza 3, and coxsackie A were only detected in afebrile patients. In this pilot study, patients with FN demonstrated a higher frequency and different pathogen profile of viral detections compared to afebrile controls. This study demonstrates the feasibility of deploying next-generation sequencing in Uganda to expand microbiological diagnostics. Larger studies are needed to better define the seasonal patterns of circulation in this context.

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SEROPREVALENCE OF SARS-COV-2 AMONG YOUNG ADULTS: A CROSS-SECTIONAL ANALYSIS OF INFECTION AND VACCINATION

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A cross-sectional study was conducted among young adults, aged 18 to 30 years, on a university campus to investigate the prevalence of SARS-CoV-2 antibodies and to assess prior vaccination and infection. Participants completed surveys on demographic and behavioral factors and to ascertain health status and symptoms. Blood was tested by SARS-Cov-2 Neutralizing Antibody Detection Kit (GenScript), a semiquantitative rapid antibody assay. A total of 313 young adults (39% male, 60% female; median age 22 [range 18.2 - 30.9]) completed testing Oct 13 2022 - Jun 6 2023. Prior COVID-19 vaccination (≥1 dose) was reported by 89% of participants, with 67% reporting full vaccination status (≥2 doses). Prior test-positive SARS-CoV-2 infection was reported by 56%, and 50% reported both past infection and vaccination (≥1 dose). Infections were less frequently reported in the youngest age group (41% for ages 18-19 yrs vs. 55% for ≥20 yrs; p=0.04) and among males (36% for males vs. 57% for females; p<0.01). No such differences were noted in vaccination coverage by age (84% for ages 18-19 vs. 91% for those aged 20 and older; p=0.08) or gender (88% for males vs. 90% for females; p=0.72). Antibodies were observed in 97% of participants by rapid assay, with 43% at higher concentrations (500 - 1500+ IU/mL) by rapid assay. As expected, antibodies were more prevalent in the vaccinated group (67% with high titers) than the unvaccinated group (21%; p<0.05). Out of 7 participants with no detectable antibodies, 2 reported receiving 3 vaccine doses as well as confirmed infection; 1 reported only infection; and only 3 reported no vaccine or known infection history. Furthermore, antibodies were detected in 10 out of 12 participants who denied both vaccination and prior infection, 4 with high titers. Ongoing laboratory testing are underway to detect viral respiratory pathogens by qPCR and confirm SARSS-CoV-2 antibodies by quantitative ELISA. Despite low vaccination coverage in this young adult population, about half self-reporting a known infection, nearly all carried SARS-CoV-2 antibodies. We demonstrate unrecognized infection in approximately 80% of unvaccinated young adults.

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SARS-COV-2 ANTIBODIES SEROPREVALENCE AFTER CORONAVAC IMMUNIZATION IN GUARAMIRANGA, NORTHEAST BRAZIL, 2021-2022

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Guaramiranga, a mountain town in Ceará State, Brazil's northeast, has approximately 5,654 inhabitants. Starting on January 20, 2021, Guaramiranga became the first Ceará municipality to vaccinate all adults against COVID-19. They acquired 5,187 vaccines for the first dose (D1), of which 3,328 were CoronaVac, manufactured by Sinovac/Butantan. They fully vaccinated 4973 adults with two doses, of which 1,734 received only the CoronaVac vaccine. D1 vaccination began on January 20, 2021, and ran until April 1, 2022, while the second dose (D2) started on February 18, 2021 (28 days after D1) and ran until July 6, 2022. From January to July 2022, we conducted a seroepidemiological study among the fully vaccinated adult population of Guaramiranga with CoronaVac. We used a chemiluminescence immunoassay on blood serum samples to determine if they had neutralizing IgG antibodies to SARS-CoV-2. The median time between D1 and D2 was 24 days (20-147; IQR 61): 204 with a time ≥ 28 days (37.5 %) and 340 < 28 days (62.5 %). We analyzed 544 samples, of which 452 had a positive result (83.1%, p-value < 0.001, 95% CI 0.797-0.861). The samples mainly came from men (n = 324; 59.6%), mixed race (n = 339; 62.3%), with a median age of 34 years (18-76; IQR 18). The

median time between serum collection and application of D2 was 210 days (0-330; IQR 48): 537 with time > 15 days (98.7%), considered immunized, and seven with time ≤ 15 days (1.3%). Four of these seven samples were collected on the same day of the D2 application, two on the next day, and one after two days. Most positive samples (n = 445; 81.8%) were from immunized individuals. The median time between exam collection and D2 for these positive samples was 212 days (118-330; IQR 55). Out of 452 positive samples, 27 were from COVID-19 cases confirmed by RT-PCR or rapid test: one was collected seven days before diagnosis and 26 later (median 42.5 days). Thus, 426 (94.2%) samples had antibodies that resulted exclusively from vaccination for around seven months after D2. The findings highlight the relevance of serosurveillance in understanding viral transmission and guiding vaccine booster dose decisions.

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IMPACTS OF PAVING THE INTEROCEANIC HIGHWAY ON DENGUE IN PERU'S AMAZON BASIN

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Human mobility drives the spread of many infectious diseases, yet the health impacts of changes in mobility due to new infrastructure development are poorly understood and currently not accounted for in impact assessments. While past work linking mobility to infectious disease has had to rely on cellphone or survey data, we take a novel experimental approach, leveraging historical road upgrades as a proxy for regional human mobility changes. In collaboration with the Regional Health Directorate of Madre de Dios, Peru, we analyzed how road paving altered transmission of dengue—a high-burden mosquito-borne disease—via changes in human mobility through recently deforested areas in Peru's Amazon basin. The rapid paving of the Interoceanic Highway through a formerly isolated region of the Amazon in 2009 provides a unique opportunity to quantify the causal impact of road paving on vector-borne disease transmission. To uncover this relationship, we compared dengue case data from health centers near to the newly paved highway and those far to the highway before and after the highway was paved (a difference-in-differences causal inference approach). We used a population-weighted panel regression model that controls for differences between healthcare centers, such as variation in temperature, precipitation, and baseline dengue burden. Preliminary results show that the paving of the highway caused at least an additional 25,706 dengue cases since paving (95% confidence interval: [15,545-35,867]) compared to if the highway had never been paved, accounting for 45.4% [27.4%-63.3%] of all dengue cases recorded in the region since paving. This is the first study to directly quantify the causal impact of road paving on dengue transmission and is especially timely after two new roads were recently approved for construction throughout the region, at the protest of local communities and indigenous groups. Our findings demonstrate a novel method for studying the impacts of mobility on disease transmission and advocate for future road construction plans to account for increased infectious disease transmission during impact assessments.

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SURVEILLANCE OF SARS-COV-2 BASED ON SANGER SEQUENCING OF THE SPIKE GENE ALLOWED THE DETECTION AND TRACKING OF VARIANTS IN BOLIVIA FROM 2020 TO 2023

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During the COVID-19 pandemic, the emergence and spread of SARS-CoV-2 variants highlighted the need to rapidly identify them using alternative and cost-efficient approaches to whole genome sequencing. SARS-CoV-2 variants were identified based on a fragment of the spike gene (nt 22589-23125) amplified by Sanger sequencing using an in-house primer set corresponding to a partial region of the receptor-binding domain (RBD), which included the receptor-binding motif (RBM). For validation purposes, an NGS-based method on an Illumina Iseq100 platform was also used to examine and compare a group of samples representing different variants. The results confirmed the consistency of these two approaches. 2551 samples collected from June 2020-December 2023 from confirmed COVID-19 cases were screened for variants across the seven waves in Bolivia. A total of 29 different variants were identified, which, in order of appearance, were: Gamma, Alpha, Lambda, Beta, Epsilon, Mu, Theta, Delta, and Omicron (BA.1, BA.2, BA.2.12.1, BA.5.2, BA.5.2.24, BA.2.56, BA.2.75, BQ.1, BF.12, BF.14, BF.25, BF.39.1, BF.40, BF.7.16.1, CH.1.1, XBB.1, XBB.1.5, XBB.1.16, and XBB.4). The distribution and frequency of SARS-CoV-2 variants were initially influenced by the circulation of predominant variants circulating in South America (Gamma, Lambda, and Mu) and later by the impact of variants of global distribution such as Delta and Omicron. This study demonstrated that the designed Sanger sequencing strategy was useful in low-income settings for the identification of most of the variant types circulating in Bolivia during the study period. This approach can be extended to the analysis of other viruses with zoonotic and pandemic potential to enhance local epidemiological surveillance.

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DETECTION OF DENGUE AND METAGENOMIC ANALYSIS OF *AEDES AEGYPTI* VIROME IN KISUMU, KENYA.

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Aedes aegypti is the main vector for Dengue and Chikungunya viruses. It harbours insect-specific viruses (ISVs), which can impact mosquito ability to transmit diseases by interfering with viral processes. Limited surveillance has left the diversity of ISVs and their effect in local *Ae. aegypti* populations largely unknown. This study aimed to address this gap by conducting analysis during a dengue outbreak by characterizing the viromes of *Ae. aegypti* in Kisumu. Adult mosquitoes were collected in Jua Kali area of Kisumu using CDC miniature light traps. Mosquitoes were identified using taxonomic Keys, pooled and stored at -80 °C for virome analysis. RNA extraction and library preparation were performed followed by Illumina Miseq sequencing. Initial analysis was done on the CZ-ID platform, an integrated pipeline with capabilities to perform quality control, de-hosting, duplicate removal, as well as assembly and identification of viruses**.** Virus isolation was performed in Vero cells. A total of 2,142 female *Ae. aegypti* grouped into 86 pools and 4 superpools were processed for cell culture and metagenomic analysis respectively. Dengue virus serotype 3 was detected in 1 pool. Metagenomics analysis revealed the presence of a wide range of viruses, including *Iflaviridae* family members Tesano *Aedes* Iflavirus, Armigeres Iflaviruses, Sassandra virus, Hanko Iflavirus 1, Rabai virus, and unclassified Korle-Bu virus. Tesano *Aedes* virus was prevalent in 3 out of the 4 superpools, and Armigeres virus was present in 2 of the superpools. The present study provides initial insights into the virus diversity within *Ae. aegypti* mosquitoes in Kisumu, representing the first attempt to uncover this information in the region and particularly during a dengue outbreak. Despite current efforts, understanding the complete impact of ISVs on arbovirus transmission remains challenging due to the intricate and context-dependent nature of these interactions. Ongoing research may unravel the mechanisms and subtleties governing ISV-arbovirus interactions.

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UNDERSTANDING HUMAN-ANIMAL-TICK INTERACTION AND RISK FACTORS WHICH LEAD TO THE EXPOSURE TO CRIMEAN CONGO HAEMORRHAGIC FEVER VIRUS (CCHFV) IN UGANDA: A MULTIDISCIPLINARY STUDY

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Crimean-Congo Haemorrhagic Fever (CCHF) is a zoonotic disease with a wide geographic range. It can present with non-specific symptoms leading to a severe disease with fatality. In Uganda, we observe increased cases of CCHF, with a high case fatality rate. However, the true extent of total cases is unknown due to mild and possibly misdiagnosed cases. Furthermore, environmental and behavioural risk factors for CCHF are not fully understood in Uganda, and the populations most at risk have not yet been identified. A better understanding of exposure risks can guide educational programs and interventions. This study, therefore, integrated a quantitative serology survey with a qualitative study to understand CCHFV exposure dynamics in Uganda. We conducted focus group discussions and in-depth interviews to examine human, animal, and tick interaction dynamics in six distinct environmental and cultural districts in Uganda. These findings informed a serosurvey design to identify risk factors associated with tick exposure and CCHFV transmission. The seroprevalence study is currently underway and will provide data from 1920 participants across the six districts. Blood is collected alongside a structured survey informed by our qualitative study. CCHFV antibody testing will be performed to estimate CCHFV exposure and identify risk behaviours for exposure. Social science findings revealed various interaction practices influenced by cultural, environmental, and socioeconomic factors that may be linked with tick interactions and direct transmission of CCHFV. These included hunting wild animals and birds, tick plucking and eating, animals sleeping within the household, slaughtering sick animals for consumption, and rituals using animals, their products, or by-products. These results will be presented alongside the seroprevalence and structured survey results and discussed in relation to their implications for CCHFV transmission and control in Uganda.

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DEVELOPMENT OF A RT-LAMP ASSAY FOR LA CROSSE VIRUS

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The leading cause of arboviral pediatric encephalitis in the United States is La Crosse virus (LACV), a mosquito-borne virus in the genus *Orthobunyavirus* (*Bunyavirales*: *Peribunyaviridae*). Because of the non-specific symptomology of early LACV infection, surveillance to detect enzootic LACV circulation is key to raising awareness for prevention and alerting healthcare providers. However, LACV cases have historically occurred around specific foci instead of having dispersed circulation along the range of its primary vector, *Aedes triseriatus.* This has led to inconstancies in surveillance efforts, often resulting in reactive surveillance to identified cases. Additionally, the technical expertise, facilities, and equipment needed for qRT-PCR testing of trapped or reared adult mosquitoes, the primary tool for LACV detection in mosquitoes, is often not available in a timely fashion. To address the gap between local field personnel collecting mosquitoes and downstream testing facilities, we developed a RT-LAMP (reverse transcription loop-mediated isothermal amplification) assay for LACV. Five sets of primers targeting the S segment of the LACV genome were designed via the NEB® LAMP Primer Design Tool. These were assessed for sensitivity and specificity compared with qRT-PCR, using multiple LACV strains and other orthobunyaviruses. This assay requires minimal training and easily accessible equipment, which could reduce the barriers for enhanced mosquito surveillance, which in turn will aid public health efforts in communities at risk for LACV infection.

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ISOLATION OF LA CROSSE VIRUS FROM *AEDES TRISERIATUS* (DIPTERA: CULICIDAE) IN WESTERN NORTH CAROLINA

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La Crosse virus (LACV) (genus *Orthobunyavirus*, family *Peribunyaviridae*) is a mosquito-borne virus that causes disease ranging from non-febrile illness to meningitis or encephalitis, frequently in children. Since 2018, three high-risk geographic clusters of LACV cases identified in regions of Tennessee, North Carolina, West Virginia, and Ohio. Though LACV is maintained horizontally through mosquitoes, primarily *Aedes triseriatus* (Say), and small mammals such as squirrels and chipmunks, the virus also utilizes transovarial maintenance in an efficient manner. Therefore, standard adult mosquito surveillance is frequently supplemented with ovitrap collection, rearing, and subsequent testing of adults for LACV. Here we report detection and isolation of two LACV strains (HAY 539 and JAC 210) from *Ae. triseriatus* adult mosquitoes reared from field-collected eggs from five western North Carolina counties during June–September 2021. Virus isolates were made on Vero cells and pathogen identity was confirmed with qRT-PCR and full genome next generation sequencing. The minimum infection rate (maximum likelihood estimate) in *Ae. triseriatus* was 1.19 in 10,000 (95% CI: 0.21–3.88). A maximum likelihood phylogenetic analysis of the M segment coding regions indicated both viruses fell within the lineage I clade. Strain HAY 539 demonstrated a 99.4% identity to NC97-7306 (GU206127) collected from North Carolina in 1997 and JAC 210 demonstrated 98.5% identity with NC00-283 (GU206112), another LACV isolate collected from North Carolina in 2000. The homology of these strains with isolates from the same geographic region from over 20 years ago indicates a lack of introduction of genetically diverse strains over time. Because recent studies have indicated that LACV strains from lineage I are likely to be the most lethal in humans, these findings highlight the contribution of transovarial viral maintenance and the potential for emergence from the transovarial cycle.

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CYTOMEGALOVIRUS INFECTION AND SHEDDING IN PREGNANT WOMEN, CHILDREN, AND INFANTS IN SIERRA LEONE

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Congenital Cytomegalovirus (cCMV) infections are the leading non-genetic cause of hearing loss and neurodevelopmental delay in infants. Risk factors for non-primary CMV infection (npCMV) in pregnant people, primarily occurring in low-income countries, are largely unknown. In primary CMV infection, exposure to young children shedding virus is a significant risk factor in pregnancy; the *objective* of this study is first to identify prevalence and magnitude of CMV and npCMV in pregnant women in Sierra Leone, and to observe the association of CMV shedding in young children and

npCMV in pregnant people. A longitudinal cohort of 31 pregnant women (before the third trimester), 38 children less than 36 months of age (1-2 children per household), and then 17 infants were enrolled. Saliva samples were collected once weekly, and in the pregnant/postpartum subjects, urine, blood, and breast milk (after birth of the infant) was collected once a month. DNA was extracted and quantitative CMV DNA PCR was performed. Shedding was defined as at least two positive samples detected consecutively. Women were included only if they had at least three samples collected over at least 60 days (N = 25). Over the duration of the study, 21 women (84%) demonstrated shedding, and 14 (56%) shed while pregnant. Of children less than 36 months of age, all but one (27/28, 96%) demonstrated shedding. There was a positive correlation between viral load of the young child and viral load of the pregnant/postpartum subject on any given data point date. Behaviors which may increase CMV exposure were common; there was no association between these behaviors and viral shedding. Our study shows that in Sierra Leone, occurrence of shedding of CMV in saliva is common in pregnant women and nearly universal in children under 3 years of age. This is the first study which demonstrates a statistically significant correlation between the magnitude and occurrence of CMV viral shedding in young children and pregnant or postpartum women in the same household, supporting the hypothesis that the care of young children is a possible risk factor for npCMV in pregnant women.

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SPATIOTEMPORAL FORECASTING OF NIPAH VIRUS SPILLOVER RISK IN BANGLADESH, 2007-2023

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Zoonotic spillover occurs when infected flying fox bats come in contact with humans or indirectly through contaminated food sources. Surveillance primarily prioritizes locations with historical cases during the winter season. We suspect Nipah virus transmission from flying fox bats to humans occurs when temperatures are cool during these winter months. Early identification of Nipah virus infections is important to initiate early treatment and limit person-to-person transmission. However, the determinants of annual heterogeneity in spillover density and the geographic distribution of spillover are very poorly understood. This analysis aimed to assess environmental and temporal predictors of Nipah virus spillover and develop a model to make one-month-ahead forecasts of spillover risk of Nipah virus in Bangladesh districts. The model with the best predictive accuracy was identified using cross validation of training data from 2007-2019 and was then tested on data from 2020-2023. This “final” model was compared with a “base” model that only used information on the month of year and historical cases per district as predictors. After model training, the month-weighted cross validation AUC on the test data was 0.81, whereas the month-weighted AUC of the base model was 0.60. Ratios between the estimated spillover risk from the full and base models showed that the full model produced higher spillover risk estimates in district-months that reported cases compared to the base model, and also had better specificity in identifying district-months that did not report a spillover event. Similarly, spillover risk ratios above 1 were also seen in districts that saw a case when compared to their own historical average estimated risk. These results suggest that environmental data can be used to improve forecasts of Nipah virus spillover risk and improve the efficiency of public health surveillance efforts.

7860

VIRAL SURVEILLANCE IN CAVE-DWELLING BATS FROM KAPCHORWA DISTRICT IN EASTERN UGANDA REVEALS DETECTION OF MULTIPLE CORONAVIRUSES, PARAMYXOVIRUSES, AND RHABDOVIRUSES

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Bats are known to harbor a variety of viruses with capacity for co-circulation and impact on medical and veterinary health worldwide. Thus, surveillance of bat-associated viruses is crucial to developing novel public health response strategies. Furthermore, human encroachment into caves for shelter, mineral harvesting, and tourism pose additional risk to viral spillover. Bats within the genera *Rhinolophus*, *Hipposideros*, and *Miniopterus* are known to co-roost in caves and harbor a variety of viruses related to those with potential to affect human health. We hypothesize that if these bats are reservoirs for multiple potential pathogens then longitudinal surveillance will uncover the dynamic bat/virus relationships between and across cave structures. Bat oral and rectal samples were collected from bats captured in three caves in Eastern Uganda in January (dry season) 2022-2023 and May (wet season) 2021-2023. Samples were subjected to RNA extraction followed by viral nucleic acid detection using consensus PCR assays targeting six viral families: *Coronaviridae*, *Filoviridae*, *Flaviviridae*, *Peribunyaviridae*, *Paramyxoviridae*, and *Rhabdoviridae*. Coronavirus nucleic acid was detected in oral and rectal swab samples from *Hipposideros ruber* (n = 14), *Rhinolophus* spp. (n =8), and *Miniopertus* sp. (n =10). Additionally, oral and rectal swabs representing all genera of bats and caves sampled were putatively positive for paramyxoviruses (n = 24) and rhabdoviruses (n = 2). Testing and sample sequence confirmation is ongoing, as are attempts to isolate virus from positive samples. Overall, this work will contribute to our understanding of viral ecology and spillover risk at the human/bat interface and aid in discovery of novel viral strains.

7861

ROLE OF MULTIPLEXED IMMUNOASSAYS TO DETERMINE IMPACT OF NON-SPECIFIC BINDING ON IMMUNOASSAYS: IMPLICATIONS OF “STICKY SERA” IN DISEASE SEROSURVEILLANCE IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Serological tests have long been used to determine antibody reactivity to antigenic pathogen-specific targets. While not a definitive measure of biologic protection, these assays can help determine population-level pathogen circulation, and in some cases, exposure status. The multiplex bead-based immunoassay (MIA) is quickly becoming a popular approach due to its testing reactivity to multiple antigens simultaneously. However, with these results, seroreactivity is identified through determination of a cut-off value specific to each target. As part of a larger study assessing the antibody durability following vaccination for *Ebolavirus* (EBOV), 10009

serum samples collected in various cohorts across the Democratic Republic of the Congo (DRC) were tested. With seven total targets, this pan-filovirus MIA included EBOV glycoprotein (GP), nucleoprotein and viral matrix protein 40 (VP40), as well as *Bundibugyo ebolavirus* GP, *Sudan ebolavirus* GP, and *Marburgvirus* GP and VP40, and a bovine serum albumin (BSA) control. Using a geometric mean approach to determine the threshold for reactivity for all targets, cut-offs were set for each antigen (all falling within a range of 4000 - 12000 Median Fluorescence Intensity (MFI)). With a conservative cut-off for BSA of 10,000 MFI, 140 (1.4%) of all samples tested were be considered seroreactive to BSA. Of these samples, 39.2% were considered reactive to all filovirus antigen targets - potentially indicating that the samples were "sticky". While the biological explanation of the "sticky sera" is unknown, geographical associations between those with pan-reactive samples were observed, which may be linked to diet or lifestyle norms. Further research is needed to assess the true mechanism of these samples' seroreactivity. These data suggest that control targets should be regular additions in the development of serological testing strategies as they can help to identify sera which show unspecific binding to a variety of protein targets. Controls such as BSA in an MIA assay may help to identify samples which would otherwise be overestimated by traditional single-plex serological approaches.

7862

SEROPOSITIVITY TO BOVINE CORONAVIRUS IN DAIRY WORKERS AND COMMUNITY DWELLERS: RESULTS OF A PILOT STUDY

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Among human coronaviruses, there is evidence that some currently adapted to humans may be zoonotic in origin, including bovine origin. Bovine coronavirus (BCoV) is a betacoronavirus associated with diarrheal disease in calves and respiratory disease in feedlot cattle. To date, there has been little study of the zoonotic potential of BCoV. In this study, the seroprevalence of BCoV antibodies in a cohort of dairy workers was assessed for evidence of zoonotic exposure to BCoV. We performed a pilot cross sectional seroprevalence study of BCoV antibodies in a cohort of 28 dairy farm workers and 15 community controls. Study participants were drawn from a longitudinal study of Washington State dairy workers and corresponding community controls living in the same region. Community controls could not have worked on a dairy farm in the past 10 years nor had anyone in the household who did. We obtained and tested serum for antibodies to BCoV using a fluorescent focus neutralization assay with BCoV antibody positive and negative control cattle sera. Antibodies to SARS- CoV-2 were tested using Abbott Architect IgG (nucleocapsid) and IgM (spike). Chi-squared tests were utilized to assess any correlation between seropositivity to SARS-CoV-2 (IgM or IgG) and seropositivity to BCoV. Using the serological positivity cutoff of 1:128, 2 community controls were positive for BCoV. Among the workers, 1 was positive at 1:128 and 1 was positive at a titer of 1:512. The geometric mean of titers did not differ significantly between groups. We did not observe any correlation between seropositivity to SARS-CoV-2 (IgM or IgG) and seropositivity to BCoV. This pilot study of dairy workers and community controls did not demonstrate significant evidence of zoonotic exposure to Bovine coronavirus. At the same time, the fact that we observed the highest seropositive titer in a dairy worker suggests that sporadic exposure may occur. Further studies should investigate this possibility, as well as the possibility of cross-reaction with related betacoronaviruses such as human coronavirus OC43.

7863

EVALUATION OF AMINO ACID DETERMINANTS OF DIFFERENTIAL SERUM NEUTRALIZATION BETWEEN DIVERGENT AND EPIDEMIC DENGUE TYPE 1

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DENV is sustained in ecologically discrete but overlapping non-human primate sylvatic and human urban transmission cycles. Sylvatic DENVs form independent clades and are genotypically distinct from other endemic variants within a given serotype, and the full impact of genetic variability on differences in susceptibility to neutralization by neutralizing antibodies (NAbs) in human immune sera remains to be assessed. The primary target of NAbs is the virus envelope (E) glycoprotein. We sought to characterize epitopes which contribute to different neutralization phenotypes between DENV-1 strains isolated from sylvatic and urban epidemic transmission settings. The neutralizing potency of DENV-1 primary immune sera against DENV-1 P72-1244, a variant isolated from canopy-dwelling monkeys, was characterized using sera from endemic (n=18) and non-endemic (n=8) donors 1-30 years post infection using a foci reduction neutralization assay (FRNT50). We found that all primary immune sera had > 8-fold reduced neutralization potency between P72-1244 and epidemic strains belonging to DENV-1 genotypes I, IV and V. We identified 5 and 23 residues within the envelope glycoprotein of P72-1244 and sylvatic strain Brun2014 respectively, which are uniquely different from prototypical and contemporary clinical reference strains, and likely contribute to differences in the neutralization phenotypes observed. To test our hypothesis, we constructed a panel of recombinant DENV-1 infectious clones containing E residues which vary between DENV-1 strains West Pac '74, BIDV852, P72-1244, Malaysia.36046/05 and the sylvatic strain Brun2014 to recapitulate potential epitope variability between epidemic and sylvatic DENV-1. We interrogated neutralization potency and breadth of endemic and non-endemic primary immune sera against DENV-1 chimeras relative to the parental viruses. These results characterize the effects of divergent DENV-1 residue substitutions on viral resistance to neutralization and highlight epitope targets potentially involved in evasion of antibodies elicited by infection with endemic DENV-1.

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SEROLOGICAL EVIDENCE OF EMERGING HENIPAVIRUSES AND PARAMYXOVIRUSES IN PTEROPODID BATS IN THE PHILIPPINES

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Pre-emergence pandemic preparedness against deadly zoonotic viruses involves active biosurveillance of potential wildlife reservoirs to inform spillover risk predictions. Since its initial emergence in 1998 in Malaysia, Nipah virus (NiV) of the genus *Henipavirus*, family *Paramyxoviridae,* has caused deadly outbreaks in Singapore, Bangladesh, and India. In 2014, an outbreak of NiV disease occurred in two villages in the province of Sultan Kudarat, island of Mindanao, Philippines, and was linked to the slaughter and consumption of horse meat. Flying foxes are the presumed wildlife host for NiV and horses an intermediate host, consistent with the transmission

chain of the close relative Hendra virus (HeV) in Australia. Despite the presence of flying foxes in the Philippines and a NiV-like virus outbreak, there has been limited follow-up to determine the current circulation of NiV in native pteropodid bats across the Philippines archipelago. Here, we sampled five species of pteropodid bats, including flying foxes (*Pteropus vampyrus*, *Pteropus hypomelanus, Acerodon jubatus*), rosette bats (*Rousettus amplexicaudatus*), and dawn bats (*Eonycteris speleae*, *Eonycteris robusta*) native to the Luzon Island of the Philippines to confirm evidence of NiV circulation and explore the presence of other paramyxoviruses. Sera samples were collected monthly for one year and tested by a multiplex microsphere-based immunoassay for immunoglobulin (Ig) G reactivity against a panel of five henipaviral glycoproteins (GP; Nipah, Hendra, Cedar, Ghana, and Mojiang virus) and three related paramyxoviral receptor binding proteins (RBP; Sosuga, Yeppoon, and Grove virus). Serologic evidence of NiV was predominantly detected in flying foxes at an estimated seroprevalence of 13.1% (42/320), providing the first indications of NiV circulating in flying fox hosts in the Philippines. In addition, we found serological evidence of Asiatic paramyxoviruses most closely related to Sosuga virus, Yeppoon virus, and Grove virus. Further biosurveillance efforts will needed to assess areas at-risk for spillover within the Philippines.

7865

INTERROGATING THE ECOLOGY OF NO-KNOWN VECTOR FLAVIVIRUSES THROUGH *IN VITRO* VALIDATION OF MODEL-BASED HOST-VECTOR-VIRUS PREDICTIONS

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Flaviviruses (genus *Flavivirus*, family *Flaviviridae*) cluster phylogenetically based on host-virus-vector relationships. Most flaviviruses cycle between hematophagous arthropods (*i.e.,* mosquitoes, ticks) and vertebrate hosts, while others have been isolated strictly from arthropods (*i.e.,* insect-specific flaviviruses) and others only from vertebrate hosts (*i.e.,* no-known vector (NKV) flaviviruses). NKV flaviviruses have been isolated from either rodents or bats (referred to as r-NKV and b-NKV, respectively), and in rare occasions, humans. Previous work suggests some b-NKV flaviviruses replicate to low titers on mosquito cells, and one report describes a b-NKV flavivirus isolated from field-caught ticks. Barring these reports, little is known surrounding true host range and ecology of b-NKV flaviviruses. Using existing machine learning models designed to predict host-vector-virus associations based on a virus' genomic composition, we demonstrate a framework for validating these model predictions by performing single-step growth curves on a number of different arthropod cell lines. This framework has potential to enhance our understanding of flavivirus ecology, as results will be used to strengthen predictive models and inform biosurveillance efforts. Results are discussed within the context of validating predictive models using experimental approaches.

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PLASMA IGM ANTIBODIES CONTRIBUTE TO VIRUS NEUTRALIZATION IN EARLY IMMUNE RESPONSES TO SECONDARY DENGUE VIRUS INFECTIONS

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Dengue virus serotypes 1-4 (DENV1-4) cause 100 million infections per year, and a portion progress to severe disease. IgM antibodies are thought to arise early in the primary immune response, but their neutralizing role during secondary immunity is unclear. We sought to understand the role of plasma IgM antibodies during acute secondary DENV infection, which is the time of risk for progression to severe disease. To investigate contribution of IgM antibodies to plasma DENV-neutralizing activity, we utilized pediatric plasma samples from acute secondary DENV1 infections (n=27). Each sample was IgM- and mock-depleted, and their neutralization potency was assessed with a Focus Reduction Neutralization Test (FRNT) using mature DENV 1-4. Percent IgM contribution to plasma neutralizing activity was assessed as a ratio of the difference of the two fractions and normalized for IgG concentration. We found that acute secondary plasma neutralized the infecting serotype of DENV1 (Mean NT_{50}=1429) in 22 out of 27 samples. Thirteen of these 22 samples demonstrated contribution of IgM antibodies towards plasma DENV1 neutralizing activity, with a mean contribution of 42%. We found that while 17 of 22 plasma samples demonstrated neutralization of 3 or more DENV serotypes, only 6 of these showed any contribution of IgM to broad neutralization. Moreover, IgM contribution was highest towards the infecting serotype (mean DENV1 = 40%) as compared to other serotypes (mean DENV2 = 23%, DENV3 = 27%, and DENV4 = 34%). Interestingly, our analysis suggested a potentially protective role for acute IgM antibodies during the secondary infection as there was a trend towards greater contribution of IgM in milder DENV1 cases (median=51%, n = 9) than in those with severe dengue disease (median=24%, n=4; p = 0.1063, Mann Whitney Test). Thus, acute IgM antibodies contribute substantial plasma neutralizing activity during acute secondary infection, especially towards the infecting serotype. IgM antibodies may have a role in controlling secondary DENV infection and promoting early protective immunity.

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INCREASED FREQUENCY OF ANTIGEN-SPECIFIC CD4+ T CELL RESPONSES FOLLOWING VACCINATION WITH ORAL LIVE ATTENUATED POLIO VACCINES

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Despite enormous progress, polio eradication remains elusive. An enhanced understanding of polio vaccine-induced immunity is needed. While the importance of serum neutralizing antibodies for disease protection is well established, relatively little data on the role of cell mediated immunity following oral or injectable vaccines is available. We investigated differences in polio antigen (Ag)-specific T cells following vaccination with inactivated (IPV) versus oral live attenuated (OPV) polio vaccines using peripheral blood mononuclear cells from volunteers enrolled in two polio vaccine studies. In the first, twenty-nine (n=29) healthy adults were randomized to receive intradermal fractional dose IPV with or without a novel mucosal adjuvant (dmLT). In the second trial, healthy adults were randomized to monovalent Sabin strain OPV1 or novel OPV1; samples from a subset of twenty-eight (n=28) volunteers in this trial were available. Younger adults (18-25 yr) in both studies received IPV-based series in childhood (OPV-naïve) while older adults (26-45 yr) were OPV-primed. A flow cytometric activation induced cell marker (AIM)-based approach was used to assess the frequency of Ag-specific CD4+ and CD8+ T cells using structural (n=293) and non-structural (n=368) polio peptide megapools. Following vaccination, we detected CD4+ and/or CD8+ Ag-specific T cells in 57.9% of volunteers (mean T cell frequency 0.09%; range 0.02-0.41%). Ag-specific CD4+ T cells were more often identified following vaccination with live attenuated OPVs (18/28 (64.3%)) as compared to IPV (4/29 (14%)) while Ag-specific CD8+ T cells were identified equally (7/29 (24%) vs. 7/28 (25%)). The frequency of Ag-specific T cells increased over time, especially observed in CD4+ T cells at Day 28 in OPV-primed volunteers (p=0.05). Clear structural versus non-structural immunodominance was not observed however OPV-primed volunteers revealed more frequent non-structural T cell

responses compared to OPV-naïve cohorts. Ongoing investigations seek to understand the relationship between Ag-specific T cell responses and PV shedding dynamics.

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DISTINCT CELLULAR IMMUNE RESPONSES ARE ASSOCIATED WITH PATHOGENESIS, DISEASE PROGRESSION, AND LATE-RELAPSING HEPATITIS IN YELLOW FEVER PATIENTS

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Yellow fever (YF) is a hemorrhagic, infectious, febrile viral disease of great importance to public health due to its clinical severity and high potential for dissemination in urban areas. Few studies have addressed humoral and cellular immunity during human infection with the YF virus. Thus, this work aimed to evaluate the cellular immunity of individuals infected by the YF virus through in vitro antigen-specific stimulation of peripheral blood mononuclear cells. A range of memory T-cell features was evaluated including: Naïve/N, Early Effector/eEf, Central Memory/CM, Effector Memory/EM, Naïve*/N*, Early Activated/eA, Non-Interferon Mediated/IFN-nM, Interferon-Mediated/IFN-M $CD4^+$ and $CD8^+$ T-cells. The study population included 45 patients with YF in the acute phase (Days 1 to 15 after symptoms onset/D1-15) and 16 healthy individuals (HC). The data demonstrated that patients with acute YF presented increased frequency of CMCD4, eACD4, eEfCD8, EMCD8, CD4IL-5, and CD8TNF along with lower ratios of N*CD4, IFN-nMCD4, NCD8, IFN-nMCD8 as compared to HC. When the YF group is classified according to the clinical outcome, there was observed a higher frequency of CMCD4, eEfCD8, and EMCD8 and a lower frequency of N*CD4, NCD8, and IFN-nMCD8 in patients progressing to discharge, while those evolving to death showed an increased profile of eACD4, CD4TNF and CD4IL-5 and decrease profile of NCD4 and IFN-MCD8. In addition, were observed high levels of CMCD4, eACD4, CD4IL-5, eEfCD8, and EMCD8 and low levels of NCD4 and N*CD4 in YF patients without late-relapsing hepatitis (nL-Hep). Those YF patients who progressed to late-relapsing hepatitis (L-Hep) presented an increase of CD4IL-5, N*CD8, and IFN-MCD8 and a decrease of NCD4, IFN-MCD4 and IFN-nMCD4. This study provided a comprehensive overview of cellular immunity during acute YF infection, highlighting that distinct cellular immune responses are associated with pathogenesis and disease progression in wild YF infection.

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FLAVIVIRUS ANTIGENIC CARTOGRAPHY OF PREEXISTING NEUTRALIZING ANTIBODIES IN A PEDIATRIC COHORT IN MERIDA, MEXICO, A HYPERENDEMIC AREA FOR ARBOVIRUSES

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Flaviviruses (*Flaviviridae* family) such as the dengue (DENV 1-4) and Zika (ZIKV), are closely related viruses whose infection leads to cross-reactive antibody responses. In 2021, a set of serum samples collected from a pediatric cohort in Merida, Yucatan (n=662) were identified as previously exposed to flaviviruses by IgG ELISA. These samples were further characterized by focus reduction neutralization tests (FRNT) to quantify their neutralizing antibody titers (50% neutralization titer= NT_{50}) against DENV (1 to 4) and ZIKV *in vitro*. Analysis of the NT_{50} values identified that 44% (n=289), 51% (n=336), 22% (n=149), and 37% (n=245) of all children had detectable levels of neutralizing antibodies against the DENV serotypes -1, -2, -3 and -4, respectively. Interestingly, 75% (497/662) showed neutralizing activity against ZIKV as well. A comparative analysis of NT_{50} values suggested that 47% (311/662) of children experienced a prior monotypic infection with ZIKV; 5.3% (n=35) with DENV-2; 4.5% (n=30) with DENV-1; 2.7% (n=18) with DENV-4, and only 0.4% (n=3) with DENV-3, based on >4-fold higher neutralizing titers against a single virus compared to the others. Additionally, multitypic flavivirus-exposure was inferred in 40% (265/662) of children. Finally, the antigenic distances between the DENV serotypes and ZIKV were calculated. An antigenic cartography map revealed two main clusters for serum reactivity, one grouped against DENV-1 and DENV-2 (94%, n=249) which clustered relatively close to each other in antigenic space, and another cluster showing high reactivity (84.3%, n=223) against ZIKV. The increased seropositivity against ZIKV suggests a previous exposure to this flavivirus in children of Merida; however, the timing of ZIKV infection and how these neutralizing responses decline overtime are yet to be determined. Overall, these results represent a critical set of epidemiological data vital to understand how exposure history affects the emergence of newly introduced flaviviruses within individuals and populations, and supports the future evaluation of vaccine candidates.

7870

CHARACTERIZATION OF NLRP3 INFLAMMASOME ACTIVATION IN HUMAN MONOCYTES AND MACROPHAGES INFECTED WITH OROPOUCHE VIRUS

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Oropouche orthobunyavirus (OROV), a member of the genus *Orthobunyavirus* in the family *Peribunyaviridae*, is transmitted by arthropods such as midges or mosquitoes. Oropouche fever (ORO) is endemic to Central and South America, with over 30 past outbreaks affecting more than half a million individuals. ORO presents clinical signs like dengue fever and is one of neglected tropical diseases. The high morbidity rate associated with ORO has spurred the hypothesis that proinflammatory cytokines play a pivotal role in its pathogenesis. Previous studies have suggested that OROV infection occurs in peripheral blood mononuclear cells (PBMCs). Our research aims to investigate whether OROV can replicate and induce inflammasome formation, accompanied by pyroptosis, in human monocytes and macrophages. We utilized the human-derived monocytic THP-1 cell line (parental Null 2) and the NLRP3-knockout THP-1 (NLRP3-KO). These monocytes were further differentiated into M0 macrophages by stimulation with phorbol 12-myristate 13-acetate (PMA). Our study on virus replication kinetics revealed that OROV infection at 5 MOI (multiplicity of infection) transiently increased infectious virus titers by up to tenfold between 16- and 72-hours post-infection (hpi) in macrophages, or between 24 and 72 hpi in monocytes. Indirect immunofluorescent assay detected the speck-like protein containing a caspase recruitment domain (ASC) in OROV-infected Null-2 macrophages, but not in NLRP3-KO macrophages. Further characterization of NLRP3 inflammasome activation in OROV-infected macrophages or monocytes is currently underway.

7871

VIRUS SPECIFIC T CELL RESPONSES IN A CONTROLLED HUMAN ZIKA CHALLENGE MODEL

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Zika virus (ZIKV), a flavivirus predominantly transmitted by infected Aedes mosquitoes, poses a significant public health threat due to its potential to cause neurological complications, notably microcephaly in infants born to infected mothers. The notable outbreak in Central and South America during 2015-2016 underscored the urgent need for both a deeper understanding of ZIKV infection and the development of preventive measures, particularly in the absence of an approved vaccine.Addressing this urgency, the NIAID and Johns Hopkins University has developed a Controlled Human Infection Model for ZIKV. The primary objective of the model is to evaluate countermeasures to control ZIKV infectivity and to elucidate the immune response to ZIKV infection. Volunteers who participate in this study undergo intensive monitoring until ZIKV clearance. Blood samples are collected at various intervals post-inoculation (day 0, 2-10, 12, 14, 16, 21, 28, 56, 90, and 180) for analysis.Our research is focused on characterizing the kinetics and magnitude of human T cell responses within peripheral blood mononuclear cells (PBMCs) during ZIKV infection, and their correlation with viral clearance. We utilize ZIKV-specific peptide mega pools, enabling T cell response analysis irrespective of donor HLA types, and employ high spectral flow cytometry to assess cell activation status, memory phenotype, and cytokine secretion. This investigation into the early immune response to ZIKV infection offers invaluable insights that can guide the development of novel vaccines and therapeutics.

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IMPACT OF DENGUE VIRUS INFECTION ON COMPLEMENT ACTIVATION AND REGULATION

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Dengue virus (DENV) is a flavivirus with four known circulating serotypes (DENV 1-4). Infection with DENV can result in a wide spectrum of disease: primary infections tend to produce milder disease while secondary infections can be associated with more severe disease, though the mechanisms behind the progression to severe disease are not well defined. Dysregulation of the complement cascade, especially the alternative pathway and the amplification loop, has been shown to correlate with disease severity. In particular, cleavage of complement component C3 produces high levels of anaphylatoxins C3a and C5a, which have a potent effect on the permeability of the capillary vasculature. In this study, we aimed to investigate the effect of infection on the expression of complement regulatory molecules CD46, CD55, and CD59 on both infected and bystander cells. HepG2 cells were infected with DENV-2 16681 (MOI = 1) for 24, 48 and 72 hours post infection (hpi). Cells were then stained with anti-CD55, anti-CD46, anti-CD59 and anti-DENV antibodies and analyzed by flow cytometry to determine the expression of complement regulatory molecules. During DENV-2 infection, a significant increase in the expression of complement regulatory molecules CD46, CD55, CD59 was observed for all timepoints in DENV-infected cells compared to bystander cells. This phenomenon was seen at all MOIs tested (MOI =0.1 through MOI=10), and across multiple DENV serotypes. Our results suggest that DENV-infected cells can augment expression of complement regulatory molecules and prevent cell death. Furthermore, C3 inhibition with treatment of compstatin during DENV-2 appears to modulate cell survival and viral infection. Going forward, we plan to utilize a human skin explant model to investigate the role of complement activation in DENV infection.

7873

PREMATURE HIGH LEVELS OF ANTIBODY-DEPENDENT COMPLEMENT ACTIVATION IS ASSOCIATED WITH SEVERE DISEASE IN SECONDARY DENV3 INFECTIONS

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Dengue viruses (DENV1-4) are a group of four serologically distinct arboviruses. In 1997, the WHO defined disease caused by DENV as dengue fever (DF) and more severe disease as dengue hemorragic fever (DHF). A small proportion of DF cases can progress to DHF hallmarked by plasma leakage, and leading to cardiovascular shock or organ failure. Clinical disease is characterized by an inflammatory-driven pathology, with complement dysfunction implicated as a risk factor for progression to DHF. The role that antibody-dependent complement activation (ADCA) has in this progression is unknown. Using sera from a cohort of DENV3 patients, we invesitigated the capacity of dengue antibodies to perform ADCA. Sera was collected from patients diagnosed with primary and secondary DENV3 infections, from both DF and DHF cases. Serial samples were collected during early disease, the critical phase, when patients are at risk of severe symptoms, and disease recovery. We used a bead based assay to quantify the capacity of anti-DENV3 non-structural protein 1 (NS1) antibodies to perform ADCA in serial samples from a subset of patients. Anti-DENV3 NS1 IgG and IgG3 titers were measured in sera samples by ELISA. When comparing complement activation in this cohort, we determined that secondary DENV3 infections have higher complement deposition than primary DENV3 infections. In primary DENV3 infections, ADCA increased over time regardless of severity. Secondary DENV3 infections demonstrate greatest ADCA during the critical phase for DHF patients and during disease recovery for DF patients. Anti-DENV3 total IgG and IgG3 titers correlated with ADCA during the critical phase, while only IgG titers correlated during early disease, and neither correlated during disease recovery. This data supports the hypothesis that ADCA plays a critical role in the progression to DHF, and demonstrated that total IgG and IgG3 titers are partly responsible for increases in ADCA. Future work will focus on assessing the capacity of anti-DENV3 envelope protein antibodies to perform ADCA, and measure endogenous complement levels, to elucidate the relationship between ADCA and severe disease.

7874

ASSESSING THE ANTIBODY RESPONSE AND SOLUBLE MEDIATOR PROFILES INDUCED BY WILD-TYPE AND VACCINE STRAINS OF THE YELLOW FEVER VIRUS: LESSONS FROM THE 2016-2018 OUTBREAK IN BRAZIL

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Between 2016-2018, Brazil experienced major sylvatic yellow fever (YF) outbreaks. Patients from these outbreaks represented a unique opportunity to assess the immune response triggered by wild-type (WT) South American strains of yellow fever virus (YFV) in humans. Our study aimed to evaluate the systemic immune response of patients from these outbreaks compared to healthy vaccinees and seronegative individuals. Using a high-throughput 48-plex Luminex assay, we quantified the circulating levels of pro-inflammatory (IFN-α2, IFN-γ, TNF-α, TNF-β, IL-1α, IL-1β, IL-6, IL-

12, IL-15, IL-16, IL-18, TRAIL, MIF, LIF) and regulatory cytokines (IL-1ra, IL-2ra, IL-3, IL-4, IL-5, IL-9, IL-10, IL-13, IL-17A), chemokines (CXCL1, CXCL8, CXCL9, CXCL10, CXCL12, CCL2, CCL3, CCL4, CCL5, CCL7, CCL11, CCL27), and growth factors (basic FGF, PDGF-β, VEGF, G-CSF, GM-CSF, M-CSF, β-NGF, HGF, SCGF-β, SCF, IL-7, IL-2), in serum samples from YF patients and individuals who received a single dose of the 17DD YF vaccine, collected 30 to 60 days post-infection/vaccination. Samples from healthy seronegative individuals were used as controls. Plaque reduction neutralization tests were also performed to measure neutralizing antibodies (nAb) levels in all participants. Our preliminary findings revealed the occurrence of a massive storm of mediators with mixed immune profiles in YF patients, with a significant elevation of 36 mediators compared to vaccinees and seronegatives. When compared only to vaccinees, this number increased to 43, suggesting that vaccine and WT strains of YFV can induce distinct immune profiles. Furthermore, nAb levels indicated that the natural infection elicited a stronger humoral response compared to vaccination. Further analysis and construction of integrative networks between nAb and soluble mediators are being performed for all groups. Thus far, our study has helped to fill the knowledge gap concerning the immune response against WT YFV and provided a better understanding of important differences between the responses to natural infection and vaccination, which have implications for the effective management of this disease.

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BREAKTHROUGH INFECTION ENHANCES SARS-COV-2 SPECIFIC T CELL RESPONSES AND GENERATES NOVEL EPITOPE SPECIFICITIES

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Relatively little is known on how different SARS-CoV-2 variants shape the magnitude, breadth and repertoire of the T cell responses after breakthrough infection (BTI). We addressed these points in a cohort that experienced symptomatic BTI during Delta or Omicron waves with samples collected before and/or after infection. Interestingly, a subset of donors with no previous reported infection showed pre-existing immunity against non-spike antigens consistent with responses in individuals with asymptomatic infections. In general, following symptomatic BTI, we observed: i) a boost in spike-specific CD4 and CD8 T cell responses, particularly in donors without previous asymptomatic infection. ii) broadening of the response to non-spike CD4 and CD8 T cell responses. No differences were observed as a function of the variant wave of exposure. We then mapped the T cell epitopes recognized post-BTI to dissect the molecular mechanisms of variant cross-recognition. As expected, only a minor fraction of the T cell epitopes identified was affected by variant mutations, with few mutations associated with either decrease or increases in the responses. In addition, BTIs led to novel epitope responses generated by variant-specific mutations, highlighting a third mechanism, beyond increases in magnitude and breadth of antigens targeted, by which BTI shapes T cell responses. Overall, this study suggests that at the T cell level, the BTIs boost spike-specific responses, increase the breadth to non-spike antigens and additionally induce novel responses to peptides containing variant mutations.

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DENGUE ADAPTIVE IMMUNE RESPONSES AND HLA DIVERSITY IN A PUERTO RICAN COHORT

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Dengue virus (DENV) is the most common mosquito-borne viral disease globally, causing an estimated 40,000 deaths yearly. There's no specific treatment, and the only US-FDA-approved vaccine for dengue, CYD-TDV(Dengvaxia®), has limited approval. Host genetic factors, like Human Leukocyte Antigen (HLA) genes, play a crucial role in the immune system response by encoding proteins that present antigens to T cells and influence disease susceptibility. Studies highlight robust T-cell responses linked to specific HLA alleles in DENV infection. However, research must identify DENV-specific HLA-restricted T-cell responses across diverse populations, including Puerto Rico**.** We aim to characterize the magnitude of the T-cell response when HLA-restricted with DENV-specific peptides in a Puerto Rican cohort. We first performed HLA genotyping by NGS using buccal samples from seropositive DENV participants and the MHC Core Library & Capture Kit from BioDynami. We then analyzed the sequences using NextGENe Software. We observed that the allelic variants that are found at a frequency greater than 1% in Puerto Rico and when compared globally are DPA1*01:03, DPB1*02:01, DPB1*105:01, DQA1*01:01, DQA1*01:02, DQB1*03:02, DRB1*07:11, DRB1*13:44, DRB1*14:46. Following the complete description of the HLA alleles from our Puerto Rico cohort, we will perform HLA peptide binding predictions using the Immune Epitope Database prediction tool and then be able to complete the functional assays. Understanding these population-specific patterns and examining the intricacies of HLA and T-cell-mediated responses deepens our understanding of the genetic factors involved in immune responses and gives insights into innovative disease prevention and treatment approaches.

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PROTEOMIC DECONVOLUTION OF CIRCULATING ANTIBODY REPERTOIRES ELICITED BY SECONDARY DENV INFECTION

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The four serotypes of dengue virus (DENV1-4) collectively infect an estimated 400 million people annually and can cause severe and sometimes fatal complications. No specific treatments exist, and vaccine development remains challenging. Antibodies from a primary DENV infection protect against the same serotype but may enhance subsequent infection with a different serotype. However, after secondary infection, broad and durable immunity develops, reducing the risk for severe disease. Yet, a molecular-level understanding of serological immunity to dengue viruses has been frustrated by the complexity of the polyclonal antibody response. In particular, the identities and epitopes of envelope (E) protein type-specific and cross-reactive plasma antibodies following a secondary heterotypic DENV infection and their contributions to broad protection remain unknown. Here we apply high-throughput B cell receptor sequencing (BCR-seq) during acute secondary dengue infection coupled with high-resolution proteomic analysis of DENV E dimer-specific circulating immunoglobulin at late convalescence to quantitatively profile the plasma antibody repertoire with monoclonal resolution in a Nicaraguan pediatric cohort (N=2 DENV2, N=2, DENV3). We recombinantly expressed and characterized abundant antibody lineages to dissect their specificities and neutralization breadth. Using a panel of engineered chimeric dengue viruses with E domain exchanges, we further mapped the epitopes of broadly neutralizing antibodies. Our data contributes to a better understanding post-secondary DENV immunity and the antibody features which characterize persistence of serological immunity to dengue viruses. These insights have implications for the development of vaccines and therapeutics targeting this significant global health challenge.

7878

ANALYZING THE IMMUNOGENICITY PROFILE OF ARIPO-ZIKA

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Flaviviridae is a family of enveloped positive-strand RNA viruses that can be classified as mosquito-borne, tick-borne, insect-specific, and those with no known vectors. Zika (ZIKV), Dengue (DENV), West Nile (WNV) and yellow fever (YFV) viruses have caused epidemics leading to debilitating illnesses in the Americas and regions of Africa. For example, ZIKV infection during pregnancy can result in congenital ZIKV syndrome, which includes microcephaly, which is marked by reduced brain size, ocular damage, and neurological defects. ZIKV infection in the elderly has been associated with Guillain Barré Syndrome, paralysis, and death. To combat the morbidity and severe disease burden associated with ZIKV, we developed a chimeric vaccine strategy using an insect-specific flavivirus as a vaccine vector (ARPV). Herein, we investigated the immunogenicity of our Aripo-Zika (ARPV/ZIKV) vaccine by immunotyping the immunoglobulin response, assessing the durability of ARPV/ZIKV-induced immunity, and determining if ARPV/ZIKV is cross-protective against other flaviviruses. Immunotyping of IgG, IgA, IgM, IgD, and IgE pre- and post-challenge indicated IgGs are the most prominent immunoglobulins elicited by Aripo-Zika immunization. ARPV/ZIKV immunization conferred complete protection against a lethal dose of ZIKV in an immunocompetent mouse model ten months post-immunization. PRNTs of ARPV/ZIKV serum 30 days post-immunization revealed ARPV/ZIKV does not show evidence of cross-neutralization against DENV 2, YFV, or WNV. Overall, our results continue to indicate the chimeric vaccine platform is a viable option for developing flavivirus vaccines.

7879

DESIGNING DENGUE VIRUS 2 (DV2) SUBUNIT VACCINE USING A STRUCTURE-GUIDED APPROACH TO REFOCUS NEUTRALIZING ANTIBODIES (NAB) TO POTENT, QUATERNARY NAB EPITOPES OF DV2

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The four dengue virus (DV) serotypes cause millions of infections annually, with varying degrees of severity from mild symptoms to severe dengue cases that can be fatal. Current dengue vaccines are based on tetravalent live-attenuated DV formulations. However, their efficacy and safety in dengue-naïve individuals are poor due to imbalanced responses to the four DV serotypes in the vaccine. One of the causes of this imbalanced response is the unbalanced replication rate of the four DV which is challenging to control. Dengue subunit vaccine could be a promising alternative as its immunogenicity is independent of virus replication. DV Envelope (E) protein is the main target of DV neutralizing antibody (nAb). Several recombinant DV E-protein (rE) have been assessed as subunit vaccine antigens but have performed poorly. One of the reasons is that secreted wild-type (WT) rE is mostly monomeric at physiological temperature while many known potent human nAb target quaternary structure epitopes on the native E dimer of the virion. We had previously shown that using molecular modeling software, Rosetta, we can stabilize DV2 rE dimer (SD rE) under physiological conditions. The resulting SD rE was able to be recognized by quaternary-targeting nAb while WT rE did not. Here, we report on the result of using DV2 WT vs SD rE as vaccine antigens in mice and the nAb specificity elicited by each rE. Using Ab depletion techniques to remove sub-populations of DV-specific Ab and DV chimeras, we found that nAb elicited by WT vs SD rE target different domains of DV2. While the traditional WT rE elicited DV2 nAb that target simple epitopes on EDIII, SD rE induced nAb that target more complex epitopes and covered all three E-domains of DV2. Our results demonstrate that structure-guided design can preserve quaternary epitopes on subunit vaccine and can refocus the resulting nAb profile to epitopes that are targeted by known potent DV2 nAb. This data suggests the importance of DV rE's oligomeric state, and that structure-guided design is a viable option for developing a successful dengue subunit vaccine.

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TOOLS FOR ANALYZING THE IMMUNE RESPONSE TO VIRUS INFECTION AND VACCINES

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To provide tools for characterizing antibody and vaccine efficacy, we have developed reporter virus particles (RVPs) that encompass a broad range of viruses. RVPs can be used in neutralization assays in place of live virus but are non-replicative and safe at BSL-2. The appropriate virus envelope proteins on the RVP surface mediate entry and fusion while a reporter gene expressed in infected cells provides a luminescent or fluorescent readout. Ease of use, quantitative readouts, and consistency between reagent lots make RVPs a higher-throughput alternative to live virus, which can require staining or imprecise and laborious plaque assays. Flavivirus RVPs are produced by co-expressing C/prM/E structural genes with full-length replicon in which these genes are replaced with a luciferase reporter gene. Viruses include dengue (serotypes 1-4), Zika (SPH2015), yellow fever (Asibi, 17D), and West Nile (NY99) viruses and additional virus variants. For SARS-CoV-2 studies, we have produced lentiviral pseudotyped RVPs representing over 90 different strains, including all variants of interest and concern. Flavivirus and SARS-CoV-2 RVPs have been extensively characterized and validated by us and others in publications and are widely used in vaccine development. We have developed additional lentiviral RVPs, including for Zaire ebolavirus, Marburg, Chikungunya, Nipah, Hendra, Lassa, and other viruses, creating an extensive RVP portfolio of prototype pathogens and providing non-replicative models for viruses requiring BSL-4 containment. Influenza RVPs containing the appropriate HA and NA protein are effective in cell-based neutralization assays but given the importance of hemagglutination inhibition assays (HAI) we developed a substitute for live virus to be used in HAI (TiterSafe). Like RVPs, TiterSafe displays HA and NA surface proteins and shows the expected strain-specific activities in HAI assays with both sera and MAbs, providing a rapid and safe alternative to the use of live virus in HAI.

7881

IMMUNOGENICITY OF COVID-19 MRNA, VIRAL VECTOR, AND INACTIVATED VIRUS VACCINES REGIMENS

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InVITE is an international study characterizing immunogenicity of COVID-19 vaccines offered through national immunization programs. This analysis focused exclusively on participants receiving an initial vaccine regimens. We report on 2344 individuals receiving an initial dose of vaccine enrolled from August 2021 to June 2022 in the Democratic Republic of Congo, Guinea, Liberia, and Mali. Participants received COVID-19 mRNA vaccines (Comirnaty, Pfizer/BioNTech; Spikevax, Moderna), non-replicating viral vector vaccines (Jcovden, Johnson & Johnson/Janssen; Vaxzevria, Oxford/AstraZeneca), or inactivated vaccines (Covilo, Sinopharm; CoronaVac, Sinovac). Blood was collected at two visits within 24 hours of vaccination

(Visit 1) and two months following the vaccine regimen (Visit 2). SARS-CoV-2 anti-Spike (anti-S) IgG and anti-Nucleocapsid (anti-N) pan-Ig antibody levels were measured in serum. A regression model of log10 anti-S level at Visit 2 compared immunogenicity between vaccines, adjusting for country. Women comprised 49% of participants. At study enrollment, 57% of participants were 18-39 years old and 4% were ≥ 60 years old. At Visit 1, 83% and 67% of participants had positive anti-S and anti-N antibodies, respectively. At Visit 2, Spikevax recipients had significantly higher anti-S levels than all other participants, while Comirnaty recipients had significantly higher levels than participants who received non-replicating viral vector and inactivated-virus vaccines. Enrollees who received non-replicating viral vector vaccines had significantly higher values than those who received inactivated virus vaccines. Anti-S levels did not differ significantly between the recipients of the two non-replicating viral vector vaccines or between the recipients of the two inactivated vaccines. Most participants had evidence of SARS-CoV-2 infection prior to vaccination. Anti-S IgG antibody responses to COVID-19 vaccines offered through national vaccination programs differed significantly in immunogenicity, based on vaccine platform. These data can help inform future public health decisions.

7882

ASSESSING THE INFLUENCE OF ASSUMPTIONS ON VACCINE EFFICACY AGAINST ASYMPTOMATIC DENGUE CASES ON IMPACT OF DENGUE VACCINATION STRATEGIES: A MODELING STUDY

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Dengue vaccines clinical trials usually prioritize assessing vaccine efficacy against symptomatic cases over asymptomatic cases, although a majority of dengue infections are asymptomatic. This modeling study aims to assess how influential are different assumptions regarding Vaccine Efficacy against Asymptomatic dengue cases (VEA) on two key aspects: (a) the impact of dengue vaccination programs in averting total dengue cases, and (b) determining the optimal target age for routine vaccination to avert the maximum number of dengue cases. We developed a dynamic transmission model for dengue infection and transmission, incorporating age stratification and multiple serotypes. For this study, the model was parametrized and calibrated using demographic and epidemiological data from Indonesia. We considered a hypothetical vaccine of 90% efficacy against symptomatic cases for both seropositive and seronegative individuals with different duration of protection (VD) (5-30 years) and coverage rate (VCR) (30-90%). While keeping other model parameters constant, we varied the VEA between 27% and 63%, which correspond to 30% and 70% relative to its efficacy against symptomatic cases, respectively. For 30% VCR, when VEA increased from 27% to 63%, routine vaccination resulted in an increase of 17.82% to 18.79% of the total number of averted dengue cases at VD of 5 and 30 years, respectively. For a VCR of 60%, a similar trend was observed with a 17.87% to18.34% increase of averted dengue cases. However, with 90% VCR, when VEA increased from 27% to 63%, the total averted cases went from 19.30% increase at VD = 5 years to 13.99% increase at VD = 30 years. This indicates that change in VEA may have a lower impact for longer VD when high VCR levels are reached. Furthermore, the optimal age for dengue vaccination was estimated to be 2 to 3 years old for all VEA, VD, and VCR assumptions. Assumptions regarding VEA in modeling studies could significantly influence the results regarding the potential impact of a dengue vaccination program to avert symptomatic cases. However, in this case, we found them to have minimal impact on the optimal age for dengue vaccination strategies.

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PHASE 1 TRIAL TO MODEL PRIMARY, SECONDARY, AND TERTIARY DENGUE INFECTION USING A MONOVALENT VACCINE

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There is an urgent need to better understand the drivers of dengue severity and the broadly neutralizing protection that may arise after secondary dengue virus (DENV) exposure. We are conducting a partially blinded phase I vaccine trial (NCT05691530) to examine how natural immunity influences the signs and symptoms, viremia, and immune responses to a dengue vaccine. Healthy adults living in a non-endemic area are screened for neutralizing antibodies to zero (seronegative), one non-DENV3 (heterotypic), or more than one (polytypic) DENV serotype, vaccinated with a live attenuated DENV3 monovalent vaccine, rDEN3Δ30/31-7164, and followed at 10 visits over 6 months. We hypothesize that the vaccine will be safe, and all groups will have a significant rise in neutralizing antibody titers in the first month. Moreover, compared to the seronegative group, the heterotypic group will have higher vaccine viremia due to enhancement, while the polytypic group will have lower viremia due to the protection associated with prior infection. We have vaccinated 20 of 45 individuals, representing all three groups, with no unexpected or severe adverse events. Seroconversion or 4-fold rise in DENV3 titer was observed in 12 of 14 (86%) tested individuals at day 28 and day 57. A rise in titer to a non-DENV3 serotype occurred in 12 of 14 (86%) volunteers at day 28 and 8 of 14 (57%) participants at day 57, suggesting a broadening of the immune response. Viremia measured by DENV culture with a limit of detection of 0.7 plaque forming units (PFU)/mL occurred in 5 of 14 (36%) participants with a maximum observed titer of 1.9 $\log_{10}$PFU/mL, confirming safe and appropriate viremia levels. Once all individuals have completed day 57, the study will be unblinded and neutralizing antibody titers, viremia, and adverse events will be compared among groups. Ongoing work will evaluate neutrophil and T cell responses, and germinal center changes using sequential fine needle lymph node aspirates. This study will elucidate the immunological factors driving the induction of cross-serotypic protective immunity, inform correlates of protection, and highlight potential therapeutic targets.

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EVALUATION OF T-CELL RESPONSES TO TETRAVALENT DENGUE VACCINE TAK-003 BY AGE GROUP

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TAK-003 is a tetravalent dengue vaccine based on an attenuated dengue 2 serotype backbone. Results from a phase 3 trial of TAK-003 in children aged 4-16 years in dengue-endemic regions (NCT02747927) showed long-term efficacy and safety against symptomatic and hospitalized dengue. While an efficacy trial has not been conducted in adults, comparable antibody response has been shown between children and adults. Alongside antibody response, a robust T cell response is useful for severe dengue protection. We report an exploratory analysis of TAK-003 induced T cell response by age in baseline seronegative children (4-16 years) and adults (22-43 years) from two phase 2 trials (NCT02948829 and NCT02425098 respectively). Participants from trial NCT02948829 received final dosing schedule, 2 doses of TAK-003 at Days 1 and 90; while participants from an earlier single-dose trial NCT02425098 received 1 dose at Day 1. T cell response comparison was conducted at 1 month post first vaccination. To minimize confounding factors, seronegative participants from trial NCT02948829 (n=81) and seronegative participants dosed with the final TDV formulation from NCT02425098 (n=18) who received TAK-003 at Day 1 and had a positive T cell response were selected for analysis. Dengue serostatus was tested at baseline (seropositivity: reciprocal neutralizing antibody [NAb; MNT_{50}] titer ≥10 for ≥1 serotype). Peptide pools for non-structural (NS) proteins NS1, NS3, and NS5 matching DENV-1, -2, -3, and -4 were used for peripheral blood mononuclear cells stimulation. T cell interferon-gamma (IFN-γ) enzyme-linked immunospot assay [ELISPOT] was used to analyze T-cell response. Median magnitude of T cell IFNγ ELISPOT response against any peptide pool for children and adults was 847 versus 742 spot forming cells/10^6 PBMCs, respectively, at 1 month post first vaccination and comparable DENV 1-4-serotype matched T cell IFNγ ELISPOT responses were observed between children and adults. Overall, we show for the first time that TAK-003 induced comparable T cell responses against all four DENV serotypes in dengue seronegative children and adults at 1 month post first vaccination.

7885

A NON-INFERIORITY TRIAL COMPARING TWO VACCINES (RABIX-VC VS. RABIPUR) FOR RABIES AMONG ADULTS IN DHAKA, BANGLADESH

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The purpose of the clinical trial was to evaluate the safety and immunogenicity of Rabies vaccine (Rabix-vc), and demonstrate non-inferiority of Rabix-vc compared to the comparator Rabipur vaccine in healthy participants of 18 to 75 year of age. No significant safety events and adverse effects were observed in test vaccine Rabix-vc or the comparator vaccine Rabipur recipients. The total occurrence rate of adverse events and adverse drug reactions was similar in both test and comparator group. It has been confirmed that the test vaccine Rabix-vc is non-inferior to the comparator vaccine in the primary efficacy endpoint, both in terms of seroconversion response (seroconversion rate difference is equal to or greater than pre-defined non-inferior margin of -10%) and GMT (ratio is equal to or greater than pre-defined non-inferior margin of 0.70). Therefore, this clinical trial was determined to be sufficient to confirm the immunogenicity and safety of Rabix-vc vaccine for Rabies virus infection. These results suggest that locally manufactured Rabix-vc vaccine is non-inferior to the well-known licensed Rabipur vaccine.

7886

BARRIERS AND FACILITATORS OF YELLOW FEVER VACCINE UPTAKE AMONG CHILDREN AGED 12-23 MONTHS IN WEST POKOT SUB-COUNTY, WEST POKOT COUNTY, KENYA

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Yellow Fever is a vaccine-preventable disease, Yellow Fever Vaccine (YFV) is routinely administered in areas deemed high risk. West Pokot Sub-County an arid high-risk area in Kenya has consistently reported a low uptake of below 50%, against the recommended 80% since the introduction of YFV in 2019. We sought to identify factors associated with vaccine uptake, in the sub-county. We used a mixed method approach and the WHO cluster sampling method to enroll children aged 12-23 months in July 2023. Data were collected from the children's caregivers using pretested questionnaires. We conducted key informant interviews (KII) with nurses offering vaccination. Data were analyzed using descriptive and inferential statistics. Crude odds ratio and adjusted odd ratio their respective 95% confidence intervals and p values less than 0.05 were used as a measure association and were considered independently associated with YFV uptake at the multivariate level. A total of 633 children were recruited. Their mean age was 22.9 (SD= 3.9) Months. The estimated YFV coverage was 47.2% (299/633). At the bivariate level, family socioeconomic status (wealth quartile) (cOR 2.63, 95% CI 1.87-3.70, p:0.001), child vaccination status for routine vaccines (cOR 3.8, 95% CI 2.2–6.6, p:0.001), and knowledge of the vaccine- (cOR = 3.4, 95% CI 2.4–4.5, p:0.001), were significantly associated with YFV uptake. The Caregiver's knowledge of the vaccine (aOR = 3.67, 95% CI 2.6–5.3, p:0.001) and family socioeconomic status (wealth quartile) (aOR 2.6, 95% CI 1.8-3.70, p:0.001) were significantly associated with YFV uptake at the multivariate level. In the KII inconsistent supply of vaccines and inadequate staffing were identified as key barriers to vaccination while caregivers' attitudes and knowledge of the vaccine were facilitators of vaccine uptake. This is associated with inadequate knowledge of the vaccine and periodic vaccine stockouts. We recommended targeted awareness campaigns to improve YFV knowledge, regular vaccine supply, and planned outreaches to improve YFV coverage.

7887

SAFETY AND TOLERABILITY OF A VSV-BASED LASSA FEVER VACCINE (RVSVΔG-LASV-GPC) IN HEALTHY ADULTS: UPDATES OF A FIRST-IN HUMAN, PLACEBO-CONTROLLED DOSE ESCALATION AND DOSE EXPANSION TRIAL (IAVI C102)

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Lassa fever (LF), a viral hemorrhagic illness endemic to West Africa, causes about 10,000 deaths annually. The development of an effective LF vaccine is a global priority. Buoyed by the success of the Ebola VSV-based vaccine, ERVEBO, IAVI has developed a vaccine by replacing VSV surface G protein with LASV glycoprotein complex (rVSVΔG-LASV-GPC). A Phase 1 trial was conducted in three sites in the US and one in Liberia. The trial had

two parts, dose escalation (US) and dose group expansion (US & Liberia). Participants received rVSVΔG-LASV-GPC IM at the following doses: $2x10^4$pfu (tested only in the dose escalation), $2x10^5$ pfu, $2x10^6$ pfu, $2x10^7$ pfu, or placebo. Eleven participants in the $2x10^7$ pfu escalation group were boosted 6-20 weeks later. We collected solicited adverse events (AEs) and unsolicited AEs for 14 and 28-days post-vaccination, respectively. Pure tone audiometry was done at baseline and post-vaccination to screen for sensorineural hearing loss. rVSV-LASV-GPC shedding and infectivity analyses in serum, saliva, and urine samples have been completed for 52 US study participants. The trial enrolled 113 participants, (22 placebo and 91 active vaccine recipients). Solicited events were reported in 67 (73.6%) vaccinees compared to 13 (59.1%) placebo recipients; Grade 3 solicited systemic adverse events were most frequent at the highest dose and reported in 7 (29.2%) vaccine recipients compared to 1 (4.5%) in the placebo group. No Grade 3-4 related unsolicited AEs, vesicles, arthritis, nor related SAEs were reported. Pure tone audiometry revealed no hearing loss. While attenuated VSV vaccine virus RNA has been detected by reverse-transcription polymerase chain reaction (RT-PCR) in blood and in saliva, no replication competent infectious VSV vaccine virus could be detected by infectivity assay in cell culture.The rVSVΔG-LASV-GPC vaccine was well tolerated in both US and Liberian populations. There was a dose dependent increase in severity and frequency of solicited systemic AEs. A phase 2 trial in West Africa will assess the safety and tolerability of the product in adults, adolescents and children aged at least 18 months.

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INFORMING LASSA FEVER VACCINE TRIAL IMPLEMENTATION THROUGH COMMUNITY ENGAGEMENT

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Lassa fever remains a significant public health concern in West Africa, with an annual incidence of approximately 300,000 cases. Recognizing the urgent need for vaccine development, the International AIDS Vaccine Initiative (IAVI), in collaboration with the Partnership for Research on Vaccines and Infectious Diseases in Liberia (PREVAIL), initiated a phase 1 clinical trial for a Lassa fever vaccine, with support from CEPI. Community engagement was identified as crucial for the successful implementation of the study. This paper outlines the community engagement efforts undertaken in Liberia to inform trial implementation and facilitate participant recruitment. The PREVAIL team conducted eight focus group discussions with key stakeholders to understand community views on Lassa fever and the vaccine trial. Findings highlighted significant gaps in knowledge about Lassa fever and widespread distrust in vaccine trials, emphasizing the need for strong community engagement strategies. The PREVAIL Social Mobilization and Community Engagement Team implemented a comprehensive recruitment plan to encourage community participation in the Lassa fever vaccine trial. We identified gatekeepers through stakeholder mapping and held advocacy meetings with health authorities and local leaders to facilitate community entry. Community engagement meetings were organized at local centers, with over 750 community members participating. The study education sessions explained the trial's objectives, processes, risks, and benefits. About 350 volunteers expressed interest and were referred for screening and enrollment. Sixty-one eligible participants were enrolled in the trial, highlighting the effectiveness of community engagement in clinical trials. These findings underscore the significance of community engagement in vaccine trials. Embracing a collaborative approach that respects community perspectives and fosters trust is essential for overcoming obstacles and ensuring local acceptance and participation in Lassa fever vaccine trials.

7889

ASSESSING IMMUNOGENICITY OF VACCINES AGAINST FILOVIRUSES: CHALLENGES AND PROSPECTS

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Accurate assessment of immune responses following immunization plays a pivotal role in evaluating the efficacy of vaccine candidates in clinical settings. Robust immunological tools are crucial for such investigation and need to be developed and proved fit for purpose. Evaluation of immunogenicity of vaccine candidates against filoviruses, such as Marburg (MARV) and Sudan (SUDV) virus, can be challenging due to limited availability of critical reagents for immunoassay development and qualification. Main obstacles include complexities in production and purification of key antigens; scarcity of human convalescent samples, coupled with safety considerations; availability of human monoclonal antibodies targeting vaccine antigens can also be limited. Vaccines against MARV and SUDV are currently in IAVI's pipeline, based on replication-competent recombinant vesicular stomatitis viral vector, encoding either MARV (rVSVΔG-MARV-GP) or SUDV (rVSVΔG-SUDV-GP) glycoprotein. To support progressing and testing of these vaccine candidates, we developed and qualified a panel of immunoassays to investigate both the humoral and cellular responses. Assays include GP binding ELISAs, VSV-based Plaque Reduction Neutralisation Test (PRNT), Interferon-gamma (IFN-γ) ELISpot, and flow cytometry-based Intracellular Cytokine Staining (ICS). Furthermore, we developed these assays with reagents cross-reactive between human and non-human primates (NHPs), to allow pre- to clinical bridging and comparison of responses across species. This aspect is crucial in advancing our knowledge of species-specific similarities and differences, and it will be essential in the event of licensure by U.S. Food and Drug Administration (FDA) Animal Rule. In this study we discuss strategies we employed to overcome the challenges in the field. We will present the development and qualification data of several immunoassays specific to measuring anti-MARV-GP and anti-SUDV-GP immune responses. Our work highlights the importance of advancing immunological methodologies for the rigorous evaluation of vaccine candidates against filoviruses.

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DENGUE VIRUS GENETIC DIVERSITY IN SAMPLES FROM PARTICIPANTS ENROLLED IN THE BUTANTAN-DENGUE VACCINE PHASE 3 TRIAL IN BRAZIL

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Brazil is hyperendemic for dengue and facing an outbreak in 2024. A locally produced, live, attenuated, tetravalent dengue vaccine (Butantan-DV), is in late stages of development at Instituto Butantan. A single dose of Butantan-DV aims to prevent cases of dengue caused by all dengue virus (DENV) serotypes. We evaluated the genetic diversity of DENV-1 and DENV-2 in placebo (Pb) and Butantan DV (Vx) recipients who had virologically confirmed dengue 28 days postvaccination, between 2016 and 2022 in a Phase 3 trial. Serum samples were processed for DENV-RNA detection, deep sequencing, phylogenetic analysis, and diversifying selection analysis. Of 16,235 participants, we analyzed 298 PCR positive samples which 145 tested positive for wild-type DENV-1 between 2017 and 2022 (73.2% Pb and 26.8% Vx). Additionally, 153 individuals tested positive for wild-type DENV-2 between 2018 and 2021 (62.5% Pb and 37.5% Vx). From the PCR-confirmed samples, it was possible to generate 152 near-full/full DENV genomes. Phylogeny of 77 DENV-1 sequences (85.7% Pb; 14.3% Vx) showed that all genomes were classified as genotype V,

distributed into three clades. Most of the sequences (90.9%) belong to Clade II (57.1%) with sequences from North and Northeast regions or Clade III (33.8%) with sequences from Midwest and Northeast, showing a polyphyletic distribution associated to other viruses from all Brazilian regions mostly sampled through National Surveillance between 2019 and 2023. All 75 DENV-2 sequences were distributed across three clades within genotype III (American/Asian), with most sequences (94.6%) grouping into the BR4 lineage together with other sequences from the Northeast, North, Southeast, and Midwest regions. Most of the DENV-2 samples are from 2019 (67.6%), the year with a major DENV-2 outbreak in the country. Our findings indicate a spatiotemporal distribution relationship between sequences following the circulation and epidemics of each serotype in Brazil, reinforcing the importance of genomic surveillance to track the evolution of circulating strains. An intra-host genetic diversity analysis is ongoing and will be presented soon.

7891

CHIKUNGUNYA: ONGOING DOSE-RESPONSE, SAFETY, AND IMMUNOGENICITY PHASE 2 TRIAL OF SINGLE-DOSE LIVE-ATTENUATED VACCINE (VLA1553) IN CHILDREN AGED 1 TO 11 YEARS

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VLA1553 is a live-attenuated chikungunya virus (CHIKV) vaccine designed for active immunization as a prophylactic measure. With the US FDA approval in November 2023, Valneva's vaccine VLA1553 (brand name IXCHIQ®), became the first and only licensed vaccine for use in adults aged 18 years and older who are at increased risk of CHIKV exposure. For children there is currently no licensed chikungunya vaccine available. This abstract provides an overview of an ongoing Phase 2 clinical trial in the pediatric population which is part of a pediatric investigational plan (PIP) agreed with regulators. VLA1553-221 (NCT06106581) is a prospective, randomized, blinded, dose finding Phase 2 clinical trial ongoing at three trial sites in the CHIKV endemic countries Dominican Republic and Honduras. Approximately 300 healthy children aged 1 to 11 years are to receive a single shot of two different dose levels of VLA1553 or an active control (tetravalent meningococcal vaccine) in a 2:2:1 ratio. The aim of this trial is to evaluate the tolerability, safety, and immunogenicity of VLA1553 in a generally healthy pediatric population and to identify the appropriate dose level for testing in Phase 3. Current recruitment status (April 2024) is 108 vaccinated out of planned 300 with the first child (Cohort: 7-11 years old) vaccinated in January 2024. An independent DSMB regularly reviews accruing safety data and has not raised any concern to date. Once available, these Phase 2 results will potentially support the initiation of a Phase 3 pediatric pivotal trial with the objective to broaden the IXCHIQ® label to the age group in the pediatric population. This would follow the initial regulatory licensure obtained in adults and possibly also in adolescents (NCT04650399).

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PRECLINICAL IMMUNOGENICITY AND EFFICACY OF A VESICULAR STOMATITIS VIRUS-BASED SUDAN VIRUS VACCINE AND AN UPDATE ON ITS PERFORMANCE IN A PHASE 1 CLINICAL TRIAL

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Sudan virus (SUDV; species *Orthoebolavirus sudanense*) is responsible for outbreaks primarily in East Africa and to date, there have been 8 outbreaks caused by SUDV in South Sudan and Uganda. SUDV causes viral hemorrhagic fever in humans with fatality rates ranging from 41% to 100%. Unlike Zaire ebolavirus (ZEBOV), there are no licensed vaccines or therapeutics targeting SUDV, which highlights an urgent unmet need. IAVI is developing a SUDV vaccine based on a recombinant replication-competent vesicular stomatitis virus (rVSV) as used to develop ERVEBO®, the licensed single-dose ZEBOV vaccine produced by Merck. Here, we report on the preclinical immunogenicity and efficacy of the SUDV vaccine (rVSVΔG-SUDV-GP) in cynomolgus macaques and provide safety and immunogenicity results from a phase 1 clinical trial. In macaques, a single intramuscular (IM) injection of a research construct produced by IAVI protected 90-100% of animals challenged with SUDV (Gulu variant) 28 days post vaccination. All unvaccinated animals succumbed to infection by day 9. Anti-GP IgG ELISA titers were detectable in all vaccinated animals indicating that a single administration of rVSVΔG-SUDV-GP, even at the lowest dose, induced serum antibodies. Neutralizing antibodies evaluated by plaque reduction neutralization test (PRNT) based on rVSVΔG-SUDV-GP were detectable in 8/8 macaques vaccinated with $2x10^7$ pfu, as well as 5/6 macaques vaccinated with $2x10^4$ pfu. After demonstrating efficacy in NHPs, IAVI and its partners initiated a first-in-human phase 1 placebo-controlled, single-blind clinical trial (IAVI C108) at two U.S. sites using an investigational product manufactured by Merck. Safety and immunogenicity were assessed in 36 healthy adult volunteers vaccinated with one IM injection at three dose levels. There were no serious adverse events and most adverse events were transient, mild or moderate local reactions limited to local reactogenicity. All dose levels generated detectable humoral immune responses as measured by anti-GP IgG ELISA providing strong support for continued development of rVSVΔG-SUDV-GP for vaccinating people at risk for SUDV infection.

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SAFETY AND IMMUNOGENICITY OF MRNA ZIKA VIRUS VACCINE: RESULT FROM PHASE 2 TRIAL OF MRNA-1893

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mRNA-1893 is a novel lipid nanoparticle-encapsulated messenger RNA (mRNA)-based vaccine directed against the pre-membrane and envelope (prME) structural protein of Zika virus. In this randomized, observer-blind, placebo-controlled, Phase 2 study conducted in the continental US and Puerto Rico, 808 adults were randomized in 1:1:1:1 ratio to receive either 30 µg or 100 µg mRNA-1893 as a 2-dose regimen in 28-day interval, or 100 µg mRNA-1893 as a 1-dose regimen, or a normal saline placebo control. This final analysis includes all safety and immunogenicity through study day 196 (approximately 6 months after the last vaccination). Approximately half of the participants in each study arm were baseline

flavivirus positive. Overall, solicited adverse reactions were more frequently reported in participants that received mRNA-1893 than placebo, particularly 2 doses of 100 µg mRNA-1893. Reactogenicity was higher after the second dose regardless of serostatus and dose but remained mostly mild and moderate in severity. Treatment emergent adverse events (TEAEs), severe TEAEs, medically attended adverse events, and serious adverse events, were similar across treatment arms. Two doses of mRNA-1893 resulted in higher geometric mean titers (GMTs) of neutralizing antibodies at Day 57 in baseline flavivirus seronegative participants compared to 1-dose 100 µg mRNA-1893. GMTs were similar in the 2-dose 30 µg and 100 µg arms at Day 57, regardless of baseline flavivirus status. In baseline flavivirus positive participants, 1-dose 100 µg regimen resulted in comparable GMT to the 2-dose regimes (30 and 100 µg) on Day 57. The results of this Phase 2 trial are consistent with the safety and immunogenicity trends noted in the Phase 1 trial. Overall, both 30 µg and 100 µg doses and the dosing regimens (1-dose 100 µg vs 2-dose 30 µg, and 2-dose 100 µg) were well-tolerated. A single dose may be sufficient to generate a robust immune response in baseline flavivirus positive participants while a two-dose regimen is likely needed to elicit robust immune response in baseline flavivirus negative participants.

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CHIKUNGUNYA VIRUS-LIKE PARTICLE VACCINE INDUCES CROSS-NEUTRALIZING ANTIBODIES AGAINST ALL THREE CHIKUNGUNYA GENOTYPES AND OTHER ALPHAVIRUSES

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The chikungunya virus (CHIKV) virus-like particle (VLP) vaccine candidate (known previously as PXVX0317) is a single intramuscular dose comprising three recombinant CHIKV structural proteins derived from the West African CHIKV Senegal strain 37997 formulated with aluminum hydroxide adjuvant. One likely mechanism of protection against chikungunya disease is by inducing serum neutralizing antibodies (SNA) measured by neutralization assays. This study was performed to assess the capability of anti-CHIKV antibodies induced by vaccination with CHIKV VLP vaccine to cross-neutralize other CHIKV strains (15661, 181/25, LR2006 OPY-1, PM2951) representing all 3 genotypes (Asian, East/Central/South African (ECSA), and West African); various arthritogenic alphaviruses (Mayaro virus (MAYV), Una virus (UNAV), Ross River virus (RRV), O'nyong-nyong virus (ONNV)); and encephalitic alphaviruses (eastern equine encephalitis virus (EEEV), western equine encephalitis virus (WEEV)). The SNA response and durability of this immune response were measured at 21- and 181-days post-vaccination. Peak neutralization titers against the four CHIKV strains were observed at 21 days post-vaccination, suggesting that a single dose of CHIKV VLP vaccine can induce cross-protective serum neutralizing antibody (SNA) against all 3 genotypes. As expected, CHIKV VLP vaccine was able to induce cross-neutralizing antibodies against the closely related arthritogenic alphaviruses tested, with the highest titers observed against ONNV and the lowest against RRV but was unable to induce neutralizing antibodies against either encephalitic alphavirus, EEEV or WEEV.

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CHARACTERIZATION OF IMMUNE RESPONSES TO THE RVSVΔG-LASV-GPC VACCINE CANDIDATE IN HEALTHY ADULTS

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Lassa Fever is an acute viral haemorrhagic disease caused by Lassa Virus (LASV) and is endemic to several parts of West Africa. A 2023 outbreak in Nigeria involved 4702 suspected cases and 152 deaths. A safe and effective vaccine against LASV could prevent or control outbreaks. We report on a dose-escalation phase I study in 114 healthy adult volunteers conducted at sites in US and Liberia, investigating safety and immunogenicity of a replication-competent recombinant vesicular stomatitis viral vector vaccine encoding LASV glycoprotein (rVSVΔG-LASV-GPC). Vaccine was administered intra-muscularly as a single injection or in a homologous prime-boost regimen using a 6-20-week interval and was well tolerated. We present in detail analyses of the immune responses up to 12 months after vaccination, demonstrating the induction of serum IgM and IgG antibodies recognizing homologous and heterologous LASV GPC. In addition, we detected neutralizing antibody titers in sera collected at various time points post vaccination that were also able to neutralize LASV of heterologous lineages. Furthermore, rVSVΔG-LASV-GPC vaccination induced Th1-biased CD4+ T cell responses characterized by interferon-γ, IL-2 and tumour necrosis factor-α secretion and CD8+ T cells of monofunctional, polyfunctional and cytotoxic phenotypes. Additionally, we used a systems vaccinology approach to identify early biomarkers and immune signatures associated with rVSVΔ-LASV-GPC vaccination in humans. We identified a signature of early innate markers correlating with anti-LASV-GPC IgM and IgG binding and neutralizing antibody levels on day 28 and beyond. Consistently, we also found an early cytokine signature linked to anti-vector antibodies and LASC GPC-specific T cell responses. Overall, our results show replication-competent rVSV-vector induces a milieu of innate antiviral responses that can orchestrate rapid development of durable adaptive immunity against LASV GPC. Taken together, these results suggest a favourable immune profile induced by rVSVΔG-LASV-GPC vaccine, supporting the progression of this vaccine candidate to phase 2 trials.

7896

CONSISTENCY OF IMMUNOGENICITY AND SAFETY IN THREE CONSECUTIVE LOTS OF A TETRAVALENT DENGUE VACCINE CANDIDATE (BUTANTAN DV): A RANDOMIZED PLACEBO CONTROLLED TRIAL IN DENGUE NAIVE BRAZILIAN ADULTS

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A randomized, double blind, placebo controlled trial was conducted to demonstrate the immunogenic equivalence of three consecutive lots of the dengue vaccine candidate (Butantan DV) and assessed its safety. The aim was to evaluate the consistency of the immune response at Day 28 post vaccination with three consecutive lots of Butantan DV and to describe the frequency of adverse reactions from vaccination through Day

21.We included healthy adults aged 18 to 59 years dengue naive from non endemic areas in Brazil. Subjects were allocated in a 2:2:2:1 ratio to four parallel arms. The consistency of the immune response to the three lots of the Butantan DV vaccine was evaluated by analyzing the serum neutralizing antibody titers against four dengue serotypes using the virus reduction neutralization test performed at baseline and Day 28. The criterion for lot to lot consistency was a 95% confidence interval (95% CI) of the geometric mean titer ratio within the margins of equivalence of greater than 0.5 and lower than 2.0 for the 12 possible pairwise comparisons of the three vaccine lots and four serotypes in the Per Protocol Set (PPS). Adverse events were analyzed according to frequency, and the Miettinen & Nurminen method was used to construct 95% CIs for the difference in the binomial proportions of each batch compared to the placebo group. Between November 4th, 2022, and January 16th, 2023, 700 participants were randomized, and 616 were included in the PPS. Of the 12 possible pairwise comparisons between the three lots and four serotypes of DENV, 10 met the endpoint of lot equivalence, while 2 failed marginally. Most of the adverse reactions were solicited, with incidence rates of 90% and 74% in the vaccine and placebo arm, respectively. The most common adverse reactions were headache (66.5%) and rash (65.5%). The frequency of unsolicited adverse reactions was 27% in the vaccine arm and 19% in the placebo arm. Three serious adverse events occurred but none related to the vaccination.Conclusions: Three lots of Butantan DV were safe and achieved the endpoint of lot equivalence.

7897

ANTIMALARIAL ACTIVITY OF COMMONLY USED HERBAL PRODUCTS IN GHANA: DECIPHERING THE UNACCOUNTED DRUG PRESSURE ON *PLASMODIUM* PARASITES

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The emergence of resistant *Plasmodium* parasites to standard antimalarial drugs poses a significant threat to malaria control. This phenomenon has necessitated the development of new and effective chemotypes with novel target (s) and multistage activity against the parasite. In Ghana, there is a heavy reliance on herbal formulations for treating malaria. However, the role of overreliance on these herbal preparations in the emergence of resistance to standard antimalarials has not been adequately explored. Thus, this study sought to evaluate the efficacy of selected antimalarial herbal drugs against *P. falciparum* parasites and assess their ability to potentiate resistance to conventional antimalarials. We sampled twenty-one commercially available antimalarial herbal formulations within Madina-Accra, Ghana. Using *in vitro* growth inhibition assays, we assessed the antiplasmodial activity of these formulations against four laboratory strains and two clinical isolates of *Plasmodium falciparum*. We further studied the changes in parasite morphology and growth rates after exposure to the sampled drugs. We employed *in vitro* resistance selection techniques to assess the potential of these parasites developing of resistance to the formulation understudy. Of the 21 formulations studied, 8 had "good" activity across the six strains screened with half-maximal inhibitory concentration (IC50) values of less than 50 ug/ ml. Also, analysis of microscopy images and growth pattern curves have shown the stage-specificity of some of the formulations and have the potential to be parasite invasion inhibitors. In total, 3 of the 8 potent formulations were shown to have specific activity in ring-stage parasites whereas the rest showed varied activity in the various intraerythrocytic stages. The outcomes of the study will shed light on the possible contribution of over-reliance on herbal drugs to the emergence of resistance to standard antimalarial drugs. It will also highlight the need for regulations by the appropriate authorities to monitor herbal drug preparation and treatment regimens.

7898

ASSESSMENT OF ANTIMALARIAL RESISTANCE AND ASSOCIATED MARKERS IN GAMBIAN *PLASMODIUM FALCIPARUM* CLINICAL ISOLATES

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Chemotherapy remains a crucial strategy in combating malaria; however, its efficacy is continuously challenged by the emergence of antimalarial resistance. Recent reports of increasing resistance to artemisinin in Sub-Saharan Africa requires robust continuous surveillance. We investigated the effect of antimalarials on expression and variations in drug resistance-associated genes of Gambian *Plasmodium falciparum* isolates. The effect of six major antimalarials on clinical *P. falciparum* from The Gambia were measured to determine IC_{50} and growth rate inhibition (GR_{50}). Subsets of clinical isolates underwent drug survival assays (DSA) to determine parasite survival rates (SR) post-exposure to sub-therapeutic drug doses. Amplicon sequencing was used to determine drug resistance markers in *pfcrt, pfmdr, pfdhps, pfdhfr* and *pfkelch13* genes. Significantly, differences in median IC_{50} and GR_{50} values are as follows: Amodiaquine (8.143nM, 10.43nM); Chloroquine (86.92nM, 48.39nM); Dihydroartemisinin (1.22nM, 1.38nM); Lumefantrine (54.99nM, 194.99nM) Mefloquine (38.6nM, 47.74nM) and Piperaquine (80.8nM, 85.20nM). Significantly, DHA was more effective compared to the other drugs, with increased SR observed in one isolate 24h and 48h post-treatment. Chloroquine lumefantrine and piperaquine were less effective with higher SR observed. Targeted sequencing showed 58.4% as wild-type and 41.6% as resistant based on haplotypes of *Pfcrt* loci. Correlation analysis of IC_{50}, GR_{50}, DSA, and observed resistance markers from 2021-2023 indicating drug tolerance, highlights continuous effective drug resistance surveillance using combination of advanced phenotypic testing and genomics. This integrated approach sheds light on treatment effectiveness and spread of known and emerging drug resistance markers, offering valuable insights in treatment strategies.

7899

FORECASTING VOLUMES OF ARTEMISININ COMBINATION THERAPIES UNDER VARIOUS ANTIMALARIAL RESISTANCE SCENARIOS AND MULTIPLE FIRST-LINE THERAPY STRATEGIES IN SUB-SAHARAN AFRICA

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Artemisinin partial resistance and biomarkers associated with partner drug resistance have emerged in Africa. Although some countries in Africa have registered multiple Artemisinin Combination Therapies (ACTs) as part of their treatment guidelines, artemether lumefantrine remains the main first-line therapy. Currently, most national malaria programs lack clear guidance on managing drug-resistant infections. In November 2022, the World Health Organization published guidelines on mitigating antimalarial resistance in Africa, suggesting exploring interventions like multiple first-line therapy (MFT) strategies. The Malaria Commodities Forecasting Consortium is analyzing the deployment of MFT strategies to estimate commodity volumes and required budgets for meeting ACT demand under each strategy. This analysis integrates projections for artemisinin and partner drug resistance spread using a model from Imperial College London. Baseline scenarios use Malaria Atlas Project treatment estimates. Assumptions around treatment type are derived from available data on current country strategies as described in existing grant agreements. Projections cover six years (2024-2030) and are displayed on an interactive dashboard. The dashboard

includes maps illustrating the 10-year spread of resistance in Africa, and functionalities that enable users to switch MFT strategies for geographies, select a treatment failure rate that triggers treatment policy changes, and customize ACT product split and prices to visualize their effects on ACT volumes and budgets. Depending on the MFT strategy selected, lower volumes of main ACTs (artemether lumefantrine or artesunate amodiaquine) are expected annually, with their market share shifting to dihydroartemisinin piperaquine and/or artesunate pyronaridine. Shifting to more expensive ACTs, which have not yet experienced high treatment failures in Africa, will require a higher financial investment in commodity procurement unless drug costs are reduced. We will present a summary of key, likely MFT strategies that have clear modeled outputs on treatment volumes and associated costs.

7900

LESSONS LEARNED FROM MALARIA DRUG EFFICACY STUDIES IN EQUATORIAL GUINEA

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Malaria control efforts in Equatorial Guinea are crucially supported by periodic drug efficacy studies (DES) to ensure the continued effectiveness of treatments like artemether + lumefantrine (AL) and artesunate + amodiaquine (ASAQ). These studies not only inform local malaria treatment policies but also contribute to global malaria control strategies. Here, we explore the operational insights and adaptations derived from two major efficacy studies conducted in 2018 and one scheduled for 2024. Both studies were designed to assess the therapeutic response of uncomplicated *Plasmodium falciparum* malaria to both drug treatments across varying epidemiological zones, including Bioko Island where malaria incidence has notably declined since the inception of the Bioko Island Malaria Elimination Project (BIMEP). The 2018 study underscored several operational challenges, particularly in sustaining participant enrollment and managing multi-site logistics. The diminished malaria incidence on Bioko Island further complicated these issues, leading to extended study durations compromising data integrity. Key adjustments have been planned for the 2024 study to include more robust community engagement practices, flexible recruitment strategies, and enhanced training for local health workers to ensure timely and efficient study execution. Our analyses will explore how successfully were these innovations during the new study compared to the 2018 one. The lessons learned from both malaria DES are vital for refining future epidemiological research in Equatorial Guinea. By adapting research methodologies to better fit local conditions, these studies should help pave the way for more effective and sustainable malaria elimination efforts.

7901

EX VIVO ANTIMALARIAL DRUG SUSCEPTIBILITIES AND MOLECULAR MARKERS OF DRUG RESISTANCE IN UGANDA

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The management of malaria in Africa is challenged by drug resistance. In Uganda, resistance to aminoquinolines was common, but has been decreasing, resistance to antifolates is widespread, and partial resistance to artemisinins has emerged. We assessed susceptibilities of up to ~700 *P. falciparum* isolates to 8 antimalarial drugs in samples from individuals presenting with uncomplicated falciparum malaria from 2016-23 at 3 clinics in eastern Uganda and from 2021-23 at a clinic in northern Uganda. We utilized 72-h growth inhibition assays with SYBR green detection and genotyped samples using molecular inversion probe deep sequencing. Median IC_{50}s were measured in 2016-20 and 2021-23 in eastern Uganda for: lumefantrine (5.3 vs 9.0 nM, dihydroartemisinin (1.5 vs 3.0 nM), chloroquine 19.0 vs 11.6 nM), monodesethylamodiaquine (6.8 vs 7.9 nM), and mefloquine (10.0 vs. 15.3 nM); p for all comparisons <0.0001; susceptibilities to most drugs decreased over time. In 2021-23, median IC_{50}s were lower in eastern compared to northern Uganda for lumefantrine (9.0 vs 14.7 nM, p<0.0001) and monodethylamodiaquine (7.9 vs 9.1 nM, p=0.002), but no differences were detected for dihydroartemisinin, chloroquine, or mefloquine. To assess genotype-phenotype associations, we sequenced ~70 genes of interest in samples collected since August, 2021 (results for earlier samples are published). Preliminary analysis identified polymorphisms in PfMDR1, PfK13, falcipain cysteine proteases, and other proteins associated with variation in lumefantrine IC_{50}s. Association with one mutation, PfMDR1 500N, was identified independently in both the 2016-21 and 2021-23 samples. In addition, genotyping of surveillance samples from across Uganda showed that PfMDR1 500N prevalence increased from 0-5% in 2016 to up to 25% in 2022 in multiple districts in northern Uganda. Decreased susceptibility to artemisinins and lumefantrine suggest that the efficacy of artemether-lumefantrine, Uganda's first-line drug, may be decreasing. Continued surveillance and genotype-phenotype association studies to facilitate timely responses to emerging resistance are needed.

7902

TRNA REPROGRAMMING AS A FEATURE OF ARTEMISININ RESISTANCE IN *PLASMODIUM FALCIPARUM*

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Plasmodium falciparum has developed partial resistance to artemisinin (ART). Resistance, driven by mutations in Pfk13, is multifaceted but quiescence plays a central role. Epigenetic regulation may contribute, given that only a percentage of parasites survive a pulse of the active drug metabolite dihydroartemisinin (DHA). The identities or roles of these epigenetic factors have yet to be discovered. tRNA modifications are a conserved epitranscriptomic translational control mechanism, whereby cellular stress leads to modification reprogramming and codon-biased translation. Here we use liquid chromatography-mass spectrometry to profile tRNA modifications in ring-stage ART-sensitive (ART-S) Dd2 and ART-resistant (ART-R) $Dd2^{PfK13\_R539T}$ parasites before and after drug pulse. ART-R parasites differentially reprogram their tRNA modification profiles in response to DHA, specifically by mcm^5s^2U hypomodification. Proteomic and codon usage analyses revealed that the ART-R parasite proteome displays codon bias, uncovering a new layer of proteomic regulation in drug-resistant parasites. A subset of these proteins was not transcriptionally regulated, suggesting codon-biased translation. Upregulated proteins were enriched for Lys^{AAA}, His^{CAT} and Asp^{GAT} and downregulated proteins were enriched for their cognate codons. PfK13 was among the codon-controlled upregulated proteins. mcm^5s^2U occurs on the U_{34} of $Lys^{AAA/AAG}$ codons to regulate translational fidelity, providing a mechanistic link between the tRNA modification and proteomic data. A conditional knockdown (cKD) of the terminal s^2U thiouridylase, PfMnmA, made in an ART-S parasite background displayed increased ART survival, signifying that hypomodification alone can mediate an ART-R parasite response to DHA. cKD parasites also had altered responses to proteotoxic and mitochondrial antimalarials, uncovering overlaps between epitranscriptomic stress response pathways. This study describes a novel epitranscriptomic pathway via tRNA s^2U reprogramming that ART-R parasites may use to help survive ART-induced stress.

7903

EMERGENCE OF QUADRUPLE MUTATIONS IN *PLASMODIUM FALCIPARUM* DIHYDROFOLATE REDUCTASE ENZYME IN NORTHWESTERN TANZANIA

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Plasmodium falciparum dihydrofolate reductase is a key enzyme targeted by the antimalarial drug pyrimethamine which is a component of sulfadoxine-pyrimethamine (SP) used for intermittent preventive treatment of malaria in pregnancy (IPTp). Mutations in the gene at codons 16, 51, 59, 108 and 164 confer resistance of *P. falciparum* to pyrimethamine, potentially undermining the efficacy of SP for IPTp. The emergence of 164L mutation in Kagera, along with existing triple mutations (S108N, C59R, N51I), forms quadruple mutations (51I, 59R, 108N, 164L) resulting in the highest level of SP resistance. This study outlines the trend of quadruple mutations by examining single nucleotide polymorphisms (SNPs) from 1118 samples collected across Karagwe, Muleba, and Ngara districts in Kagera region from 2021 to 2023. DNA was extracted using the Chelex-Tween protocol, followed by targeted sequencing using molecular inversion probes, with the Illumina platform. The prevalence of 164L mutation varied significantly between districts ($p = 0.001$), with Karagwe consistently reporting the highest rates: 34.5%, 38.8%, and 24.2% in 2021, 2022, and 2023, respectively. Conversely, Muleba and Ngara had lower rates, ranging from 1.4% to 2.9% and 9% to 14.4%, respectively. The prevalence was not statistically different across the years ($p=0.422$); however, it varied over time, with notable increases in 2022 followed by slight declines in 2023. The 108N, 51I, and 59R mutations were observed at higher levels (>80%) across the districts, with prevalence fluctuating over time. The 108N mutation showed a high prevalence (near fixation) across all districts and years ($p > 0.05$). In contrast, the prevalence of the 51I mutation remained constantly high in Karagwe and Ngara but showed some variations in Muleba. Similarly, the 59R mutation exhibited relatively high prevalence rates across all districts, with slight variations over time. The high prevalence of the 164L mutation threatens SP efficacy in IPTp, though the exact impact remains uncertain. Continuous surveillance is vital to inform malaria control strategies and maintain IPTp effectiveness.

7904

PFCRT MUTATIONS CAN MEDIATE PIPERAQUINE RESISTANCE ON SELECT AFRICAN HAPLOTYPES IN *PLASMODIUM FALCIPARUM* PARASITES WITH A MINOR FITNESS COST

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The recent increase in *Plasmodium falciparum* malaria cases and deaths in sub-Saharan Africa, mostly impacting young children, requires expanded strategies to reduce the malaria burden. Piperaquine (PPQ), used in combination with dihydroartemisinin (DHA), has been identified as a promising partner drug for uncomplicated malaria treatment and prevention efforts, including seasonal malaria chemoprevention and perennial malaria chemoprevention. However, the rapid emergence and spread of PPQ resistance in Southeast Asia a decade earlier, mediated by mutations in the drug efflux transporter PfCRT, generates concern for the long-term efficacy of DHA-PPQ in Africa. The recent emergence of African parasites with partial resistance to artemisinin increases selective pressure on partner drugs and highlights the compelling need to assess whether PPQ will remain effective in this region. We demonstrate that *pfcrt*-edited parasites expressing the more contemporary Asian T93S or I218F mutation on the FCB African PfCRT haplotype demonstrate moderate- to high-level PPQ resistance (~10% survival at 200 nM). Parasites expressing these mutations on GB4 and Cam783 African PfCRT haplotypes exhibited increased survival only at lower PPQ concentrations. T93S and I218F mutants showed increased susceptibility to chloroquine and no change in susceptibility to other first-line partner drugs or DHA. Competitive growth assays reveal differing impacts of these PPQ-resistant haplotypes on fitness depending on the parasite background. These studies help proactively predict the path to PPQ resistance in Africa, which is especially relevant to global health efforts to identify region-specific antimalarial treatments and to combat the spread of multidrug-resistant *P. falciparum* parasites.

7905

EXPANDING ANTIMALARIAL RESISTANCE SURVEILLANCE: AN INTEGRATED GENOMIC AND PHENOTYPIC APPROACH

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In the fight against malaria, the emergence of partial artemisinin resistance presents a significant hurdle, necessitating a comprehensive surveillance strategy that goes beyond sequencing existing genetic molecular markers. Recent studies in Africa indicate a prevalence of *Pfkelch13*-independent partial artemisinin resistance, underscoring the indispensable need to generate phenotypes alongside genotypes for accurate resistance detection. Furthermore, the preponderance of polygenomic infections in some regions of Africa, i.e., the complexity of infection (COI), further confounds surveillance efforts and highlights the need for innovative *in vitro* methods that are both sensitive and amenable to higher throughput than is accomplished by the standard ring-stage survival assay (RSA). Here we expand on our extended recovery ring-stage survival assay (eRRSA), to explore the potential of pooling samples to improve phenotypic antimalarial resistance surveillance and assess the efficacy of eRRSA for identifying resistance in nonclonal and pooled populations. Preliminary data using *in vitro* construction of mixed parasite pools of sensitive and resistant parasite isolates with increasing COI does not mask the resistant phenotype. We are extending this approach to examine parasites post-drug exposure to distinguish pools with varying drug sensitivities and proportions of individual genotypes to approximate natural infections. In addition, we can ascertain competitive fitness dynamics among pooled parasites for up to 40 days. Through a combination of genomic and phenotypic methodologies, this investigation sets the stage for improved throughput resistance surveillance alongside deeper investigations into parasite biology that underpins the emergence and spread of drug resistance.

7906

REDUCED PEROXIDATION OF *PLASMODIUM FALCIPARUM*-INFECTED RED BLOOD CELLS AS A MAJOR MECHANISM BY WHICH ARTEMISININ-RESISTANT PARASITES ESCAPE SPLENIC RETENTION

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Plasmodium falciparum resistance to artemisinin (ART) is associated with delayed clearance of infected red blood cells (RBCs) in malaria patients. The mechanism by which the ART-resistant parasites persist remains not totally understood. To unveil the mechanism involved, we explored the changes induced by artemisinin in ART-sensitive and ART-resistant *P. falciparum*-infected red blood cells in 88 patients, in an ex vivo human spleen recrudescence model and also in specific rheological models and analyzed lipid membrane properties following treatment with ART. We found that delayed parasite clearance is associated with delayed splenic pitting both in vivo in clinical isolates in patients and ex vivo with ART-resistant laboratory strains exposed to ART and perfused in a human spleen. Only ART-resistant strains were able to grow following spleen perfusion. Compared to ART-sensitive parasites, RBCs infected by ART-resistant parasites showed less pronounced loss of deformability after treatment by ART and crossed microsphere filters more efficiently than sensitive strains. These features were associated to a significant increase in peroxidation of arachidonic acid (AA) to hydroxyeicosatetraenoic acid (HETEs) and linoleic acid to hydroxyoctadecadienoic acid (HODE) in ART-sensitive strains compared to ART-resistant strains, in RBCs infected with laboratory or clinical isolates. These results suggest that lipid peroxidation is reduced in ART-resistant parasites protecting them from phenotypical damage caused by artemisinins, allowing them to escape spleen retention and to persist in circulation.

7907

EX VIVO SUSCEPTIBILITIES TO NEW ANTIMALARIALS UNDER DEVELOPMENT AND ASSOCIATIONS WITH GENOTYPES IN *PLASMODIUM FALCIPARUM* ISOLATES FROM BURKINA FASO

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Among novel compounds under development as potential antimalarials are inhibitors of the proteins PfATP4 (KAE609, SJ733, PA92), PfPI4K (MMV1901539, EQV620), and resistance mediators PfCARL, PfACT and PfUGT (ganaplacide). We assessed ex vivo susceptibilities to these novel antimalarials in fresh *P. falciparum* isolates collected from subjects with malaria in Bobo-Dioulasso, Burkina Faso in 2021 and 2022. Susceptibilities were determined using a 72h SYBR-green assay. Median IC_{50}s were 0.8 nM for KAE609, 9.1 nM for PA92, 73.8 nM for SJ733, 15.2 nM for MMV1901539, 6.9 nM for EQV620. We characterized isolate genotypes using dideoxy and molecular inversion probe sequencing. We found associations between the PfATP4 G223S mutation (seen in 27% of isolates) and decreased susceptibility to all three PfATP4 inhibitors (mean IC_{50} SJ733: 55.6 nM for WT, 88.6 nM for mutant; PA92: 6.6 nM for WT, 10.4 nM for mutant; KAE609: 0.8 nM for WT, 1 nM for mutant; $p<0.05$ for all comparisons). Previously, KAE609 selected for resistant parasites with a mutation (G223R) at the same codon, and the G223S mutation was also associated with a moderate decrease in susceptibility to the three PfATP4 inhibitors in Ugandan parasites. PfPI4K was highly polymorphic (77 mutations, indels, and deletions), but isolates had no mutations previously identified after in vitro drug selection or that were associated with altered susceptibilities. We also assessed genotypes of PfACT, PfCARL and PfUGT, we detected a stop mutation at codon 119 of PfACT in 6.5% of isolates. Stop mutations in PfACT have been linked to decreased inhibitor susceptibility, but due to solubility limitations with ganaplacide we were unable to assess susceptibilities of these isolates. Our results indicate that malaria parasites circulating in Burkina Faso are generally susceptible to inhibitors under development. We identified several polymorphisms in potential drug targets and resistance mediators, and a natural occurring mutation in PfATP4 was associated with modestly decreased ex vivo inhibitor susceptibility.

7908

ARTEMISININ-BASED COMBINATION TREATMENT FAILURE IN TRAVELERS RETURNING FROM SUB-SAHARAN AFRICA WITH *PLASMODIUM FALCIPARUM* MALARIA- A SYSTEMATIC REVIEW

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Artemisinin-based combination therapies (ACTs) are recommended as first-line treatment against uncomplicated *P. falciparum* infection in Sub-Saharan Africa (SSA) where the vast majority of *P.f* occurs. Emergence of ACT failure was first reported in Southeast Asia (SEA) where the resistance was attributed to mutations in the *PfKelch13* propeller domain. Recently, increasing reports of ACT treatment failure in travelers returning from SSA are emerging. Since travelers can serve as sentinels for this emerging resistance, we aimed to summarize the available information. A systematic literature search for ACT failure in travelers from Africa with *P. falciparum* malaria was performed. In total, 52 cases were identified. The first case was reported in 2006 with a total of 14 cases reported in the 1st decade and another 38 cases reported in the 2nd decade. Cases had traveled from 23 African countries. Almost all patients did not take malaria prophylaxis. Their initial ACT treatment was an artemisinin-lumefantrine (AL) combination in 45/52 (87%), the rest were treated mainly by piperaquine-dihydroartemisinin combinations. The majority of treatment failure 46/52 (88%), presented as a late recrudescence, with the recurrent febrile illness at a mean of 18.6±10 days after initial diagnosis. The other 6 patients exhibited early failure (within 3 days). Genetic evaluation of the *PfKelch13* propeller domain was done in 46 of the cases, of them only 3 (7%) had *PfKelch13* mutations with clinical significance. ACT treatment failures in *P. falciparum* malaria imported from SSA seems to be increasing in the last decade. The common presentation is as a late recrudescence, which typically cannot be diagnosed in the endemic setting since it is indistinguishable from re-infection. In contrary to SEA situation, the genetic basis of the resistance mechanism cannot be explained by *Pfkelch13* mutations, and thus warrants further elucidation. Since late recrudescence is the common manifestation, it is not clear whether it is artemisinin failure or failure of the slow-acting partner drug.

7909

LUMEFANTRINE PERFORMANCE IN AFRICA - A REVIEW OF LITERATURE

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Previously known as benflumetol, Lumefantrine was discovered to have schizontocidal activity against malaria parasites. Due to their synergistic effect against *Plasmodium falciparum,* Lumefantrine was combined with Artemether and consist of one of the most popular Artemisinin-Combination Therapy (ACT) being used to treat non-complicated malaria in Africa (Artemether-Lumefantrine, AL). However, several African studies reported that this combination performed bellow WHO recommended threshold (90%). Despite that partial resistance to artemisinin was confirmed in some of those countries, treatment failure in Africa has been hypothesized to associate to the partner drug, Lumefantrine. Hypothesis are based on the fact that significant delayed parasite clearance after AL treatment (the definition of artemisinin partial resistance) was not observed in some countries. Also, molecular markers associated with quinoline resistance (namely *pfcrt* and *pfmdr1* genes) are being selected by this combination. Phenotype and genotype data are scattered and the current situation in Africa is unclear. Lumefantrine decreased susceptibility need further

clarification. Additionally, because Lumefantrine and Amodiaquine exert opposite genetic forces on the parasite, they could potentially lead to incompatible resistance mechanisms if combined. In accordance, AL could be recued into a Triple (AL+ Amodiaquine) combination and become a short-term available solution. Furthermore, Lumefantrine is also being rescued into a non-artemisinin combination, along with Ganaplacide (KAF156). This combination is currently the most advanced new generation antimalarial therapy in development. In this study, we review the state of art, regarding Lumefantrine potential decreased performance, the mechanisms and factors that could be associated with its decreased performance in Africa and its recycling into new therapeutic alternatives.

7910

THERAPEUTIC EFFICACY OF ARTEMETHER-LUMEFANTRINE, DIHYDROARTEMISININ-PIPERAQUINE, AND ARTESUNATE-AMODIAQUINE FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN MAINLAND TANZANIA, 2023

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Antimalarial drug resistance threatens malaria control in Africa. In 2022, Tanzania confirmed artemisinin partial resistance (APR) by therapeutic efficacy study (TES) in Kagera region and suboptimal AL efficacy in Pwani region. Tanzania conducts annual TES of its first-line (artemether-lumefantrine, AL) and alternate first-line (artesunate-amodiaquine, ASAQ; Dihydroartemisinin-piperaquine, DP) antimalarial drugs to inform policy. Children with uncomplicated falciparum malaria were enrolled, treated, and followed to assess response to treatment per the 2009 World Health Organisation (WHO) TES protocol at Mbeya (AL, ASAQ), Mtwara (AL, ASAQ), Mwanza (AL, DP) and Tabora (AL, DP) sites. Molecular correction was conducted using a 3/3 *msp1/msp2/glurp* approach with gel electrophoresis. From March to September 2023, 703 participants were enrolled and 696 (99.0%) completed the study. Respective uncorrected and corrected Kaplan-Meier efficacies for AL were 87.5% and 98.9% in Mbeya, 84.9% and 95.2% in Mtwara, 82.1% and 98.8% in Mwanza, and 62.1% and 97.7% in Tabora. For DP, they were 95.4% and 98.7% in Mwanza and 93.0% and 95.3% in Tabora. For ASAQ, they were 100% and 100% in Mbeya and Mtwara. One participant experienced early treatment failure (AL, Mtwara). Day 3 parasitemia was observed in 1/175 (0.5%) Mbeya, 2/174 (1.1%); Mtwara, 4/175 (2.3%) Mwanza, and 3/171 (1.8%) Tabora participants. No APR or suboptimal AL, ASAQ, or DP efficacy was shown in Mbeya, Mtwara, Mwanza, or Tabora, but low uncorrected AL efficacies in Tabora indicate high selective pressure for lumefantrine resistance. Pwani and Kagera remain priority regions for change to alternate first-line, closely followed by regions with low uncorrected AL efficacies. ASAQ's 100% efficacy and antagonistic resistance mechanism make it a strong AL replacement candidate.

7911

PFPRELI: A NOVEL MOLECULAR MEDIATOR OF RESISTANCE TO *PLASMODIUM FALCIPARUM* SERINE HYDROLASE INHIBITORS

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The increasing incidence of drug resistance in *Plasmodium falciparum* has diminished the efficacy of almost all available first-line antimalarials. Consequently, new antimalarial treatments with novel modes of action are needed. Salinopostin A (Sal A) is a potent natural-product antimalarial with a high barrier to resistance that is thought to act via inhibition of parasite α/β serine hydrolases. Given the difficulty of employing natural products as therapeutic agents, our group synthesized an analog of Sal A, JB-128, that exhibited submicromolar activity against *P. falciparum* asexual blood stages (mean EC_{50} 180nM), with the schizont stage being particularly sensitized. Earlier results demonstrated that Sal A-resistant parasites generated from *in vitro* resistance selections in a hypermutable Dd2-Polδ mutant line harbored mutations in a PRELI domain-containing protein (PfPRELI), with 20-fold EC_{50} increases against SalA. These mutants were cross-resistant to JB-128 (7- to 10-fold EC_{50} increase). *In vitro*-evolved JB-128-resistant Dd2-Polδ parasites derived following JB128 selection pressure also acquired an overlapping set of mutations in PfPRELI. PfPRELI localizes primarily to the mitochondria and is vital for parasite growth, as demonstrated by a conditional PfPRELI knockdown. Strikingly, parasites with reduced PfPRELI protein levels became 12-fold more sensitive to JB-128. Additionally, resistance selection experiments with other serine hydrolase inhibitors also resulted in resistant parasites with PfPRELI mutations, emphasizing its central role in mediating resistance to candidate antimalarials targeting serine hydrolases.

7912

MAPPING THE RESISTANCE DETERMINANTS OF SMALL PEPTIDE-LIKE MOLECULES AGAINST *PLASMODIUM FALCIPARUM* PARASITES

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Malaria, caused by *Plasmodium* parasites, is one of the most prevalent infectious diseases in tropical regions. Artemisinin resistance against *P. falciparum* has been arising in some endemic areas, creating a need to develop new antimalarial compounds. Peptidomimetic molecules have been reported as antimicrobial agents and their antiplasmodial activity as protease inhibitors has been investigated in the last few years. Our work has focused on the parasitological profile of dipeptidyl protease inhibitors against *P. falciparum* asexual blood stage parasites. The most potent compound (Neq1153) showed a mean±SD IC_{50} of 600 ± 100 nM and a selectivity against HepG2 cells of 350. Neq1153 is a slow-acting inhibitor with pronounced inhibitory activity against trophozoites. Interestingly, Neq1153 exhibited a 10-fold increase in potency when tested against the chloroquine-resistant Dd2 strain when compared to its potency against the chloroquine-sensitive 3D7 strain. Neq1153 was found to be antagonistic with artesunate or chloroquine. This compound also caused swelling of the digestive vacuole, suggesting a possible mode of action related to the vacuole transmembrane proteins PfCRT or PfMDR1. PfCRT mutations in a Dd2 background (T93S, F145I, and I218F) and PfMDR1

mutations in a NF54 background (M841I+M924I) led to a two-fold loss of potency for all the mutants assessed. Interestingly, decreasing the *pfmdr1* copy number in FCB parasites led to two-fold increased sensitivity. Increasing the *pfpm2/3* copy number desensitized the parasite 2-4 times against Neq1153. Neq1153 seems to be a protease inhibitor involved in hemoglobin digestion and its potency is apparently affected by PfCRT, PfMDR1, and PfPM2/3 as low-level mediators. Parasites recently obtained under Neq1153 drug selection pressure are currently being characterized to elucidate resistance mediators. These findings highlight the importance of an in-depth investigation to indicate the true potential of a new series of compounds as antimalarial candidates. Our data also provide evidence that dipeptidyl derivatives could be attractive hits for an antimalarial drug discovery program.

7913

SELECTION AND CHARACTERIZATION OF AN ELQ-596 RESISTANT CLONE OF *PLASMODIUM FALCIPARUM*

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Endochin-like Quinolones (ELQs) are a potent new class of Cytochrome bc_1 inhibiting antimalarials currently in preclinical development by the Medicines for Malaria Venture (MMV). For the first time, a clone of multidrug resistant *Plasmodium falciparum* (Dd2-B2) was successfully selected for resistance to ELQ-596, a next-generation biaryl ELQ currently under study. The resistant clone D5 harbors a C18F mutation in the cytochrome b gene coding sequence which alters the Q_i site of the cytochrome bc_1 complex. In vitro antiplasmodial testing shows that D5 exhibits ~100-fold resistance to ELQ-596 compared to the parental Dd2-B2 strain. The D5 clone also appears to have a growth defect that is likely due to a fitness cost associated with the mutation. We evaluated the comparative activities of analogs of ELQ-596 in order to gain an understanding of the structural features that were important in the acquisition of resistance in the D5 clone. Taken together, our results indicate that the resistance mechanism targets primarily the 6-position chlorine atom and the 3-position biaryl projection. Surprisingly, cross-resistance to the structurally similar ELQ-300 was only modest, ~2 to 3-fold. We also evaluated the sensitivity of the D5 clone to other inhibitors of the electron transport chain and observed a dramatic enhancement in its susceptibility to Q_o targeting drugs including Atovaquone, selected ELQs, and prototypical Q_o targeting agents. For example, our results show enhanced sensitivity of the D5 clone to Q_o-targeting Atovaquone and ELQ-400 of between 10-100-fold compared to the parental strain. In summary, our results show that the acquisition of ELQ-596 resistance confers a fitness cost and a surprisingly enhanced susceptibility to Q_o-targeting compounds, which could represent a "pharmacological trap" created by compounds targeting both the Q_o and Q_i sites of cytochrome bc_1 complex. Our presentation will include a biochemical and structural rationale for these findings, and a discussion of their potential translational impact.

7914

POST ARTESUNATE DELAYED HEMOLYSIS IN PEDIATRIC PATIENTS IN THE UNITED STATES

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Intravenous artesunate is the current first line therapy for severe malaria and has substantially reduced its mortality. Some patients develop hemolysis after artesunate therapy, termed post artesunate delayed hemolysis (PADH). Thus, the U.S. Food and Drug Administration recommends that patients treated with artesunate receive weekly monitoring of hemoglobin and hemolytic markers for four weeks after therapy.The frequency and severity of PADH in pediatric patients is not known. Understanding the risk of PADH in pediatric patients is essential to determine appropriate monitoring for this condition. In the Multicenter Retrospective Chart Review we identified patients treated with artesunate at nine U.S. hospitals, between April 2019 and December 2023. We reviewed post-discharge laboratory values and clinic visits to identify patients with laboratory findings of PADH, and determine clinical outcomes. In the Pediatric Health Information System (PHIS) Database Review we identified patients who were treated with artesunate in a database of 49 children's hospitals (Pediatric Health Information System (PHIS) Database). We reviewed patient visits within eight weeks of treatment to identify patients with repeat presentations related to anemia or hemolysis. In our retrospective chart review, 24% of patients (6 of 24) treated with artesunate had laboratory evidence of PADH. No patients were symptomatic or medical intervention. Haptoglobin and lactate dehydrogenase levels were similar in patients with or without PADH. Of 92 patients treated with artesunate in the PHIS database, three (3.3%) had a repeat presentation within four weeks with diagnoses suggestive of new onset anemia. PADH is common in US pediatric patients treated with artesunate for severe malaria. However, severe hemolysis requiring medical intervention is rare. Haptoglobin and LDH levels were not useful as initial screening labs for PADH in pediatric patients. Our findings call into question the utility of weekly laboratory monitoring, as opposed to symptom-based monitoring, to identify pediatric patients at risk of readmission for PADH.

7915

NEXT GENERATION 3-BIARYL-ELQS FOR LONG DURATION PROTECTION AGAINST MALARIA

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ELQ-300 is a potent antimalarial drug with activity against blood, liver and vector stages of the disease. A prodrug, ELQ-331, exhibits reduced crystallinity and improved in vivo efficacy in preclinical testing and currently it is in the developmental pipeline for once-a-week dosing for oral prophylaxis against malaria. Due to the high cost of developing a new drug for human use and the high risk of drug failure it is prudent to have a back-up plan in place. Here we describe ELQ-596, a member of a new subseries of 3-biaryl-ELQs, with enhanced potency in vitro against multidrug resistant *Plasmodium falciparum* parasites. ELQ-598, a prodrug of ELQ-596 with diminished crystallinity, is more effective against murine malaria than its progenitor ELQ-331 by 4 to 10-fold, suggesting that correspondingly lower doses could be used to protect and cure humans of malaria. With a longer bloodstream half-life in mice compared to its progenitor ELQ-596 highlights a novel series of next generation ELQs with the potential for once-monthly dosing for protection against malaria infection. Advanced chemical methods for preparing 3-biaryl-ELQs will be presented along with preliminary results from experiments to explore key structure-activity relationships for drug potency, selectivity, pharmacokinetics and safety. Additionally, studies

relating to resistance propensity, characterization of resistant mutants, parasite killing profile, along with simulated docking of ELQ-596 into the enzyme active site will also be included.

7916

CHEMOGENOMIC PROFILING OF POOLED *PLASMODIUM FALCIPARUM* MUTANTS FOR DRUG ANNOTATION

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The malaria parasite *Plasmodium falciparum* is evolving resistance to the current frontline treatments with artemisinin combination therapies (ACTs). In ACTs, a short-acting artemisinin derivative rapidly decreases parasitemia while a long-acting partner drug is supposed to clear out any surviving parasites. While combination therapies are intended to deter development of resistance, evolving resistance in *P. falciparum* is occurring to both artemisinin and its partner drugs. Resistance first emerged in South East Asia, but recently evidence for emerging ACT resistance has been detected in Sub-Saharan Africa. The World Health Organization reports that widespread resistance to artemisinin combination therapies will result in 360,000 additional severe cases of malaria a year and an additional 80,000 deaths annually. Understanding drug mechanism of action can aid in the rational design of combination therapies that can evade the evolution of drug resistance. To speed up this process we have designed a drug screen and analysis protocol that uses a pool of isogenic *P. falciparum piggyBac* mutants to create unique chemogenomic response profiles related to the antimalarial compound's mechanism of action (MOA). Comparing chemogenomic response profiles to drugs of known MOA to compounds or drugs with unknown MOA aids in the annotation of the compounds. This approach provides an empirical method to select compounds with novel MOA that target distinct pathways and have opposing mechanisms of resistance. The ultimate goal is to select 'anticorrelated' ACT partner drugs that limit the parasite's ability to evolve resistance to ACTs.

7917

SYSTEMATIC REVIEW OF BIOGEOGRAPHIC PATTERNS OF *PLASMODIUM FALCIPARUM* DRUG RESISTANCE DYNAMICS

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The emergence of antimalarial drug resistance continues to threaten the use of control interventions in reducing transmission intensity and in turn the burden of the disease. How the interplay among transmission intensity, population immunity, and drug usage changes influences the dynamics of drug resistance is not well understood. Understanding the relationship between these factors and the changes of drug resistance will have implications on how to better plan drug administration under different transmission settings. We examined the association between parasite rate (a metric for transmission intensity) and the change in antimalarial drug usage with the prevalence of key Chloroquine (CQ) *pfcrt*-76T and Sulfadoxine Pyrimethamine (SP) (*pfdhfr*-108N and *pfdhps*-437G) resistant markers. We synthesized three types of data to inspect the question: drug usage over the years, local parasite rate (PR), and resistant marker prevalence. Global drug usage data collated at the country level was estimated from the Demographic Health Survey (DHS) and Multiple Indicator Cluster Survey (MICS) databases using customized codes. We then compiled prevalence data on key CQ (pfcrt-76T) and SP (pfdhps-437G and pfdhfr-108N) resistance markers in over 1000 studies from the WorldWide Antimalarial Resistance Network (WWARN) database. Subsequently, we retrieved parasite rate (PR) data corresponding to the areas where the drug resistant marker data were obtained from the Malaria Atlas Project (MAP) database. A mixed-effect regression model was then used to assess the association between parasite rate and drug usage with the prevalence of the resistant markers. We found a general decrease in the prevalence of *pfcrt*-76T and CQ usage, but an increase in the prevalence of *pfdhps*-437G and *pfdhfr*-108N, and SP usage. Results also suggest that transmission intensity may have varying impact on the evolution of antimalarial resistance. Furthermore, drug (CQ and SP) usage was found to be a good predictor of drug resistant marker changes under high transmission setting. However, under low transmission that influence may not be so clear as other factors may be at play.

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PROFILING OF DRUG RESPONSES AND ANTIMALARIAL DRUG RESISTANCE MARKERS IN *PLASMODIUM FALCIPARUM* CLONES FROM A GHANAIAN DIHYDROARTEMISININ (DHA)--SELECTED CLINICAL ISOLATE

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Failing antimalarial drugs due to the development of drug-resistant parasites is a serious threat to malaria control efforts. More severe is the emergence of artemisinin resistance in endemic regions, with indigenous mutations reported in some areas. This raises questions about the universality of currently validated markers for surveillance of artemisinin resistance. Uncovering molecular markers that drive artemisinin resistance in parasites with Ghanaian genetic background is critical, especially in the context of the emerging artemisinin resistance. This would be pivotal for identifying invaluable molecular markers for surveillance efforts and effectively informing targeted strategies to combat artemisinin resistance. This study demonstrated that dihydroartemisinin (DHA)-selected *Plasmodium falciparum* clones exhibited a range of sensitivities to artemisinin derivatives. When exposed to DHA and artesunate (AS), the parasites exhibited similar survival rates. Furthermore, each clone contributed to the overall drug-resistant phenotype with varying levels of drug susceptibility. Interestingly, we also discovered that this reduced sensitivity to artemisinin was not associated with non-synonymous mutations in the *Pfkelch13* gene and *Pfmdr1* gene. The findings suggest the possibility of artemisinin resistance developing independently of mutations in the *Pfkelch13* gene, aligning with observations noted in prior research. This opens the likelihood of mutations occurring in other genes or different regions of the *Pfkelch13* gene, especially since our study did not investigate the entire gene. These results underscore the complex nature of artemisinin resistance, extending beyond the currently recognized molecular markers. This complexity highlights the urgent need for exhaustive research to fully characterize the mechanisms behind artemisinin resistance. Such research is vital without novel and more effective antimalarial drugs to replace existing artemisinin-based treatments. Understanding these complex resistance mechanisms is critical for sustaining the efficacy of malaria therapies.

7919

EVALUATION OF HISTIDINE-RICH PROTEIN 2-BASED RAPID DIAGNOSTIC TESTS FOR MALARIA DIAGNOSIS AND PREVALENCE OF *PFHRP2*/*PFHRP3* DELETIONS IN UGANDA, 2021-2023

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Histidine-rich protein 2 (HRP2)-based rapid diagnostic tests (RDTs) are widely used to diagnose *Plasmodium falciparum (P. falciparum)* malaria in resource-limited settings. However, false positive results due to persistent

antigenemia, *P. falciparum* infections in which *pfhrp2 and pfhrp3* are deleted and non-*falciparum Plasmodium* infections threaten the efficacy of HRP2-based RDTs. Samples from two cross-sectional studies of participants aged at least 2 years, carried out between 2021 and 2023 in Uganda, were used to evaluate the performance of HRP2-based RDTs by comparison with microscopy and quantitative PCR (qPCR). Discordant samples testing negative by RDT and positive by microscopy underwent qPCR to confirm and quantify *P. falciparum* malaria. Samples confirmed to be positive for *P. falciparum* were tested for *pfhrp2* and *pfhrp3* deletions using digital PCR while those confirmed to be negative underwent *Plasmodium* species testing. Microscopy and RDT were performed on 6353 samples from the cross-sectional studies. Overall, the sensitivity of HRP2-Based RDTs was high at 92% but the specificity was low at 57%. The Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were 49% and 94% respectively. Using qPCR as the gold standard on a random sample, the sensitivity of HRP2-based RDTs was 90% and the specificity was 64%. There were 166 (6%) discordant samples out of 2684 microscopy-positive samples. Of these, 90 (54%) were confirmed to be *P. falciparum* whereas 76 (46%) were negative by qPCR. One *P. falciparum* positive sample was confirmed to have a deletion in *pfhrp3.* The overall prevalence of *pfhrp3* deletions was estimated to be 0.04%. There were no observed deletions of *pfhrp2*, and therefore, no double deletions of *pfhrp2/pfhrp3* were observed. Discordant samples testing negative by qPCR were determined to be majorly non-*falciparum* species (n = 37, 49%) or false positives by microscopy (n = 31, 41%). While HRP2-based RDTs remain sensitive in Uganda, false positives are common due to persistent antigenemia. Microscopy-positive, RDT-negative discordance was uncommon and deletions of *pfhrp2* and *pfhrp3* remain rare in Uganda.

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EVALUATION OF A QUANTITATIVE DRIED BLOOD SPOT PLATFORM FOR MALARIA PARASITE DETECTION, SEQUENCING, AND HOST RESPONSE PROFILING

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While the gold standard in malaria diagnosis remains microscopic observation of *Plasmodium* parasites in blood smears, subclinical and submicroscopic infections evade detection by standard diagnostic protocols. Such infections form a reservoir for further transmission, maintaining the spread of malaria. Highly sensitive molecular techniques, such as quantitative PCR (qPCR) can identify low-density parasitemias in dried blood spots (DBS) in a laboratory setting; however, parasitemia estimates can greatly vary due to an imprecise estimation of blood volume in each "punch" from a DBS. Quantitative dried blood spot (qDBS) microsampling cards for volumetric blood sampling may be stored, transported, and later analyzed for a variety of analytes, including parasite and host proteins, metabolites, and genetic or genomic material. Here, we tested qDBS as a means of collecting, storing over a long period (>8 months), and ambient transport of samples over great distances (from Lagos, Nigeria to Gainesville, Florida, USA), determining the suitability of DNA extracted from blood collected on qDBS cards for use in molecular and metabolomic analyses. The qDBS cards (N=87) with paired Pf RDT data were collected in July 2023 from patients presenting to the clinic with acute febrile illness and were split into four groups. DNA was extracted from one of the two paper discs from each qDBS card using Chelex-Tween20, retaining the second disc for further study using LC/MS metabolomic profiling of positive samples or nanopore sequencing of negative samples. Quantitative polymerase chain reaction (qPCR) for four *Plasmodium* species (*P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*) confirmed parasite infection for 76% Pf RDT-positive and identified "RDT-missed" samples. Initial multi-omic host response analyses of confirmed positives and parallel parasite sequencing data indicate that qDBS cards preserve high-quality DNA and metabolites, offering improved quantification of parasites and multi-analyte biomarker detection.

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FIELD EVALUATION OF THE NOVEL ONE STEP MALARIA PF AND PF/PV RAPID DIAGNOSTIC TESTS AND THE PROPORTION OF HRP-2 GENE DELETION IDENTIFIED ON SAMPLES COLLECTED IN THE PWANI REGION, TANZANIA

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Malaria rapid diagnostic tests (mRDTs) have played an important role in the early detection of clinical malaria in an endemic area. While several mRDTs are currently on the market, the availability of mRDTs with high sensitivity and specifcity will merit the fights against malaria. We evaluated the field performance of a novel One Step Malaria (P.f/P.v) Tri-line and One Step Malaria (P.f) rapid test kits in Pwani, Tanzania. Methods. In a cross-sectional study conducted in Bagamoyo and Kibiti districts in Tanzania, symptomatic patients were tested using the SD BIOLINE, One Step Malaria (P.f/P.v) Tri-line and One Step Malaria (P.f) rapid test kits, microscope, and quantitative Polymerase Chain Reaction (qPCR). An additional qPCR assay was carried out to detect Histidine-Rich Protein 2 (HRP-2) gene deletion on mRDT negative but microscope and qPCR positive samples. Microscope results confirmed by qPCR were used for analysis, where qPCR was used as a reference method. Results The sensitivity and specifcity of One Step P.f/P.v Tri-line mRDTs were 96.0% (CI 93.5–97.7%) and 98.3% (CI 96.8–99.2%), respectively. One Step P.f mRDT had sensitivity and specifcity of 95.2% (CI 92.5–97.1%) and 97.9% (CI 96.3–99.0%) respectively. Positive predictive value (PPV) was 97.6% (CI 95.4–98.7%) and negative predictive value (NPV) was 96.2% (CI 95.5–98.3%) for the One Step P.f/P.v Tri-line mRDTs respectively, while One Step P.f mRDT had positive predictive value (PPV) and negative predictive value (NPV) of 97.0% (CI 94.8–98.3%) and 96.7 (CI 94.9–97.9%) respectively. 9.8% (CI 7.84–11.76) of all samples tested and reported to be malaria-negative by mRDT had HRP-2 gene deletion. Conclusion One Step Malaria P.f/P.v Tri-line and One Step Malaria P.f rapid test kits have similar sensitivity and specifcity as the standard mRDT that is currently in the market, demonstrating the potential to contribute in the fight against malaria in endemic settings. However, the identified malaria parasites population with HRP-2 gene deletion pose a threat to the current mRDT usability in the field and warrants further investigations.

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AVAILABILITY AND APPROPRIATENESS OF MALARIA MANAGEMENT SERVICES AT DRUG SHOPS IN TWO HIGH-BURDEN REGIONS IN UGANDA

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In Uganda, amidst controversy about their mandate, drug shops are popular health service outlets. PMI Uganda Malaria Reduction Activity conducted a cross-sectional study in the Busoga and Lango regions, endemic settings in Uganda, to determine capacity of drug shops to provide malaria management services. The sampling frame was a list of drug shops from the National Drug Authority. Facilities were proportionately randomly sampled across districts, targeting 384 in each region. Drug shops were assessed for licensure status, availability of antimalarials and mRDTs, and their malaria management practice. 389 drug shops in Busoga and 359 in Lango participated. Of 579 (77%) drug shops that had an operating license, 85% were up-to-date. Most respondents had tertiary-level education (83%) and were enrolled nurses (45%) and nursing assistants (32%). Only 296 (83%) drug shops in Busoga and 261 (76%) in Lango reported having attended to a febrile patient in the week prior to the interview. Considering the last febrile patient seen, 64% in Busoga and 82% in Lango had a malaria test performed and the majority (92%) were positive. Considering patients with a positive and negative result, 97% and

30% were prescribed an antimalarial, of which most were given (99% and 90%) the antimalarial as a full (97% and 80%) dose, respectively. Of 154 patients not tested, 97 (63%) were prescribed an antimalarial and 96 (99%) were given treatment; but only 71 (74%) received a full dose. Artemether-lumefantrine (AL; 75%), followed by dihydroartemisinin-piperaquine (DP; 10%), and intravenous artesunate (IVAS; 99%) were the most frequently prescribed antimalarials. Considering stock, AL (88%), DP (39%), and IVAS (26%) were available. Less than half (289, 39%) of the drug shops had RDTs. Overall, 515 (72%) of drug shops reported selling AL by the tablet and not as a complete dose. Drug shops are actively and inappropriately managing patients for uncomplicated malaria. There is an urgent need to engage drug shops in providing appropriate malaria management and further understand interventions to change behavior of drug shop attendants.

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LONGITUDINAL SURVEILLANCE OF PFHRP2/3 DELETIONS TO SUPPORT FUTURE ANTIGEN-BASED MALARIA DIAGNOSTICS IN KENYA

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Kenya reported an estimated 3.4m malaria confirmed cases and 219 deaths because of malaria in 2022. Accurate malaria diagnosis is essential for malaria case management, surveillance, and elimination. About 74% of malaria diagnoses globally use malaria Rapid Diagnostic Test (RDT). The accuracy of *P. falciparum* Histidine-rich protein 2 (PfHRP2)-based RDTs can be impaired by either deletion in PfHRP2 or related PfHRP3 gene. The WHO criteria that require >95% accuracy as the threshold for selection or withdrawal of RDTs argue for active mapping of the distribution of PfHRP2/3 deletions. To improve case management, the Kenya Ministry of Health conducted surveillance of clinically- significant Pfhrp2/3 deletions according to recommended WHO protocol. Eligible participants meeting the case definition of malaria 6 months-85 years old. Training was conducted on recruitment of study participants, collection of samples, data entry using Open Data. Collection application. Positive and negative predictive value (PPV/NPV) of HRP2-based malaria RDT was calculated. A total of 5,394 dry blood spots were collected. All participants were concurrently tested for malaria using both the HRP2-based and Pf-pLDH-based RDTs. 2401 (45%) of the individuals tested positive by at least one of the RDTs. A total of 72 (1%) of the infections had discordant results that tested negative by HRP2-based RDT but positive for the *Pf*-pLDH -based test- hence suspected to be harboring HRP2/3 deletions. Trans Nzoia county had the highest number of suspected deletions. The coastal endemic region recorded the highest PPV of 99.3% and low transmission zone recorded the lowest PPV (96.8%) while seasonal transmission zone recorded the highest NPV 99.3% and lake endemic region recorded the lowest NPV 95.3% of HRP2-based RDT. Our preliminary findings suggest that the HRP2/3 deletion frequency in Kenya is still <2%. As such, there is need to repeat these surveys every two years for early detection of increase in frequency of these deletions. All the discordant samples, along with 5% of the entire general sample is scheduled for genomic analyses to ascertain the deletion rate.

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THE PREVALENCE OF *PLASMODIUM OVALE* AMONG SYMPTOMATIC INDIVIDUALS FROM THE EASTERN REGION OF GHANA

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Malaria is a major public health concern in Ghana, with *Plasmodium falciparum* being the primary causative agent. Current reports indicate that the prevalence of falciparum malaria has generally decreased worldwide, which has drawn significant attention to the non-falciparum Plasmodium species: *Plasmodium* malariae and *P. ovale*. Given this, data on the prevalence of these *Plasmodium* species is crucial for guiding effective intervention strategies. This study aimed to determine the prevalence of *P. ovale* among symptomatic individuals from the Eastern Region of Ghana. We conducted a comprehensive analysis of 1,949 clinical samples collected from individuals with suspected malaria across three towns in the Eastern Region of Ghana. Genomic DNA was extracted from the samples, and nested polymerase chain reaction (PCR) assays were performed to detect *P. falciparum* and *P. ovale*. Among the suspected malaria cases, 53.9% (1,050/1,949) were identified as *P. falciparum* infections, while Plasmodium ovale mono-infection accounted for 1.6% (32/1,949). *P. falciparum* and Plasmodium ovale co-infection accounted for 3.9% (75/1,949) of the cases. A total of 40.6% (792/1,949) of participants suspected of malaria tested negative for both *P. falciparum* and *P. ovale.* The prevalence of *P. ovale* observed in this study underscores the importance of the availability of reliable diagnostic tools at point-of-care facilities. These findings emphasize the necessity for tailored malaria control measures that encompass a broader spectrum of *Plasmodium* species to effectively manage and eventually eradicate malaria.

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MALARIA DIAGNOSIS IN URBAN AREAS USING LOOP MEDIATED ISOTHERMAL AMPLIFICATION

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Cities in sub-Sahara Africa are increasingly becoming receptive to malaria. With sub-Saharan Africa projected to attain 75% urbanization in 2050, urban malaria ought to be taken seriously. Continuous real time surveillance is needed to inform policy strategy and disease monitoring. Low-cost molecular tools are thus needed in carrying out large-scale surveillance studies to limit missing out on low density sub-microscopic malaria infections. Loop mediated isothermal Amplification (LAMP) is an easy to use, cost effective and sensitive molecular diagnostic tool with the capacity to be used in large scale surveillance studies. The aim of this study was to assess the capacity of LAMP assay in on-going malaria epidemiological studies.A cross-sectional study was carried out in Accra, Ghana to access the dynamics of malaria transmission in the three transmission seasons (dry, heavy rain and post rainy season). 13-health facilities within the city and 100 households per facility were randomly selected at each survey timepoint. Individuals within these households who consented to the study were tested for malaria and anemia. RDT, thick and thin smears and dried blood spots were prepared. DNA from the filter blots were purified using Chelex® sodium form and analyzed using the LAMP assay. Preliminary results from the dry-season survey showed a 2.2% (65/2930) malaria prevalence by RDT across the 1313 households sampled. Out of this, 689 people have been sampled with full results to date. Malaria prevalence was 1.3% (9/689) by RDT, and 6.4% (44/689) by LAMP. All samples that were positive by RDT

were also positive by LAMP. The results to date confirm the importance of an effective low-cost molecular tool such as the in-house LAMP assay for malaria surveillance. The LAMP assay has the potential to provide a programmatic alternative to detect low-density malaria infections and better elucidate malaria epidemiology in an urban context.

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THE ADDITIVE VALUE OF PARAMAX-3™ PAN/PV/PF MALARIA RAPID DIAGNOSTIC TEST USE FOR IMPROVING *PLASMODIUM VIVAX* MALARIA DETECTION IN MAEVATANANA, MADAGASCAR

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Since 2006, Madagascar has been using malaria rapid diagnostic tests (mRDT) that detect both the *Plasmodium* pan-specific LDH antigen and the *P. falciparum* HRP2 antigen. As of today, the Malagasy Ministry of Health (MoH) is interested in obtaining more specific information on the prevalence *P. vivax* malaria. This will help in developing better strategies for achieving malaria elimination. To provide the MoH with information for the selection of appropriate mRDTs, we conducted an assessment of the relative performance of the commercially available mRDT Paramax-3™ Pan/Pv/Pf with a focus on its ability to detect *P. vivax* antigens. This study was conducted in August 2023 in Maevatanana in the northwestern area. For each outpatient with suspected malaria, both Paramax-3™ Pan/Pv/Pf testing and microscopy were carried out to diagnose malaria. Out of the 298 patients who were tested, 118 patients (39.6%, CI95%: 34 – 45.2%) had positive mRDT and 111 patients (37.1%, CI95%: 31.6 - 42.9%) had positive microscopy. Using microscopy as the reference method, the Paramax-3™ Pan/Pv/Pf had a sensitivity of 96.4% [CI95%: 91.1 – 98.6%] and a specificity of 94.1% [CI95%: 89.8 – 96.7%] for detecting any plasmodial infection (Kappa = 0.9). The test's sensitivity was 94.3% [CI95%: 90.1 – 96.8%] (Kappa = 0.9) for detecting *P. falciparum* and 100% [CI95%: 51 – 100%] and a specificity of 98.6% [CI95%: 96.6 – 99.5%] (Kappa = 0.6) for detecting *P. vivax*. The positive and negative predictive values of Paramax-3™ for detecting *P. vivax* malaria were 100% [95% CI: 98.7 – 100%]. Overall sensitivity and specificity values of the test were above the cut-off defined by the WHO (90%). In concluding remarks, there was almost perfect agreement between microscopy and the Paramax-3™ Pan/Pv/Pf test for diagnosing malaria. It's worth noting that the Paramax-3TM Pan/Pv/Pf test is effective in detecting *P. vivax*. This makes it a valuable diagnostic tool for mapping the distribution of *P. vivax* in Madagascar, especially during national surveys.

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CONTRIBUTION OF THE OTSS+ SUPERVISION APPROACH IN IMPROVING THE QUALITY OF MICROSCOPIC MALARIA DIAGNOSIS IN CÔTE D'IVOIRE, 2022-2023

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A national assessment of biotechnologists conducted in July 2019 by the PMI Stop Djekoidjo project and the Côte d'Ivoire National Malaria Control Program in 104 referral hospitals revealed that half of the referral hospitals did not have WHO-certified microscopists to read malaria slides. After training biotechnologists from 31 referral hospitals, the Outreach Training and Supportive Supervision Plus (OTSS+) approach was initiated to further improve skills for quality microscopic malaria diagnosis and was implemented by a national pool of supervisors. The project provided each supervisor with an observation questionnaire digitized in a tablet for automated data collection. Each supervisee was observed while practicing standard procedures in malaria microscopy and reading 10 WHO-certified slides (10min/slide) including three negative slides, three *Plasmodium falciparum* slides, one mixed infection slide (*P. falciparum* plus one other species), and three slides with *P. malariae*, *P. vivax*, and *P. ovale*. Results provided by the supervisees were compared to those validated for each certified slide. Competence was assessed according to the WHO level three criteria for parasite detection (>70%), species identification (>70%) and determination of parasite density (>30%). From May 2022 to May 2023, three OTSS+ laboratory supervision visits were conducted with the referral hospitals biotechnologists. Data collection was carried out by 12 supervisors using KoboCollect software. Data were then analyzed based on the WHO criteria to compare the proportion of competent microscopists between the first and third OTSS+ supervision visits. In a cohort of 41 laboratory technicians, the proportion deemed competent between the first and third OTSS+ visits increased from 80.5% (33/41) to 100% for parasite detection; from 12.2% (5/41) to 39.0% (16/41) for parasite Species identification; and from 41.5% (17/41) to 90.2% (37/41) for parasite density. Results showed the effectiveness of the OTSS+ supervision approach in building skills for malaria microscopy. Scaling-up would improve the quality of microscopic malaria diagnosis in Côte d'Ivoire.

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AI-ASSISTED SOFTWARE FOR RAPID AND ACCURATE BLOOD SMEAR ANALYSIS OF RODENT MALARIA MODEL

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Rodent malaria models are vital for preclinical testing of antimalarials and vaccines. Typically, evaluating these models involves counting *Plasmodium*-infected RBCs manually, which is time-consuming and repetitive. We have developed an AI-assisted software, Malaria Screener R, to expedite these studies by automating the counting of infected RBCs. This application requires a built-in or top-mounted camera for capturing field-of-view images through the microscope. The software features an intuitive graphical user interface that facilitates image processing and visualization of the results. It is being developed as an offline desktop application for Windows and Mac OS. Our AI-powered algorithm reliably measured *P. yoelii* and *P. berghei* infected RBCs at a wide parasitemia range (0.13-74.12%) using only a few images from each slide (about 3 images with ~150 RBCs per image). Automated counts strongly correlated with manual counts. The program was highly accurate for parasitemia >1% (mean relative error: *P. yoelli* – 10.74% and *P. berghei* – 8.31%). Low parasitemia (<1%) affected count accuracy (up to 2-fold). However, our software was designed to allow user verification and correction, an especially quick process at parasitemia <1%. The software demonstrated significantly better precision and consistency than four parasitologists in a test study that measured standard deviation and relative error. We also tested the system's generalizability with three different microscope settings (Nikon E800 with 100x objective, Nikon E600 with 40x objective, and Nikon E600 with 100x objective). Following fine-tuning, it was able to perform with a mean relative error lower than 25% (15.64%, 23.07% and 24.84% respectively). In addition, the AI model is currently being trained to differentiate parasite stages. Initial training presented promising results by showing lower than 25% mean relative error across the 4 classes that were included (Ring, Trophozoite, Schizont and Uninfected). Overall, Malaria Screener R showed the potential to help in the rapid evaluation of novel vaccines and antimalarials in an easily accessible *in vivo* malaria model.

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PERFORMANCE OF RAPID DIAGNOSTIC TESTS, MICROSCOPY, AND REAL-TIME PCR FOR THE DETECTION OF MALARIA INFECTIONS AMONG ASYMPTOMATIC INDIVIDUALS FROM VILLAGES WITH CONFIRMED ARTEMISININ PARTIAL RESISTANCE IN NORTH-WESTERN TANZANIA

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In high transmission areas, asymptomatic infections with low parasitemia and gametocytes are commonly encountered and are capable of sustaining transmission. Such infections need to be properly detected and radically treated for successful control and elimination of malaria. This study evaluated the performance of rapid diagnostic tests (RDTs), microscopy, and quantitative PCR (qPCR) for detecting asymptomatic infections in the Kyerwa district of Kagera region, where artemisinin partial resistance has been recently confirmed**.** This cross-sectional community survey of asymptomatic individuals aged ≥6 months was conducted in July and August 2023. Dried blood spots (DBS) and blood slides were collected from 4,454 individuals. DNA was extracted from DBS using the Chelex method and qPCR was used to amplify the 18S ribosomal RNA gene. Malaria prevalence was 44.3% (n = 1,979), 32.1% (n = 1,431), and 39.8% (n = 1,771) by RDTs, microscopy, and qPCR, respectively. Using qPCR as a reference method, the sensitivity and specificity of RDTs were 94.0% (95% CI = 92.8-95.1) and 87.5% (95% CI = 86.2-88.7), respectively; the low specificity was potentially due to prior antimalarial medication. For microscopy, the sensitivity and specificity were 74.6% (95% CI = 72.5-76.6) and 95.2% (95% CI = 94.3-96.0), respectively; and with a higher positive predictive (92.8%) value compared to RDTs (83.4%) and vice-versa for negative predictive value (85.3% for microscopy and 95.2% for RDTs). The sensitivity of microscopy at <100, 100-1000, 1001-5000, 5001-10,000, and >10,000 (parasites/µl) was 60.7%, 93.9%, 97.8%, 100%, and 97.7% respectively; compared to 88.8%, 99.8%, 99.5%, 100% and 97.7% for RDTs. Sensitivities of both microscopy and RDTs increased with an increase in parasite densities indicating both tests are effective for the detection of malaria parasites, particularly in asymptomatic individuals. The performance of RDT and microscopy should be regularly checked for accurate detection of malaria parasites for effective surveillance and case management particularly in this area with confirmed artemisinin partial resistance

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MOLECULAR EXAMINATION OF FALSE NEGATIVE HISTIDINE-RICH PROTEIN 2 (HRP2)-BASED RAPID DIAGNOSTIC TESTS (RDTS) FOR MALARIA IN DIORO, MALI

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Previous studies in Mali have found high frequencies of false negative HRP2-based RDTs in subjects with *Plasmodium falciparum* malaria (chills, fever, headache and other symptoms plus a positive thick smear for asexual *P. falciparum* parasites). In Dioro (Mali), the frequencies of false negative RDTs were higher in the dry season (when parasite densities are low) than in the rainy season (when parasite densities are high). Molecular studies based on 1] a bead-based immunoassay that detects sub-picogram levels of HRP2 antigen, 2] PCR amplification of a conserved parasite gene (*18S rRNA*) and *hrp2* and 3] *hrp2* Sanger sequencing were performed to examine the potential for 1] lower or undetectable levels of HRP2 antigens, 2] spontaneous deletions of the *hrp2* gene or 3] variant HRP2 sequences that are undetected by the antibodies used in most immunoassays to explain those false negative RDTs. As expected, the likelihood of a negative molecular test result increased as parasite densities decreased among subjects with true positive and false negative RDTs. In contrast, subjects with true positive RDTs were more likely to be positive for HRP2 than those with false negative RDTs (50/55 vs. 14/65, p=0.001). Subjects with true positive RDTs were also more likely to be positive for *18S rRNA* and *hrp2* than those with false negative RDTs (*18S rRNA*: 47/55 vs. 7/65, p=0.001 and *hrp2*: 34/55 vs. 7/65, p=0.001). Interestingly, *hrp2*-positive subjects with false negative RDTs were more likely to have variant *hrp2* sequences than those with true positive RDTs (3/3 vs. 2/17). These findings suggest low-density parasite infections from the dry season with false negative RDTs may produce HRP2 antigens that are more difficult to detect using immunoassays than those of high-density parasite infections from the rainy season with true positive RDTs, potentially due to lower levels of HRP2 production and/or variant HRP2 sequences missed by immunoassay capture antibodies. These findings highlight a critical obstacle to detecting malaria in Mali during the dry season - when parasite densities are low and interventions to interrupt transmission may have their greatest impact.

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HISTIDINE-RICH PROTEIN (HRP) 2-BASED RDT FALSE-NEGATIVES AND *PLASMODIUM FALCIPARUM* HRP 2 AND 3 GENE DELETIONS IN LOW, SEASONAL AND INTENSE PERENNIAL TRANSMISSION ZONES IN CAMEROON

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False negative rapid diagnostic tests accruing to the non-detection of *Plasmodium falciparum* histidine-rich protein 2/3 (*Pfhrp2/3*) is threatening the diagnosis of malaria. Although regular monitoring is necessary to gauge the level of efficacy of the tool, studies in Cameroon remain limited. This study assessed *Plasmodium* spp. prevalence and *Pf*hrp2/3 gene deletions across ecological zones in Cameroon.This is a cross-sectional, multi-site, community- and hospital- based study, in 21 health facilities and 14 communities from low seasonal (LS) and intense perennial (IPT) malaria transmission zones between 2019 - 2021. Participants screened for malaria parasite using *Pf*hrp2 mRDT and light microscopy. DNA extracted from dried blood spot using chelex®-100 and *P. falciparum* confirmed using *var*ATS real-time quantitative Polymerase Chain Reaction (qPCR), *P. malariae* and *P. ovale* by real-time qPCR of Plasmepsin gene, and *P. vivax* using a kit. Isolates with amplified *Pf*csp and *Pf*ama-1 genes were assayed for *Pf*hrp 2/3 gene deletions by PCR. A total of 3,373 participants enrolled, 1,786 *Plasmodium* spp. infected, with 77.4% *P. falciparum*. Discordant RDT and qPCR results (False negatives) were reported in 191 (15.7%) samples from LS (29%, 42) and IPT (13.9%, 149). The *Pfhrp2+/Pfhrp3+* genotype was most frequent, similar between LS (5.5%, 8/145) and IPT (6.0%, 65/1,076). Single *Pfhrp2* and *Pfhrp3* gene deletions occurred in LS (0.7%, 1/145 each) and IPT (3.6%, 39/1,076 vs 2.9%, 31/1,076), respectively. Whilst a single sample harboured *Pfhrp2-/Pfhrp3-* genotype in LS, 2.4% (26) of 1076 were double deleted and the *Pfhrp2+/Pfhrp3-* (0.3%, 3) and *Pfhrp2-/Pfhrp3+* (1.2%, 13) genotypes only observed in IPT. *Pfhrp2,*

Pfhrp3 deletions and *Pfhpr2-/Pfhrp3-* genotype accounted for 78.8% (26), 64.9% (24) and 63.6% (21) RDT false negatives, respectively.*Plasmodium falciparum* remains the dominant species in Cameroon. Although the low prevalence of *Pfhrp2/3* gene deletions supports the use of HRP2-based RDTs for malaria diagnosis, the high proportion of false-negatives due to gene deletion necessitates continued surveillance to inform malaria elimination efforts

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EVIDENCE-BASED CLINICAL TRIAL DESIGN: A MODELLING STUDY OF THE *PLASMODIUM VIVAX* SEROLOGICAL TESTING AND TREATMENT IN ETHIOPIA AND MADAGASCAR (PVSTATEM) CLUSTER-RANDOMIZED TRIAL

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The high frequency of negative or counterintuitive results even among adequately powered clinical trials calls for the development of additional methods to guide clinical trial design. We demonstrate the potential of mathematical modelling to maximise trial effect size and optimise its roll-out using the ongoing *Plasmodium vivax* Serological Testing and Treatment in Ethiopia and Madagascar (PvSTATEM) cluster-randomised trial as a case study. Effective control of *P. vivax* requires targeting the hidden liver-stage reservoir of hypnozoites. *P. vivax* serological testing and treatment (PvSeroTAT) represents a novel intervention targeting hypnozoite carriers. The PvSTATEM trial underway in Ethiopia and Madagascar randomises villages to intervention (two rounds of PvSeroTAT, 6 months apart) and standard of care. We use mathematical modelling methods to 1) characterise factors influencing the impact of PvSeroTAT under a range of verisimilar conditions, and 2) optimise the PvSTATEM trial design. We use an existing *P. vivax* transmission model to simulate a village-based *P. vivax* intervention consisting of two rounds of PvSeroTAT, 6 months apart. To address the first aim, we quantify the impact of the intervention across a range of transmission settings (varying e.g. *P. vivax* transmission intensity, intervention coverage, *P. vivax* seasonality and timing of intervention, treatment adherence). The second aim is investigated by simulating each of the villages screened for participation in the PvSTATEM trial. We will simulate candidate clusters by calibrating the transmission model to data from PvSTATEM census surveys (concluded in autumn 2023) and baseline observational surveys (expected date of completion May 2024). Simulation modelling reveals that the proposed cluster randomized trial is likely to yield a significant result across a broad range of parameter assumptions, with particular sensitivity to cluster size, intervention coverage, *P. vivax* seasonality, and transmission intensity.

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UNTARGETED RNA SEQUENCING ANALYSIS OF BLOOD SAMPLES REVEALS NO PFHRP2/3 DELETION IN FALSE NEGATIVE RDTS IN SENEGAL

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Molecular pathogen surveillance is an important emerging strategy to monitor infection risk. In the context of a broader pathogen surveillance study, a focused sub-analysis was conducted to explore the utility of untargeted RNA metagenomic Next-Generation Sequencing (RNA-mNGS) to detect histidine-rich protein 2/3 (*Pfhrp2/3*) gene deletions among malaria Rapid Diagnostic Test (RDT) false negative samples. We applied this strategy to plasma from 163 malaria RDT-negative febrile individuals. For these samples we created cDNA then performed RNA-mNGS on pooled and indexed samples to obtain at least 2 million sequencing reads per sample. Quantification of *Plasmodium falciparum* was calculated by comparing *P.falciparum*-specific reads to total raw read counts. Cleaned and de-duplicated *P.falciparum* reads were then aligned to *Pfhrp2* and *Pfhrp3*. We detected *P.falciparum* sequences among 11/163 febrile samples that were negative by malaria RDTs. We next evaluated the expression levels of *Pfhrp2* and *Pfhrp3*, the target antigens of the malaria RDTs used in this study, as deletion of these genes has been observed at low rates in Senegal. We observed significantly more reads aligned to *Pfhrp2* in RDT+/mNGS+ (n=26) samples compared to RDT-/mNGS+ samples (n=11). However, the fact there were some reads mapped to both genes in RDT-/mNGS+ suggested these genes were present. Further molecular assays targeting the *Pfhrp2* exon 2 region and adjacent genes confirmed the absence of deletions in qPCR-verified *P. falciparum* infections, correlating with the low incidence of *Pfhrp2* gene deletion in Senegal previously reported. Further work is ongoing to explore the implications of differences in *Pfhrp2/3* gene expression levels on protein levels and to perform molecular analysis for *Pfhrp3*. Our findings suggest that *Pfhrp2/3* deletions continue to be rare in Senegal, and suggest that RNA-mNGS offers an avenue for simultaneous surveillance of these deletions alongside identifying non-malarial causes of fever.

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MALARIA MASS DRUG ADMINISTRATION WITH DIHYDROARTEMISININE PIPERAQUINE (DHAPQ) IN TWO DIFFERENT SETTINGS OF MALARIA TRANSMISSION IN MALI

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Despite the efficient implementation of the current malaria control strategies in Mali (universal net coverage, detection and treatment of cases, seasonal malaria chemoprevention and intermittent preventive treatment for pregnant women), malaria morbidity and mortality remain high in the country. The Word Health organization (WHO) currently recommends mass drug administration (MDA) for the interruption of transmission of *P. falciparum* malaria in areas approaching elimination. However, the gap in our knowledge is how MDA during the transmission can impact the disease burden when provided a month before the peak of cases. This study assesses the feasibility and the effect of MDA with DHAPQ on the prevalence and incidence of malaria in Sirakorola (low transmission setting) and Frentoumou (High transmission setting) in the peak month which is October. We performed an uncontrolled before-and-after study in both sites. It consists of assessing the prevalence of asymptomatic infection before and four weeks post-administration using microscopy, provide full antimalaria treatment with DHAPQ to participants (only the first dose was given by community health workers), run a passive case detection at health centers to determine the incidence of clinical malaria post treatment. A total of 7,093 participants were enrolled with 2,038 in Frentoumou and 5,055 in Sirakorola respectively. MDA coverage and compliance averaged 99.40% and 92.90% respectively. In Frentoumou, prevalence of asymptomatic *P. Falciparum* carriage was 52.71% before and 5.43% after the MDA (OR=0.10; 95% IC 0.01-0.92; p<0.001) whereas it was 21.05% before and 2.83% after MDA in Sirakorola (OR=0.10; 95% IC 0.00-0.15; p<0.001). Malaria cumulative incidence dropped from 10.74% to 4.31% in Frentoumou (RR= 0.40; 95% CI 0.32-0.49) and from 2.65% to 1.64% in Sirakorola (RR= 0.62; 95% CI 0.55-0.69). Chills, diarrhea, or headaches

were the adverse drug reactions reported after the MDA. In Mali, regardless the transmission intensity, MDA with DHAPQ targeting the high transmission season could be benefic for the reduction of the diseases burden among communities.

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PROGRESS IN THE FIGHT AGAINST MALARIA USING COMMUNITY-BASED CASE MANAGEMENT IN THE DISTRICT OF VANGAINDRANO, MADAGASCAR, 2023

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For years, Vangaindrano District has had the highest malaria incidence in Madagascar, however, community health workers (CHWs) have not provided malaria services there since 2011. Delayed care-seeking is frequent for a variety of reasons, including suboptimal access to community-level healthcare. In response, the Ministry of Health and the MCGL project are collaborating to implement malaria community-based case management (mCCM) for people of all ages, while also bolstering management and technical capacity among district- and facility-based actors. We summarize changes in access to health services following the April 2023 introduction of these activities. We accessed data from the routine health information system and MCGL administrative documents for analysis. We included data from the 100 CHWs associated with all 7 health facilities to complete training about these activities (Apr 2023), and analyzed data from April to November 2023. Following training, all 100 CHWs began providing malaria diagnosis and care, and all CHWs submitted all their data reports from April - November. In total, CHWs assessed 14,524 febrile people of all ages, 99.5% (14,453/14,524) of whom were tested with a rapid diagnostic test (RDT). Of those tested, 10,403 (72.0%) were confirmed to be infected with malaria and all of these were treated with an artemisinin-based combination therapy by the CHWs. Each CHW received a median of 17 (interquartile range [IQR] 15, 24) febrile people and treated a median of 12 (IQR 10, 17) cases of uncomplicated malaria per month. CHWs performed 20.1% (14,453/71,810) of RDTs and diagnosed 22.4% (10,403/46,357) of cases in these five communes during this period. According to quarterly structured assessments by HF chiefs, 95 of the 100 CHWs strengthened their clinical skills. These data suggest that properly trained and supplied CHWs, who had been non-functional for a decade, rapidly succeeded in providing quality malaria care to persons of all ages within their communities. This model is promising, and these initial efforts will be expanded to increase access to malaria prevention and control interventions across the district.

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INCREASING ACCESS TO QUALITY MALARIA SERVICES THROUGH ON-THE-JOB CAPACITY BUILDING OF FRONT-LINE HEALTH WORKERS: LESSONS FROM HEALTH FACILITY MONITORING VISITS IN THREE SOUTHERN NIGERIAN STATES

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Nigeria bears the highest global malaria burden, accounting for 27% of cases worldwide (World Malaria Report 2022). Accurate diagnosis and treatment are crucial for effective malaria control. The U.S. President's Malaria Initiative for States (PMI-S) collaborated with state governments to train health workers on malaria case management, documentation, and intermittent preventive treatment of malaria in pregnancy (IPTp) to increase access to quality malaria services. From 2021 to 2023, 80 health facilities (HFs) received at least three health facility monitoring (HFM) visits. During these visits, data on health workers (HW) performance were collected electronically and on-the-job capacity building and targeted mentoring were used to address observed gaps in the HW's skills. This study assessed the impact of HFM visits on the performance of selected malaria quality of care indicators in HFs across three southern Nigerian states by comparing indicator achievements at first visit, which was 3 months after training, and the third visit, which was 22 months after training. Major improvements were observed, with the proportion of HWs conducting Rapid Diagnostic Tests (RDTs) satisfactorily increasing from 75% to 100% and the proportion of HFs correctly classifying malaria cases respectively rising from 45% to 100%. Similarly, the proportion of HWs who administered IPTp in alignment with WHO protocol improved from 39% to 78%, and the availability of malaria charts at the facilities improved from 25% to 100%. IPTp administration did not have maximum improvement like malaria case management indicators and key factors, such as SP availability (25% and 36% stock out rate at the 1st and 3rd visits), or women's access and practices within the facilities. Further research is needed to understand the impact of systemic factors on quality prevention services. We conclude that just one HFM following a training is not enough to ensure appropriate quality services, and this underscores the need for increased effort to understand the specific factors that impact malaria services.

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ESTABLISHMENT OF MALARIA ELIMINATION CONSORTIUM (MEC) STRATEGIC PLANNING AND EXECUTION TO ELIMINATE MALARIA FROM PAKISTAN BY 2035

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Malaria is a major public health problem in Pakistan, with more than one million estimated and almost 371,828 confirmed cases reported in 2020. However, published figures do not reflect the real malaria burden due to fragmented data sources. Pakistan has difficulty obtaining reliable data for malaria surveillance, therefore it has become crucial to upscale the current plan for radical approach to eliminate malaria. An initiative was taken up by the Aga Khan University in March 2023to strengthen the existing framework of Pakistan Malaria Elimination Operational Program (PMEOP). To effectively enhance the measures, AKU has established the Malaria Elimination Consortium (MEC) comprising of field and policy experts, data scientists, academicians, and experts from federal and provincial governments. The establishment of MEC was a crucial and important step towards effective Malaria elimination having the intricacy of diverse group of international experts. A data scoping exercise was conducted in the Sindh province particularly in Thatta district to find out the existing status and gaps in the effective measures. MEC has proposed a charter and Terms of Reference, which has been agreed upon by all the members. To make the formal structures and specific responsibilities, the consortium has developed Technical Working Groups (TWG) which are in line with the national TWGs and will support the National Malaria Elimination Operational Plan. The collaborative efforts of AKU-MEC has brought all the national and international stakeholders on board towards Malaria elimination in Pakistan. The consortium is going to hold an international Malaria Elimination Symposium at AKU, Pakistan in May 2024. A diagnostic and case management workshop is planned in the coming months, to

train the relevant staff. The establishment of MEC is an important and a timely initiative towards achieving the goal of Malaria elimination by 2035, in Pakistan. The data scoping report is expected to be published as a scientific research article.

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ACHIEVING ZERO INDIGENOUS MALARIA CASES, SUB-NATIONAL MALARIA ELIMINATION VERIFICATION IN KING CETSHWAYO DISTRICT, SOUTH AFRICA. A FIRST IN SUB-SAHARAN AFRICA

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South Africa has reduced its malaria burden over the recent years, and it is part of the WHO e2025 countries targeted for elimination within sub-Saharan Africa. The risk of importation, presence of vector mosquitoes and climate change have affected malaria transmission patterns, thus, achieving national elimination is challenging and a long-term goal. Subnational verification of malaria elimination therefore is an option for large countries that have achieved interruption of local transmission in certain parts of their territory (provinces or Districts). South Africa adopted a health strengthening systems approach in the process of verifying subnational elimination in King Cetshwayo District. Nationally in 2020 the Malaria Elimination Audit Tool (MEAT) and indicator checklist was implemented. A Cascade of the MEAT tool and Indicator checklist in KwaZulu Natal Province and King Cetshwayo respectively in 2021. This was supplemented by technical interventions through the development, implementation, trialing, and refinement of a subclassification algorithm to distinguish local cases as either introduced or indigenous cases between 2019 and 2023. This was followed by a national led internal review of the utilization of the subclassification algorithm in 2022 & 2023, and programmatic implementation of the foci program conducted on cases without travel history. Annual validation exercises were conducted in with regional team constituting of surveillance, program management, epidemiology, and public health. In conclusion addressing strategic, technical, and operational issues concurrently is critical in achieving sub-national elimination in South Africa and lessons can be extended to the continent. A country led process is also recommended, adopting and contextualizing WHO tools to sub-national levels, formation of independent committees to conduct internal and external reviews and provide guidance on declaring an area malaria free.

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ASSESSING THE POTENTIAL OF USING DIHYDROARTEMISININ PIPERAQUINE FOR MALARIA MASS DRUG ADMINISTRATION IN AN ENDEMIC AREA OF GHANA

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Globally, malaria results in millions of cases and 625,000 deaths in 2020 including 481,000 children <5 years in Africa. Ghana ranks 11th among countries that contributed 70% of the global malaria burden. Targeting asymptomatic carriage in endemic countries in Africa using mass drug administration (MDA) could lead to malaria pre-elimination in endemic areas. Data to inform policy on MDA implementation is urgent. We hypothesize that implementing MDA will interrupt transmission paving the way to malaria pre-elimination in these endemic communities. A population of 6,000 (4000 in the intervention arm and 2,000 in the control arm) was targeted in the Pokrom sub-district of Ghana. One round of bimonthly MDA was conducted in December 2023. Community health volunteers go from door-to-door testing all participants using RDTs and treating using dihydroartemisinin piperaquine (DHAP). MDA was administered every two months. Treatment was directly observed. Data was analysed using SPSS Statistics 26. Parasitaemia decreased significantly from 27.5% (95% CI: 25.4, 29.6) at the baseline to 2.8% (95% CI: 2.3, 3.2) after the first MDA. Across genders, a significant drop in prevalence was observed between the baseline and after the MDA period in males (from 28.3% to 2.9%) and females (from 27.3% to 2.8%). Within all age groups, parasitaemia prevalence after the first MDA significantly dropped to < 3.0% (X^2 = 18.89, p-value = 0.002) except for patients 5 to 14 years. The first intervention was significantly associated with a 93.0% reduction in the odds of malaria parasitaemia (odds ratio = 0.07, 95% CI: 0.63, 0.94, p-value < 0.001). Reduced odds of parasitaemia were observed for patients 15 years and above (odd ratio = 0.75, 95% CI: 0.67, 0.833, p-value <0.001). Prevalence among follow-up communities after the first MDA was <4.0% except in Kwesi Dei (15.4%, 95% CI: 0.9, 21.8). These preliminary findings suggest that malaria parasitaemia could be reduced to pre-elimination levels following implementation of MDA using DHAP. More data is being collected for a robust that could inform on policy on MDA implementation.

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EVALUATION OF EXTERNAL QUALITY ASSURANCE EFFORTS ON MALARIA DIAGNOSIS IN FOUR NIGERIAN STATES (2021-2023)

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The World Health Organization recommends that every suspected malaria case must be confirmed by microscopy or a rapid diagnostics test prior to treatment. In May 2020 Nigeria updated its malaria guidelines to use malaria microscopy strictly for secondary and tertiary health facilities where a trained Medical Laboratory Scientist is present and good quality equipment and reagents are available, while RDTs may be used at all levels of healthcare services. Importantly, the guidelines include quality assurance recommendations for available diagnostics methods. This evaluation aims to explore the gains of adopting external quality assurance (EQA) for malaria microscopy services in secondary and tertiary service points in Akwa Ibom, Cross River, Oyo, and Zamfara States, between August 2021 to December 2023. The EQA approach involves quarterly visits to a total of 87 secondary and tertiary health facilities by the state malaria EQA reference team using the National Malaria Elimination Program tool deployed via Kobo Toolbox to enable real-time, and remote monitoring of malaria diagnosis activities. The visit consisted of blinded re-checking of 15 randomly selected (10 positive and 5 negative) routine smears for true detection and speciation of plasmodium spp by WHO expert microscopist, over the period of August 2021 - December 2023. In Oyo state, accurate microscopy diagnosis increased by 27% in secondary and tertiary health facilities, Akwa Ibom was 37%, Cross River increased by 50%, and Zamfara State by 36%. Additionally, since the start of the EQA exercise in 2021, the test positivity rate (TPR) decreased by 10.0%, 12.0%, 10.0% and 2.0% in Akwa Ibom, Cross River, Oyo, and Zamfara State respectively, independent T-test was done to compare effect of accurate diagnosis on TPR with a statistically significant decline (t=3.522, P= 0.02). EQA are critical for

preventing overdiagnosis and layer of accountability, leading to overall more accurate microscopy diagnosis, reduction in TPR, and supports appropriate diagnosis-based treatment, preventing unnecessary anti-malarial drugs use.

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SILENT CIRCULATION OF *PLASMODIUM VIVAX*: FIRST ASYMPTOMATIC MALARIA CASE POST MALARIA ELIMINATION IN ARGENTINA

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For eight years prior to the certification of malaria in Argentina in 2019, there were no instances of local transmission of malaria. In order to achieve certification from the World Health Organization (WHO) as a malaria-free country, epidemiological surveillance efforts were focused on detecting any presence of *Plasmodium vivax* in the area where the last cases had been reported.. During an epidemiological surveillance conducted by the national malaria program over the summers of 2016, 2017 and 2018 in Salvador Mazza, situated in the extreme northwest of the country (Salta province), several neighborhoods were randomly selected for the collection of human blood samples. Malaria parasites diagnosis relied on traditional microscopy observing the tick and blood smears and the molecular detection of *Plasmodium* infections of filter paper on which one drop of blood are added. Blood samples were screened for the presence of *P. vivax* infections through amplification and sequencing of a portion of the *Plasmodium cytochrome b* gene. An autochthonous case of *P. vivax* malaria was identified in an asymptomatic 64-years-old individual residing in La Bendición neighborhood, located in Salvador Mazza, Salta province. This individual had never travelled in any *P. vivax* endemic region. This case is the first one detected following the analysis of 94 samples collected from various localities situated along the border with Bolivia (northwest region) and Brazil (northeast region) of Argentina. This finding highlights the possibility of silent circulation of *P. vivax* in areas previously assumed to be free of malaria and raises questions regarding the timing prior to certification and prompts the reevaluation of the current situation based. The extent circulation of *P. vivax* among asymptomatic individuals remains largely unknown, with this report being the first of its kind for Argentina and the Southern Cone region.

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IMPROVING MALARIA CASE MANAGEMENT QUALITY BY REDUCING IRRATIONAL USE OF ANTIMALARIALS: A SYSTEMS THINKING APPROACH IN FOUR SOUTHERN STATES (AKWA IBOM, CROSS RIVER, EBONYI, AND OYO) IN NIGERIA

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Nigeria accounts for 27% and 31% of global malaria cases and deaths respectively in 2022. Accurate diagnosis and treatment are essential for effective malaria control, reducing presumptive treatment and irrational use of antimalarial medicines. Non-adherence to guidelines, non-availability of commodities, and poor-quality reporting affects quality case management. In four states (Akwa Ibom, Cross River, Ebonyi, and Oyo), the President's Malaria Initiative for States project supported the government to train 5,174 health workers, conducted regular supervision, and introduced a strategy where archived "used" malaria Rapid Diagnostic Test (RDT) cartridges are validated to verify the accuracy of reported cases. PMI provides malaria commodities to 65% of the 2,978 public health facilities in the four states to improve commodity availability. Four years data from National Health Management Information System (October 2019 to September 2023) from 2,978 public health facilities across four states was analyzed for trends in clinical diagnosis, RDT stock out rates, and RDT test positivity rates (TPR). Clinically diagnosed cases reduced from 24,853 (Akwa Ibom), 34,619 (Cross River), 7,214 (Ebonyi), and 146,008 (Oyo) representing 8.4%, 11.7%, 1.2%, and 26.3% of all malaria cases in year one to 3,775 (Akwa Ibom), 6,263 (Cross River), 946 (Ebonyi), and 6,264 (Oyo) representing 1.5%, 2.2%, 0.3%, and 1.4% of all malaria cases in year four. Also, RDT stock out rates dropped from 33%, 44%, 14.4%, and 33.2% to 4%, 3.8%, 4.1%, and 9.3% in Akwa Ibom, Cross River, Ebonyi, and Oyo respectively in same period. Likewise, TPR reduced from 76%, 79%, 81%, and 76% to 49%, 60%, 55%, and 51% in Akwa Ibom, Cross River, Ebonyi, and Oyo respectively in same period. Presumptive treatment significantly reduced by 85%, 82%, 87%, and 96% from year 1 to year 4 ($t=5.77$, p value <0.0001) while malaria RDT TPR reduced by 35%, 24%, 32%, and 33% in Akwa Ibom, Cross River, Ebonyi, and Oyo respectively ($t=23.46$, p value <0.0001). Enhanced service support and lower stock out rates decreased presumptive treatment and TPR, possibly aided by insecticide treated net campaigns in the study period.

7943

MEASURING ZERO INDIGENOUS MALARIA CASES THROUGH A SUB-CLASSIFICATION ALGORITHM, LESSONS FROM DEVELOPMENT, TRIALLING AND IMPLEMENTATION

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KwaZulu-Natal province in South Africa is leading with the lowest number of local cases. Atempting to measure zero local-indignous malaraia cases, King Cetshwayo District was selected for an in-depth analysis each local case from 2019 - 2023 to determine if existing data were sufficient to sub-classify local cases into local-introduced, and local-indigenous. Each case had variables such as historical transmission patterns, entomological surveillance findings, presence of vector control interventions and environmental patterns of the case residence locality were extracted. Using spatial data proximity to other reported local or imported cases was investigated. Operationally, the exercise provided an understanding as to which data were routinely available and complete in the Malaria Information System. The algorithm was developed using guidance from the WHO Elimination Framework and with inputs from National and Provincial Malaria Program. To use the algorithm two high-level questions were considered:

1) Can an epidemiological link to another case be established, and 2) Is the source locality of the index case able to sustain local transmission? The former is determined by trying to establish a spacio-temporal link between two cases. The latter is determined by considering vector receptivity and transmission patterns within the current malaria season. Between June 2019-July 2023, King Cetshwayo District reported a total of 250, of which 25 were identified as local based on self-reported travel history. Upon application of the subclassification algorithm 23 cases were subclassified as introduced and 3 cases excluded as locally imported from another district, relying on focus descriptions and potential drivers of transmission in these foci areas. During the algorithm development, of note, in addition to scientific evidence, local knowledge of the locality and the case were essential to ensure accurate sub-classification of the malaria cases. Whereas the algorithm was developed to be as objective, it is acknowledged that a degree of subjectivity and local context are essential for reliable sub-classification of local cases.

7944

EPIDEMIOLOGICAL, VECTOR BIONOMICS AND PARASITOLOGICAL DYNAMICS IMPENDING MALARIA ELIMINATION IN A HOLOENDEMIC REGION OF ZAMBIA

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Following the scale-up of a package of malaria interventions throughout Zambia, heterogeneous malaria epidemiology emerged, with some parts of the country remaining with a high malaria burden. Efforts have been made to sustain the interventions, with substantial resources committed to increasing coverage. Evaluations that were conducted to assess the effectiveness of these interventions have revealed a complex interaction of human behaviour, vector bionomic, and parasite dynamics that need to be tackled to achieve a significant reduction in the burden of malaria in the region. In this presentation, we review the results of several studies carried out in the areas by several research groups, including the international centres of excellence in malaria research (Southern Africa), to assess the impact of the interventions and determine the main factors contributing to the sustained high prevalence in the area. We also look at the interventions that have been applied in low-endemic regions to learn lessons for improved intervention programming in the country. Over 12 years, malaria prevalence in the population has remained unacceptably high despite the scaling up of interventions in the area. The prevalence rate of over 50% in the population with children of school-going age have 7 times the odds of harbouring high parasitaemia sustained over this period. Mortality and hospital admission (40%) in the area remain high, with children living farther from the health facilities bearing the highest mortality brunt. Temporal, spatial distribution of the main malaria vectors with differential susceptibility to insecticides used on bednets and for IRS, complicated with resistance to affordable and environmentally friendly Insecticides resistance, appears to be a formidable impediment to the reduction in transmission. Human factors particularly related to socio-economic activities, including population movement to mosquito-infested temporary settlements and poor housing structures, appear to be significant contributors to refractory responsiveness to proven effective interventions.

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CONTRIBUTION OF COMMUNITY HEALTH WORKERS TO MALARIA HEALTH SERVICE DELIVERY IN RWANDA

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Prompt testing and treatment of malaria is a basic strategy for controlling disease in endemic countries. Rwanda provides testing and treatment at both health facility and community levels. Initially, only children under 5 were treated at community level, but in 2016, the Rwanda Ministry of Health expanded to treat all ages. This ten-year retrospective review examined malaria case management data from Health Management Information system (HMIS) from 2013 through 2023. HMIS data are aggregated and reported weekly for malaria surveillance and response and recorded in HMIS database monthly. Malaria data was downloaded from the national HMIS and data quality checks were performed in Excel. A secondary data analysis of all malaria cases treated in the community and at health facilities was performed using SPSS version 28. The records from 2013 to 2023 included 14,241,916 cases of malaria at health centers and 10,931,751 cases confirmed by CHWs, yielding a total of 25,173,667 confirmed malaria cases by microscopy or rapid diagnostic test. The proportion of malaria cases managed by CHWs increased over the ten years from 8% in 2013 to 28% in 2016, and then to 58 % in 2023. Overall, the number of malaria cases tested and treated quadrupled from 1,016,018 in 2013 to 4,812,883 in 2017, then declined to 3,122,437 by 2019, though still three times higher than 2013, and slightly more than the total 3,005,212 malaria cases tested and treated in five years between 2020-2023 at both levels. This review highlights the increasing proportion of malaria cases tested and treated by community health workers in Rwanda. Given the important role and efforts that have been bestowed on CHWs in the fight against malaria in Rwanda and globally, it is important that national malaria programs in collaboration with its malaria implementing partners are able to adequately train staff, and accurately assess and ensure the quality of community-based diagnostic testing and treatment by CHWs.

7946

ELIMINATING MALARIA FROM INDIA THROUGH STRATEGIC PLANNING AND PRAGMATIC APPROACHES

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Since the discovery of malaria transmission was made in India by Sir Ronald Ross in 1897, an intensive works was carried on malaria control in India. There were different phases for malaria control to moving from control towards eradication and elimination. India achieved spectacular gains in malaria control during the 'Eradication Era' in the 1950s till the mid-1960s. The Global Malaria Eradication Programme of WHO launched in the 1950s was a huge success in India as the incidence declined from estimated 75 million cases and 8,00,000 deaths in 1947 to just 49,151 cases and no deaths in 1961 and malaria was thought to be on the verge of eradication. These gains were, unfortunately, not sustained and malaria re-emerged after 1965. After that a series of setbacks were witnessed leading to malaria resurgence in the country. A revised strategy named the Modified Plan of Operations was launched in 1977. Efforts for malaria elimination once again was accelerated in 2016 and Government of India launched the National Framework for Malaria Elimination 2016-2030 in February 2016 align with the Global Technical Strategy for Malaria Elimination 2016-2030. WHO supported malaria program for development of the National Strategic Plan for Malaria Elimination focusing on district-based planning, and its operationalization in the country. Malaria program is now moving away from "One Fit Size to All". The new strategic plan aiming to achieve zero indigenous cases by 2027 highlighting innovation in areas specific

surveillance and interventions. During the recent years, India has achieved incredible feat in reducing the disease burden and deaths due to malaria. Overall, 80.8 % decline of malaria cases and 81.2% deaths in 2023 as compared to 2015. India's progress on Malaria decline is well appreciated globally in the World Malaria Reports. However, there are challenges for the country to sustain the progress made so far and to achieve the goal for malaria elimination. Innovations and strategic reforms in the process of malaria elimination in India will be reviewed and presented.

7947

GROUND ZERO EPICENTER OF MALARIA IN PAKISTAN: THATTA, SINDH

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Pakistan emerged as a significant contributor to the global increase in malaria cases in 2022, attributed to flooding in Sindh. The burden surged to 1,824,396 cases, with Sindh province alone accounting for 53.5% of cases. This study examines the epidemiological trends of malaria in Thatta, Sindh, utilizing surveillance data from District Health Information System in Pakistan from 2018 to 2022.The collected data includes variables such as the total suspected cases, total screened cases, total positive cases, age and gender distribution, species, and the percentage of cases treated as per national guidelines. In 2018, the malaria positivity rate was 19.2%, decreasing to 9.70% amidst COVID-19 response measures. This trend peaked in 2022 due to flood devastation, where out of 419,737 suspected cases, 117,192 tested positive, indicating a positivity rate of 27.9%. Males were disproportionately affected compared to females, particularly evident in 2022, with 67,983 males and 49,209 females contracting the disease. Most positive cases occurred in the >5 years age group, notably rising in 2022 to 85,142 cases compared to 32,050 cases in the <5 years age group.Plasmodium *vivax* consistently prevailed over Plasmodium *falciparum* from 2018 to 2021, with a significant increase in both species in 2022. Vivax cases reached 63,267, and falciparum cases reached 49,781, marking a surge in overall malaria incidence. Malaria cases have continued to rise in Pakistan since 2022 due to rising temperatures and stagnant water resulting from flooding. These findings underscore the urgent need for targeted interventions and surveillance to address the multifaceted challenges of malaria transmission in Thatta district and beyond.

7948

DISTINCT HISTOPATHOLOGIC PROFILES OF PLACENTAL MALARIA HAVE DIFFERENT ASSOCIATIONS WITH BIRTH OUTCOMES

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Placental malaria is characterized by the accumulation of parasites in the placenta, leading to adverse birth outcomes, including preterm birth (PTB) and small for gestational age (SGA). The timing and severity of placental malaria may affect birth outcomes differently. To better understand the impacts of placental malaria on perinatal outcomes, we characterized associations between different measures of placental malaria and birth outcomes. We analyzed data from 1835 Ugandan women enrolled in a randomized controlled trial evaluating intermittent preventive treatment regimens in pregnancy. Placental malaria histopathology was categorized as: (1) active infection, defined as the presence of parasites regardless of malaria pigment, (2) past infection, defined as the presence of pigment in the absence of parasites, and (3) the density of pigment deposition in fibrin, categorized as mild (<10% of high-powered fields), moderate (10 to <30%), or severe (≥30%). The following birth outcomes were evaluated: PTB (delivery <37 weeks gestation), SGA (birth weight <10th percentile for gestational age), and low birth weight (LBW, <2500 grams). We found PTB was strongly associated with active infection (RR=3.16 [95% CI: 1.53-6.51]), but not past infection (RR = 1.00 [0.64-1.57]). In contrast, SGA was associated with past infection (RR=1.31 [1.09-1.57]), but not active infection (RR=1.08 [0.67-1.73]). After excluding women with active infection (n=75), SGA risk was higher in those with moderate and severe pigment deposition compared to those without pigment ($RR_{moderate}$=1.31 [1.02-1.67] and RR_{severe}=2.38 [1.62-3.50]). LBW was associated with active infection (RR=3.28 [1.88-5.70]), but not past infection (RR=1.10 [0.77-1.57]). In summary, active placental malaria was strongly associated with PTB and LBW, while past infection was associated with SGA. Our results suggest that different histopathologic profiles of placental malaria have differential impacts on birth outcomes and assessment of birth weight alone does not fully capture the effects of past placental infection on fetal growth.

7949

CROSS SECTIONAL SURVEY ASSESSING PREVALENCE AND PREDICTORS OF MALARIA PARASITAEMIA AMONG CHILDREN UNDER 13 YEARS IN KARAMOJA REGION, UGANDA.

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Uganda has one of the highest malaria transmissions worldwide, ranking third and fifth, for malaria morbidity and mortality respectively. Interventions to prevent malaria have predominately targeted children under five, who are most at risk of developing severe forms of the disease. However, emerging evidence suggests that older children also bear a significant burden of malaria. This study was conducted to assess the prevalence and factors associated with malaria parasitaemia among children younger than 13 years in Karamoja region of Uganda. A baseline malariometric survey was conducted in May 2022 prior to the introduction of seasonal malaria chemoprevention (SMC) in five districts in Karamoja region. A total of 6,350 children from 7,684 households were randomly sampled. Of these, 2,539 children were tested for malaria using microscopy and malaria rapid diagnostic tests (mRDTs). Prevalence was estimated using descriptive statistics. Multivariate logistic regression was used to identify factors associated with parasitemia, with results expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CI). Overall, malaria prevalence among children under 13 years in the five districts was 45%. Age-specific prevalence was 43%, 48% and 47% in children under 5, 5-9 years and 10-12 years, respectively. Older children aged 5-9 years were 38% [OR: 1.378 (1.124, 1.686)] more likely to have malaria than those under five. Children who had anaemia were also more likely to have malaria [OR:2.269 (1.868, 2.758)]. Other predictors at household and child levels were not significantly associated with malaria prevalence among children. The study demonstrates the substantial prevalence of malaria among children under 13 years in this context, with notably high prevalence among children older than 5 years. Findings suggest that that age-appropriate interventions are warranted to address malaria burden across age groups of children under 13 years. Further studies are needed to better understand trends in the burden and predictors of malaria prevalence, severity, and mortality among children.

7950

EPIDEMIOLOGY AND STATISTICAL MODELLING OF *PLASMODIUM VIVAX* AND *P. FALCIPARUM* MALARIA CASES IN MANDOTO, MADAGASCAR.

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Mandoto is one of Madagascar's districts, characterized by diverse topography and climate, and experiences ongoing transmission of malaria throughout the year. In this district, *Plasmodium vivax* and *Plasmodium falciparum* are co-endemic. Approximately 50% of individuals are Duffy positive, and thus susceptible to *P. vivax* infection. It has been selected as a study site to assess the efficacy of an intervention to reduce *P. vivax* transmission based on serological testing and treatment with primaquine. Prior to the beginning of the clinical trial, it is crucial to have a deep understanding of the malaria situation in the district of Mandoto. Conducted as a time series study spanning from 2019 to 2023, data on monthly malaria cases were gathered from health centres across the district, complemented by climatological data. Using descriptive analysis, cross-correlation, spatial analysis, and ARIMA (Autoregressive Integrated Moving Average) forecast models, we aimed to understand the dynamics of malaria transmission. A total of 202,014 RDT tests were performed over the study period across all 27 healthcare facilities within the district, as reported in 1,158 reports. There were 79,323 malaria cases with a positivity rate of 39.2%. *P. vivax* and *P. falciparum* were co-endemic in all health centres within the district, and 49.5% of malaria cases were attributed to *P. falciparum* infections while 18.6% were attributed to *P. vivax*. The species of 31.9% of the cases were not identified. Malaria cases were most prevalent among children aged between 6 and 13 years old for both *P. vivax* and *P. falciparum* infections. Malaria cases exhibited a temporal pattern, peaking following the end of the rainy season between April and June while the lowest malaria cases occurred between July and September. A strong positive correlation was found for *vivax* and *falciparum* malaria time series lagging two to four months behind precipitation. The western region of the district poses a significant risk of transmission. Complete outcomes of ARIMA models will be detailed during the presentation.

7951

ASSOCIATION BETWEEN MALARIA INFECTION AND UNDER-NUTRITION IN CHILDREN AGED 6-59 MONTHS IN KISUMU COUNTY, KENYA

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Under-nutrition and malaria contribute to child morbidity and mortality globally, and this has shown little progress in Africa and Asia. Globally malnutrition affects various countries but sub-Saharan countries bear the burden. Under-nutrition accounts for 45% deaths in children 6-59 months. Sub- Saharan Africa and Asia reports under-nutrition accounting for 44.8% deaths from malaria, 52.3% deaths from pneumonia and 60.7% from diarrhea. Kenya reports 942,000 cases of under-nourished children below five years. This study aim to determine the relationship between malaria and nutrition cases among children below five years. It is impressive to investigate the relationship between malaria and nutrition cases among children below five years. This study is part of an on-going surveillance study, where we characterized children aged 6-59 months with baseline of malaria infection upon enrollment. We compared the mal-nourished children from nourished children of the same age for their past exposure to malaria in Kisumu County Kenya. Blood samples were drawn for microscopy and a valid structured questionnaire was used to collect epidemiological data. The collected data were analysed for descriptive statistics using STATA data analysis software.A total of 300 (70 malnourished and 230 nourished) under-five children participated in the study. Previous exposure to *Plasmodium* infection was found to be a predictor for the manifestation of malnutrition in under-five children ($P=0.02$ [$OR=1.87$, $CI=1.115$-3.138]). Children with high plasmodium density were 4.5 more likely to be malnourished as compared to nourished children ($P=0.001$ [$OR=0.422$, $CI=0.181$-0.978]).Study finding reveals exposure to plasmodium falciparum has an impact on nutritional status. Therefore, future research should be prioritised to generate data on the individual level. Further, malaria control interventions could be tailored to integrate nutrition programmes to disrupt indigenous malaria transmission in a population.

7952

QUANTIFYING THE LAGGED EFFECTS OF CLIMATE VARIABLES ON MALARIA RISK: A CASE STUDY IN IGANGA-MAYUGE HEALTH AND DEMOGRAPHIC SURVEILLANCE SYSTEM SITE IN UGANDA

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Climate change is expected to have a significant impact on malaria transmission, particularly affecting vulnerable populations in low-income countries. Prior research indicated lagged non-linear associations between climate variables and malaria risk, and these exposure-lag-response relationships were found to be highly context-specific. Using weekly malaria case data collected between July 2018 and February 2023 from a single hospital in the Iganga-Mayuge HDSS site in Uganda and remotely sensed temperature and rainfall data, we quantified the associations between temperature and rainfall and malaria risk employing a distributed lag non-linear model. Further, given age-specific vulnerability to malaria infections, we explored if these associations varied by age group using age-specific case data for three sub-groups—namely, children under 5 years of age, school-age children between 5-14 years, and others who are aged 15 years and older. We observed a lag of 2-8 weeks between exposure to rainfall exceeding 200 mm per week and a significant increase in the risk of symptomatic malaria cases, with the highest observed relative risk (1.28, 95% CI: 1.08, 1.52) at a lag of 4 weeks when exposed to a weekly total rainfall of 270 mm. On the other hand, we did not find a statistically significant lagged association between temperature and malaria. Our analysis showed that the risk of symptomatic malaria cases in school-aged children was less sensitive to the climate variables compared to other age groups. Rainfall above 220 mm per week was found to be associated with an increased malaria risk at a lag of two months in the study area, guiding local health authorities on the optimal timing of preventive interventions and preparedness plans for managing the increasing demand for case management. The observed differences in increased malaria risk across different age groups stresses the importance of targeted interventions for specific populations. Moreover, the significant associations between climate and malaria underscore the need for context-specific and adaptive malaria control strategies alongside broader climate change mitigation efforts.

7953

SEASONAL MALARIA AMONG SCHOOL-AGED CHILDREN IN SIX WESTERN CONFLICT-AFFECTED BORDER PROVINCES IN THAILAND

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Thailand aims to achieve national malaria elimination by 2024. Most existing national and subnational malaria interventions target adult populations and overlook school-aged children (SAC) ages 5-14 years, which represent 12% of the population but contribute nearly 25% of malaria cases nationwide. In the six provinces (Tak, Mae Hong Son, Kanchanaburi, Patchaburi, Ratchaburi, Prachuab Khiri Khan) along the Thai-Myanmar border currently experiencing a resurgence of malaria, cases among SAC represent nearly 70% of all SAC cases nationally. This mixed methods study used October 2020 to September 2023 surveillance data from the national malaria information system to describe malaria epidemiology among SAC in these provinces. We collected qualitative data regarding behavioral risks for infection among SAC from interviews with key stakeholders across all six provinces. We conducted a time series analysis to examine associations with seasonality; travel abroad or outside of the province; ownership and use of bed nets; place of residence; and overnight exposure among SAC. The sample included 71.8% (n=4,920) of confirmed cases among SAC with complete investigation and classification data. Between October 2020 to September 2023, SAC consistently had the highest incidence across all age groups (range: 1.32-5.24/1,000 people versus adults: 0.60-3.54/1,000 people). During this time period, confirmed infection in SAC rose significantly in March (1.6-fold increase over other months) and October (1.9-fold increase)—periods corresponded with school breaks and return to school. Infections were more likely to be locally acquired (i.e., no reported travel history) compared to adults ($p<0.05$) and were due to lack of protection from mosquitoes before bedtime. Currently, Thailand distributes bednets to all high-risk populations; however, there are no interventions that target SAC specifically. Further research exploring behavioral risks among SACs is needed. Following this analysis, Thailand's Division of Vector-borne Diseases is now including school names and locations in the country's health information system.

7954

EXPLORATORY MODELLING OF THE INFLUENCE OF CLIMATE ON MALARIA TRANSMISSION

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A significant gap in our knowledge of malaria transmission lies in understanding its responsiveness to climate. Malaria is a highly climate sensitive disease, with both parasite and vector dynamics demonstrating competing and non-linear dependencies upon both temperature and rainfall across multiple traits. Incorporating these impacts into transmission models could help targeting control efforts effectively and, importantly, for assessing how climate change might influence the burden of disease. We examined the sensitivity of malaria transmission to changes in temperature and rainfall using a fully mechanistic compartmental transmission model which incorporates a set of mosquito-parasite thermal dependency relationships quantified in laboratory experiments. Results indicate a reduction in the effectiveness of insecticide treated nets at higher temperatures in some settings but not others. It highlights how temperature could significantly alter the pattern of malaria transmission, challenging the timing and planning of intervention programmes. In exploring the role of rainfall, a sub-model estimating potential vector breeding areas has demonstrated good effectiveness at estimating observed density of Anopheles mosquitoes in some settings, particularly within the *gambiae* complex. Future work intends to improve estimations of the *funestus* complex through explicit modelling of the more lagged relationship between rainfall and semi-permanent breeding sites. This research can start to explore how intervention effectiveness and disease burden might change under possible future climatic conditions.

7955

CHARACTERIZING THE TRANSMISSION RESERVOIR OF *PLASMODIUM FALCIPARUM*

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Malaria control has stalled in many high-transmission settings despite widespread uptake of malaria control measures. One potential explanation for the lack of progress is a failure to eliminate parasite reservoir populations. There is a need to understand the population-level distribution of transmission-relevant infections to design targeted interventions to decrease malaria. We followed 947 individuals in 238 households for 1 year for *Plasmodium falciparum* (*Pf*) infection and tested for transmission-stage parasites (gametocytes) at both scheduled follow-up visits and sick visits. We examined predictors for: both ever having and the rate of any gametocytes and high gametocyte density infections, as well as gametocyte detection over time. We also examined the spatial distribution of gametocytes and the total burden of gametocytes in the population. Among the total population, 72% had *Pf* infections, 23% had gametocytes detected, and 5.7% had high density gametocytemia during the study. Children aged 5-15 years were more likely than adults and children under 5 to have any gametocytes detected (Odds Ratio=9.5, 95%CI:4.2, 21.8), to have repeated gametocyte-containing infections ($p<0.001$), to have high-density gametocyte infections ($p<0.001$), and had significantly more frequent gametocyte detection (Rate Ratio=2.6, 95%CI:1.6, 4.2). Gametocyte detection was clustered spatially, and households with high proportions of school-aged children were more likely to have high frequency and density of gametocyte detections ($p=0.05$) but not parasitemia ($p=0.9$). After accounting for non-enrollment, we estimate that 53% of all gametocytes circulating in the population over the course of the study were found in school-aged children who made up 33% of the population. At a population level, school-aged children carry the majority of gametocytes and the association between gametocyte detection and school-aged children is above that expected due to presence of *Pf* parasitemia alone. There is a vital need for targeted interventions, particularly focusing on school-aged children, to effectively reduce transmission in high-burden settings.

7956

PATIENT REPORT VERSUS PROVIDER REPORT, A POST-MODERN ANALYSIS OF MRDT TESTING AND DRUG DISPENSING DATA FROM A TRIAL IN THE PRIVATE RETAIL MEDICINE SECTOR IN WESTERN KENYA

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Private retail outlets remain a major source of antimalarials for individuals experiencing febrile illnesses in malaria-endemic countries. However, there remains a challenge in how the decision to dispense antimalarials is made. The lack of diagnostic testing in the retail sector leads to presumptive diagnosis and overuse of ACTs. The TESTsmART study trained retail outlet attendants to perform malaria rapid diagnostic tests (mRDTs) in conjunction with a mobile application to capture testing and drug dispensing data. Simultaneously, outlet clients with history of fever in the preceding 48 hours were randomly selected for exit interviews after seeking care. Comparison of these two concurrent data sources showed similarities but also significant differences. Half (51%, 25446/49804) of clients reported in the app were tested, of which only 11% had a positive mRDT. Photographs of the mRDT captured in the app confirmed these results. In contrast, 43% (2436/5695) of exiting clients reported receiving testing in the outlet, with 35% reporting a positive test. Outlets reported dispensing ACTs to 97% of test-positive patients compared to 77% at exit. For test-negative clients, 35% received an ACT based on outlet report, compared to 25% by client report. Among untested clients, 91% received an ACT according to the outlet report, compared to 71% by client report. To help understand the differences in reported test-positivity between the two datasets, we enrolled 145 clients for secondary exit testing. Among 36 clients who reported having completed testing in the shop, 11 (31%) had discordant results at exit testing. Among the remaining 109/145 clients who did not test in the shop, 4 were positive at exit testing. Contrasting outcomes reported by the providers and the clients highlight barriers to improving testing, adherence to malaria drugs, and challenges for monitoring case management in the retail sector. These include accurate communication of results to the client, poor confidence in negative results, and reluctance to withhold antimalarials from test-negative clients.

7957

HIDDEN RESERVOIRS OF *PLASMODIUM VIVAX* INFECTIONS IN DUFFY-NEGATIVE POPULATIONS FROM CENTRAL AFRICA

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In sub-Saharan Africa, malaria control measures are primarily focused on *Plasmodium falciparum* (Pf), despite an upward trend of *P. vivax* (Pv) across the continent and in Duffynegative individuals. The epidemiological characteristics of Pv in regions predominantlyDuffy negatives are unclear. This study investigated the prevalence and transmissiondynamics of *Pv* infections across various landscapes of Cameroon. Blood samples from1,584 individuals were collected from communities and hospitals in Buea (western lowland), Bertoua (eastern forest), and Bamenda (northwestern highland) of Cameroon. Overall, 18%of these samples were positive for *P. vivax* based on 18S-based quantitative PCR and furtherconfirmed by *PvDBP*1 PCR assays. Among them, 151 (10%) were mixed infection with Pf.The majority (99%) of these cases were in Duffy-negative individuals. No significantdifference was observed in parasitemia between mono-Pv and mixed Pv-Pf infections. Theaverage parasitemia of community samples was slightly higher, though non-significantcompared to the clinical samples. Parasitemia levels were not significantly different by agegroups and gender. Among the three regions, samples from Buea had a higher rate of Pvinfections as well as higher parasitemia than the others. This discrepancy highlights thepotential differences in transmission dynamics by landscapes and population density. Relatively high parasitemia in community-based infections implies high transmissionpotential and frequent circulation of the parasites in Duffy negative populations. Thesefindings underscore the importance of surveillance and diagnosis in malaria-endemic areasof West/Central Africa where Pv is assumed to be rare. Our ongoing investigations on thegenetic origin and relatedness of these infections based on next generation sequencingshed light on the extent of vivax malaria spread in Africa.

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COMPARISON OF BAYESIAN OPTIMIZATION FRAMEWORKS FOR PARAMETER CALIBRATION IN AN AGENT-BASED MODEL OF MALARIA TRANSMISSION

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Malaria transmission is a complex process, which is challenging to model due to latent parameters that can't be measured directly and must be inferred through calibration to population-level data. In calibration, new parameter values are simulated, and outputs are compared to reference data. However, for computationally expensive simulators, this can take a lot of time and memory. Another challenge is the "curse of dimensionality": the number of possible parameter combinations rises exponentially as more parameters are included. In this work, we explore different algorithmic approaches to calibrate the agent-based malaria transmission model EMOD. Our goal was to recalibrate 13 parameters describing modeled infections, immunity, and parasite dynamics to accommodate an increase in the maximum concurrent infections per individual, and a new custom model of innate immune variation. We tested two Bayesian Optimization Frameworks (BOFs) with Gaussian process (GP) models to emulate correlations between EMOD parameters and simulation goodness-of-fit to 18 total data objectives describing incidence, prevalence, parasite density, or infectiousness from 8 study sites across Sub-Saharan Africa. We then use tailored acquisition functions to strategically sample new parameter sets for further simulation and GP training. BOF 1 uses a single-task GP to model overall fit to all reference data objectives together, and a trust-region based Thompson sampling strategy. BOF 2 uses a multitask GP to model fit to each of the data objectives separately, and a two-step pareto frontier acquisition function. We validated BOF 1 against prior baseline EMOD parameterization and then compared BOF 1 vs. BOF 2 to explore parameter sensitivity and find tradeoffs between objectives along the frontier of critical parameter sets. Both approaches quickly outperform previous calibrations, resulting in improved model fit to in-sample and out-of-sample data targets. This framework accelerates and increases transparency in multi-objective calibration of a widely-used malaria model, facilitating the inclusion of new field data moving forward.

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DESIGNING CLUSTER RANDOMIZED TRIALS FOR MALARIA: INSIGHTS FROM MATHEMATICAL MODELLING

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Randomised control trials are the gold standard for evaluating the impact of novel control tools against malaria. To assess the full impact of certain interventions, such as insecticide-treated nets (ITNs), randomisation is carried out at a group ('cluster') level. This is because ITNs not only protect those sleeping under them but also those living nearby, due to the action of the insecticide(s). This makes trials more logistically challenging and increases the required sample size. Here we explore how mathematical modelling can help guide the design of cluster randomised trials (CRTs). We use an established model of malaria transmission to explore the evolution of key quantities (e.g. effect size and between-cluster heterogeneity) during the follow-up period of a hypothetical CRT, designed to compare a next-generation ITN to a pyrethroid-only ITN. This helps to estimate how study power (assessed via simulation-based methods) varies over time. We show how the age-group followed up during the trial can affect the statistical power of a CRT. We also illustrate how other ongoing interventions against malaria, such as seasonal malaria chemoprevention can affect observed outcomes in CRTs. In the case where between-cluster heterogeneity in malaria prevalence is estimated in a pre-baseline survey, we show how the estimated value is influenced by the timing of the survey. In this work, we highlight some of the challenges involved in designing well-powered CRTs with feasible sample sizes. Whilst we stress that a number of challenges (small cluster-level populations, inter-year seasonal variation, within-cluster heterogeneity in malaria transmission) limit a model's ability to accurately predict the outcome of a CRT, we provide suggestions that can help increase a CRT's statistical power.

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PREDICTING MALARIA PARASITEMIA IN MALI USING *PLASMODIUM* DEGREE-DAY

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Over 200 million people contract and over 600,000 die from malaria annually, justifying its continued priority in global public health efforts. Degree-day (DD) modeling is a proven approach for modeling vector-borne diseases with limited environmental data. *Plasmodium falciparum*, the primary human pathogen of malaria in Africa, has optimal environmental temperatures for parasitic development in its *Anopheles* vectors. In tropical regions where transmission depends on covariation both of temperature and rainfall, literature on malaria lacks DD thresholds for high transmission. If DD threshold estimates for high transmission risk can be validated, these models can be used to inform endpoint collection periods for studies and trials. The Malaria Research and Training Center at University of Bamako and the Laboratory of Malaria Immunology and Vaccinology at NIAID have conducted several transmission-blocking vaccine studies in Mali. During these trials, data collected included incidence of parasitemia, clinical malaria, and parasite transmission by direct skin feeds (DSF, an assay used to measure human-to-vector transmission). Using local weather data in Bamako, we extrapolated temperature and rainfall measurements to our nearby study sites. We observed increased incidence in clinical malaria after 78 DDs (early September) and 66 DDs (mid-August) in 2018 and 2019, respectively, with incidence peaking in early October (98 and 78 DDs) for both years. Blood smears positive for *P. falciparum* parasitemia were most frequent in the days following 105 DDs (mid-October) in 2018 and 79 DDs (early October) in 2019. Preliminary exponential models of cumulative DDs and clinical malaria and parasitemia returned significant correlate estimates with moderate correlations. Cox models incorporating rainfall as a time-dependent covariate and time-to-parasitemia models will be presented. These findings suggest DD have utility in predicting high transmission risk periods at vaccine study sites, improving statistical power by reducing the amount of negative outcome data collected.

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RELATIONSHIPS OF INTERMITTENT PREVENTIVE THERAPY AND INSECTICIDE-TREATED BED NETS TO RISK OF MALARIA DURING PREGNANCY IN MAFERINYAH, GUINEA

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In sub-Saharan Africa, malaria continues to be the primary cause of morbidity and mortality in young children and pregnant women. According *to the annual* WHO *Malaria R*eport, i*n 2022 malaria caused 608,000 deaths*, of which 94% occurred in Africa. *These estimates do not include* poor outcomes associated with *malaria infection during pregnancy*, *which poses* substantial and often fatal risks for the mother, her fetus, and the neonate. Currently, the only available measures to protect pregnant women from malaria are intermittent preventive therapy and insecticide-treated bednets (ITN). We examined the impact of these measures in a cohort of pregnant women in Guinea. From Jul 13, 2020 to Sept 7, 2023, we enrolled 2007 pregnant women at antenatal care (ANC) visits; average age was 24 years, ranging from 14 to 43. Blood smears (BS) were performed on all women, of which 1634 (81.4%) were negative and 373 (18.6%) were positive. In the 1755 participants for whom gestational age was recorded, 34/43 (79.1%) of women enrolled during their first trimester tested BS-positive; 230/1122 (20.5%) during the second trimester; and 96/590 (16.3%) during the third trimester. During the dry season, 143/966 (14.8%) of women were BS-positive compared to 230/1041 (22.1%) in the rainy season. We observed a general decrease in the proportion of positive BS with increasing number of sulfadoxine-pyrimethamine (SP) doses starting from one dose to four doses. 47/306 (15.4%) of women were BS-positive with zero doses of SP; 326/1083 (30.1%) with one dose of SP; 52/266 (19.5%) with 2 doses of SP; 13/116 (11.2%) with 3 doses of SP and 1/30 (3.3%) with 4 doses. 185/1166 (15.8%) of women who used an ITN the previous night had a positive blood smear as did 188/841 (22.4%) of those who did not. These results demonstrate a concerning rate of malaria infection among asymptomatic pregnant women in Maferinyah, Guinea. Continued efforts are needed to increase coverage of effective preventive measures. Future planned assays include malaria PCRs, evaluation of hrp2/3 deletions and antimalarial resistance markers in parasites, parasite binding assays, and serological assays for helminths.

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EXPLORING THE IMPACT OF *SCHISTOSOMA HAEMATOBIUM* INFECTION ON THE EXPANSION OF THE HUMAN RESERVOIR FOR *PLASMODIUM FALCIPARUM* IN GHANA

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Chronic Schistosoma infections reduce the host's responsiveness to infections, making them a significant challenge in malaria control efforts. Asymptomatic schistosomiasis infections are particularly problematic in tropical regions with high coinfection rates, such as Sub-Saharan. A study aimed to investigate the cytokine responses associated with *Schistosoma*

haematobium and *Plasmodium falciparum* and their impact on interactions and malaria parasite persistence within the host. The study included 279 Ghanaian individuals aged 6–30 years, including those infected (82) and non-infected (197) with *S. haematobium*. Urine and blood samples were examined for *S. haematobium* and *P. falciparum* parasites. Cytokine levels were determined by cytometric-bead array technology and Flow Cytometry. Results showed that 92% of participants who received praziquantel treatment had clearance of *S. haematobium* after the first dose and 98% after the third dose. Coinfection of 2.89% coinfection was recorded. Th2 dominated the panel of cytokines evidence in the host, possibly favouring the survival and replication of *P. falciparum*.

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BURDEN OF MALARIA IN THE KINSHASA PROVINCE, DEMOCRATIC REPUBLIC OF CONGO

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The Democratic Republic of Congo bears one of the highest global burdens of malaria, accounting for 12.3% of malaria cases and 12.6% of malaria deaths. The World Health Organization recommends that high-burden, high-impact countries reduce malaria transmission through greater investment and targeting interventions in rural and peri-urban areas. However, data are limited to inform intervention targeting, specifically how the malaria burden and associated risk factors evolve. This cohort study was conducted to estimate the trend in malaria prevalence and associated factors in different settings in Kinshasa Province. Between 2018 and 2021, a cohort study was conducted in areas of varying malaria endemicity in Kinshasa Province (Voix du Peuple, Kimpoko, and Bu). Study households were visited twice yearly, once in the rainy and once in the dry seasons. At each visit, study teams collected information on malaria symptoms and insecticide-treated net (ITN) use and performed rapid diagnostic tests (mRDT). During the same study period, adult mosquitoes and larvae were collected to study vector bionomics and insecticide resistance by allelic kdr gene frequency. At baseline, 1635 participants were enrolled from 239 households. The median number of participants per household was six (IQR 5-9). Over half (54%) were female, 15% were children under five, and 31% were aged 5-14. Across the 3.5-year study period, household net ownership was consistently low (51%) despite recent bed net campaigns. The overall malaria prevalence by mRDT was 35% (Bu: 58%, Kimpoko: 39%, and Voix du Peuple: 19%). The burden of malaria was greatest among 5-14 years old (47%), followed by participants ≥15 years (35%) and children <5 years (19%). Malaria prevalence differed by season (rainy= 60% and dry=41%). Entomological surveillance confirmed pyrethroid resistance. Despite increased efforts to control malaria in the DRC, prevalence remains elevated in Kinshasa Province, particularly in school-aged children and in rural and peri-urban areas. The weak health system and limited use of effective ITNs must be addressed to improve the impact of malaria interventions in DRC.

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UNDERSTANDING MALARIA TREATMENT PATRONAGE: INSIGHTS FROM URBAN INFORMAL HEALTHCARE PROVIDERS IN NIGERIA

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Informal healthcare providers (IHCPs), including proprietary patent medicine vendors (PPMVs), drug sellers, and traditional/herbal healers, play a significant role in the healthcare system of sub-Saharan countries like Nigeria. They serve as the initial point of contact for approximately 55% of suspected malaria cases in Nigeria, a major contributor to the global malaria burden. Despite lacking formal training and registration with regulatory authorities, these entrepreneurial providers are widely patronized, even in urban areas, as evidenced by recent studies. While much attention has been given to assessing their practices in rural settings, where patronage is presumed to be higher, there is a lack of information regarding their practices in urban settings. Understanding the reasons for patronage of IHCP's is crucial for effective intervention planning. Urban cities are known to be heterogeneous with differing settlement types, which might impact on the patronage reasons. This study aimed to explore IHCPs' perspective on why community members seek malaria treatment from them.In-depth interviews were conducted among 12 IHCPs including PPMVs, drug peddlers, traditional doctors, and herbal drug sellers in two cities in Nigeria. These IHCPs were drawn purposively from three different settlement types (formal, informal and slum) and data was collected using a pre-tested interview guide. Thematic content analysis was used to draw insights. From the perspective of IHCPs in formal settlements, the primary reason for community members patronizing PPMVs is the high cost of drugs from hospitals. Other factors include time constraints, long distances, and access to credit facilities mainly in the informal settlements. Notably, herbal/traditional doctors are sought after in slums due to strong community beliefs and positive experiences . The provision of subsidized malaria drugs and the implementation of healthcare cost reduction strategies will reduce out-of-pocket expenditure, making malaria case management at formal health care facilities more accessible .

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MALARIA TEST POSITIVITY RATES AND ASSOCIATED FACTORS IN KINSHASA PROVINCE, DEMOCRATIC REPUBLIC OF THE CONGO

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Malaria remains the world's leading cause of morbidity and mortality, with sub-Saharan countries bearing the heaviest burden. According to the World Malaria Report 2023, malaria incidence and mortality rates have increased after the COVID-19 pandemic in the DR CONGO despite a recent Long-Lasting Insecticide-treated Net (LLIN) campaign. We assessed malaria prevalence and associated factors over one year after LLIN distribution. The study was conducted across three health areas in different settings in Kinshasa Province: one urban (Lingwala), one semi-urban (Kimpoko), and one rural (Bu). Three household surveys were conducted over 1 year. Participants were interviewed, and a rapid diagnostic test (RDT) performed. Data were analyzed using STATA for bivariate and multivariate statistical

analyses. A total of 1,574 participants were enrolled in the study. Over half of the participants (56%) were female. Children <5 years represented 14% of the study population, 41% were school-aged children 5-17, and 45% were over 17 years old. LLIN ownership and use were high (83% and 80%). The mean test positivity rate (TPR) by visit was 36%, 33%, and 49%. Women were more likely to be RDT positive in Kimpoko (p-value=0.040 at visit 1 and p-value=0.008 at visit 2) compared to women in other sites. Age was strongly associated with positive RDT results across all visits, especially among school children in Bu and Kimpoko (p-value=0.000). Participants in Bu were more likely to have a positive test result compared to the other sites (visit 1: aOR=1.66, 95% CI, 1.40-1.98; visit 2: aOR=1.93 95% CI 1.57-2.36 and visit 3: aOR= 1.77 95% CI 1.39-2.25). No association was found between the possession of LLINs and RDT positivity. However, not using a net the night before the survey was associated with a positive RDT during visit 1 in Bu and visit 2 in Kimpoko. The factors most closely associated with positive RDT results were the participants' age, sex, and whether they lived in the city or a rural or semi-urban area. These factors did not vary across the study period. Control programs should target interventions for these groups to reduce the burden of malaria.

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TEMPORAL TRENDS IN THE PREVALENCE OF *PLASMODIUM* SPECIES ACROSS REGIONS OF VARYING MALARIA BURDEN IN MAINLAND TANZANIA FROM 2021 TO 2023

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Recent studies indicate that non-*Plasmodium falciparum* species may be more prevalent than previously perceived in sub-Saharan Africa. Although *P. malariae*, *P. ovale spp*., and *Plasmodium vivax* are less severe than *P. falciparum*, treatment and control are more challenging, and their geographic distribution is not well characterized. Their characterization is important for the National Malaria Control Programmes in formulating malaria diagnosis and treatment guidelines. This study evaluated the temporal dynamics of malaria species over three years (2021-2023) through molecular characterization using samples collected in 13 regions with varying transmission intensities in Mainland Tanzania. A total of 4024, 4962 and 3070 dried blood spots (DBS) were selected from samples collected in 2021, 2022, and 2023 respectively. Genomic DNA was extracted from DBS and used for detection of malaria parasites by quantitative real-time polymerase chain reaction targeting the 18S ribosomal subunit. In 2021 and 2022, 90.0% of the samples had *P. falciparum* mono-infections followed by *P. falciparum/ P. ovale* co-infections (4.8%). Overall, *P. falciparum* positivity decreased from 51.5% to 48.1%. For non-falciparum species, the positivity decreased from 1.8% to 1.4%, 4.6% to 2.6%for *P. malariae, P. ovale*, respectively (p>0.05). *P. vivax* was only detected in 3 (0.1%) samples in one region in 2021. Although the overall variation was minimal, notable variations were observed within regions. *P. falciparum* decreased from 50.6% to 40.1% in seven regions and increased in six regions from 53.0% to 61.8%. *P. malariae* decreased from 2.6% to 1.3% in eight regions, slightly increased from 2.1% to 2.5% in 3 regions, and remained constant in two regions. *P. ovale* declined from 5.2% to 2.6% in 10 regions. Results from the ongoing analysis of samples collected in 2023 will be presented later. Both *P. falciparum* and non-falciparum species are prevalent in Mainland Tanzania and depict marked temporal dynamics in some regions. Malaria elimination efforts require continuous surveillance and an improved understanding of the dynamics of all malaria species.

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A PRELIMINARY ANALYSIS OF DELAYED TREATMENT FOR SEVERE MALARIA DISEASE AT SUSSUNDENGA-SEDE HEALTH CENTER

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Severe malaria disease must be treated within 24 hours of symptom onset, which is supported by National Malaria Control Programme in Mozambique. In rural, moderate transmission settings access to care and prompt treatment can be a challenge and is understudied in Western Mozambique. Existing research has identiied the important role caregiver education and distance care, but rarely also account for provider delays. Our aim was to quantify the individual, household, and provider determinants of delayed treatment among individuals seeking care at the Sussundenga-Sede health center in Sussundenga, Mozambique, a rural village bordering Zimbabwe in Manica Province. We conducted a time-matched case control study from April 2023-2024. We used systematic sequential sampling to enroll 120 individuals with severe malaria disease and 120 individuals with non-malaria disease who are hospitalized at the Sussundenga-Sede health center. Cases were defined as a hospitalization with malaria tested by blood smear or positive malaria rapid diagnostic test (RDT) and one or more severe malaria symptoms. Controls were defined as a hospitalization without malaria tested by a negative blood smear or negative malaria RDT and not seeking care for conditions related to an accident. Eligible participants were: 1) older than 3 months; 2) full time residents in Manica Province; 3) had the capacity to provide consent; and 4) presented to Sussundenga-Sede health center within 72 hours of enrollment. The study excluded military members, children younger than 3 months, and pregnant women. All consenting participants completed a survey about their neighborhood level access to care, malaria prevention behaviors, and process to seek care at Sussundenga-Sede health center. The survey included a medical records abstraction tool to record severity of disease and treatment. The findings of this preliminary analysis will provide additional insight into multi-level determinants of treatment delays for severe malarial disease.

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IMPACT OF DIFFERENT TIMINGS OF THE FOURTH DOSE OF RTS,S MALARIA VACCINE IN PERENNIAL SETTINGS: A MODELLING STUDY

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The RTS,S/AS01 malaria vaccine, which has been introduced into the Expanded Program on Immunization (EPI) for use in children in moderate to high malaria transmission areas, provides another tool in the fight to reduce malaria morbidity and mortality. However uncertainty around ideal deployment, feasibility, and impact of a fourth dose remains. This study compares modelled estimates of impact of a fourth dose of RTS,S vaccine given between 15-27 months of age using OpenMalaria, an individual-based, stochastic model of malaria transmission and disease progression. We simulated the impact of the fourth vaccine dose timing schedules and coverage on malaria cases, severe disease, hospitalizations, and deaths across different archetypal transmission settings. Our modelling suggests that the three-dose primary series of RTS,S vaccine substantially reduces the malaria burden across transmission settings, regardless of timing of the fourth dose. The fourth dose could avert additional malaria cases and

deaths compared with the primary series alone, and we find potential flexibility in timing this dose, particularly from 6 to 12 months after dose three. Overall, vaccine coverage remains the most important determinant for impact on age patterns of malaria burden and should be maximized. A fourth dose delivered between 15- and 21-months of age (corresponding to a 6- to 12-month interval after dose three) with high population coverage of both the primary series and subsequent dose, will likely avert the largest proportion of cases of clinical malaria, severe malaria, and deaths in perennial settings, across transmission intensities.

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MANAGEMENT OF UNCOMPLICATED MALARIA IN RURAL AND URBAN AREAS IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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The Democratic Republic of Congo (DRC) is the second most affected country by malaria worldwide. One of the reasons for this high mortality rate may be poor management of cases of uncomplicated malaria that progress to severe malaria, or even cases of antimalarial drug resistance due to misuse of antimalarial drugs. The national policy recommends that uncomplicated malaria be treated in health centers, using Artemisinin-based combination therapies (ACTs) The objective of this article is to compare the management of uncomplicated malaria in rural and urban areas. A drug use study was carried out in DRC in 2018. In each of the former 11 provinces of DRC, one Rural Health Centre (RHC), one Urban Health Centre (UHC), and one General Referral Hospital (GRH) were selected. In each of them, 100 patient's files containing a prescription of antimalarials were randomly selected. Among them, all the files with a diagnosis of uncomplicated malaria were included in this study. Prescribed antimalarials, biological confirmation, and compliance with national policy were analyzed. A total of 2,213 cases of uncomplicated malaria were recorded. Children under the age of five were the most affected, with an incidence of 32.97%. Two ACTs were the most used drugs: artesunate/amodiaquine (45.33%) and artemether-lumefantrine (20.09%). The compliance to national policy and cure rates were significantly higher in CSRs (80.8% and 97.12% respectively), compared to UHC (61.2% and 87.31% respectively), $p<0.0001$. The remote position of RHC mean that only recommended medications are provided there, by government institutions or NGOs. On the other hand, the location of UHC in urban areas gives them access to all circulating medications, including non-recommended ones. Despite limited resources, RHCs manage more effectively uncomplicated malaria than urban ones. Prevention and treatment strategies for uncomplicated malaria, including control of circulating drugs should be strengthened. Rational use of antimalarials should also be promoted especially for children under 5.

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MANAGEMENT AND OUTCOMES SEVERE MALARIA IN HEALTH FACILITIES IN THE DEMOCRATIC REPUBLIC OF CONGO

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Malaria is the leading cause of death in the DRC, especially among children under the age of five. The national policy in DRC recommends the use of injectable artesunate, followed by a full course of oral ACT for the management of severe malaria. Health centers need to transfer severe malaria cases to Referral Hospitals which are better equipped to manage these cases. The aim of this study is to evaluate the use of drugs and outcomes in patient treated for severe malaria. A drug use study was carried out in 2018, in all the former 11 provinces of DRC and, in each of them, one Rural Health Centre (RHC), one Urban Health Centre (UHC), and one General Referral Hospital (GRH) were selected. In each of them, 100 patient's files containing a prescription of antimalarials over a one-year period were randomly selected. Among them, all the files with a diagnosis of severe malaria were included in this study. Biological confirmation, compliance with national policy, and outcome were analyzed. Of a total of 659 patients, 34.45% were treated in RHCs, 13.05% in UHCs, and 52.50% GRHs. The under-5 age group was the most represented, with 49.61%. Injectable quinine was the most used treatment (39.54%), followed by injectable Artésunate in 36.64%. Treatment was initiated without biological confirmation of malaria in 36.87% of patients. Proportion of death was 13.09% (7.91%, in the RHCs and 5.18% in the GRHs). No death was recorded in the UHCs which can easily transfer sick patients to GRHs. The under-5 age group recorded 14 deaths (63.63%) of all deaths. The most used drug is not the recommended one, RHCs manage a disproportionately high number of severe cases and death rates are high among treated patients especially in under five years old children. Measures to mitigate these issues need to be put in place.

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FACTORS ASSOCIATED WITH MALARIA TRANSMISSION IN BENIN - A RETROSPECTIVE STUDY OF DATA COLLECTED BETWEEN 2017 AND 2021

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From 2017 to 2021, Benin experienced an increase in malaria incidence, from 167 to 212 per 1000 people at the national level (a 27% increase) while case fatality rates also increased from 1.4% to 1.6% despite the implementation of WHO-recommended interventions (e.g., net mass distribution, routine net distribution to newborns and pregnant women, and the introduction of SMC). This study aimed to understand malaria transmission dynamics in Benin and identify factors with insights used to target interventions and control measures crucial to the 2023 Global Fund financial request. Data from the National Health Information System (DHIS2) and data from campaigns, surveys, and meteorological repositories were used. The indicators reflecting the effectiveness of malaria interventions (i.e., data quality, prevention, and case management interventions, campaigns, and impact) were identified. Descriptive analyses were applied to observe the distribution of malaria burdens and interventions, using visualization methods (line and bar graphs, boxplots, and maps) at the communal level. After adjusting for confounding variables to cancel links among independent variables, a multiple regression analysis was performed to determine the factors significantly associated with malaria transmission. Benin indeed experienced an increase in transmission with a peak in 2019. The malaria burden was highest in the northern regions, with 47% of Benin's cases and 54% of deaths while representing only 34% of the population. The regression model indicated significant predictors of transmission, including the increased case reporting with the strengthened surveillance systems responsible for 30% of the change in incidence, improved screening practices leading to increased detection and 27% of the change in incidence, and increased rainfall resulting in 9% of the change in incidence mainly in 2019. The findings of this analysis, which underscore the critical need for sustained and scaled surveillance systems, testing capacities, and environmental management strategies, were instrumental in Benin's successful funding proposal to the Global Fund.

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UNDERSTANDING THE IMPACT OF HOUSEHOLD WEALTH INDEX ON MALARIA RISK BY SETTLEMENT TYPE USING THE WET SEASON DATA FROM IBADAN

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Malaria persists as a significant public health challenge in urban Nigeria, particularly amid the changing urbanization landscape, with informal settlements and slums being the focal points of vulnerability. This study This study evaluates the relative strength of different wealth indicators in predicting malaria risks across urban settlements in Nigeria, leveraging on the our wet season data collected between July and November 2023 in selected wards of Ibadan, Oyo state. A total of 7,123 individuals were surveyed and tested for malaria from various wards accross different settlement types in Ibadan. The study employed quantitative techniques, for gathering of data on household assets ownership, treated net ownership and use, quality of housing, treatment and health seeking behavour and rapid diagnostic tests for malaria conducted with each participant during the wet season. Wealth index was computed by using principal component analysis the following indicators 1) household assets, 2) net ownership and use, 3) quality of housing, and 4) treatment seeking behavour which may directly influence malaria risk. Univariate analysis revealed that Wealth Index is associated with test positivity rates. investigation is the first step in evaluating a range of wealth and consumption indices, across Nigeria to determine their association with malaria risk. Although wealth indices remained predictive of malaria risk after adjusting for variables directly related to malaria, the association's strength was reduced. In Nigeria's varied settings, bed net ownership and use were identified as stronger predictors of socioeconomic disparities in malaria risk than quality of housing and household asset ownership highlighting the importance of comprehensive socioeconomic evaluations in malaria control strategies. Evidently, after computing the PCA, slum has a lower wealth index with (median: -1.05), contrasting with formal and informal settlements which appear not to be distinguishable with (median: -0.32), suggesting potential methodological refinements in the criteria for classification of formal and informal settlements.

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FACTORS ASSOCIATED WITH THE PREVALENCE OF SUBMICROSCOPIC *PLASMODIUM* SPP. INFECTIONS IN NATIVE COMMUNITIES OF THE RIO SANTIAGO DISTRICT, AMAZONAS-PERU

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In Peru, malaria is endemic in the region of Amazonas, with cases concentrated in the Rio Santiago district. In 2022, the Malaria Elimination Plan was launched, focusing on community-level implementation strategies. Therefore, directing our efforts towards submicroscopic infections and their associated factors is important, as they constitute a silent reservoir that sustains malaria transmission. A descriptive cross-sectional study was conducted in six native communities in the Rio Santiago district from November 2021 to October 2022. Active case detection was employed to determine factors associated with submicroscopic infection prevalence, using a survey and finger-prick sampling for microscopy and qPCR. Out of 1267 participants, 8.1% tested positive by microscopy, and 14.2% by qPCR (9.0% *Plasmodium vivax*, 4.1% *P. falciparum*, and 1.1% mixed infections), with 49.4% being submicroscopic and 55.5% asymptomatic. The Alianza Progreso community had the highest number of cases, and *P. vivax* was the most prevalent species using both methods, while Caterpiza community reported the highest proportion of submicroscopic cases at 21.6%. Multivariate analysis revealed that presenting symptoms (p=0.005; 95% CI: 0.27-0.78%) and using mosquito nets (p=0.032; 95% CI: 0.36-0.96%) decreased the likelihood of having a submicroscopic infection by 53% and 41%, respectively. Additionally, being from Caterpiza increased the risk of submicroscopic infection by 2.18, whereas residing in Chapiza decreased the risk by 71% (p=0.006; 95% CI: 0.11-0.68%) compared to Alianza Progreso. This study demonstrates a high prevalence of submicroscopic infections in the Amazonas region, highlighting the need to use more sensitive diagnostic tools and prioritize active case detection-finding, to strengthen and focus interventions within the framework of malaria elimination.

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COMPARING CHANGES IN MALARIA TRANSMISSION USING THE MOLECULAR FORCE OF INFECTION VERSUS INCIDENCE DURING A MALARIA RESURGENCE IN TORORO, UGANDA

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Individuals in high endemic settings are often infected with multiple falciparum clones, and many infections do not result in symptoms. Thus, the molecular force of infection (mFOI, the incidence of genetically distinct parasite clones acquired over time), may more directly reflect changes in transmission than incidence of symptomatic disease. To assess mFOI and its relationship to incidence during a resurgence of malaria in Tororo, Uganda associated with a change to less effective IRS, we genotyped apical membrane antigen-1 in all asymptomatic and symptomatic malaria infections in a cohort of 651 individuals enrolled in three locations: Tororo away from the border with Busia, Tororo near the border with Busia, and Busia (no history of IRS). Poisson regression with generalized estimating equations for repeated measures was used to estimate monthly mFOI and malaria incidence per person-year (ppy). In Tororo away from the border, incidence increased nearly 7-fold after Oct 2021 and by 1.9-fold in Tororo near the border; there was no change in incidence in Busia. At the peak of the resurgence in March 2022 in Tororo away from the border, mFOI was 15.7 infections ppy vs. malaria incidence of 4.8 cases ppy, and in Tororo near the border, mFOI was 15.1 infections ppy vs incidence of 2.5 cases ppy. This provides evidence for similar transmission intensity in these two locations despite differential increases in malaria incidence. Overall, mFOI was greater than incidence by a factor of 4.8 but there were differences by age, site, and time period. As expected due to age-related immunity, the ratio of mFOI to malaria incidence was highest in adults (6.9), followed by children 5-15 (4.5) and children <5 years (2.8). In addition, prior to the resurgence, the ratio of mFOI to malaria incidence was lowest in Tororo away from the border (3.0) and was similar in Tororo near the border (5.9) and Busia (5.5), suggestive of less immunity in Tororo away from the border - the site that experienced the greatest resurgence in malaria. mFOI is a more sensitive measure of transmission intensity compared to incidence and can be used to study differences in exposure and immunity.

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PREVALENCE AND EPIDEMIOLOGICAL CHARACTERISTICS OF ASYMPTOMATIC MALARIA IN SUCRE, VENEZUELA: A CROSS-SECTIONAL STUDY

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Venezuela remains the country accountable for most malaria cases in Latin America. Bolivar, Amazonas, and Sucre state account for more than 80% of the cases in the country. Unlike in the other two states, in Sucre the malaria transmission hot spots are not related to mining activities. Asymptomatic malaria carriers were reported more than two decades ago in this state; however, an unprecedented malaria epidemic has developed in the last decade, changing the epidemiological landscape. This study aims to determine the current prevalence of asymptomatic malaria in Sucre using molecular techniques. We carried out a cross-sectional study on asymptomatic individuals (N=351) in 4 rural communities (El Paujil, Cristóbal Colón, Yaguaraparo and Chacopata) of Sucre state. Patients were interrogated in their households and were tested by rapid diagnostic tests (RDT), polymerase chain reaction (PCR) and thick and thin blood smears for malaria. The overall prevalence of asymptomatic malaria by PCR was 24,8% (CI:20,5-29,5), greater in men (28,3%, CI:21,7-35,6) than in women (21,9%, CI:16,5-28,1). The prevalence in older than 15 years was 27,1% (CI:21,6-33,1), while in younger than 5 years was 16,7% (CI:6,7-32,7). Teachers (41,7%, CI:18-68.8) and farmers (34.5%, CI:23.2-47.2) had the highest prevalence; However, there were no statistically significant differences. Only one of the cases detected by PCR was also detected by RDT and microscopy. Most cases accounted for *Plasmodium vivax* (73,6%), followed by *P. vivax/falciparum* (mixed) disease (14,9%), *P. falciparum* (9,2%), and 2 cases of *P. malariae* (2,3%). Chacopata was the region with greater prevalence (30,6%, CI:17,4-46.7). Neither the amount of time living in the area nor a record of malaria showed statistical significance among PCR positive and negative groups. Less than 2% of patients with asymptomatic malaria were diagnosed by rapid diagnostic tests and microscopy. Active surveillance systems using highly sensitive tests provide a more accurate prevalence of asymptomatic malaria, estimation required for elimination.

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EVOLUTION OF PREVENTIVE AND CURATIVE BEHAVIORS, VITAL AND PARASITOLOGICAL PARAMETERS OVER THE COURSE OF EPISODES OF MALARIA IN CHILDREN LIVING IN LIBREVILLE, GABON

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Introduction: Despite the fight against malaria, there are transmission spots in Africa but studies on repetition of malaria episodes are carried out mainly in Asia and Latin America. In Africa, clinical trials explore this side without attempting to observe the evolution of parameters and behaviors of malaria patients over episodes. While these changes could favor the persistence of malaria endemicity. This work aims to determine the correlation of preventive and curative behaviors, vital and parasitological parameters over episodes of malaria in children.Methods: This study was a passive cohort conducted at the Malaria Clinical and Operational Research Unit which is an epidemiological surveillance site located in Libreville, Gabon. This work focused on children with several episodes during between 2020 and 2022. The Mac Némar and Spearman Chi square tests were used to compare behaviors and parameters over episodes of malaria.Results: This work identified 59 children with 2 episodes of malaria among 8,497 observations. Among these children, 50.85 % were male. Median parasitemia was 1540 parasites/µL (233 – 15050) at first episode and was 800 parasites/µL (243 – 5400). Also, at malaria first episode, median duration was 4 days (3 – 6) and was 2 days (1 – 4) at second episode. Temperature ($p = 0.38$), use of impregnated mosquito net at bedtime ($p = 0.39$) and practice of self-medication ($p = 0.28$) were similar from one episode to another in the participants. Parasitemia ($p < 0.01$) and duration of fever ($p < 0.01$) were different over the 2 episodes. The concordance of stage and species of parasite could not be assessed because of the almost totality of trophozoites and *Plasmodium falciparum* respectively in each episode. Conclusion: The temperature during the malaria episode seems influenced by immunological capacities unlike duration of fever and parasitemia which could be linked to characteristics of the episode such as the inoculum during the mosquito meal. On the other hand, the indifference to prevention practices and self-medication despite a previous episode of malaria in children shows a persistence of bad habits among parents/guardians.

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IMPACT OF COVID-19 ON MALARIA: CLINICAL CHANGES BEFORE AND DURING THE COVID-19 PANDEMIC, A RETROSPECTIVE STUDY IN A REFERENCE CENTER

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Malaria is a parasitic disease that has always been controlled by national programs worldwide**.** The management of Covid-19 and the malaria is difficult because they share the same symptoms and require regular screening. Data showed that the death of malaria could increase compared if there was no Covid-19 pandemic, but is still limited regarding the impact of Covid-19 on epidemiological clinical profile of malaria. In that context, our study aimed to evaluate the impact of the Covid-19 pandemic on the epidemiological and clinical profile of malaria in a referral center in Madagascar. It was a retrospective comparative study, the study period was subdivided into two: before Covid-19 1st January to 31 December, 2019 and during Covid-19 1st January to September 31, 2021.We retained 113 patients including 69 cases before Covid-19 and 44 cases during Covid-19. The frequency of malaria decreased to 44(38.94%), severe malaria is the predominant clinical form during Covid-19 44(42.31%). The mean duration of disease progression to severe malaria decreased to 3 days, the length of stay increased by 8 days and the death rate was 7 (16%) during Covid-19. The death rate was 12(17%) before Covid-19 versus 7(16%) during Covid-19. On univariate analysis, the presence of confusion (p=0.80), convulsions (p=0.61), respiratory failure (p=0.50) and anemia (p=0.82) were factors associated with malaria mortality. The disruption of malaria control related to COVID-19 has an impact on symptom severity and mortality. Prevention of this disaster through increased screening and awareness of healthcare workers should be a priority in the Covid-19 response.

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SIMPLEGEN: A MODELING APPROACH (DE)COUPLING EPIDEMIOLOGY AND GENOMICS TO INFORM MALARIA SURVEILLANCE

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Malaria genomic surveillance has gained notable traction in recent years with the value of *Plasmodium* genetic data being increasingly recognized as a useful source of epidemiological intelligence. However, a major hindrance is the lack of a well-defined framework for evaluating the utility of genetic data ahead of obtaining samples. This makes it difficult to "power" and benchmark sampling designs for genetic applications in different transmission settings. In addition, without models that link processes that generate parasite genetic diversity with epidemiological processes, the practical application of genomic epidemiology will be limited. We are developing SIMPLEGEN, a simulation-based pipeline that combines mathematical models of malaria transmission with genetic models that can be used to systematically explore the utility of genetic data under different epidemiological conditions. Transmission trees from the transmission model detail host-vector infection events, with individual parasite strain tracking including recombination events in the mosquito midgut. The population can be sampled using specific survey designs (e.g. cross-sectional) and the tree

is pruned to only events relevant to the infections in the sample. We then overlay a genetic model to simulate the parasite strain pedigree describing relatedness between all strains within all sampled individuals and simulate genetic diversity evolution via mutation and recombination backwards-in-time. Finally, an observation model captures issues with real sequencing data. The final SIMPLEGEN output is simulated genetic data that can be passed into downstream data analysis tools. Decoupling epidemiology from genetics leads to a significant speed-up in simulation, allowing us to explore different questions (e.g. spatial patterns). SIMPLEGEN is a tool for exploring parasite genetic features that capture epidemiological parameters and has the potential to serve as a framework for rigorous benchmarking of different analysis methods and genomic sampling designs, a currently unexplored area in malaria genomic surveillance.

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DISENTANGLING *PLASMODIUM FALCIPARUM* GENETIC RELATEDNESS NETWORKS TO STUDY MALARIA TRANSMISSION PATTERNS ACROSS SENEGAL

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Genomic surveillance and genetic relatedness analyses have emerged as powerful tools for studying infectious disease transmission. Previously, malaria relatedness studies have relied on summarizing the genetic relatedness using networks that reveal pairwise relatedness values between individual parasites. In this study we assessed the genetic relatedness network structures using established network science metrics (including graph density, clustering coefficient, and degree centrality) to quantitatively assess how genetic relatedness networks correlate with transmission intensity. Genetic relatedness networks from monogenomic *P. falciparum* infections collected across eight sites of varying malaria incidence (2.7‰ - 369.3‰) across Senegal were constructed using Identity by descent based (IBD) Hidden Markov Model (hmmIBD). Relatedness relationships were also classified as clonal (IBD >0.95), inbred (IBD 0.8-0.95), first degree (IBD 0.4 -0.8), second degree (IBD 0.2-0.4) and third degree (IBD <0.2) to further quantify network structure. Overall, we found that the genetic relatedness networks of low-incidence populations (<30‰) had more interconnected network structures compared with high-incidence populations. Ordinary Least Square Regression analysis showed several network statistics strongly correlated with log incidence such as average edge weight (R^2 = 0.406), graph density (R^2 = 0.367), and average clustering coefficient (R^2 = 0.352). Multivariate goodness-of-fit analyses using a series of Poisson Generalized Linear Models showed that relying on single metrics could lead to inaccurate predictions (AIC 1264.17- 1224.19) and that combinations of network statistics metrics are needed to generate accurate predictions. This study has demonstrated that genetic relatedness networks can be reliably quantified, allowing us to further resolve malaria transmission structures. Incorporating these analyses into a predictive tool could be valuable for global malaria control efforts.

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A *PLASMODIUM VIVAX* STRAIN THAT EXPRESSES FLUORESCENT PROTEINS THROUGHOUT THE LIFE-CYCLE

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Plasmodium vivax persists due to its ability to form dormant liver-stages, known as hypnozoites (HZs). Understanding the molecular makeup of HZs is key to developing new treatments to eliminate HZs, but these experiments have been hindered by the inability to isolate *Pv* HZs for molecular characterization. A transgenic *Pv* that expresses fluorescent proteins throughout the life-cycle would overcome this limitation and make molecular characterization possible. To address this need, *Pv* Chesson parasites were harvested from *Saimiri boliviensis* monkeys and transfected with a plasmid containing *gfp, mCherry*, and *nanoluc* reporter genes under two different promoters. GFP was placed under the constitutively expressed *hsp70* promoter, whereas mCherry and Nanoluc were placed under the *lisp2* promoter to enable the exclusion of activating forms from dormant HZs in future isolations. Pyrimethamine resistant asexual stage parasites were recovered about 31 days after transfection and inoculation into a naïve animal. Eighty-nine percent of the resistant parasites expressed GFP. Infected blood was then collected and fed to *Anopheles stephensi* mosquitoes, and GFP+ oocysts and sporozoites were detected. Primary human hepatocyte cultures were inoculated with sporozoites, and both small and large forms expressing GFP were detected by live imaging. Large forms also expressed mCherry as expected. There were no effects on the parasite's development in the liver-stages. This study establishes a fluorescent, transgenic *P. vivax* strain that can be used to isolate hypnozoites for molecular characterization and methods for genetically manipulating *P. vivax* to test specific proteins that may be involved in dormancy

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SIMPLSEQ + CI: A HIGHLY-SENSITIVE MALARIA MULTIPLEXED AMPLICON SEQUENCING PROTOCOL AND CLOUD-BASED BIOINFORMATIC WORKFLOW WITH CONTAMINATION DETECTION FOR INTERVENTION STUDIES

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Multiplexed PCR amplicon sequencing is a powerful tool for genetic profiling of malaria-causing *Plasmodium* parasites; however, drug and vaccine efficacy studies demand high sensitivity levels to detect parasites in low-parasitemia samples, a capability not provided by large amplicon panels designed for epidemiological surveillance. Here, we present SIMPLseq, an amplicon panel of six highly diverse *P. falciparum* markers (CSP, TRAP, SURFIN, KELT, SERA8, and WD-repeat containing protein) designed for high-sensitivity parasite genotype tracking, especially for longitudinal infection analyses. In addition, we introduce a new system to detect inter-sample contamination based on the use of combinatorial indices (CI) during the first round of nested PCR amplification. We tested SIMPLseq + CI in samples with varying parasitemia levels. All SIMPLseq loci amplified at concentrations as low as 0.5 parasites/µl, with partial detection continuing below 0.125 parasites/µl - a significant improvement in sensitivity relative to our previous 4CAST panel. The addition of CI to the first round PCR primers produced a minimal reduction in read yield compared to non-barcoded SIMPLseq primers for moderate-to-high parasitemia samples. Tests of intentional inter-sample contamination proved CI's capacity to enhance the fidelity of sample-to-genotype mapping. To facilitate the integration

of SIMPLseq + CI in routine monitoring of therapeutic interventions, we developed an interactive, open-access bioinformatic workflow in the cloud-native platform Terra.bio. This workflow automates the detection of inter-sample contamination, denoising of sequencing artifacts, and reporting of amplicon sequencing outputs. It also provides results as easily interpretable report files. We present examples of how SIMPLseq + CI and its associated bioinformatic workflow may be used for clinical trials and make recommendations for its implementation in longitudinal studies of malaria interventions.

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EVOLUTION OF MOLECULAR MARKERS OF ANTIMALARIAL DRUG RESISTANCE IN UGANDA, 1999-2022

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The primary therapy for uncomplicated malaria in Uganda was chloroquine until 2001, chloroquine plus sulfadoxine/pyrimethamine (SP) in 2001-2006, and artemether-lumefantrine beginning in 2006. Evolution of the genome of *Plasmodium falciparum* in association with changes in treatment policy has been well-described, but not previously from a single site across two decades. To better characterize resistance marker changes over time, we used molecular inversion probe deep sequencing of *P. falciparum* isolates collected in Kampala, central Uganda, in 1999, and Tororo, eastern Uganda, in 2003-04, 2008, 2012, 2016, and 2022. For markers of aminoquinoline resistance, the prevalence of the resistance-associated PfCRT 76T, PfMDR1 86Y, and PfMDR1 1246Y mutations changed from 100%, 88%, and 70% in 1999 to 0%, 0%, and 7% in 2022, respectively. For markers of sulfadoxine resistance, the prevalence of the resistance-associated 437G, 540E, and 581G mutations changed from 56%, 56%, and 0% to 100%, 100%, and 7%, respectively. For markers of pyrimethamine resistance, the prevalence of the resistance-associated 51I, 59R, 108N, and 164L mutations changed from 96%, 58%, 98%, and 0% to 100%, 100%, 100%, and 16%, respectively. For markers of artemisinin partial resistance, the prevalence of resistance-associated PfK13 mutations was 0% through 2016, but rose to 10% for 469Y and 16% for 675V in 2022. In summary, we found major changes in drug resistance markers over time. Key markers of aminoquinoline resistance mostly disappeared after removal of chloroquine from recommended treatment regimens. Multiple markers of antifolate resistance were present even before widespread use of SP, but prevalence increased over time, with markers of high level resistance appearing recently. Markers of artemisinin partial resistance, first noted in 2016 in northern Uganda, were detected in Tororo in 2022. Overall, our results demonstrate profound changes in the prevalence of resistance markers in Uganda over two decades, coincident with changing malaria treatment practices, emphasizing the importance of continued surveillance for genomic markers of drug resistance in Africa.

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ASSESSMENT OF GENETIC DIVERSITY OF *PLASMODIUM FALCIPARUM* PF230 GENE AS A POTENTIAL CANDIDATE FOR MALARIA VACCINE DEVELOPMENT

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Evolutionary events in the Malaria parasite's genome leading to high genetic variability have been shown to affect the performance of malaria vaccine candidates. This study aimed to assess the genetic diversity of the *Plasmodium falciparum Pf230* gene as the promising transmission-blocking (TBV) vaccine candidate to predict its efficacy. A total of 1312 chromosome two VCF data files from the four study countries (Tanzania (n=589), Kenya (n=690), Uganda (n=12), and Ethiopia (n=21) were retrieved from the MalariaGEN database and utilized to study the genetic diversity of the *Pf230* gene using various genetic matrices and bioinformatics techniques. Different R packages, outstanding software such as DnaSp, and other population genetics tools running under Unix were used to determine the *Pf230* gene nucleotide diversity, SNPs density, Wright's fixation index (Fst), Principal component analysis (PCA), Haplotype diversity, signatures of selection using Tajima's D and performing phylogenetic analysis. The nucleotide diversity results indicated very low levels of genetic diversities of 6.1e-4, 5.8e-4, 6.4e-4, and 4.3e-4 for Tanzanian, Kenyan, Ugandan, and Ethiopian parasite populations. The SNP density results showed very low SNPs occurrence across the entire *Pf230* gene, with a little variation at around 2200 bp position for all four counties. The mean Fst indicated very low genetic differentiation in the *Pf230* gene within Tanzania (Fst = 5.1e-3), Kenya (Fst = 5.2e-3), Uganda (Fst=5.0e-3), and Ethiopia (Fst=1.3e-3). The DnaSP results showed evidence of purifying selections and lower haplotype diversity values of 0.1288, 0.1319, 0.0000, and 0.3047 for Tanzania, Kenya, Uganda, and Ethiopia respectively. The PCA showed no genetic structure for the *Pf230* gene and a little to moderate level of sequence divergence based on the phylogenetic analysis. The *Pf* genomic data analyzed in this study provides evidence of very low genetic diversity of the *Pf230* gene. The findings strongly suggest that the *Pf230* gene is highly conserved and is not under selection pressure. Therefore, it can be considered a suitable and potential TBV candidate.

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EVIDENCE FOR SUSTAINED LOCAL TRANSMISSION IN A LOW TRANSMISSION SETTING IN SOUTHERN ZAMBIA: EXAMINING PARASITE GENOTYPE RELATEDNESS USING AN AMPLICON PANEL

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In low-prevalence malaria settings, transmission is persistent though nearly undetectable. Importation and introduced transmission become increasingly important as local transmission decreases, but with low incidence of clinical disease, traditional epidemiological measurements and surveillance strategies cannot discern one from the other. Parasite genomics provides more information on individual infections through relatedness measures that support inferences on transmission dynamics. This study used a 24-marker amplicon panel to examine relatedness patterns in 350 clinical samples collected from low-transmission Choma District, Zambia between 2018 and 2023. Complexity of infection (COI) and identity-by-descent (IBD) were used to assess for spatial-temporal patterns in relatedness, associations between relatedness and travel history, and used to construct and examine networks of related parasites. Mean COI was 2.1 and 55% of samples were polyclonal. There were no statistically significant individual associations between demographic characteristics of sampled individuals, year of collection, parasite density, or COI. COI in individuals who reported travel was 2.2 parasites clones higher than COI in individuals without reported travel by. Individuals who were diagnosed less than 14 days apart, individuals living in the same health facility, and individuals living within the

same zone (cluster of 2-3 villages) had infections of more closely related parasites by IBD, while traveler case parasites were on-average less related to the rest of the parasite population. The majority of cases were in one highly-related cluster of parasites spanning the entire study period and providing strong evidence of ongoing local transmission. There were two short transmission chains (each with five or fewer total infections) that suggested travel-related introductions, but these did not result in sustained transmission. Given the strong evidence of local transmission, local prevention efforts remain essential in this pre-elimination area.

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HLAG 01:05N NULL ALLELE FREQUENCY IN NEWBORN IN BENIN POPULATIONS AND HLA-G EXPRESSION

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HLA-G, a non-classical HLA class Ib molecule, is involved in the feto-maternal immunologic tolerance. *HLA-G*0105N* presents a single base deletion, preventing translation of HLA-G1, HLA-G5 and HLA-G4 isoforms. The non-translation of sHLA-G isoforms in *HLA-G*0105N* homozygous individuals could lead to better defense against pathogens in host and could also lead to spontaneous miscarriages in women, due to low secretion of HLA-G isoforms and therefore a reduction in immune tolerance. Previous studies showed a high frequency of *HLA-G*0105N* in some African populations but this information is lacking in Benin. Here, we evaluate the *HLA-G*0105* null allele frequency in Benin populations and its association with soluble HLA-G expression in plasma samples. This study was carried out on two cohorts in southern Benin. The first cohort monitored 656 children from birth to 18 months of age and the second cohort monitored 400 children from birth to 24 months. *HLA-G*0105N* null allele frequency was accessed by PCR/RFLP. Plasma sHLA-G concentration was measured by ELISA and correlated to the *HLA-G*0105N* genotypes. A high frequency (13%) of the *HLA-G 01:05N* allele was observed in the Benin populations compared to other populations of non-African origin (0 to 4%) from 1000 Genomes project. *HLA-G*0105N* allele frequency was 11% and 14% respectively in the first and second cohorts, corresponding to the highest frequencies of African populations from 1000 Genomes project. The mean level of sHLA-G at birth from homozygous wild-type *HLA-G*0105N* individual was significantly higher than those from heterozygous individuals (p=0.010) and higher than those from homozygous *HLA-G*0105N* allele (p=0.005). Similarly, we found that heterozygous individuals had higher means of sHLA-G than homozygous *HLA-G*0105N* individuals (p=0.007). Our results showed an association between *HLA-G*0105N* genotypes and plasma sHLA-G concentration suggesting a genetic control of sHLA-G expression. The high frequency of *HLA-G*0105N* allele observed in Benin suggests that the reduced HLA-G expression in *G*0105N* carriers may improve the defense against infectious tropical diseases.

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UNRAVELING THE GENETIC DIVERSITY AND TRANSMISSION NETWORKS OF *PLASMODIUM FALCIPARUM* IN SOUTHWESTERN UGANDA: A LOW TRANSMISSION SETTING

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In Uganda, malaria transmission varies across regions, with the southwestern area experiencing low transmission. Understanding factors sustaining transmission is crucial for malaria elimination efforts. Travel history is used to classify cases as local or imported, but it suffers from recall bias. Parasite genetic data may offer less biased insights. We aim to characterize malaria cases using both genomic data and travel history to elucidate transmission networks and assess importation's role. We collected dried blood spots and travel data from malaria cases at three low transmission sites in southwestern Uganda: Chahafi, Maziba, and Muko. We employed highly multiplexed amplicon sequencing targeting 165 diversity loci. Demographic and travel data were analyzed in R. Genetic data analysis was conducted using MOIRE and Dcifer packages to decipher complexity of infection and relatedness. We collected 348 samples across the sites, with most cases reporting travel within Uganda. Initial genetic analysis revealed substantial within-host diversity, with mean complexity of infection varying across sites. Dcifer analysis showed differing levels of between-host relatedness, with Chahafi and Maziba having no related samples and Muko showing some relatedness to both. Chahafi exhibited more clusters, indicating greater relatedness among samples. High rates of overnight travel among cases suggest significant imported malaria. Genetic data suggest increased diversity and relatedness between sites. Further investigation is planned to understand transmission networks better.

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FIKK GENE EXPRESSION SPECIFIC TO SEVERE MALARIAL SYNDROMES IN MALIAN CHILDREN

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Plasmodium falciparum is the most common and virulent malaria parasite. As the primary species responsible for severe malaria, it continues to be a leading cause of mortality in the developing world. Children under the age of five are overwhelmingly affected, accounting for most deaths from malaria. *P. falciparum* is unique among *Plasmodium* species for having multiple members of the *fikk* multigene family, which encodes serine/threonine kinases. During intra-erythrocytic infection, *P. falciparum* actively exports 18-26 FIKKs into the infected erythrocyte. These kinases are predicted to facilitate the activation and trafficking of membrane proteins within infected erythrocytes, contributing to the remodeling of the erythrocytic membrane and its highly variable surface antigens. Given the association of parasite erythrocyte surface antigens and severe malarial disease, we hypothesized that severe malaria cases feature elevated expression of a subset of *fikk*s compared to matched uncomplicated malaria controls. We investigated the differential expression of *fikk* kinases in severe clinical syndromes of *P. falciparum* malaria in a matched case-control study in Mali. Using RNA-seq and *de novo* assembled transcripts, we compared *fikk* expression in cases of cerebral malaria (CM), severe malaria anemia (SMA), and a combined syndrome featuring both CM and SMA (CM+SMA) to matched uncomplicated malaria controls (UM). Preliminary findings with 64 total subjects indicate the differential expression of several *fikk*s in severe disease compared to matched controls. One *fikk* gene had significantly increased expression in CM cases compared to matched uncomplicated malaria controls (N=14 pairs, P<0.02; Wilcoxon signed-rank test). We identified a characteristic *fikk* expression profile specific to the combined CM+SMA syndrome involving four FIKKs. We are examining host immune responses

to FIKK proteins using a custom protein microarray. A subset of FIKKs could be suitable targets for vaccine and therapeutic development for severe malaria, particularly if they are natural targets of the host immune system.

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SNP-SLICE RESOLVES MIXED INFECTIONS: SIMULTANEOUSLY UNVEILING STRAIN HAPLOTYPES AND LINKING THEM TO HOSTS

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Multi-strain infection is a common yet under-investigated phenomenon of many pathogens. For example, genomic sequences from field samples of malaria often need to be excluded as many downstream analyses require monogenomic inputs. Such a protocol impedes our understanding of pathogens' underlying genetic diversity, co-infection patterns, and genomic relatedness. In molecular epidemiology, a scalable tool to learn and resolve the SNP-haplotypes from polygenomic data is urgently needed. Here, we develop a slice sampling Markov Chain Monte Carlo algorithm, named SNP-Slice, to learn not only the SNP-haplotypes of all strains in the populations but also which strains infect which hosts. Our method reconstructs SNP-haplotypes and individual heterozygosities accurately without reference panels and outperforms state-of-the-art methods at reconstructing SNP-haplotypes or estimating the multiplicity of infections and allele frequencies. Thus, SNP-Slice introduces a novel approach to address polygenomic data and opens a new avenue for resolving complex infection patterns in molecular surveillance. We illustrate the performance of SNP-Slice on empirical malaria and provide recommendations for using our method on empirical datasets.

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RELATIONSHIP BETWEEN SEASONAL MALARIA CHEMOPREVENTION AND GUT MICROBIOME DIVERSITY IN BURKINA FASO

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Sulfadoxine-pyrimethamine (SP) is used for intermittent preventive treatment in pregnancy (IPTp) and, with amodiaquine (AQ), for seasonal malaria chemoprevention (SMC) in children. SP has antibacterial activity, and studies in pregnant women have shown that IPTp with SP positively impacts maternal nutrition and weight gain, leading to improved birth outcomes. However, the mechanism by which SP offers nutritional benefits is unknown. We hypothesize that SMC with SP-AQ improves overall nutrition by effecting changes in the gut microbiome. The goal of this study was to investigate whether the gut microbiome is altered after receipt of SMC with SP-AQ and whether repeated exposures to SP-AQ have compounded effects on microbiome diversity. We prospectively studied 24 children 3-59 months of age who were eligible for SMC in Sourkoudougou, Burkina Faso. Households were approached for participation and 24 children were enrolled one month prior to the start of the SMC campaign and followed longitudinally through the malaria transmission season (June-December, 2023). Four monthly SMC doses were directly observed. Rectal swabs were collected at enrollment, during routine visits on days 3, 14, and 28 after the first three SMC cycles, and approximately two months after the fourth and final SMC cycle. At each visit, a physical exam was performed and anthropometric and dietary intake data were recorded. Of the 24 children, 22 (92%) received all three doses of SP-AQ for each of the four SMC cycles. A total of 264 rectal swabs were collected. Analyses to characterize the relative abundance, richness, and diversity of the gut bacterial community are ongoing, and results will be presented.

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BENCHMARKING THE PERFORMANCE OF POPULATION-LEVEL SEQUENCE FREQUENCY ESTIMATION TOOLS IN MALARIA RESEARCH AND PUBLIC HEALTH

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Computational tools for estimating population-level sequence frequencies (PLSF), defined as the fraction of parasite strains characterised by a given multilocus genotype within a population, are necessary to monitor drug resistance. However, the performance of these tools has not yet been systematically evaluated. In this study, we present a benchmarking analysis of existing PLSF estimation tools, including SNP-slice (SS), FreqEstimationModel (FEM), and MultiLociBiallelicModel (MLBM). Through a systematic evaluation framework, we compare the accuracy, computational efficiency, scalability, and usability of these tools. We executed all tools with default settings on simulated datasets featuring presence/absence indicators, incorporating a range of population sizes (10, 100, 1000), mean multiplicity of infection (MOI: 2, 3, 5), strain detection sensitivity within samples, and two sets of genotype frequencies: highly skewed and more evenly distributed. All true genotypes were detected in all runs by MLBM and FEM, with an average relative error of 0.29 and 0.34 respectively; only 83% were returned by SS with an average relative error of 0.60. Over 40% of the genotypes returned by MLBM and FEM were false positives, predominantly characterized by low reported frequencies (MLBM: median 2.64e-21 range, 3.17e-321-0.076; FEM: median 0.004, range 0.0003-0.069). In contrast, SS returned 15% false positives with relatively higher reported frequencies (median 0.007, range 0.0003-0.21). Even with high MOI values and large population sizes, MLBM always ran in less than a second. FEM and SS face scalability challenges, with runtime scaling with both MOI and population size. All tools produce reproducible results. Prior to the conference, we plan to evaluate additional tools, optimise model parameters to improve accuracy, and conduct read count simulations to evaluate models incorporating within-host frequencies. We will identify areas for improvement and suggest best practices for selecting and utilising the tools depending on factors such as data complexity, computational infrastructure, and specific research objectives.

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LEVERAGING DENSELY SAMPLED MALARIA CASES AND PARASITE GENETICS TO INFER TRANSMISSION NETWORK STRUCTURE

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When malaria transmission declines and becomes more heterogeneous, standard epidemiological surveillance may not provide sufficiently granular data to inform malaria control. Inferring transmission details from genetic data has proven useful for viral and bacterial diseases, but these methods cannot be applied to malaria due do differing biology, e.g. superinfection. To address this, we developed a Bayesian framework to incorporate temporal, epidemiological and genetic data with a model of malaria transmission to infer person to person transmission events. Using simulations reflecting various transmission settings, we demonstrate our ability to identify directed transmission events with high accuracy (AUC-ROC = .82), classify imported cases (AUC-ROC = .87), as well as confidently associate infections within

outbreaks (mean precision = .97 when retaining edges with greater than 1% posterior probability). Performance suffered when using less diverse genomic markers, underscoring the importance of leveraging diverse genotyping panels. We applied our method to data from a study in Zanzibar, which collected data and samples from confirmed malaria cases presenting at health facilities over the course of two transmission seasons. A total of 1,861 samples from 99 administrative units were successfully genotyped at 26 microsatellite markers, with ongoing multiplexed amplicon sequencing of samples using 166 highly diverse microhaplotype loci to increase resolution. Applying our method revealed substantial evidence of local, geographically isolated transmission, with 72% of all cases connected to at least one other observed case when filtering edges with less than 1% posterior probability, and of these edges, 41% were to another case within the same administrative unit. Several instances of transmission connectivity spanned the two transmission seasons, as well as across geographical regions, suggesting the presence of persistent local transmission during the study period along with long distance transmission events.

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DIFFERENCES IN INNATE CELLULAR IMMUNE RESPONSES DISTINGUISH PROTECTED FROM NOT PROTECTED INDIVIDUALS IN A PFSPZ VACCINE TRIAL

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In animals, protection after immunization with irradiated sporozoites (SPZ) is primarily mediated by CD8+ cells in the liver that target infected hepatocytes. The mechanism is likely similar in humans, although hard to prove because liver resident cells are not sampled. However, correlates of protection measured in the periphery have been identified, including antibodies to PfCSP and levels of Vδ2 γδ T cells. The Warfighter 3 trial immunized 42 persons with radiation-attenuated *Plasmodium falciparum* (Pf) SPZ Vaccine ($9.0x10^5$ PfSPZ per dose) and 12 persons with normal saline on days 1, 8 and 29. Three vaccine groups received controlled human malaria infection (CHMI) at 2, 6, or 10 weeks after last immunization but were pooled for initial immunogenicity analyses. Peripheral blood mononuclear cells sampled at baseline, 2 weeks post 2nd and 3rd doses and prior to CHMI were analyzed by intracellular cytokine staining (ICS) and cell phenotyping by flow cytometry and mass cytometry. Vaccine efficacy to heterologous CHMI at 2, 6 or 10 weeks was 71, 43 and 50%, respectively. Two weeks after the 2nd immunization, ICS after PfSPZ stimulation yielded higher median percentages of γδ T cells and mucosal-associated invariant T cells (MAIT, characterized as Vα7.2+CD26+CD161+) expressing IFN-γ and/or IL-2 in protected vs. not protected vaccinees (2.35 vs. 0.88% of T cells, p=0.01 and 1.19 vs. 0.13% of T cells, p=0.005, respectively). Over 88% of vaccinees had positive CD4+ T cell responses by ICS after PfSPZ stimulation 2 weeks after the 2nd immunization with a trend towards higher median responses in protected vaccinees after the 3rd dose and prior to CHMI (0.40 vs. 0.25%, p=0.06 and 0.33 vs. 0.17%, p=0.09, respectively). Mass cytometry phenotyping confirmed higher levels of Vδ2 γδ T cells in protected vaccinees 2 weeks after the 2nd and 3rd immunizations. Consistent with previous studies, Vδ2 γδ T cells were increased in protected vaccinees. A unique finding was that MAIT cells, which span the innate and adaptive arms of the immune response, were significantly elevated in protected compared to non-protected vaccinees - a finding requiring further studies.

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TRANSMIGRATION OF MATERNAL MONOCYTES AND FETAL MACROPHAGES IN RESPONSE TO ACTIVE VERSUS PAST PLACENTAL MALARIA AND ASSOCIATIONS WITH BIRTH WEIGHT

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Placental malaria (PM) is characterized by the accumulation of *Plasmodium falciparum*-infected erythrocytes (iRBC) in the placental intervillous space (IVS). This leads to hemozoin (Hz) deposition and placental damage, even after successful treatment and parasite clearance. Maternal and fetal monocytes/macrophages (Mϕ) play an important role in the placental inflammatory response to pathogens. To investigate the spatial distribution and activation phenotypes of Mϕ in the context of active (where iRBCs are present in IVS) vs. past (where Hz, but not iRBCs, is present) PM, we performed multiplex fluorescent in situ hybridization (RNAscope HiPlex v2) to detect mRNA encoding CD68 (pan-Mϕ marker), CD163 (anti-inflammatory M2 Mϕ marker), FOLR2 (tissue resident macrophage marker- fetal Hofbauer cells (HBCs)), and KRT7 (trophoblast marker) in human placental biopsies. In the maternal IVS, the densities of maternal M1 (pro-inflammatory) Mϕ (FOLR2-CD163-), maternal M2 (anti-inflammatory) Mϕ (FOLR2-CD163+) and fetal M2 HBCs (FOLR2+CD163+) showed a 3-, 3-, and 4-fold increase, respectively, in active compared to past PM ($p<0.05$). The density of M2 HBCs (FOLR2+CD163+) in the IVS was positively correlated with greater Hz deposition in the placenta ($r= 0.55$, $p<0.05$). In the fetal placental villi (PV), the density of maternal M1 Mϕ was increased 5-fold in past compared to active PM ($p<0.05$). Linear regression analysis revealed that infant birth weight was negatively correlated with higher densities of maternal M1 Mϕ in the IVS ($p<0.05$) and maternal M2 Mϕ in the PV ($p<0.01$), suggesting that these cell populations have a negative impact on fetal growth. Our results show that with active PM, fetal M2 HBCs transmigrate into the IVS, alongside both M1 and M2 maternal Mϕ that are recruited from peripheral circulation. In past PM, maternal M1 Mϕ were identified within the fetal PV. These findings suggest that divergent maternal vs. fetal Mϕ responses to iRBC and Hz deposits within the IVS result in maternal-fetal microchimerism and may mediate perturbations of fetal growth in pregnancies complicated by PM.

7994

PROTECTIVE EFFICACY OF *PLASMODIUM VIVAX* PRE-ERYTHROCYTIC ANTIGENS PVSSP3 AND PVSPECT1

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The development of an efficacious vaccine against *Plasmodium vivax* malaria remains a top priority for global health. Anopheline mosquitoes inject sporozoites into the dermis when probing for a blood meal and eventually the parasites reach the liver through blood stream to infect the liver and upon completing development initiate clinical blood-stage infection. *P. vivax* tend to form hypnozoites, dormant forms of the parasite in the liver that resume development after a few months to several years causing relapse malaria and transmission. Therefore, targeting antigens expressed during the pre-erythrocytic (PE) stages offers the potential to prevent clinical malaria from being initiated from primary and relapse infections. Circumsporozoite protein (CSP) remains the leading vaccine candidate and shown to exhibit limited protection in the targeting population. So, there

is an urgent need to explore additional PE antigen targets to develop a more effective malaria vaccine. To evaluate PE antigens for a multivalent *P. vivax* vaccine we selected PvSSP3 and PvSPECT1 that are functionally important and are upregulated in activated sporozoites correlated with infectivity. Since clinical evaluation of protective efficacy of these antigens is technically challenging and access to *P. vivax* sporozoites is limited, we pursued an alternate strategy creating transgenic *P. berghei* that expresses PvSSP3 and PvSPECT1. The protective efficacy of PvSSP3 and PvSPECT1 are being evaluated by well-established *in vitro* functional assays for their potential efficacy as part of a multistage multivalent vaccine against vivax malaria.

7995

COMPREHENSIVE CHARACTERIZATION OF *PLASMODIUM VIVAX* ANTIGENS USING HIGH-DENSITY PEPTIDE ARRAY

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During vivax malaria infection, *Plasmodium vivax* parasites can remain dormant in the liver for months in the form of hypnozoites, before reactivating to reestablish relapse infection. These dormant parasites represent a major challenge in *P. vivax* elimination since these liver infections are asymptomatic, and we lack biomarkers of hypnozoites. In addition, we still have an incomplete understanding of which *P. vivax* genes are recognized by the host immune system. To comprehensively characterize which *P. vivax* proteins are seroreactive, we designed a high-density peptide array containing 5.7 million peptides (16 amino acids in length) covering the entire coding sequences of all known and putative *P. vivax* proteins. We probed this array with serum samples from 10 malaria naïve individuals and 10 Cambodian adults sampled i) during a symptomatic vivax malaria infection and ii) four weeks later when they either relapsed (n=5) or remained clear of parasites (n=5). Our preliminary analyses revealed 2020 putative antigens from 1649 *P. vivax* proteins with high seroreactivity shared across at least 5 Cambodian patients and 91 antigens (from 89 proteins) recognized in at least 8 of the 10 patients. These antigens include known antigenic proteins such as CSP, AMA1 and MSP5, as well as many new and exciting candidates. Since *P. vivax* and *P. falciparum* are endemic in Cambodia, we also assessed the specificity of the seroreactivity to *P. vivax* infections by probing the *P. vivax* peptides with serum from *P. falciparum*-infected Malian children. Overlapping the *P. vivax* seroreactivity data with stage-specific gene expression data revealed that many putative *P. vivax* antigens are most expressed in late schizont proteins and sporozoites, although some antigens are derived from ubiquitously expressed proteins. Overall, these results identified *P. vivax* proteins from different developmental stages that are highly seroreactive and may enable identification of whether an infection is derived from an infected mosquito bite or from reactivated liver-stage parasites, paving the way to identification of novel biomarkers for *P. vivax* hypnozoites.

7996

SPATIAL HOSPITAL BASED SEROPREVALENCE AND RISK OF INFECTION FROM *PLASMODIUM VIVAX* AND OTHER *PLASMODIUM* SPECIES USING MULTIPLEX QUANTITATIVE SUSPENSION ARRAY ASSAY IN CAMEROON

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Although *Plasmodium vivax*, one of the malaria causing species has the widest geographical distribution, it is restricted in sub-Saharan Africa due to the absence of a red blood cell receptor (Duffy antigen) in black Africans. *P. vivax* has, however, been observed as single infection in up to 5% of Duffy-negative febrile patients in Dschang, West region of Cameroon. While important, the significance is limited from an epidemiological point of view, concerning the source, transmission, distribution range of *P. vivax.* We performed a cross-sectional hospital survey among 1100 febrile patients (aged 1-70 years) with symptoms suggestive of acute uncomplicated malaria in a gradient of malaria transmission ecologies in Cameroon in 2023-2024. We used a multiplex quantitative suspension array assay by the Luminex xMAP technology to quantify IgG and IgMs to nine blood stage antigens (species specific Merozoite Surface Protein-1 19kD (MSP-1) and Apical Merozoite Antigen-1 (AMA-1), three *P. vivax* antigens (PvMSP-1 and PvAMA-1, pvRBPII) belonging to 4 species including *P. vivax, P. malariae*, *P. ovale* and *P. falciparum*, in geo-referenced dried blood spot samples from fingerpricks. Crude median fluorescence intensities (MFIs) was exported using xPONENT software and seropositivity and levels of antibodies used for subsequent analyses. The spatial prevalence of IgGs to different antigen and malaria parasite species from diverse transmission facets will be determined and standard risk factor analysis performed using regression analysis. Bayesian hierarchical modelling to predict the risk of infection with *P. vivax* and other species in different transmission settings in Cameroon.

7997

ASSESSING HUMAN ANTIBODY RESPONSES TO THE *PLASMODIUM FALCIPARUM* RH5-CYRPA-RIPR INVASION COMPLEX; QUANTIFICATION OF RESPONSES TO THREE BLOOD-STAGE TARGET ANTIGENS

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Reticulocyte-binding protein homologue 5 (RH5) interacts with 4 other parasite proteins essential for *Plasmodium falciparum* invasion of erythrocytes. Of these, RH5, cysteine-rich protective antigen (CyRPA) and RH5-interacting protein (RIPR) have been the main targets of vaccine development and form a heterotrimeric complex called “RCR-complex”. RH5.1 is a protein immunogen based on RH5 and is the most advanced blood-stage *Pf* malaria vaccine candidate antigen. A Phase I clinical trial is now underway (NCT05385471) to investigate whether combining RH5.1 with a second fusion protein vaccine candidate called “R78C” (based on CyRPA and EGF domains 7-8 of RIPR), and formulated with 50µg Matrix-M adjuvant, can improve upon responses induced by RH5.1 alone with Matrix-M previously tested. We established a new standardised ELISA protocol to report anti-RCR total IgG responses to quantify human antibody responses in cohorts vaccinated with different antigen combinations targeting the wider RCR-complex. The standardised ELISA assay format involves coating the ELISA plate with equimolar amounts of the three full-length soluble antigens (RH5.1, CyRPA, and RIPR). A reference standard curve of high concentration human serum derived from volunteers vaccinated with R78C in combination with RH5.1 in Matrix-M allowed for a total response to the RCR-complex to be measured in arbitrary units (AU). This newly established human R+C+R ELISA enables analysis of antibody quantity versus functional assessment by growth inhibition activity (GIA) assay to indicate the relative quality of the vaccine-induced antibody response across all current blood-stage vaccine candidates in humans targeting the wider RCR-complex. This assay will enable important comparisons to inform future down-selection and advancement of the most promising *Pf* blood-stage vaccine candidates.

7998

IL-15 COMPLEX ENHANCES T RESIDENT MEMORY FORMATION AND FUNCTION FOLLOWING GENETICALLY ATTENUATED *PLASMODIUM* VACCINATION IN MICE

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Malaria, which results from infection with *Plasmodium* parasites, remains a major public health problem. With growing antimalarial drug and insecticide resistance, new therapeutic strategies and highly effective vaccines are urgently needed. Stopping *Plasmodium* infection at the liver stage prevents the disease-causing blood stage and transmission. While antibodies can mediate protection, liver resident memory T (Trm) cells will likely be required for robust and durable protective immunity to malaria. Memory CD8 T cells induced by whole sporozoite vaccination kill parasite-infected hepatocytes during the liver stage. Generating sufficient CD8 T cells in the liver that persist at high frequency is critical for liver stage-specific vaccine efficacy. Indeed, a vaccine adjuvant that specifically boosts liver Trm number and function could decrease the number of vaccine doses by increasing vaccine durability. Liver Trm formation is highly dependent on IL-15. Combining IL-15 with IL-15Rα to create an IL-15 complex (IL-15C) extends the half-life and mimics the interaction of IL-15 with its receptor components in vivo. Using a *Plasmodium yoelii* late liver stage-arresting, replication competent (LARC) genetically attenuated parasite (GAP) whole sporozoite vaccine model, we show that IL-15C increases the number of CD8 and CD4 Trm cells in the liver, increases IFN-γ production by splenic T cells, and increases *Plasmodium*-specific antibody levels. Furthermore, we found that IL-15C improves vaccine efficacy following challenge with sporozoites. In sum, IL-15C boosts Trm formation and/or maintenance, T cell effector function, as well as antibody production. Overall, our findings will facilitate improved control of malaria and protection from disease by informing vaccine design.

7999

UNDERSTANDING THE IMPACT OF LOW, MEDIUM AND HIGH MALARIA PRE-EXPOSURE STATUS ON SARS COV-2 -SPECIFIC ANTIBODY PROFILES AND FUNCTIONALITY IN TANZANIAN INDIVIDUALS

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Infection with SARS COV-2 remains a major global public health concern worldwide. So far, the sub-Saharan region reported relatively low number of SARS COV-2 cases and associated deaths compared to other settings. Tropical climate and exposure to various pathogens such as *Plasmodium* spp predominantly found in most sub-Saharan settings are among factors thought to contribute to these outcomes. *Plasmodium falciparum* in particular, has been linked to induction of immune modulation that likely influences immunity to other diseases as well as vaccination outcomes. However, the extent to which malaria infection or pre-exposure influences humoral SARS COV-2 specific immune responses has not been extensively explored. With the continued rise of variants of concern, it remains important to understand how endemic infections like malaria influence SARS COV-2 specific immunity and protection dynamics. In this study involving 249 SARS COV-2 positive and negative Tanzanian individuals, we investigated the impact of malaria pre-exposure status and systemic immune activation on the SARS COV-2 induced antibody profiles and functionality. Serum cytokine and chemokine concentrations and neutralizing activity were quantified *ex vivo* using a panel of validated legendplex and flowcytometry. Malaria pre-exposure was measured using anti-schizont ELISA and individuals characterized in low, medium and high titres. Data on breadth of SARS COV-2- induced antibody responses stratified by varying malaria exposure and immune activation status will be presented.

8000

ELUCIDATING THE KINETICS AND DYNAMICS OF GROWTH-INHIBITORY IMMUNE RESPONSES TO *PLASMODIUM FALCIPARUM* STRAINS

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Malaria, caused specifically by *Plasmodium falciparum* (*Pf*), is a major global health threat. Identification of conserved antigen targets proven to be true correlates of immune protection could be transformational. To do this, there is need to better understand the mechanisms underlying the development of natural immunity to malaria. We performed *in vitro* growth inhibition assays (GIA) using field-isolated *Pf* isolates to better understand the kinetics and dynamics of functional immune responses to merozoite antigens longitudinally, while considering natural genetic diversity of circulating parasite genotypes. Samples used were from a longitudinal study in Thiès, Senegal, a low endemic setting with mostly monogenomic infections. Patients with malaria were enrolled and followed for 2 years with plasma collected at 8 timepoints. *Pf* parasite isolates from day 0 infections were preserved and genomically characterized by a 24-SNP barcode. GIAs were performed with homologous (0 SNP) parasite strains from the individual's day 0 infection (n=21) and heterologous (8 SNP) parasite strains (n=17). Neutralizing antibody patterns for homologous strains longitudinally were identified as long persisting high inhibitory responses, inhibition that peaks at week 2 and declines to baseline, and long persisting low inhibitory responses. Mean differences in longitudinal neutralizing responses for individuals with long persisting high inhibitory responses were significantly higher than that of individuals with long persisting low inhibitory responses (95% CI 42.9-65.2, $p<0.001$). Comparing each individual's longitudinal neutralizing response from their day 0 homologous strain to a heterologous strain, 41% of all individual's responses to a heterologous strain were significantly decreased. Future work aims to identify merozoite antigens and antibody biophysical features that are associated with functional neutralizing immune responses. Understanding determinants of functional immune responses and the ability to generate strain-transcending responses will help to define immune correlates of protection and aid vaccine development.

8001

LONGITUDINAL RESPONSES IN THE TISSUES AND BLOOD OF NON-HUMAN PRIMATES DURING IMMUNIZATION WITH WHOLE *PLASMODIUM* SPOROZOITES

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A hallmark feature of malaria is that an individual can be repeatedly infected with the same *Plasmodium* species, and even the same parasite clone, with induction of little functional immunity. With years of exposures, the likelihood of symptomatic infection decreases and malaria becomes an often chronic, asymptomatic infection. The exact mechanisms underlying this complex immunology are incompletely understood, but involve a myriad of innate and adaptive immune responses from the host with numerous compensatory immune evasion tactics by the parasite. The impact of this broad immune regulation on vaccine responses is unclear, but the efficacy of live-attenuated whole sporozoite vaccines is clearly lower in malaria endemic areas. Studying this interaction between previous infection and vaccine responses in humans is difficult, owing to heterogeneity in exposure to parasites and inaccessibility of the tissues where much of the parasite infection and immunology occur. To address this, we have used a non-human primate model of malaria, *P. knowlesi* infection of macaques. We vaccinated with live sporozoites under chemoprophylaxis ("CVac") with or without previous infection as a means to study the interaction between infection and complex, tissue-resident immunity following vaccination. Using minimally-invasive tissue sampling, we studied the longitudinal immune response to infection and vaccination in n=16 animals. At multiple time points we sampled the liver, bone marrow, lymph nodes and spleen and analyzed these at the single cell level. Data collection is complete and analysis is ongoing. Our early analysis has demonstrated that the tissues hold unique immunological signatures as compared to the blood, and our strategy has allowed us to see the *in situ* cellular response to parasite infection/immunization in the liver by sampling early after sporozoite inoculation. We will present the latest findings with a focus on innate and innate-like cells as well as classic adaptive immune subsets and how these responses relate to previous exposure and protection from sporozoite challenge.

8002

TREATING CEREBRAL MALARIA IN AFRICAN CHILDREN, TRANSLATING MECHANISTIC INSIGHTS TO BEDSIDE RESULTS

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Mosquito-transmitted *Plasmodium falciparum* infections cause malaria, an infectious disease that is disproportionately fatal in young children in Africa. Malaria-associated fatalities are overwhelmingly caused by the most severe form of malaria, cerebral malaria (CM). CM does not adequately respond to intravenous antimalarial therapy and at present we have no adjunctive therapies to treat CM. The abundance of infected red blood cells observed accumulated in the cerebral vasculature of children that die of CM led to the dogma that brain-sequestered infected red blood cells were the lead cause of CM. A widely used mouse model of CM provided evidence that $CD8^+$ T cells play a critical role in pathogenesis but because few studies reported lymphocytes in human cerebral vasculature in CM, the findings in mice were largely ignored, stymying efforts to identify therapies that target human T cells in CM. Using the mouse model, we sought to identify drugs that rescued mice from CM even after disease onset including blood brain barrier breakdown and brain swelling. We also looked for clues that disease pathogenesis in mice closely mirrored human disease and discovered remarkable similarities between mice and humans in both the frequency and distribution of $CD8^+$ T cells in brains, and in brain pathology by MRI. Based on our findings we identified a strong candidate for CM therapy, DON, and initiated a Phase I/IIa clinical trial of DON as an adjunctive therapy for CM in African children in Malawi involving healthy adults, adults with uncomplicated malaria and children with CM. Thus far DON has proven to be safe in adults and we are poised to begin DON studies in children. We are also continuing studies to determine the cellular and molecular mechanisms underlying disease pathology and the role of immunologic responses along the CNS borders in the mouse using intravital imaging and multiparameter immune histochemistry with a view towards the development of future CM therapies.

8003

THE PUTATIVE RECEPTOR BINDING REGION IS THE IMMUNODOMINANT REGION OF PLASMODIUM MALARIAE RETICULOCYTE BINDING PROTEIN 1A

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The adoption of highly sensitive molecular diagnostic techniques has highlighted the underreporting of *Plasmodium malariae* infections. *P. malariae* has been linked to severe complications, including nephrotic syndrome, cholecystitis, and fatal anemia. The mechanisms behind these complications remain poorly understood. Moreover, the oversight of *P. malariae* in malaria elimination programs may contribute to the continued prevalence and spread of this parasite. Among the P. malariae reticulocyte binding proteins (*Pm*RBPs), *Pm*RBP1a is notably distinct, suggesting its potential role as a critical factor in host specificity and a key mediator in erythrocyte invasion. To explore this, the large antigen was segmented into five fragments, carefully preserving functional domains. These fragments were then expressed, purified, and assessed for the presence of acquired antibodies using indirect ELISA in human plasma samples collected from four localities in Ghana: Akwakrom, Kintampo, Navrongo, and Suhum. Seropositivity was high across the fragments, indicating significant exposure: 70% for fragment one, 62% for fragment two, 65% for fragment three, 57% for fragment four, and 58% for fragment five, compared to 85% for *Pf*DBL-2 and 61% for *Pf*Rh5. Notably, fragment one, which contains the putative receptor-binding domain, showed the highest antibody levels, underscoring its importance in host-pathogen interactions. Additionally, antibody responses correlated positively but marginally with age and exposure, particularly for fragment one again. This data not only reveals a higher exposure to *P. malariae* than previously reported but also emphasizes the need for further research into the receptor-binding domain. Future studies should also investigate the cross-reactivity of these antibodies with homologous antigens in other Plasmodium species.

8004

CHARACTERIZATION OF COINFECTION WITH SOIL TRANSMITTED HELMINTHS CAUSED BY *PLASMODIUM VIVAX* BASED ON CITOKINE BALANCE IN A CHILD POPULATION FROM AN ENDEMIC AREA OF COLOMBIA

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Characterizaction of *Plasmodium vivax* geohelminth coinfection from the cytokine balance in a child population in a Colombian endemic area.The balance of the immune response mediated by the plasma balance of pro/anti-inflammatory cytokines in the infantile population

of an endemic area for geohelminths - *P. vivax* coinfection allows to know its behavior in front of the coinfection, which through antagonistic answers consent the homeostasis of the immune system. The effect of geohelminths - *P. vivax* coinfection on the balance of pro/anti-inflammatory cytokines in children population of Colombian endemic area was measured. An analytical observational study was carried out, fifty-eight (58) children were selected and studied in two groups (coinfected and control). Stool samples were processed by Kato Katz for identification and quantification of geohelminths and blood plasma was used for flow cytometry quantification of cytokines and chemokines. The prevalence of confection was 46% (33.1-58.8). When comparing cytokines and chemokines between groups, those of the proinflammatory profile IL-6 (19.4(14.7-83.9)P<0.0001), IFN-γ (98.8 (6.8-20.4)P<0.0001) and IP-10 (1036 (159. 4 - 2611)P<0.0001) showed higher concentrations in coinfected than in controls; as did the anti-inflammatory cytokines IL-10 (121.4 (49.7 - 1654)P<0.0001) and TGF-β (162.4 (13.5 - 412.1)P= 0.0007). The results of IL4 (4.3 (3.7 - 5.4) P= 0.0354) did not show biologically important elevation in plasma concentrations in the coinfected children; which supports the idea that the concentrations of this cytokine depend on the levels of host parasitemia, in this study it was found that both geohelminths and *P. vivax* in the coinfected group had mild to moderate intensities of infection. In conclusion, cytokine and chemokine variations of proinflammatory and anti-inflammatory profiles in coinfected individuals exhibit marked increases in IL10 concentration when individuals are infected with *P. vivax*, acting as a regulator of the expression of these molecules; geohelminths do the same with increased plasma concentration of TGF-β1.

8005

PLASMODIUM INFECTION AND ANTIBIOTIC USE DURING SEVERE MALARIA INDUCE GUT BACTERIA DYSBIOSIS THAT INCREASES THE RISK OF MORTALITY IN CHILDREN

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The gut microbiome has been implicated in malaria pathogenesis in murine models and limited cross-sectional human studies. However, it remains unknown if severe malaria impacts the gut microbiome in humans or if the gut microbiome contributes to the pathogenesis of severe malaria in African children. To investigate how the gut microbiome contributes to severe malaria, we analyzed gut bacteria populations in stool samples from children under 5 years old collected during hospital admission for severe malaria in 449 children and 71 healthy age-matched community children in Uganda. Differential bacterial abundance analysis revealed that the Enterobacteriaceae family was elevated in children with severe malaria as well as Bacteroides, Enterococcus, and Parabacteroides genera. Expansion of Enterobacteriaceae was associated with death in children with severe malaria and was found to mediate death through multiple comorbidities like lactic acidosis and intestinal damage. The Enterobacteriaceae family contains potential pathogens including Shigella, Escherichia, Klebsiella, Enterobacter, and Salmonella that can cause serious complications if they enter the bloodstream. Of the children with positive blood cultures, over half of the bacteria were members of the Enterobacteriaceae family. Factors associated with the expansion of these bacteria include prior antibiotic use, increased time since eating, neutrophil abundance, and hemeoxygenase-1. Increased inflammation and changes in the nutrient niche through the removal of commensals and enhanced oxygen and nitrogen respiration may support the expansion of Enterobacteriaceae. Consistently, metagenome sequencing confirmed the potential for aerobic respiration of alternative carbon sources in Enterobacteriaceae in children with severe malaria. Collectively, severe malaria is associated with gut bacteria dysbiosis, including the expansion of Enterobacteriaceae that may contribute to severe malaria-related deaths. Treatments that prevent the expansion of or target Enterobacteriaceae may help reduce mortality in children with severe malaria.

8006

VAR2CSA EXPRESSION IN CEREBRAL MALARIA IN MALIAN AND MALAWIAN CHILDREN

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VAR2CSA is the most conserved *Plasmodium falciparum* erythrocyte membrane protein-1 (PfEMP1) antigen and mediates binding to chondroitin sulfate A in placental malaria. Recent studies have found that *var2csa* transcription may also reflect *var* switching and regulation. To identify PfEMP1 variants expressed in severe malaria, we conducted a case-control study in children in Mali, West Africa from 2014-2018. We enrolled cases of cerebral malaria (CM), severe malarial anemia (SMA), concurrent CM+SMA, and matched uncomplicated malaria controls with or without a history of CM. Using RNA-seq and *de novo* assembled transcripts, we identified PfEMP1 transcripts expressed in clinical infections and quantified expression by calculating the metric transcripts per million. *var2csa* transcripts were present in more than half (62%) of infections. Across all severe malaria cases, we found significantly greater expression of *var2csa* compared to controls without a history of CM (Wilcoxon signed-rank test, N=34 pairs, P=0.0096) and controls with a history of CM (N=18 pairs, P=0.016). Unique *var* transcript count within each infection was significantly higher in severe malaria cases compared to both control groups (without history of CM: P=0.0075; with history of CM: P=0.0038). In the CM subset, there was significantly greater expression of *var2csa* compared to controls without a history of CM (N=14 pairs, P=0.00061) but not compared to controls with a history of CM (N=8 pairs, P=0.27). Unique *var* transcript count was significantly greater in CM compared only to controls without a CM history (P=0.049). Interestingly, we did not observe any significant differences in *var2csa* expression in SMA or CM+SMA cases compared to matched controls. We detected levels of *var2csa* expression in Malawian children with CM (9/10 cases) that were similar to that in Malian CM cases. Significant expression of *var2csa* in CM may reflect higher rates of *var* switching, which could allow infection to persist. Further investigation of *var2csa* in CM may provide insights into how patterns of *var* expression contribute to disease severity.

8007

CIRCULATING PLATELET-LEUKOCYTE AGGREGATES CORRELATE WITH THROMBOCYTOPENIA AND DEATH IN PEDIATRIC CEREBRAL MALARIA

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Cerebral malaria (CM) is a severe manifestation of malaria that is characterized by coma and seizures. Parasite load, virulence factors, host-derived molecules and cellular interactions contribute to pro-inflammatory mechanisms leading to pathophysiological exacerbation. Monocytes and platelets are independently implicated in the pathogenesis of CM and

found at sites of parasite sequestration in the brain microvasculature. Platelet-Monocyte Aggregates (PMA) in the periphery serve as a marker of platelet activation and inflammation. Increased levels of PMA are associated with severity in cardiovascular disease, autoimmune disease, and other infections (Dengue, HIV, tuberculosis, sepsis and COVID-19). Using flow cytometry, we analyzed circulating PMA and circulating activated platelets (aPLT) in the blood of children with CM (N=45) relative to children with uncomplicated malaria (UM, N=45). Levels of both PMA (%CD41+ monocytes/total monocytes) and aPLT (%CD62p+/total platelets) were lower in the blood of CM patients relative to UM patients (PMA: 23% vs. 51.1%, p=0.001; aPLT: 7% vs. 12%, p=0.01). In CM cases, PMA levels correlated positively with aPLT levels (R_s=0.53, p=0.001), with platelet count (R_s= 0.67, p<0.001), and with soluble CD62p, an acute phase marker of platelet activation (R_s=0.51, p<0.001). PMA and aPLT levels were inversely related to levels of TNFα, a marker of inflammation (R_s=-0.45, p=04), and host cell-free DNA levels (R_s=-0.47, p=0.04), a marker of NETosis which we have previously shown to be associated with death, and with parasitemia (R_s=-0.47, p=01). Logistic regression analysis associated decreased levels of PMA (LR=3.97, AUROC=0.731, p=0.046) and aPLT (LR=5.39, AUROC=0.791, p=0.02) with death in CM patients. Collectively, these data suggest platelet activation and coagulation processes occur early in acute malaria with platelet consumption as inflammation progresses during severe disease. The inverse relationship between platelet activation and disease severity, different from that seen in other pathologies, emphasizes the unique role of consumptive coagulopathy in the pathogenesis of CM.

8008

INVESTIGATING THE ROLE OF HOST C1QBP IN *PLASMODIUM FALCIPARUM* INFECTED ERYTHROCYTE BINDING TO HUMAN BRAIN MICROVASCULAR ENDOTHELIAL CELLS

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Sequestration of *P. falciparum* infected erythrocytes in human brain microvasculature is the hallmark of cerebral malaria. Sequestration is mediated by the interaction between *P. falciparum* erythrocyte membrane protein one (PfEMP1) family members and receptors expressed on human endothelial cells. Severe and cerebral malaria are associated with the expression of specific PfEMP1 subtypes, while the identity of the key host receptors involved in brain sequestration remains controversial but may include endothelial protein C receptor (EPCR) and intercellular adhesion molecule one. Previous work suggests that C1q Binding Protein (C1QBP) may also play a role in sequestration in the brain, but this has rarely been studied. In this study, we used a) immunofluorescence assays to examine the cellular localization of C1QBP and b) adhesion experiments to determine the role of C1QBP in *P. falciparum* infected erythrocyte (IT4VAR19 and HB3VAR03) adhesion to the human brain microvascular endothelial cell (hCMEC/D3). Resting and TNFα-activated hCMEC/D3 showed intracellular staining for C1QBP but cell surface staining was not observed. However, incubation with soluble C1QBP or human plasma (which contains soluble C1QBP), hCMEC/D3 did exhibit positive surface membrane expression of C1QBP. In static binding assays to purified receptors, IT4VAR19 showed low-level but consistent binding to C1QBP and high-level binding to EPCR. Adhesion inhibition assays showed that a monoclonal antibody (mAb) to EPCR blocked the interaction between IT4VAR19 and hCMEC/D3, whereas a mAb to C1QBP did not. HB3VAR03 did not bind to C1QBP, nor to any other known endothelial receptors in the static assays, despite showing good binding to hCMEC/D3 cells. C1QBP is not constitutively expressed on the surface of human brain endothelial cells but can become membrane-associated after exposure to human plasma. However, the *P. falciparum* lines tested here did not show high level binding to C1QBP and their adhesion to human brain endothelial cells was not substantially inhibited by a mAb to C1QBP. Overall, the results do not support C1QBP being a key host receptor in cerebral malaria.

8009

CHILDREN WITH CEREBRAL MALARIA LACK IMMUNITY TO SPECIFIC RIFIN AND STEVOR ANTIGENS

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In severe malaria, *Plasmodium falciparum* parasites sequester in the microvasculature and adhere to erythrocytes, processes mediated by variant surface antigens. Protection against severe malaria is associated with antibodies targeting parasite antigens and host traits like blood type O. The roles of the RIFIN and STEVOR antigen families in severe malaria and their interactions with host ABO blood antigens remain poorly understood. We hypothesized that severe malaria cases exhibit lower antibody responses to virulence-associated RIFIN-A and STEVOR variants than uncomplicated malaria controls during acute infection, indicating immune deficits that may predispose children to severe outcomes. These "gaps" may vary by disease phenotype and ABO blood type. We analyzed sera from 236 Malian children aged 0-14 years enrolled in a 1999-2003 severe malaria case-control study, including 67 age-matched pairs. Severe cases had cerebral malaria (CM; 37 pairs), severe malarial anemia (SMA; 20 pairs), or a syndrome featuring both CM and SMA (CM+SMA; 10 pairs). We used protein microarrays to measure serological responses to 116 RIFIN-As, 51 RIFIN-Bs, and 35 STEVOR variants, including 189 3D7 and 13 non-3D7 sequences. Antibody gaps were defined as statistically significant seroreactivity deficits in cases vs. controls (p-value < 0.05), assessed using paired Wilcoxon tests or unpaired, age-adjusted linear regressions. Sera of CM cases had antibody gaps against 16 RIFIN-As, including two variants that inhibit B cells via LILRB1 binding, and two RIFIN-Bs. CM+SMA cases had gaps against two RIFIN-As, four RIFIN-Bs, and eight STEVORs. SMA cases had no significant gaps to RIFINs or STEVORs. CM cases with blood type O (n=7) had gaps against 37 RIFINs and two STEVORs vs. unmatched type O controls, including two LILRB1-binding RIFIN-As and one RIFIN-A involved in rosetting. CM cases with non-O blood (n=25) had no gaps to RIFINs or STEVORs. Antibody gaps to RIFIN and STEVOR antigens varied significantly by malaria syndrome and host ABO blood type. Our future serologic and transcriptomic studies will continue to decipher these complex host-pathogen interactions.

8010

DECIPHERING THE HOST RESPONSE TO *PLASMODIUM FALCIPARUM* BY PLASMA PROTEOMICS

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Plasmodium falciparum malaria may present with a wide range of disease severity, depending, among other factors, on genetic background and previous exposure to the parasite. Here, we applied high-throughput LC-MS/MS plasma proteomics to identify signatures of disease severity and varying immunity in 263 malaria patients from an endemic region and returning travellers, including 25 asymptomatic (APF), 180 uncomplicated (UPF), and 58 severe (SPF) cases with varying degrees of semi-immunity (i.e., childhood and residency in an endemic region, previous malaria episodes), as well as healthy controls (HC). Patients were enrolled in two prospective cohort studies at Centre de Recherches Médicales de Lambaréné (CERMEL), Gabon, and Charité - Universitätsmedizin Berlin, Germany. Clinical data and samples were collected at d0, d3, d7, and d14. Of 330 detected proteins, 209 were differentially regulated depending

on disease severity, mainly reflecting the acute phase response (e.g. SAA1, AHSG), immune reaction (e.g. C1, immunoglobulins), and tissue reconstitution (e.g. GSN, EFEMP1). The degree of dysregulation generally correlated with severity, reflecting a continuous increase in the host response. Notably, many protein levels were similar in APF and HC. In UPF, proteome alterations were more pronounced in patients in Germany: numerous markers associated with inflammation (e.g. LBP, SAA1) were significantly lower in patients in Gabon than in Germany, regardless of descent, and proteins associated with milder disease (e.g. GSN) were higher, indicating a modulated immune response in frequently exposed patients. Applying an SVM-based machine learning (ML) classifier, we were able to accurately distinguish between disease severities and immunity. Combining plasma proteomics and routine clinical data with ML techniques allows for better understanding of the specific host response to P.f. malaria in different populations with varying degrees of immunity. This is especially important in light of increasingly effective management of malaria and consequently less exposure and waning semi-immunity in formerly endemic regions.

8011

HYPERPARASITAEMIA: A CONSISTENT PRESENTATION IN *PLAMODIUM FALCIPARUM* MALARIA IN THE UK SINCE COVID

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Malaria caused around 240 million cases and over 600,000 deaths in 2020, a marked increase on 2018-19, largely attributable to the COVID-19 pandemic.. Although most malaria deaths occur in endemic countries, imported malaria in the UK continues to cause avoidable deaths.
The UK Health Security Agency (UKHSA) Malaria Reference Laboratory (MRL) runs a passive case detection system. All notified malaria cases are initially diagniosed by blood film microscopy or rapid diagnostic tests at the referring hospital. For subsequent confirmation and/or diagnosis by the MRL, thick and thin blood films for microscopy and an aliquot of EDTA blood for molecular analyses and archiving are requested from the referring hospital. The MRL carries out retrospective qPCR molecular surveillance on all received blood samples to confirm species and drug resistance genotypes in relation to geographical origin. For each notified case, demographic, clinical and epidemiological data supplied are entered onto a database by MRL staff. From mid-2020 onwards we noticed increased numbers of cases with high parasitaemia (>2%) and hyperparasiatemia (>5%) presenting, a post-pandemic trend which has continued. To investigate, we analysed all *available P. falciparum*-positive blood samples received by the MRL from Jan 2019 to Dec 2022. We used an in-house probe-based qPCR protocol targeting the 18S rRNA gene, normalised to the WHO International Standard for P. falciparum DNA, to estimate *P. falciparum* parasitaemia in all samples. Results were compared with estimated parasite densities from microscopy, available for only a subset of blood samples. For data analyses, samples were separated into pre- (n=1332) and post-pandemic (n=2022) using 1st March 2020 as pivotal date. We present data from 3,354 successfully quantified UKHSA MRL samples collected during this period. Our results suggest an increase in the prevalence of P. falciparum hyperparasitaemia among notified UK malaria cases from the coronavirus pandemic onset until the present time. Risk factor analysis for hyperparasitaemia in this patient group will also be presented.

8012

PLASMODIUM FALCIPARUM ESTABLISHES CHRONIC INFECTIONS THROUGH HIGH *VAR* GENE EXPRESSION SWITCHING RATE

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How can *Plasmodium falciparum* parasites evade the immune system for months to establish long chronic asymptomatic infections? The prevailing hypothesis, mainly based on *in vitro* data from cultured parasites, is the antigenic variation of *var* genes, a family encoding PfEMP1 antigens located at the surface of the erythrocyte. The parasite would regularly switch between the expression of one of its ~60 *var* genes, therefore escaping the immune response built from pre-existing host antibodies. Here, in a study conducted in The Gambia where malaria is seasonal, we investigated the pattern of *var* gene expression in 26 *P. falciparum*-infected individuals during the wet season and in 16 chronically-infected individuals with 6 monthly blood samples. *Var* transcription was determined by amplicon sequencing of the semi-conserved *var* DBLa domain. In parallel, full length *var* gene sequences were retrieved from DNA long-read sequencing (PacBio). The Shannon entropy index, which measures the breadth of *var* gene expression within an isolate, was significantly lower in the dry season compared to the wet season, suggesting of immune selection pressure. Thanks to the longitudinal monthly timepoints, we observed distinct *var* gene transcription patterns from one month to the next, indicating a high *var* turnover rate. Against expectations, our investigation of monoclonal infections revealed the widespread presence of *var* genes that were recurrent, i.e. expressed at multiple timepoints within the same infection. These results suggest that a pattern of low *var* gene immunogenicity could contribute to the establishment of long chronic asymptomatic malaria infections, with parasites populations capable of re-utilizing a subset of their *var* genes throughout the infection.

8013

TRANSCRIPTIONAL ANALYSIS OF DIFFERENTIALLY EXPRESSED GENES AND PATHWAYS IN THE DEVELOPMENT OF SEVERE MALARIA

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The occurrence of malaria in immune-naïve individuals or individuals with low immunity can be severe and lethal. The severity of malaria is partly due to an excessive pro-inflammatory immune response and the virulence of *Plasmodium*. *Plasmodium falciparum* parasites that cause severe malaria are mainly a subpopulation expressing specific *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) which binds endothelial protein C receptor (EPCR) on endothelial cells. Peripheral blood mononuclear cells (PBMCs) are comprised of lymphocytes and monocytes that are differentiated and activated by inflammatory and pathophysiological conditions including febrile temperature, pipecolic acid (PA) & depleted lysophosphatidylcholine (LPC) and they equally affect the expression of PfEMP1. Can *P. falciparum* sense if there is immune pressure & alter its virulence phenotype? We will assess the differential transcriptional responses that occur in an *in vitro* system that mirrors blood-stage infection in malaria. Using a co-culture model, we will evaluate the transcriptome of pooled PBMCs from malaria-naive individuals or semi-immune individuals and parasites isolated from children with severe malaria. The PBMCs and parasites will be grown on a layer of human dermal endothelial cells expressing EPCR. Co-culture will be repeated in the presence of PA and depleted LPC. RNA sequencing of the PBMCs and parasites, and bioinformatics analysis of the resulting immunological and parasite responses will identify genes and pathways

involved in the regulation of anti-disease immunity and parasite adaptation to immune pressure. Our findings will help in the identification of modifiable host and parasite factors involved in the development of severe malaria. Our preliminary findings show that in the presence of endothelial cells majorly expressing EPCR, heat shock can increase the expression of PfEMP1 EPCR-binding domain, CIDR α1.5a, in the parasite. We did not see the impact of the immune cells used in the co-culture because we were only able to use immortalized monocytes/macrophages. Further studies of this parasite-host immune interaction are ongoing.

8014

UNDERSTANDING HOW VARIABILITY IN CULTURE TECHNIQUE IMPACTS THE LEVEL OF OXYGEN TENSION IN *PLASMODIUM FALCIPARUM* IN VITRO STUDIES

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Plasmodium falciparum is exposed to variations in environmental oxygen during its development within different organ systems having different oxygen concentrations, in humans. The effect of this oxygen tension variation within-host on the parasite is not well understood. Foundational work done for making in vitro study of the parasite possible established that the parasite thrives best in lower oxygenated environments, making it a microaerophilic organism. This allowed researchers to be able to study the parasite in the lab and to date, the technical execution of in vitro parasite studies varies considerably by research groups. The range of culture containment devices and oxygen administration methods used are grounded in feasibility in maintaining long-term culture. What is not often considered is the effect of these devices on the dissolved oxygen concentration reaching the parasite cultures and the impact that variable oxygen tension has on parasite multiplication rate. We tested different containment devices and assessed the dissolved oxygen concentration of the parasite cultures for those contained in plugged flasks, in petri dishes within modular chambers, and for cultures contained within a tri-gas incubator with 1% O2 and 13% O2 administered to the parasite cultures. We also quantified the amount of oxygen binding to hemoglobin within erythrocytes of these parasite cultures via a colorimetric plate reader assay measuring the amount of oxyhemoglobin, deoxyhemoglobin, and methemoglobin. Furthermore, we measured parasite multiplication rate (PMR) in each condition to determine how oxygen conditions in culture impacted growth rate. Gaining a better understanding of oxygen diffusion within parasite culture will contribute to an enhanced understanding of how oxygen variation impacts the parasite's biology.

8015

IMPACTS OF CONCURRENT SEVERE MALARIA AND ENTERIC INFECTION ON CHILD HEALTH OUTCOMES

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Malaria and enteric infection - which may cause diarrheal disease - are major global health challenges and leading causes of childhood mortality and morbidity. There is a critical need to advance our understanding of the role that concurrent enteric infection and severe malaria has on child mortality and morbidity. These co-infections present a complex challenge in the management of severe malaria, as they may exacerbate the severity of the disease. Limited studies, which have typically focused on helminths, have shown that concurrent infections may modulate the host's immune response to *Plasmodium falciparum*, potentially contributing to deleterious long term health effects among children. We tested stool samples from children diagnosed with severe Malaria in Uganda to advance our understanding of these co-infections on health outcomes. From 2014 to 2017 we enrolled 598 children with severe malaria and 120 matched community controls ages 6 months to 4 years. Enrollment was conducted at Mulago National Referral Hospital in Kampala and Jinja Regional Referral Hospital in Uganda. At enrollment we collected stool and whole blood and characterized severe malaria by type. We followed up with children 12-months later and collected anthropometry data and assessed neurodevelopment via standardized tests. We analyzed a subset (n = 213) of the collected samples for 30 common enteric pathogens using real-time quantitative PCR. Among the 213 fecal samples analyzed, including children with severe malaria (n=188) and community controls (n=25), nearly all were positive for ≥1 bacterial pathogen (96%), followed by ≥1 protozoan pathogen (75%), and ≥1 viral pathogen (26%). Common enteric infections included Enteroaggregative *E. coli* (60%), *Giardia* (54%), *Cryptosporidium* (27%), *Campylobacter jejuni/coli* (24%), and *Shigella* (15%). We also detected *Plasmodium* spp. DNA in 28% of stools. Our planned analysis includes regression modelling to assess the impacts of co-infection by *Plasmodium falciparum* and enteric pathogens on long-term health outcomes (cognition, growth, and weight).

8016

THE IMPACT OF FALCIPARUM MALARIA INFECTION ON THE BRAIN: NEW FINDINGS FROM AN INDIAN COHORT

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Cerebral malaria (CM) is an acute nontraumatic encephalopathy and the most severe neurological complication of *Plasmodium falciparum* infection. Mortality is high, long-term neurocognitive deficits are frequently reported in pediatric survivors, and the pathogenetic mechanisms leading to CM are still debated. However, the recent application of advanced neuroimaging techniques to patients with CM has revolutionized our understanding of the disease. Over the past 8 years, our team has recruited severe and uncomplicated falciparum malaria patients at Ispat General Hospital in Rourkela, India. We combined serial brain magnetic resonance imaging (MRI) with cutting-edge clinical and laboratory investigations to better understand the factors influencing the development and outcome of CM. We demonstrated distinct pathogenic mechanisms in pediatric and adult CM and evidenced for the first time a frequent brain involvement in uncomplicated malaria and severe, non-CM patients. In the latter group, ~20% had MRI signatures associated with CM despite the absence of coma; this feature was strongly associated with the occurrence of acute kidney injury. Brain involvement in these patients was confirmed by elevated circulating levels of S100B and UCHL-1, two markers of brain damage and neuronal injury, respectively. Overall, our findings suggest that brain involvement is common in *P. falciparum* infection, which warrants closer neurocognitive follow-up, especially in adults.

8017

ROLE OF *PLASMODIUM FALCIPARUM* HEMOZOIN-ASSOCIATED PROTEINS IN THE PATHOGENESIS OF CEREBRAL MALARIA

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One of the hallmarks of cerebral malaria, a severe complication of *Plasmodium falciparum* infection, is the adhesion of *P. falciparum*-infected red blood cells (iRBCs) to the microvasculature of the brain, which is frequently accompanied by the weakening of the junctions between endothelial cells lining the blood-brain barrier (BBB), resulting in vasogenic edema. We have observed that incubation of human brain microvascular endothelial cells (HBMECs) with iRBCs *in vitro* results in the disruption of endothelial intercellular junctions and loss of barrier integrity. We have also observed that the rupture of iRBCs and release of its contents is necessary for the endothelial barrier disruption. Removing hemozoin, a heme crystal

that is formed during the blood stage of the parasite's life cycle, eliminates the iRBC lysate's ability to disrupt intercellular junctions in HBMECs. Furthermore, natural hemozoin purified from *P. falciparum*-iRBCs disrupts intercellular junctions in HBMECs, indicating that hemozoin carries the ability to induce the loss of barrier function in the brain endothelium. We also observed that, while natural hemozoin actively induces endothelial barrier disruption, commercially-available synthetic hemozoin does not have this effect. Since a variety of biomolecules including proteins, lipids, and nucleic acids from *P. falciparum*-iRBCs are bound to natural hemozoin, but not to synthetic hemozoin, we hypothesize that the biomolecules associated with natural hemozoin are required for endothelial barrier disruption. Further, treatment of the natural hemozoin with proteases inhibits endothelial barrier disruption, indicating that a protein bound to the hemozoin is contributing to this effect. To identify the protein(s) responsible for endothelial barrier disruption, fractionation of the hemozoin-bound proteins followed by quantitative mass spectrometry will be conducted. Further elucidating the mechanism behind brain endothelial barrier disruption in cerebral malaria may lead to the development of targeted therapeutics which could drive down the high morbidity and mortality rates of this complication.

8018

PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF MONTHLY TAFENOQUINE IN HEALTHY VIETNAMESE VOLUNTEERS FOR MALARIA PROPHYLAXIS AND ELIMINATION

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Tafenoquine (TQ) is used for the radical cure of *Plasmodium vivax* infections and prevention of malaria. Because of TQ's favourable pharmacokinetics (e.g., elimination half-life ~15 days) the drug possesses attributes for monthly dosing to enhance drug adherence. We report on blood TQ concentrations to generate a pharmacokinetic (PK)/pharmacodynamic (PD) model of TQ in healthy Vietnamese volunteers participating in a TQ dose-escalating study. Participants received consecutively three TQ regimens: Regimen 1 (loading dose of 200 mg x 3 days, then two weekly 200 mg doses), Regimen 2 (two monthly 600 mg doses) and Regimen 3 (two monthly 800 mg doses). Adverse events (AEs) were recorded. Participants were randomized to two cohorts (A and B). Cohort A had sparse PK sampling during 1st weekly and 1st monthly dosing and cohort B had PK sampling during 2nd weekly and 2nd monthly dosing. A total of 193 participants were enrolled (97 (50.3 %) males, mean age 26.8 years and mean body weight 58 kg). Of these, 165 participants completed Regimen 1, 132 completed Regimen 2, and 107 completed either the 1st or 2nd monthly dose of Regimen 3. Blood TQ and 5,6 orthoquinine TQ concentrations were measured by liquid chromatography mass spectrometry (LCMS). Of the 107 participants that received Regimen 3, steady-state mean (±SD) maximum and minimum blood TQ concentrations, respectively, were 626 ± 120 ng/mL and 416 ± 71 ng/mL after the 1st weekly 200 mg dose, 953 ± 182 ng/mL and 269 ± 58 ng/mL after the 1st monthly 600 mg dose, and 970 ± 241 ng/mL and 286 ± 62 ng/mL after the 1st monthly 800 mg dose for cohort A participants (n=53). Corresponding values for cohort B participants (n=54) were 628 ± 140 ng/mL and 421 ± 98 ng/mL after the 2nd weekly 200 mg dose, 821 ± 217 ng/mL and 221 ± 81 ng/mL after the 2nd monthly 600 mg dose, and 1,025 ± 179 ng/mL and 291 ± 61 ng/mL after the 2nd monthly 800 mg dose. Metabolism of TQ to 5,6 orthoquinine TQ was low (1.1 ± 0.3%). AEs were few, mild and transient, with an incidence of vomiting: 0.9% for Regimen 1, 1.9% for Regimen 2 and 4.7% for Regimen 3. LCMS and AE analysis is ongoing for all participants. PK/PD modeling will be reported for AEs, TQ dose and regimen optimization.

8019

THE EFFECT OF ADDITIONAL DOSES OF SULFADOXINE-PYRIMETHAMINE ADMINISTERED AS PERENNIAL MALARIA CHEMOPREVENTION (PMC) ON HEMOGLOBIN LEVELS AMONG CHILDREN IN A MALARIA ENDEMIC AREA OF CAMEROON

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The World Health Organization recommends the provision of perennial malaria chemoprevention (PMC) with sulfadoxine-pyrimethamine (SP) to children who are resident in areas of high malaria transmission. While SP can reduce malaria in children, thereby indirectly increasing hemoglobin levels, this effect isn't always consistent, especially in areas with high drug resistance or varying SP dosing regimens. Thus, the evidence base remains unclear regarding the impact of PMC with SP on hemoglobin. We began an open-cohort study of children aged 6-9 months in two Cameroon sites, Soa and Mbankomo, July 2023. Children receive SP at health facilities as part of their normal expanded program on immunization (EPI) schedule with eight total SP in Soa (intervention) and up to five doses in Mbankomo (control) according to Cameroon's National Malaria Programme (NMP). Children are followed up every 3-months for up to 7 visits; all doses of SP received through the PMC program at the facility were recorded. At each household visit, parents of all consenting children completed a questionnaire and children had their hemoglobin levels measured by Hemocue. Linear mixed effects models were utilized for analysis to account for within-subject variation and for missing visits. Preliminary results, based on 748 of 2080 targeted children over three follow-up visits, revealed a dose-dependent effect of SP on hemoglobin levels over time. After adjusting for child age, each additional dose of SP resulted in an average increase of hemoglobin levels of 0.06 g/dL (95% CI: 0.01-0.11; p=0.016). Currently, PMC planning focuses primarily on known antimalarial effects. This study will provide valuable insight for policymakers and NMPs regarding potential further health effects on hemoglobin from receiving additional doses of SP as PMC.

8020

COMMUNITY ACCEPTANCE OF A NOVEL MALARIA INTERVENTION, ATTRACTIVE TARGETED SUGAR BAIT (ATSB) STATIONS, IN THE CONTEXT OF THE ATSB ZAMBIA PHASE III TRIAL

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Community acceptance is acknowledged as an important criterion to assess in community trials, particularly for new tools that require uptake by a target population. Acceptability is also an important indicator of the feasibility of scaling-up a new tool and the level of community engagement required for the tool to be successful. Installed on exterior walls of

household structures, the attractive targeted sugar bait (ATSB) is a new tool for malaria vector control designed to attract and kill mosquitos. ATSBs were evaluated in Western Zambia during a two-year phase III cluster randomized controlled trial to assess the efficacy of ATSBs in reducing malaria transmission. Community acceptance of ATSBs was critical for successful trial implementation. A community engagement strategy was developed to outline routine and response activities to deliver key messages to promote acceptance. Annual cross-sectional surveys assessed households for presence of ATSBs and measured perceived benefits, concerns, and willingness to use ATSBs. Results suggest that community acceptance and acceptability of ATSBs was high with ATSB coverage >90%, >70% of households reported perceived benefits, and <10% reported safety concerns. Focus group discussions (FGDs) and in-depth interviews (IDIs) were conducted at the end of each ATSB deployment period to obtain a range of experiences with ATSBs. Common facilitators identified in FGDs/IDIs included the desire for protection against malaria and reduction of mosquitos, trust, and understanding of the product. Common barriers identified in FGDs/IDIs included misconceptions of product impact on mosquitos, continued cases of malaria, association with satanism, perception of "attracting" mosquitos, and damage to household structures. Future introduction and scale-up of ATSBs will likely require supporting interventions aimed at fostering community acceptance and acceptability. This presentation will describe ATSB acceptance and acceptability in the trial context, household survey and qualitative results, the community engagement strategy for ATSB acceptance, and implications on future ATSB scale-up.

8021

SEASONAL MALARIA CHEMOPREVENTION (SMC) ELIGIBILITY ANALYSIS AND IMPACT EVALUATION USING MATHEMATICAL MODELING TO GUIDE DECISIONS ON THE IMPLEMENTATION OF SMC IN GUINEA

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In areas where malaria transmission is seasonal, as in Guinea, WHO recommends SMC in children under 5 (CU5). In 2015, Guinea introduced SMC in 6 districts, followed by a gradual expansion to 17 districts by 2020. In Guinea, SMC is organized into 4 monthly cycles between July and October in 16 districts, and 5 monthly cycles in just one district (Dabola). . The National Malaria Control Program (NMCP) has recently considered extending SMC geographically to identify new eligible districts, as well as others districts that could benefit from a 5th cycle of SMC. A seasonality analysis based on rainfall data and malaria cases reported by routine surveillance was carried out using an algorithm to answer this question. A mathematical model was used to predict the impact of SMC extension and the number of preventable malaria cases by introducing an additional cycle in either June or November. Three new districts - Telimélé, Kissidougou and Kérouané - were identified as eligible for SMC extension due to their high incidence in children and favorable seasonal patterns. Mathematical modelling estimated that the potential impact of the extension, with a projected coverage of 80% in the new districts, would prevent more than 450,000 cases of malaria and nearly 700 deaths in CU5 between 2023 and 2027. Cross-analysis of meteorological and case data showed that a 5th cycle in November rather than June would be more beneficial. In all districts, the proportion of cases occurring in November was higher than in June, suggesting that a fifth cycle in November would prevent more cases. The NMC used these results to lobby its partners to mobilize resources to finance this extension.

8022

ASSESSMENT OF THE MALARIA SCORECARD'S IMPACT ON HEALTH OUTCOME THROUGH HOME-BASED MANAGEMENT IN RWANDA

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Today malaria continues to represent a real public health concern in Rwandan and continue to implement integrated different malaria control interventions including LLIN distribution through mass campaigns and routine channels, IRS, behavior change communication, and improved access to diagnostics and treatment and those combined interventions resulted in significant malaria infection reduction. The Malaria Scorecard(MS), introduced as a monitoring tool, and home-based management is pivotal in Rwanda's successful efforts to combat malaria and to bolster community-driven approaches to malaria control. This study delves into the assessment of the Malaria Scorecard's impact on health outcome through home-based management, offering vital insights to optimize strategies and empower communities in their ongoing endeavors to combat malaria. This is a retrospective study, to assess the impact of the Malaria Scorecard on community-driven home-based management. Furthermore, we assessed the change in malaria incidence, severe cases and deaths before (FY2020/21) and after the implementation of the scorecard FY 2022/23. Paired t-test analysis was employed to determine the significance difference level for Malaria Scorecard impact on HBM. The findings indicate a positive change in the implementation of the Malaria Scorecard, resulting in an increase in HBM from 54.7%; 95% CI (55.1-55.3) in FY 2020/21 to 58%; 95% CI (57.9-58) in FY 2022/23. The scorecard introduction significantly reduces malaria incidence rate from 114/1,000 population to 47/1,000 population after implementation of the SC.3, severe malaria cases from 2,592 to 1316, and deaths from 94 to 51. This study supports the positive impact of the Malaria Scorecard on community-driven home-based management in Rwanda, highlighting its potential to enhance community practices. To optimize effectiveness, recommendations include targeted activities, improved resource accessibility, and community engagement. Findings contribute to the broader discourse on innovative malaria control strategies, continued integration and refinement of tools like the Malaria Scorecard.

8023

IMPACT OF THE DISCONTINUATION OF UNIVERSAL INDOOR RESIDUAL SPRAYING (IRS) IN MAPUTO PROVINCE DURING THE 2020-2021 SEASON

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In Maputo Province, Mozambique, where malaria transmission is very low, the indoor residual spraying (IRS) strategy switched from a universal to a focal approach in 2020. Focal IRS consists of targeting only the neighborhoods (bairros) with the highest incidences within each district, which resulted in different thresholds being used by district. To evaluate the impact of IRS discontinuation on malaria incidence, we used a difference-in-difference approach. Malaria case data by bairro were extracted from health facility registers for the peak transmission season of Dec 2019-Mar 2020 (baseline) and Dec 2020-Mar 2021 (endline, first year of focal IRS). Bairros were stratified by baseline incidence quartiles (Q1: 0.2-3.1; Q2: 3.1-6; Q3: 6-14; Q4> 14-561 cases/1000) and within each stratum, the change in incidence between baseline and endline was compared in bairros that received vs barrios that did not receive IRS in 2020-21. Negative binomial regression was used to estimate the interaction between baseline/endline incidence and IRS/no IRS by strata and overall. The maximization of the

area under the ROC curve was used to find the "best threshold" above which incidence starts increasing when IRS is withdrawn. Overall, there was a significant 27% larger increase in the average number of malaria cases in bairros without IRS compared to bairros with IRS (IRR=0.73, 95% CI 0.58-0.91). When stratified by quartiles, a significant impact was only found for quartile 4. The incidence threshold that maximized the area under the curve was 6.2/1000. When stratifying by this threshold, there was a significant 47% greater increase in the average number of malaria cases in areas without IRS compared to areas with IRS (IRR= 0.53, 95% CI 0.33-0.84) only in areas with an incidence ≥6.2/1000. In conclusion, during the first four months of follow up, the discontinuation of IRS resulted in an increase in the malaria incidence only in bairros with higher transmission. Bairros with a baseline incidence of ≥6.2 cases/1000 should continue to receive IRS to avoid this resurgence. Additional follow up time would be needed to understand if the long-term impact remains the same.

8024

EVALUATION OF A PILOT IMPLEMENTATION OF INTERMITTENT PREVENTIVE TREATMENT WITH DIHYDROARTEMISININ-PIPERAQUINE TO PREVENT ADVERSE BIRTH OUTCOMES IN PAPUA, INDONESIA

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Malaria in pregnancy is a major cause of maternal and neonatal death in Papua. Our previous trial in Papua showed that monthly intermittent preventive treatment with dihydroartemisinin-piperaquine (IPTp-DP) among pregnant women from the second trimester was safe, tolerable and more efficacious than standard of care with single screening and treatment (SST). We conducted a mixed method evaluation of a Ministry of Health pilot of IPTp-DP in 10 health facilities in Mimika district. The effectiveness of antenatal clinics (ANCs) to deliver IPTp-DP alongside continuous quality improvement (CQI) was assessed through ANC exit interviews (N=1136), and women's adherence to the full regimen in a 'real life' setting through home visits (N=484). We used routine health information to assess the impact on maternal and infant outcomes. We explored health provider perceptions on drivers of successful integration to inform scale-up, and pregnant women's acceptability of IPTp-DP to refine strategies to improve uptake. Delivery effectiveness of IPTp-DP, defined as the administration of 9 tablets, the first dose by DOT, and reminders on days 2-3, was 40.7% (range). Among women who received IPTp-DP effectively, full adherence was 90.3%. The likelihood of women receiving effective IPTp-DP were lower educational status (aOR 2.1, 95% CI 1.3-3.4, p 0.004), lower socioeconomic status (aOR 1.9, 1.2-2.8, p 0.004), resident in semi-urban areas (aOR 2.3, 1.7-3.1, p <0.001) and second trimester visit (aOR 1.9, 1.5-2.6, p<0.001). Being married (aOR 3.1, 1.1-8.6, p 0.03) and having more than three ANC visits (aOR 2.6, 1.1-6.3, p 0.03) were significant predictors of high adherence. Themes associated with effective delivery were DP availability, trust in providers and active CQI. Themes linked to high adherence were history of malaria in pregnancy, support from midwives, husbands, and health education. Compared to SST, IPTp-DP≥3 was associated with significant reductions in confirmed malaria (aOR 0.5, 0.36-0.74, p <0.001) and moderate anaemia (aOR 0.64, 0.31-2.7x, p 0.003).

8025

FACTORS ASSOCIATED WITH LOW INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY (IPTP) COVERAGES IN LOW PERFORMING HEALTH FACILITIES IN GHANA 2023

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Malaria in pregnancy (MiP) poses significant risks to both mother and baby. Prevention of MiP include Intermittent Preventive Treatment of Malaria in Pregnancy (IPTp). Between 2020 and 2022, IPTp 3 coverage increased from 44% to 60%, coinciding with a decrease in MiP cases from 145,472 to 125,757. However, in early 2023, IPTp 3 coverage decreased prompting a targeted supervision to low performing facilities. We report findings from the supervision and factors that might have contributed to the low IPTp 3 coverage. Fifty-two health facilities across 6 regions were visited, all providing Antenatal Care (ANC) and IPTp services. We conducted health staff interviews (one per facility), observations and review of ANC registers. Results are summarized as frequencies and proportions. Most (71.2%) of assessed facilities were government-owned and provided Glucose-6-Phosphate Dehydrogenase (G6PD) testing services. However, there were notable gaps in staff knowledge and practices; 32.7% (17/52) of interviewed staff knew 0.4ug Folic Acid should be administered daily from registration and 73.1% (38/52) knew to avoid administering 5mg Folic Acid concurrently with Sulphadoxine Pyrimethamine (SP). Stockouts of SP were reported in 27.5% of facilities within the last three months, while discrepancies in SP stock balance were noted in 28.8% (15/52). Client education on IPTp was also lacking, with averagely 65% of the staff providing adequate information on its benefits, safety, and proper usage. Less than 45% of facilities had protocols, charts, or job aids for IPTp. Concerning data practices, 23.1% (12/52) had evidence of data validation meetings, 87.8% (43/52) had data capture in line with guidelines and 75.5% (37/52) achieved 100% data completeness. SP availability and sub-optimal client education are barriers to achieving optimal IPTp coverage. Addressing these issues, along with improving the supply of protocols and enhancing data validation practices, are crucial for improving IPTp 3 coverage and reducing MiP in Ghana.

8026

HEALTH PROVIDERS ON-SITE TRAINING APPROACH IN IMPROVING THE QUALITY OF MALARIA SERVICES DELIVERY IN COTE D'IVOIRE, 2023

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In 2019 and 2022, the Cote d'Ivoire National Malaria Control Program revised its guidelines for malaria case management and prevention and organized training workshops to upgrade health providers skills on the revised guidelines. Post-training follow-up through Outreach Training and Supportive Supervision Plus (OTSS+) revealed shortcomings in applying what was learned during the training. Two training strategies were developed in 2020 and 2023 to refresh provider skills in: 1) performing malaria rapid diagnostic tests (RDT); 2) managing uncomplicated malaria; and 3) providing insecticide treated nets (ITN) to children under five years of age. Strategy one, implemented in 2020, involved theoretical workshop trainings held at district level and facilitated by central-level trainers. Strategy two, implemented in 2023, involved theoretical workshop and

practical on-site trainings held in health centers and facilitated by district-level trainers. The OTSS+ was used to assess the skills of 550 providers within three month post each training strategy in the 34 health districts. Individual performances were scored according to skills: good for a score of 90% and above; medium between 80% and 89%, and low at less than 80%. This assessment compares the results of the two strategies. For RDT performance, 47.0% demonstrated good skills with strategy one and 79.5% with strategy two. For uncomplicated malaria case management, 27.5% demonstrated good skills with strategy one compared to 52.8% with strategy two. Regarding ITNs 30% demonstrated good skills for strategy one and 43.3% for strategy two. Number of providers trained with strategy two was higher than with strategy one, 6893 versus 2060, and the average overall per diem-related training cost was substantially lower for strategy two (16 USD) compared to strategy one (83 USD). On-site training strategy appears to be more effective than workshop trainings alone in improving provider performance. In addition, this strategy allowed for training a larger number of health providers due to its lower per diem cost. Continuing to follow up will enable understanding the longer-term impact on skills.

8027

EQUITY AND COVERAGE ANALYSIS OF POPULATION-BASED HEALTH PROGRAMS: A COMPARATIVE STUDY OF SEASONAL MALARIA CHEMOPREVENTION, INSECTICIDE-TREATED NET DISTRIBUTION STRATEGIES, AND THE ESSENTIAL PROGRAM ON IMMUNIZATION IN AFRICAN COUNTRIES

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Seasonal malaria chemoprevention (SMC) consists of administrating monthly doses of antimalarials to children aged 3-59 months old during the malaria transmission season. SMC has been identified as a potential platform for the integration of other interventions such as mass drug administration, and nutrition supplementation. Similarly, the essential programme on immunization (EPI) and insecticide-treated net (ITN) distribution campaigns have been identified as useful integration platforms for many maternal and child health programmes. Integration can help to deliver services at the same time and through fewer personnel which can lead to operational efficiencies and ultimately improves health outcomes. Achieving equity in these programmes is not only socially responsible, but it is an important disease prevention strategy. The comparison of routine population-based programme styles, and the equity achieved as a result, can be used to inform the integration of other interventions. This study aims to measure and compare the coverage of SMC and EPI programmes, and ITNs distribution strategies, and how equitable they are. In this study we are conducting a secondary analysis using data from Demographic and Health Surveys and Malaria Consortium's SMC end-of-round surveys to assess intervention coverage across 27 African countries. The analysis focuses on measuring the equity and coverage of ITNs, EPI, and SMC, comparing outcomes between and within countries. Coverage of each intervention will be assessed using binary indicators, with equity measured through concentration indices (Erreygers index). The study will provide insights into the distribution of ITNs, routine immunisation services, and SMC across wealth quintiles and their relationship to program coverage. We will present graphical comparisons and pooled concentration indices that elucidate the equity of intervention delivery within and between 27 countries. The findings will contribute to evidence-based decision-making for maximizing equitable access to preventive interventions across diverse socio-economic contexts.

8028

PREVENTING MALARIA AMONGST CONFLICT-AFFECTED COMMUNITIES IN CAMEROON SOUTH-WEST AND LITTORAL REGIONS

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Conflict in Southwest and Littoral regions of Cameroon led to reduced healthcare, internal displacement limiting access to malaria prevention and treatment services. Breaking Barriers is a 4-year implementation study researching community solutions in 80 high malaria-burden conflict-affected communities. Formative research in May 2021 resulted in introduction of a community dialogue approach (CDA), community health workers (CHW) supportive supervision, and vouchers for subsidized care from May 2022. A mid-term review (MTR) was conducted in November 2023, endline planned for June 2024, adopting qualitative and quantitative observational designs. The qualitative formative research studied barriers to care, CHW utilization, and community engagement preferences, 29 focus group discussions (FGDs), 11 in-depth interviews (IDIs). Data were analyzed thematically; open, descriptive coding combined with exploration of pre-determined investigative areas. The MTR evaluated process, 15 FGDs, 21 IDIs. Data were analyzed thematically using rapid summary analysis. Quantitative studies were cross-sectional knowledge, attitude, and practice surveys, 2,386 baseline participants, MTR, 2,523. malariometric prevalence studies, baseline 1,752 children, MTR, 2,042. Data entry was completed with Epi-Info 7.2.4.0, analysis with SPSS 25.0 and R 4.2.1. Qualitative formative research found poor prevention and treatment knowledge, health-seeking and CHW utilization. MTR results found communities value their CDA role and requested sustained capacity strengthening for community stakeholders. Voucher importance depends on health service confidence. Quantitative studies found improvements in knowledge of transmission and prevention practices; early diagnosis from CHWs, perceiving malaria a concern, prevention practices and prompt treatment for sick children. Malaria positive cases reduced from 54.5% to 33%. CDA is effective providing strengthened investment. Conflict affects CHW resourcing, supervision, and supplies. Effective cash assistance requires a continuum of care. To be concluded at endline survey and presented.

8029

ZAMBIA 2023 ITN DISTRIBUTION CAMPAIGN DIGITALIZATION EXPERIENCES: LESSONS LEARNED AND BEST PRACTICES

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In 2023, the Zambian Ministry of Health (MoH) and partners, including the Global Fund (GF), Against Malaria Foundation (AMF), and the U.S. President's Malaria Initiative (PMI) undertook a nationwide mass distribution of insecticide-treated bed nets (ITNs). ITN campaigns are conducted every three years and the 2023 campaign was the country's largest ever, targeting 18 million people with over 11.5 million ITNs and was the first to be digitized. Digitalization was a condition for accepting AMF funding for a set of provinces. However, the MoH embraced this innovation as a best

practice for adoption in all ten provinces. The digitization process involved customizing paper-based ITN registers into electronic formats; configuring them onto smartphones and training community-based volunteers (CBVs) to use these tools to capture data in real time during household registration and distribution exercises. CBVs moved in pairs, one using a traditional paper register for backup and the other using the digital tools, which auto calculated the quantity of ITNs needed for each household, captured location coordinates, and generated household identifiers. The data was transmitted to a central server and readily visualized, informing MoH's management decisions at health facility, district, and provincial levels. Observed benefits have included improved data quality, transparency, and accountability. Technological and administrative challenges ranged from the extra cost resulting from procurement of devices, training, conducting the pilot; to incomplete datasets due to poor connectivity in rural areas and inadequate supply of devices and accessories. Completion of the campaign was delayed by months in part due to these bottlenecks. Among the important recommendations for future campaigns is to ensure a comprehensive workplan with a realistic timeline supported by a detailed budget that accounts for all costs. It is also critical to conduct a pilot prior to the main campaign for viability testing. Finally, staff at all levels should be trained to be able to troubleshoot and resolve issues locally.

8030

COST AND COST-EFFECTIVENESS OF ATTRACTIVE TARGETED SUGAR BAITS (ATSB): CLUSTER RANDOMIZED CONTROL TRIALS (CRCT) IN ZAMBIA, KENYA, AND MALI

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Malaria remains a serious public health problem in sub-Saharan Africa, accounting for 580,000 deaths in 2022. Current vector control methods, Insecticide-Treated Nets (ITN) and Indoor Residual Spraying (IRS) are two of the most effective methods for reducing malaria. Insecticide resistance and evolving mosquito biting behaviours remain persisting challenges in reducing malaria transmission. Attractive Targeted Sugar Baits (ATSB) are a potential new tool for malaria vector control to address these challenges. ATSB stations containing sugar laced with toxicant are placed on housing structures, aiming to attract and kill mosquitoes after feeding from them. Three cluster randomized control trials (cRCT) were concluded in Zambia (June 2023), Kenya (March 2024), and Mali (January 2024) to assess the efficacy of ATSB. Main trial results from Zambia indicated a 9% reduction in malaria case incidence and results from Kenya and Mali are forthcoming. To assess the costs and cost-effectiveness of ATSB, costs of procurement, distribution, maintenance, and disposal were collected in the context of each cRCT. Economic and financial costs were estimated using an ingredients approach. In Zambia, from October 2021 to June 2023, the total costs were USD 1.1 Million, with cost-effectiveness of ATSB at USD 37 per clinical malaria case averted, and USD 366 per DALY averted. Data from Kenya indicate a total cost over 12 months of intervention of USD 1.7 Million. Results from the three trials indicate variation in the cost-effectiveness of ATSB, depending on site-characteristics. This variation may help to determine where and when ATSB may be utilized most efficiently to complement existing vector control.

8031

MALARIA, ANEMIA, MALNUTRITION IN PREGNANCY: PREVALENCE AND ASSOCIATED FACTORS, HIGH MALARIA TRANSMISSION AREA MALI

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Malaria and anaemia are diseases responsible for a large number of healthcare visits and deaths among pregnant women in areas of high malaria transmission, especially during the rainy season. This winter period corresponds to the hunger gap and field work, which can expose pregnant women to infections. The aim of this study is to assess the prevalence of malaria, anaemia and malnutrition among pregnant women in a high malaria transmission zone, and the associated factors. The study involved the 27 community health areas in the Dioila Health District, Koulikoro region, Mali. Data were collected from June 2022 to May 2023 in the health facilities during antenatal consultations. They included socio-demographic and economic data, malaria and haemoglobin tests, physical examination (including branchial perimeter). Descriptive analysis focused on the prevalence of malaria, anemia and acute malnutrition, with confidence intervals. We performed univariate and multivariate logistic regression analysis with prevalences (malaria and anemia), malnutrition, dietary habits and household income. A total of 829 women were included in the study, with a mean age of 25.7 (sd 6.22). The prevalence of malaria was 23.7% [95%: 0.21; 0.27], malnutrition 25% [95%: 0.22; 0.28]. The prevalence of anemia was 59% [95%: 0.55; 0.63]. Factors such as multiparity and low daily household spending were significantly associated with malnutrition, malaria and anemia in pregancy. The results show a need to integrate screening for malnutrition and anemia and their management during prenatal consultations in Mali to further reduce the burden of malaria. In addition, there is a need to develop income-generating activities for women.

8032

AN OBSERVATIONAL STUDY EVALUATING THE EPIDEMIOLOGICAL AND ENTOMOLOGICAL IMPACTS OF PIPERONYL BUTOXIDE INSECTICIDE-TREATED NETS COMPARED TO A COMBINATION OF INDOOR RESIDUAL SPRAYING PLUS STANDARD PYRETHROID-ONLY ITNS IN AMHARA REGION, ETHIOPIA, 2019-2022

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National malaria programs must weigh the relative benefits of different vector and elimination tools to prioritize resource allocation with greatest impact. An open-label, stratified block-cluster randomized trial was designed to assess the epidemiological and entomological impacts of piperonyl butoxide insecticide-treated nets (PBO ITN arm) compared to the combination of pirimiphos-methyl-based indoor residual spraying (IRS) and standard pyrethroid ITNs (IRS + Standard Pyrethroid ITN arm) in the Amhara Region of Ethiopia. Confirmed malaria cases reported during the high transmission season (September to December) were compared two years before (2019 and 2020) versus two years after (2021 and 2022) the ITN distribution and the first IRS campaign, using a multilevel mixed-effects negative binomial model. Generalized linear mixed models were used to assess the difference in *Anopheles gambiae* s.l. density per trap and indoor resting density (IRD) between the two arms during the 2021 and 2022 seasons. Estimated malaria cases decreased significantly by 53.6% in the IRS + standard pyrethroid ITN arm (mean: -53.6%; 95% CI: -72.9%, -29.8%), and by 55.9% in the PBO ITN arm (mean: - 55.9%; 95% CI: -73.0%, -32.5%). There was no significant difference in the overall epidemiological impact between these two arms (mean: -2.2%; 95% CI: -30.9%, 24.0%). However, while cases decreased non-significantly in the IRS + standard pyrethroid ITN arm from the first to second post-interventions season, there was a significant increase in the PBO ITN arm. Vector density per trap and IRD were not found to be significantly different between intervention arms in either post-intervention year (2021 Vector density per trap: IRR=0.78; 95% CI 0.47-1.31; p=0.348; IRD: IRR=0.80; 95% CI 0.37-1.75; p=0.580 or 2022 Vector density per trap: IRR=1.27; 95% CI 0.75-2.12; p=0.372; IRD: IRR=1.02; 95% CI 0.45-2.28; p=0.971). These findings indicate that while there was an overall impact observed in both intervention arms, the deployment of annual IRS alongside standard pyrethroids ITNs may provide a greater, sustained vector control impact over time compared to PBO ITNs only.

8033

INTRODUCING HAMMOCK NETS AND BEDNETS IN INDIGENOUS AND VULNERABLE COMMUNITIES OF PANAMÁ

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In 2009, Panama conducted their first Long Lasting Insecticide treated bednets (LLIN) mass campaign using long-lasting insecticide-treated bednets. However, it became apparent that a significant portion of individuals in the most malaria-affected and indigenous regions slept in hammocks, a fact that may have undercut the impact of the bednet distribution. With a renewed commitment to malaria elimination in 2018, Panama aimed to achieve comprehensive coverage with either LLINs or indoor residual spraying (IRS) in all active transmission areas. To test whether LLINs (bednets and hammock nets) were an adequate intervention for the locally affected populations, Panama devised a pilot initiative, spanning from 2019 to 2022, to evaluate the feasibility, acceptability, and use of both bednets and hammock nets among indigenous and latin communities. During this session, we will present the outcomes of the distribution phase and two subsequent rounds of monitoring, which highlight that, despite the high initial coverage and local communities expressing satisfaction with the color, fabric and size of the bednets and hammock nets, the percentage of sleeping spaces that were visibly covered with a net rapidly decreased in 6 months to 46.8% for hammock nets and 73.6% for bednets and the percentage of people using a net 6 months after distribution was merely 57%, with great heterogeneities across localities. This underscores the importance of strengthening SBCC campaigns after distribution and conducting post-distribution monitoring to capture the heterogeneity between localities and take appropriate focal actions to increase use. We will show how the findings from this pilot endeavor informed the national LLIN distribution campaign conducted in 2023. By sharing the lessons learned and best practices derived from this initiative, we aim to provide valuable guidance for other countries using LLINs and grappling with malaria elimination among indigenous and other vulnerable populations in the region.

8034

THE IMPACT OF ROUTINE DISTRIBUTION AND USE OF ITN TO REDUCE MALARIA IN PREGNANCY AND FOR CHILDREN UNDER 5 YEARS

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This abstract presents a comprehensive overview of ITN coverage and utilization in Rwanda, with data reflecting national level statistics, offering insights into the effectiveness of ITN distribution and usage strategies. We conducted a comparative analysis on annually indicators from national HMIS including pregnant women confirmed and treated malaria for pregnant and lactating (42 days) women between 15 to 49 years of age and Children under five years who was confirmed and treated malaria from 2020 to 2023. We analyzed also the indicators of ownership of ITN and use collected by RDHS and RMIS.After ownership of ITNs increasing from 81% in the 2014-15 RDHS, 84% in the 2017 RMIS, dropped to 66% in 2019-20 RDHS was again increased to 80.2% RMIS 2023. The use of ITN for pregnant women was 73% 2014-15 RDHS decreased to 69% RMIS 2017, and 56% in 2019-20 RDHS with a slight rise to 56.5% RMIS 2023 while the use of ITN for children under 5 years was 68 % 2014-15 RDHS, 68 % RMIS 2017, was decreased to 56% 2019-20 RDHS was again increased to 56.8% RMIS 2023The malaria in children under five years dropped in last four years from 300,405 in 2020, 230,137 in 2021, 145,890 in 2022 and 100,049 in 2023. This represent respective cumulative decrease of 23% in 2021, 51% in 2022 and 67% in 2023. While malaria in pregnancy was also decreased from 17,126 in 2020; 10,221 in 2021, 5,460 in 2022 to 3,106 cases in 2023, with a cumulative decrease of 40% in 2021, 68% in 2022 and 82% in 2023Overall, the data underscores the importance of continuous monitoring and evaluation of ITN distribution and utilization programs to address disparities and optimize malaria control efforts. Targeted interventions may be necessary to improve coverage and ensure equitable access to ITNs, particularly in the lower rates of utilization area. By prioritizing access and promoting consistent ITN usage among vulnerable populations, Rwanda can further strengthen its malaria prevention strategies and contribute to reducing the burden of the disease nationwide.

8035

USING NATIONAL SURVEY DATA TO LEARN IMPACT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY ON BIRTH WEIGHT IN NIGERIA

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Intermittent preventive treatment of malaria in pregnant women (IPTp) promotes health of the mother and unborn child. One noteworthy benefit is reduction of low birth weight (LBW, less than 2.5kg). Large survey data sets aid learning about such benefits on a national scale. We analyzed data from the 2018 Nigeria Demographic and Health Survey (DHS) to document the impact of IPTp on birth weight. Key variables included IPTp which based on national guidelines is given monthly at antenatal clinics from the 13th week, aiming to provide a minimum of 3 doses. DHS obtained this information from women giving birth in the previous two years. Birth weight included women giving birth in the previous five years. A quarter had a record of newborn weight reported from a health facility Since many did not, women were also asked to estimate the size of the baby at birth:

very small, smaller than average, average, larger than average, and very large. We combined the latter three categories into "average or larger". Of those giving birth in the past 2 years, 23% took only one dose, 24% took 2 doses, while 17% had 3 or more doses. In the broader sample of those giving birth in the previous 5 years 2.8% estimated that their baby was very small. Among those women with a record of birth weight, 7% were LBW. Preliminary analysis comparing perceived size and IPTp doses found 3% receiving only one dose thought their baby was "very small" at birth, as did 3% of those taking 2 doses and 4% receiving 3 or more. Among the subset with a recorded birth weight, 9% who took only one dose of IPTp had LBW baby, as did 7% who received 2 doses, and 6% who got 3 or more doses. It appears possible to compare outcomes (LBW) with interventions (IPTp), but data type and availability may limit conclusions. Even though a smaller subset of women had access to a recorded birth weight (most women delivered outside a health facility), birth weight appears to provide a better indication of IPTp effectiveness than subjective perceptions of child's size at birth. The findings even with limitations show the value of national surveys to justify policies protecting pregnant women from malaria.

8036

DECENTRALIZING MALARIA CASE MANAGEMENT SERVICES IN EQUATORIAL GUINEA: A CAPACITY BUILDING APPROACH AT THE DISTRICT LEVEL

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Historically centralized, the health system of Equatorial Guinea is transitioning to decentralization to improve local responsiveness for health programs, particularly for those related to malaria service delivery. This shift, led by the Ministry of Health (MOH) with support from the National Malaria Control Program (NMCP) and the Bioko Island Malaria Elimination Project (BIMEP), aims to improve malaria case management services by empowering district-level entities. A strategic decentralization initiative was launched in 2023 to train clinicians and lab technicians to become trainers and supervisors for malaria case management, in three phases: 1) Initial training utilizing updated clinical and lab manuals together with competency assessments, 2) Monitoring and coaching of in-service practices through OTSS (Outreach Training and Supportive Supervision) visits, and 3) Advanced training focusing on skills needed to lead impactful training sessions and supervisory visits. Participants were selected based on their proficiency identified in previous training or OTSS visits. This effort has resulted in developing a comprehensive toolkit that includes clinical and diagnostics training manuals, digitized malaria case management supportive supervision tools, and manuals focusing on trainer's and supervisor's skills, all being integrated into the NMCP. Initial training results from December 2023 show high competency scores among participants, demonstrating effective learning transfer. The complete implementation of all phases is projected for the end of Q3 2024. The aim for this initiative is that it will not only help increase the quality of malaria services and tackle challenges with the overutilization of medicines and inaccurate malaria diagnoses, but it will also strengthen local leadership and ownership for a decentralized and more effective health system. The malaria program hereby establishes a framework and precedent for a more comprehensive health system reform in line with global malaria elimination goals and with Equatorial Guinea's decentralization agenda across the different disease programs.

8037

EFFECT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN SCHOOLCHILDREN ON ANEMIA THROUGH REDUCTION OF MALARIA INFECTIONS AND CLINICAL MALARIA EPISODES: MEDIATION ANALYSIS

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Anemia undermines the health and education of children. Its causes are multi-factorial, and the relative contribution of its etiologies are heterogeneous in terms of age and geography. Malaria is a significant cause of anemia in school-age children (SAC), but effects may be mediated by both episodes of clinical malaria and chronic *Plasmodium falciparum* (*Pf*) infection. Understanding the contribution of these two helps anticipate the impact of malaria control interventions on anemia. A recent school-based open label randomized, controlled trial of malaria intermittent preventive treatment (IPT), found that the risk of anemia in children in IPT arm was lower than those in control arm. In the IPT arm, three rounds of dihydroartemisinin-piperaquine (DP) or chloroquine were delivered at 6-week intervals for parasite clearance and prophylaxis. The control arm did not receive any medication. In the current analysis, we aimed to evaluate whether the reduction in the rate of anemia was mediated by parasite clearance, and/or frequency of clinical malaria episodes. We used mediation analysis to decompose total effect (TE) of IPT on anemia into unmediated and mediated effects. At the end of the study, prevalence of anemia was 8% (20/239) in IPT arm vs 15% (35/238) in control arm yielding a TE of 0.55 [OR=0.55 (0.28, 0.90)]. Prevalence of *Pf* infection was 17% (40/239) in the IPT arm vs 53% (127/238) in the control arm [OR=0.18 (0.12, 0.27)]. Clinical malaria risk was 0.14 (40/239) in IPT arm vs 0.32 (77/238) in control arm over 6 months [RR=0.44 (0.31, 0.63)]. The odds of anemia were reduced by 26% [OR=0.74 (0.54, 0.93)] in IPT compared to control, due to a reduction in the odds of *Pf* infection, representing 45% proportion of anemia reduction mediated by reduction of *Pf* infection. There was no significant mediated effect of IPT treatment on anemia through clinical malaria (OR=1.07 (0.94, 1.18)). While IPT reduces the risk of clinical malaria among SAC, this reduction alone does not translate into a decrease in anemia prevalence. Our findings suggest that *Pf* infection clearance during IPT intervention is the primary mechanism contributing to the reduction in anemia.

8038

CHANGES IN IPTP UTILIZATION MEASURED AN ANNUAL CROSS-SECTIONAL HOUSEHOLD SURVEY WITHIN PROGRAM AREAS OF THE ISDELL: FLOWERS CROSS BORDER MALARIA INITIATIVE IN ZAMBIA

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Pregnant women are at increased risk of severe illness and death from malaria. Taking three or more doses of intermittent preventive treatment of malaria in pregnancy (IPTp 3+) is a key strategy to protect women and

their babies from malaria complications. The 2022-2026 Zambia National Malaria Strategic Plan aims to increase IPTp 3+ to at least 88% from its national baseline of 68% in 2021. This study assessed utilization of IPTp 3+ among women who gave birth in the prior 12 months in Southern and Western Province within 24 health facility catchment areas (HFCAs) that are program areas of the Isdell:Flowers Cross Border Malaria Initiative (IFCBMI), an implementing partner of Zambia's National Malaria Elimination Centre. Data were collected through cross-sectional surveys conducted from April-May 2022 (n=1982) and April-June 2023 (n=2553). Within program areas, the average proportion of women who took IPTp 3+ was already near the Strategic Plan goal in 2022 at 86.5% (83.6% - 89.0%). However, the proportion slipped by a statistically significant -4.9% (-10.2% - -0.5%, p=.025) in 2023 to 81.6% (78.5% - 84.4%). This change was concentrated most strongly in Mongu District program areas, which recorded a statistically significant (p=.011) drop of -37.9% (-72.8% - -5.5%) from 90.7% to 52.8%. More modest, non-significant losses were measured in IFCBMI HFCAs in Livingstone, Mulobezi, and Sesheke (-6.5%, -10.2%, -8.3%, respectively), while modest, non-significant gains were seen in HFCAs in Kalabo, Kazungula Shangombo, and Sikongo (+7.5%, +2.4%, +1.6%, +6.0%, respectively). In 2023, IFCBMI HFCAs in Mongu and Sikongo Districts had by far the lowest IPTp3+ levels at 52.8% (36.6% - 68.7%) and 54.3% (42.2% - 65.8%), respectively, with all other district program estimates exceeding 80%. Only the Senanga program area was measured to achieve 100% in either year, at which it was measured for both years. Strategic planning for increasing IPTp3+ utilization within Mongu and Sikongo Districts will be undertaken by IFCBMI and partners to achieve national goals. Data to be collected in 2024 will again measure IPTp3+ in these areas and assess relative changes.

8039

LEVERAGING HOUSEHOLD VISITS DURING INDOOR RESIDUAL SPRAYING TO IDENTIFY PREGNANT WOMEN AND INCREASE AWARENESS OF ANTENATAL CARE AND IPTP ADHERENCE ON BIOKO ISLAND, EQUATORIAL GUINEA

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Pregnant women are particularly vulnerable to malaria, and the Bioko Island Malaria Elimination Project (BIMEP) prioritizes reinforcing knowledge, attitudes, and practices (KAP) around malaria in pregnancy to increase antenatal care attendance, adherence to intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP), and long-lasting insecticidal net use. This study aims to evaluate the effectiveness of leveraging household visits during indoor residual spraying (IRS) activities to identify pregnant women and increase awareness of ANC and IPTp adherence on Bioko Island, Equatorial Guinea. During the annual IRS round on Bioko Island in 2023, pregnant women in sprayed households were identified and enrolled in a follow-up study after obtaining informed consent. Community outreach was conducted through household visits, during which communicators educated pregnant women on malaria prevention and health-seeking behaviors. Data on age, pregnancy age, education, phone contact, malaria knowledge, and prevention practices, such as ANC attendance and IPTp-SP, were collected. Consenting women were enrolled in a registry to receive text messages, home education, and invitations to community talks on malaria. A total of 589 pregnant women were visited in their homes and educated on malaria prevention and treatment-seeking behaviors. More than 95% of the women consented to receive text messages, home education, and invitations to community talks on malaria. The project aims to build a registry to reinforce the strategy for malaria prevention in pregnancy through targeted interventions. Leveraging household visits during IRS activities is an effective approach to identify pregnant women and increase awareness of ANC and IPTp adherence. The high consent rate for receiving educational interventions demonstrates the potential for targeted strategies to improve malaria prevention and treatment-seeking behaviors among pregnant women on Bioko Island.

8040

POTENTIAL POPULATION IMPACT OF SCALING UP SEASONAL MALARIA CHEMOPREVENTION IN EAST AND SOUTHERN AFRICA: A MODELLING STUDY

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Seasonal malaria chemoprevention (SMC) aims to prevent malaria in young children in areas of seasonal malaria transmission. Historically, SMC was contraindicated in east and southern Africa, due to high-grade resistance to sulfadoxine-pyrimethamine, one of the drugs used for SMC. In 2022, geographic restrictions for SMC suitability were removed, prompting many countries to reconsider implementation. There is a need to understand the potential population-level impact of scaling up SMC in the region. Previously, the first clinical trials of SMC with SP + amodiaquine (SP+AQ) in Mozambique and Uganda showed good efficacy. We fit a model to the clinical data to characterise drug protection over time finding that SP+AQ reduces clinical malaria cases in the 30 days following drug administration by 87.4% (95% CrI: 78.0 - 92.4%). Here, we incorporate these estimates of SMC efficacy into an established *Plasmodium falciparum* transmission model developed at Imperial College, UK. We calibrate the model using data on entomology, rainfall, demography, historical intervention coverage, and malaria prevalence before validating against routine case data from seasonal regions in Mozambique, Uganda and other countries in East and Southern Africa. We estimate the potential impact of implementing SMC under various scenarios, including the number of cycles, their timing, targeted age groups and coverage achieved. Initial results suggest that even in areas of saturated *dhfr-dhps* quintuple SP resistance, SMC with SP+AQ could have a substantial population impact. Results from Uganda suggest that if SMC were delivered in seasonal areas, for 10,000 cycles of SMC administered, 536 clinical cases (range: 69 - 1412) and 19 severe cases (range 5 - 38) could be averted. We find that despite the high drug resistance present in East and Southern Africa, SMC has the potential to be highly effective and could avert a substantial burden of malaria in young children. It will be important to consider how SMC implementation may drive resistance to SP and AQ in areas with pre-existing resistance, and if higher grade resistance may negatively affect intervention effectiveness.

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WHAT HAPPENS WHEN CHEMOPREVENTION OF SEASONAL MALARIA IS STOPPED: EXPERIENCE IN THE SOUTHERN SENEGALESE REGION OF SÉDHIOU

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In the Sédhiou region, we noted a drop in malaria incidence from 21‰ to 10.1‰ from 2015 to 2017. Thus no longer meeting the eligibility criteria for chemoprevention of seasonal malaria in children, the intervention was discontinued in Sédhiou in 2020. And in the absence of any other experience of stopping chemoprevention of seasonal malaria, we carried out a quasi-experimental study, with a mixed design taking the neighboring region of Kolda as a comparison zone, using case study

and linear regression modeling with the double-difference method. The discontinuation of chemoprevention of seasonal malaria is a source of concern for health workers and mothers/caregivers. The latter believe that this strategy reduces malaria cases, and fear a resurgence of cases when it is stopped. For the district medical officers, the cessation should be progressive, depending on the local incidence. Malaria incidence in children aged 3 to 120 months is 4.5 ‰ in 2017 and 17.47 ‰ in 2020. Correlations were sought between incidence and mortality and distance from the health center, existence of an ambulance, malaria training, structure, rainfall. No correlation was found between malaria incidence and rainfall or the implementation of mass distribution of mosquito nets. The number of malaria cases fell by 0.05% per month, with a difference of 31 cases between the Sédhiou region and the Kolda comparison ($p<0.01$). Mortality is correlated with the type of health facility, with a significant drop noted in health posts ($p<0.01$). There was no significant difference in malaria incidence between the Sédhiou region, where chemoprevention of seasonal malaria was stopped, and the Kolda region, where it was continued ($p=0.054$). No excess malaria mortality or morbidity among children or the general population was observed when chemoprevention of seasonal malaria was stopped. However, the mitigation plan, which reinforced early case management and larval nest control, may have contributed to such results.

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CONTRIBUTION TO THE IMPROVEMENT OF SEASONAL MALARIA CHEMOPREVENTION (SMC) SUPERVISION BASED ON REAL-TIME ANALYSIS OF DISAGGREGATED DATA FOR DECISION MAKING

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Seasonal Malaria Chemoprevention (SMC) is one of the key interventions for reducing morbidity and mortality in children under 5 years of age in Burkina Faso. Despite reported SMC coverage in cycles 1 & 2 surpassing 100%, health facilities identified children not covered by the SMC campaign presenting with malaria between the two cycles. Further analysis was conducted to verify whether high SMC coverage at health facility level is associated with reduced malaria cases in three project regions. Secondary analysis of daily SMC monitoring data from 581 health facilities collected via a digitized version of the national SMC daily reporting tool was conducted. Confirmed malaria cases in children under 5 collected in health facility consultation registers were disaggregated by SMC-status. Quality control was carried out based on physical copies of the daily collection sheets, which were photocopied and attached to the registered data files to check for any coverage values that might be out of line. Descriptive and spatial analysis based on GIS was used to identify clusters with high SMC coverage and high proportion of malaria cases among children not covered by the SMC campaign. Descriptive analysis of these data will enable us to draw lessons to strengthen SMC implementation so it achieves its intended impact. 54.4% (n=4065) of malaria cases reported between cycle 1 and cycle 2 among children under 5 who were not covered by the SMC campaign came from health facilities with SMC coverage of over 100%. Validated SMC data revealed that SMC coverage was less than 100% (40-80%) in 52% of health facilities during the two cycles. Spatial analysis of SMC coverage disaggregated by health facility reveals three distinct clusters in the health districts of Garango (Centre-Est region), Nanoro (Centre-Ouest region) Diébougou (Sud-Ouest region). The results indicate that high coverage rates of over 100% do not mean that all children under 5 are fully covered during each campaign and will enable SP/Palu to strengthen the supervision system, which must focus on improving SMC coverage in areas where the number of malaria cases among children not covered by SMC is high.

8043

USE OF ALTERNATIVE LLIN DISTRIBUTION CHANNELS TO IMPROVE HOUSEHOLD OWNERSHIP AND USE OF LLINS

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The Democratic Republic of Congo (DRC) has adopted the use of long-acting insecticide-impregnated mosquito nets (LLINs) as the principal means of preventing malaria infection. To promote LLIN ownership and use, the cyclical nationwide distribution of LLINs has become the primary concern of the national malaria control program. Despite these efforts, indicators of LLIN ownership and use in the country remain low and fluctuate according to whether the distribution is immediate. As a result, alternative distribution channels for LLINs have been devised to maintain their presence in households and improve their use. Based on data from the Vaccine Coverage Survey (VCS) 2022, coupled with malaria indicators, we set out to explore the contribution of alternative LLIN distribution channels to the rate of LLIN ownership and use in the country. The presence of at least one LLIN was reported in 72.8% of the 78,776 households nationwide that agreed to participate in the survey. A total of 114,185 LLINs were observed in households, of which 93.2% were insecticide-impregnated and 80.8% used to sleep under the night before the survey. For the country, 13.8% and 3.6% of these LLINs came from distribution to pregnant women at antenatal clinics (ANC) and to children under 5 at pre-school clinics (PSC) respectively. The rate of ownership of LLINs from these two sources seems proportional to the time spent post-campaign. In 9 of the country's 26 provinces, ANC-derived LLINs were in first place, with proportions ranging from 19% in Haut Katanga, 28% in Kinshasa, 30% in Haut Uele, 35% in Haut Lomami, 35% in Kongo Central, 37% in Tanganyika, 39% in Mai-Ndombe, 40% in Ituri, 41% in Sud Ubangi to 61% in Nord Ubangi. No influence of the school environment was found. Thus, ANC proves to be a reliable alternative for maintaining a stable rate of ownership and use in suitable proportions. Better monitoring of this activity will undoubtedly contribute to improving household ownership and use of LLINs and, indirectly, to reducing malaria morbidity and mortality.

8044

MALARIA IN PREGNANCY

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Malaria, a parasitic infection transmitted by mosquitoes, is one of the most devastating infectious disease killing more than one million people annually. Pregnant women, children, and immune-compromised individuals have the highest morbidity and mortality, and Africa bears the heaviest burden. Twenty-five million pregnant women are currently at risk for malaria, and, according to the World Health Organization (WHO), malaria accounts for 10,000 maternal and 200,000 neonatal deaths per year. The above statement leads the researcher to question the practices of health personnel regarding the management of malaria among pregnant women attending the Cite des Palmiers District Hospital, with the main aim to evaluate the practices of health personnel regarding the management of malaria in pregnancy.To achieve this, a quantitative, descriptive cross-sectional study was carried out and data was collected within 5 days at the ANC unit in the Cite des Palmiers District Hospital using questionnaires. During this study, 28 health personnel were identified by a simple random sampling technique, the analysis of data in word 2010, which allows us to express

our results on histogram, pie chart and tables.From our result, it appears that, most represented age range where 70% were between 21-25 years, 14% between 26-30 years, 7% between 31-35 years and 7% between 41-45 years while 0% was found between 36-49 years. For an overall practice of health personnel, 83% tell pregnant women to sleep under mosquito nets and to clean their environments while 17% do not. At the end of this study, it was concluded that 62% of health personnel had good practice towards the management of malaria among pregnant women while 38% were found to have challenges in the practice of management of malaria among pregnant women.

8045

THE SOCIO-DEMOGRAPHIC PREDICTORS OF INSECTICIDE-TREATED BED NET UTILIZATION FOR PROTECTION AGAINST MALARIA BY ASYMPTOMATIC INDIVIDUALS FROM RURAL COMMUNITIES ACROSS FIVE REGIONS IN MAINLAND TANZANIA

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Insecticide-treated bed nets (ITNs) are the core vector control intervention used to prevent transmission and reduce malaria-related morbidity and mortality. Whereas ITNs are mainly targeting under-fives and pregnant women, there are potentially other vulnerable populations/groups which are yet to be identified and targeted. This community-based cross-sectional survey was conducted to evaluate predictors of ITNs usage among individuals of all age groups from five regions of Tanzania (Kagera, Kigoma, Njombe, Ruvuma and Tanga) with varying malaria endemicity. Logistic regression was used to determine the associations between ITNs usage and different predictors, and the results were presented as crude (cOR) and adjusted odds ratios (aOR) with 95% confidence interval (CI). The survey enrolled 10,228 individuals from 15 villages in five districts (one district/region). Of these, 77.62% owned and 77.23% used ITNs the night before the survey. The highest ITNs usage was in Nyasa (Ruvuma) (91.89%) while the lowest was in Kyerwa district (Kagera) (63.81%). All five villages from Kyerwa had lower usage of ITNs (<75%) while six villages; one village in Ludewa (Njombe), two in Muheza (Tanga) and three villages in Nyasa district had higher ITNs usage (>90%). ITNs usage were higher among females (aOR=1.21; 95% CI, 1.07-1.37) and under-fives (aOR = 2.28; 95% CI, 1.62 - 3.21). Four villages; one in Muheza and three in Nyasa had significantly higher odds of ITNs usage (>10 times) compared to a village in Kyerwa district (which had the lowest usage). Individuals with higher (aOR = 2.03; 95% CI, 1.72 - 2.40) and moderate socio-economic status (SES) (aOR = 1.59; 95% CI, 1.37 - 1.84) and living in houses whose walls had no holes (aOR = 1.29; 95% CI, 1.06 - 1.56) had significantly higher odds of ITNs usage. Thus, there was low usage of ITNs among males, school children, and individuals from households with low SES and poorly constructed houses. These findings should be considered by policymakers in ITNs distribution and targeting other vulnerable groups to close the socio-demographic gaps in ITNs usage and enhancing malaria control and elimination efforts in Tanzania.

8046

BENEFITS OF INCLUSIVE INNOVATION IN THE DEVELOPMENT OF A DECENTRALIZED ROUTINE DATA QUALITY AUDIT (RDQA) IMPLEMENTATION MODEL IN THE DEMOCRATIC REPUBLIC OF CONGO (DRC)

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Problems with the quality of malaria data persist in the DRC, limiting the NMCP's ability to make informed decisions and launch a timely response to identified priorities. An effective surveillance and M&E system that produces high-quality data is essential for: i) monitoring malaria trends, ii) evaluating the impact of malaria control interventions, and iii) evidence-based decision-making. In 2023, the NMCP developed a decentralized RDQA approach targeting health zones and health facilities. This included a participatory approach involving stakeholders at all levels of the health system: national (NMCP, HMIS and technical partners), provincial (NMCP and HMIS), and health zone management teams through a series of consultative meetings. The following stages were crucial: i) landscape analysis of RDQA implementation at country level, ii) design of an RDQA model that would promote ownership and accountability of actors at provincial and peripheral levels, iii) development and updating of existing tools, and iv) adoption of a continuous learning approach during the RDQA pilot phase (June 2023 to March 2024). Integrating the perspectives of stakeholders across all heath administrative levels in the development of the RDQA approach has strengthened ownership and accountability of end-users in the implementation of RDQA and the monitoring of action outcomes. Actors are highly motivated to manage the feedback lifecycle from the national level to the province, from the provincial level to the health zone, and from the health zone to the health facilities, with increased responsibility and accountability of provincial and health zone level personnel in monitoring and supporting the implementation of corrective actions identified during the RDQA pilot phase. The proportion of recommended actions was 73% (106/145) from the first RDQA field visit, 70% (118/168) from the first formative supervision field visit, and 68% (115/167) from the second RDQA field visit.

8047

ASSESSING THE FEASIBILITY OF USING A MULTIPLEX SEROLOGICAL ASSAY TO CONDUCT SEROSURVEILLANCE FOR MALARIA EXPOSURE

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Measuring malaria exposure is critical for public health and malaria eradication efforts as well as in force health protection for military service members deployed to malaria endemic regions. Malaria disease surveillance is challenged by both natural immunity and chemoprophylaxis which can lead to under-estimate of malaria prevalence. In this effort, we test the feasibility of using a multiplex serological assay to measure malaria exposure based on antibody responses to 20 antigens including anopheline salivary antigens for vector exposure, pre-erythrocytic antigens for sporozoite exposure, and erythrocytic antigens for exposure to blood-stage parasitemia for both *P. falciparum* (Pf) and *P. vivax* (Pv) antigens. We validate this assay against samples from U.S. naïve subjects as well as subjects that underwent irradiated sporozoite treatment (IMRAS) or controlled human malaria infection (CHMI). We compare the serological profiles to those of samples collected from populations native to a region of Kenya with low

to moderate malaria endemicity and populations from Uganda with high malaria endemicity. We demonstrate that this multiplex serology assay can reliably detect exposure-induced antibody titers and we successfully applied this panel to 755 samples obtained from U.S. military service members returning from deployments to regions of Africa with significant malaria risk. Our findings reveal evidence of exposure: some individuals had anti-CSP antibody levels comparable to those found in endemic populations, suggesting exposure to sporozoites under chemoprophylaxis. We also observed isolated cases of anti-MSP1 levels that were as high as observed in endemic populations and CHMI studies, suggesting possible cases of clinical or subclinical parasitemia. The feasibility of implementation of this approach for serosurveillance in high-risk malaria settings is discussed.

8048

EVIDENCE OF *PLASMODIUM VIVAX* IN NORTHERN KENYA, AN EMERGING MALARIA CONTROL THREAT; AN INCIDENCE REPORT FROM THE OUTCOME OF THE MID-2023 EPIDEMIC RESPONSE AND FOLLOW UP SURVEY.

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Malaria mortality and morbidity in Kenya has all along been largely due to *Plasmodium falciparum* infections with no cases attributed to *P.vivax*. The northern Kenya counties are classified as zero to low-risk transmission zones. In mid-2023 an upsurge in febrile illnesses was reported in 3 such counties, requiring a pandemic response. In addition to possible viral infection that had featured in these areas previously, malaria disease was also investigated. A follow up sampling on the same spots was done six months after the initial outbreak. The presence of the diverse species present in this surveys is hereby reported. A total of 89 and later 64 blood samples were collected from patients suspected of malaria in the initial outbreak response and follow up survey. Positivity and speciation was performed using probes with species specific primers. From 3 health facilities in Marsabit, Mandera and Turkana counties a total of 24, 50, 15 and later 32 and 30 DBS samples were received respectively. There were 11, 40 and 15 in the first survey and 27 and 26, in the follow up, Plasmodium positive samples in the 3 facilities respectively. This translated to a total positivity of 74.8% in the select population. Speciation analysis recorded a total of 113 *P. falciparum* cases, 4 with a mixed infection of *P. malariae* and *P. falciparum*, 3 *P.vivax* mono infection, and 6 *P. vivax -P. falciparum* co-infected cases. No *P.ovale* was observed. A total of 4 patients in Mandera and 5 in Marsabit were found to be infected with *P.vivax* in the survey translating to an incidence rate of 7.1% and 6.3% respectively. The incidence of malaria from the response sites was quite high. Although the burden of *P. vivax* in these counties is undetermined, the presence of the observed proportions in such a small sample size is an indicator of an underlying or emerging problem of cases that are rarely diagnosed in a clinical setting and may often be asymptomatic. The presence of *Anopheles stephensi* that was recently identified in the same study region, presents a highly competent vector here, which could enhance the transmission of *P. vivax* and reverse all the malaria control gains made over the years.

8049

SOUTH-SOUTH EXCHANGE - USE OF A COLLABORATIVE CAPACITY STRENGTHENING MODEL FOR COUNTRIES APPROACHING MALARIA ELIMINATION

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The Surveillance Practice and Data Quality Committee sits within the RBM Partnership to End Malaria's Surveillance, Monitoring and Evaluation Working Group. The committee aims to increase awareness of malaria surveillance guidelines among National Malaria Control Programmes (NMCP) and key stakeholders, and provides a platform to facilitate knowledge exchange in malaria surveillance and routine data management. Several NMPCs have requested support to adapt their surveillance systems for low transmission and pre-elimination settings. To respond to these requests an exchange programme was organised from 17 to 23 March 2024. The National Center for Parasitology, Entomology and Malaria Control (CNM), in Cambodia, was selected to host the exchange due to their achievement of reducing confirmed malaria cases by over 90% between 2010 and 2020. The exchange included participants from 11 African NMCPs and aimed to understand country priorities and support countries to build effective operational plans to transition from aggregate to case-based surveillance and develop models for cross-border surveillance. The programme started with CNM and partners discussing the malaria situation in Cambodia, national elimination strategy, and implementation experience, including challenges with drug resistance and cross-border surveillance. Field visits included meetings with provincial health department and health facility staff, and mobile and village malaria workers to understand the complexities of implementing a last mile operational plan and learn from the successful elimination of *Plasmodium falciparum*. Workshop discussions focused on understanding surveillance process, the importance of high-level ownership, collaboration, flexibility, and funding of country-driven technical capacity. We present key lessons from the exchange and short- and long-term priorities to be considered by Africa countries pursuing malaria elimination. The south-south exchange model provides a platform to facilitate knowledge exchange between countries, enabling those with first-hand experience to support others to achieve elimination goals.

8050

BENIN'S MALARIA SURVEILLANCE SYSTEM: INNOVATIONS TO PURSUE AND WEAKNESSES TO IMPROVE

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In limited resources settings, the best way to optimize scarce resources in public health is to base decisions on evidence. For malaria control, countries have surveillance system, the aim of which is to guide decisions using data collected and analyzed on the epidemiological indicators of the disease. We used the Malaria Surveillance Assessment Toolkit under development with WHO in its latest pilot phase in Benin for a comprehensive assessment of the performance of the malaria surveillance system and the determinants of the level of performance. The toolkit was adapted to the Benin context for a comprehensive assessment. The assessment strategy combined; i) a desk review, ii) qualitative interviews with all the key players in malaria surveillance at central, intermediate, and peripheral levels of the health pyramid, and iii) quantitative data collection on a nationally representative sample of health facilities, including an assessment of data quality at health facility level. The low care seeking behavior in case of fever in under-5 children (53%), self-medication and the low contribution of the private sector in the routine malaria data collection system led to an estimated 17% representativeness of the cases captured by the surveillance system, according to the overall surveillance cascade figure. The monthly data reporting completeness rate is 81%, and the concordance of various indicators between the three sources: individual data registers at health facility level, monthly reporting forms and the entered data in the DHIS2 varies from 11% to 91% for the month of September 2021 which was evaluated. Routine data, campaign data, periodic survey data and routine supervision data are managed by different non-integrated parallel systems, which does not facilitate real-time data access for all stakeholders. A new strategy to improve data quality, based on the verification of used-RDT cassettes as proof of malaria confirmation, is a good practice to be pursued, and the implementation of interoperability between the different databases with DHIS2, the national repository, will be necessary to optimize the use of data for decision-making

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BED NET USE, MISUSE, AND MISCONCEPTION: A COMMUNITY-BASED CROSS-SECTIONAL STUDY IN FIVE REGIONS OF MAINLAND TANZANIA

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Bed nets are the most common vector control interventions in malaria endemic countries including Tanzania. Despite government efforts to distribute bed nets, studies have reported misconceptions and misuse of bed nets, leading to reduced effectiveness of bed nets in malaria control and elimination in Tanzania. This study aimed to upgrade the limited knowledge on the use, misuse, and misconceptions of bed nets in Tanzania. A community-based cross-sectional survey (CSS) was conducted in Kagera, Kigoma, Njombe, Ruvuma, and Tanga, regions from July to August 2023. In the CSS, anthropometric, demographic, clinical, parasitological, and socio-economic status data were collected through electronic devices using Open Data Kit software. Questionnaires with both open-ended and closed-ended questions were used to collect data on ownership, use, misuse, and misconceptions of bed nets. Descriptive statistics were used to summarize participants' responses to the questionnaires. Association between gender and bed net ownership was assessed using multivariate logistic regression analysis. A total of 10,228 individuals were recruited in the study. Most of the participants 5,005 (48.93%) were aged ≥15 years while under-fives and the school-aged children (5-15 years) were 1,538 (15.04%) and 3,685 (36.03%) respectively. The majority were females (60.25%) and 77.62% reported owning bed nets, with significant higher ownership among females (61.26%) than males (38.73%) ($p<0.001$). Of the participants, 7,899 (77.23%) reported using the nets the night before the survey. Only 659 (6.44%) participants were aware of other uses of bed nets and the most common misuse of bed nets was keeping chickens (4.81%, n=492) and making ropes (0.61%; n=63). Among the participants, 117 (1.14%) were aware of misconceptions related to bed nets and 85 (0.83%) reported heat stress as the most common misconceptions towards bed nets use. Misuse of bed nets is still a considerable challenge in Tanzania. This continues to reverse the government's efforts for malaria control and elimination. Educational programs are urgently needed to enhance use of bed and reduce misconceptions.

8052

QUANTIFY THE TREND IN MALARIA INCIDENCE AT HEALTH DISTRICT LEVEL AND IDENTIFY THE FACTORS ASSOCIATED WITH THIS INCIDENCE IN BURKINA FASO FROM 2016-2022 USING ROUTINE CASES DATA

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In recent years, Burkina Faso's national malaria control program has intensified malaria control interventions to reduce malaria morbidity and mortality. An analysis of routine malaria case data was undertaken to assess the impact of these interventions at health district (HD) level. Malaria incidence from routine surveillance was adjusted to account for incomplete testing, reporting, and care-seeking rates. We assessed the trend in malaria incidence in Burkina Faso between 2016 and 2022 by HD and identified predictors of malaria incidence. To analyze the trend, we used the seasonal trend decomposition (STL) using local regression smoothing, quantifying the significance of the trend with the Mann-Kendall test and direction and intensity of the trend with the Sen's slope coefficient. We used generalized additive mixed models with a smoothing spline function and district-level random effect to identify factors associated with malaria incidence at the district level.Between 2016 and 2022, the adjusted malaria incidence decreased by 15.2 % (from 864 to 733 cases per 1000 population) at national level. The STL method show that the trends decreased constantly for adjusted incidence in 39/70 HDs and the trend remained increasing in two HDs (N'dorola and Kampti). We found a significant positive relationship between number of days of IPTp stock-outs, bednets usage and health facility usage rate and adjusted incidence. We found a significant negative relationship between number of days of ACT stock-outs, number of years of seasonal malaria chemoprevention (SMC), number of SMC cycles and access to bednets and malaria incidence.The intensification of malaria control interventions has led to an overall reduction in the incidence of malaria. However, in some districts, a significant increase in incidence has been observed, hence the need to continue adapting strategies to meet these evolving challenges in order to reduce the incidence of malaria in these districts. In addition, the association between adjusted malaria incidence and some factors should be analyzed with caution and more in-depth analyses are needed to draw conclusions.

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FEASIBILITY OF USING GEOGRAPHIC INFORMATION SYSTEMS (GIS) TO FACILITATE POPULATION-PROPORTIONATE HOUSEHOLD SAMPLING OF ADMINISTRATIVE UNITS IN NORTHERN UGANDA, A CASE STUDY

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Population-based sampling using census population counts is the gold standard of public health sampling. In low- and middle-income countries, obtaining an up-to-date census at high spatial resolution poses a challenge in conducting population-representative sampling. Conventional methods to randomly selecting households (HH) for cluster sampling designs (e.g. WHO EPI cluster sampling or "random walk") is subject to selection bias and require multiple visits to each cluster. The use of GIS tools can mitigate these biases, preclude the need for a detailed census, and increase study validity by creating a more representative sample. Between August 2022 to January 2023, we successfully implemented a GIS-guided two-stage cluster sampling method GulART Study in Northern Uganda, which aimed to characterize the prevalence of *Pfk13* markers associated with partial resistance to artemisinin-based treatment of malaria in five districts. To the best of our knowledge, prior surveys of *Pfk13* in this region relied on convenience sampling. Our goal was to sample n=660 children <5 years of age. To do so, (1) we randomly selected n=33 parishes, stratifying by district; (2) we next obtained spatial population maps of each selected parish by masking a LandScanTM population density raster with parish boundaries obtained from Humdata in ArcGIS; (3) we used the Create Balanced Spatial Points tool to draw random points weighted by population density; points were then matched to Google Earth satellite imagery to select a human habitation within a 5km radius for a total of n=20 HHs per parish. HHs were oversampled by 1.5 times to account for unsuccessful encounters. To protect HH's geoprivacy, hand-drawn maps of parishes were used to locate sampled HHs. In our experience, GIS-guided sampling located an eligible HH participant in 70% of selected HHs and was feasible to use in field sampling. Rigorous implementation of our sampling protocol

abrogates common biases associated with "random walk" sampling, and linkage of participants and geo-location facilitates additional downstream analyses.

8054

DEVELOPING A ROADMAP FOR THE IMPLEMENTATION OF MALARIA GENOMIC SURVEILLANCE IN AFRICA

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Genomics for global health with a focus on outbreaks and endemic disease has been a long term investment by researchers and public health professionals around the world. Interest and investment in the area of genomic surveillance has accelerated in recent years, including the potential for pathogens with pandemic and epidemic potential, as shown previously. However, there has been little translation of genomics for malaria policy-decision making to date. The power of genomic surveillance when applied to endemic diseases, such as malaria, has a dual purpose - to accelerate the elimination of the disease and as a source for pandemic preparedness for future events. Africa CDC commissioned- a technical working group in April 2022 to identify public health priority use cases and develop a roadmap for the implementation of malaria genomic surveillance in Africa which is to be delivered in 2024. With a focus on sustainability, harmonisation of laboratory approaches and interoperability of data, the roadmap aims to balance the need for country leadership with a continent wide strategy. Providing an end-to-end genomic surveillance framework developed for malaria, but adaptable to other pathogens and vectors, the phased approach encourages a national strategic plan informed by and aligned with regional and continent-wide objectives. It also aims to empower a continental network of institutions for malaria genomic surveillance such as reference laboratories, regional hubs and centres of excellence and national nodes for malaria genomic surveillance. Importantly, an enduring focus on the roadmap is on sustainability and inclusion of national funding as a key part of a diversified funding landscape. While ambitious, the roadmap is also pragmatic. It aims to build on existing knowledge, partnerships and infrastructure for the overarching goal of an integrated ecosystem that accelerates malaria elimination and contributes to global health security.

8055

DRUG PHENOTYPE ASSESSMENT TO VALIDATE DRUG RESISTANCE MARKERS CHANGING AMONG NATURAL SENEGALESE *PLASMODIUM FALCIPARUM* ISOLATES

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Senegal has implemented multiple antimalarial drug-based strategies over the past two decades, including intermittent preventive treatment for pregnant women, artemisinin-based combination therapies as artemether-lumefantrine, artesunate-amodiaquine (AS-AQ) for case management and seasonal malaria chemoprevention (SMC) using SP-AQ. Previously, we profiled several known drug resistance markers (*Pfcrt, Pfmdr1, Pfdhfr, Pfdhps,* and *Pfkelch13*) using single nucleotide polymorphism (SNP) molecular surveillance and whole genome sequence collected from febrile patients with malaria at health facilities across Senegal between 2000-2022. Our molecular surveillance revealed changes in *Pfcrt, Pfdhfr* and *Pfdhps* allele frequencies over time. Of note was a decrease in the *Pfcrt* K76T allele frequency between 2003 and 2014, declining from 76% to 26% coincident with chloroquine (CQ) withdrawal as a primary first line drug. Interestingly, this trend was reversed between 2014 and 2022 with an increase in *Pfcrt* K76T allele frequency reaching a Senegal-wide frequency of 57% in 2022. Whole genome sequencing analyses suggested that this increase was associated with the emergence of a new selective sweep. We hypothesized that these changes on *Pfcrt* K76T in 2014 reflects emerging amodiaquine (AQ) resistance or amodiaquine-mediated changes in parasite fitness due to AQ use in SMC (SP-AQ) or in AS-AQ treatment. To test this hypothesis, we culture-adapted parasites with and without *Pfcrt* K76T and phenotyped them for drug susceptibility to chloroquine (CQ) and mono-desethyl-amodiaquine (MD-AQ), the active metabolite of AQ. Parasites with *Pfcrt* K76T had significantly increased CQ EC50 ($p<0.0001$) and MD-AQ EC50 ($p<0.0013$) relative to wildtype *Pfcrt* parasites. Phenotypic assessment and genetic validation using gene editing in a Senegalese background will be done to assess the impact of *Pfcrt* K76T mutation on MD-AQ susceptibility. However, these findings raise the question of the duration of AQ efficacy and suggest a need for ongoing monitoring using molecular surveillance and genetic validation to guide drug policy.

8056

DEVELOPING AN OPEN SOURCE, FREE, AND GENERALIZABLE SAMPLE AND DATA MANAGEMENT SYSTEM TO ENABLE SCALABLE AND SUSTAINABLE GENOMIC SURVEILLANCE IN SENEGAL

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Scalable and sustainable pathogen genomic surveillance, and more broadly any sizable sample or data handling, necessitates robust systems for sample and data management. Commercial solutions exist but are often expensive and inflexible to local contexts and needs, while bespoke solutions are often challenging to develop, scale, and sustain. Here we describe a sample and data management system using free and open access tools in the Google Suite (namely Google Sheets), developed to meet the needs of malaria genomic surveillance efforts in Senegal, but available and generalizable to the wider community. The system was initially developed at the Broad Institute in Boston for large-scale sample processing and management and adapted to support large-scale COVID genomic surveillance, and has several features that make it ideal for broader use, including in lower resource settings, such as integration with existing sample and data management systems, familiarity with Google tools and ease of uptake, and being an open source and free solution. Like other labs

scaling surveillance activities, CIGASS historically used several commercial and bespoke tools for smaller scale sample and data management. We are able to maintain functioning and familiar tools and seamlessly integrate them into this new system due to the flexibility of Google tools. Unlike tools that require some level of coding skills to navigate, such as a SQL database, Google tools are often familiar to users. At CIGASS, they already use a Google Workspace to manage all of their office activities including email and file sharing, which made the shift to this Google-based system fairly seamless. Google tools are free and open source, enabling generalizability to a broad range of settings. Google tools meet the highest standards of data security and privacy and access for sharing is controlled at the level of the individual user. This system has proven to be an effective tool for scaling and conducting genomic surveillance at a country-level at CIGASS and is generalizable, adaptable, and openly available to be used for other pathogens and laboratory settings.

8057

IMPACT OF A REWARD SYSTEM AND CONSISTENT FEEDBACK ON REPORTING RATE AND TIMELINESS IN OGUN STATE, SOUTHWEST NIGERIA

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The timeliness and reporting rates of data reports are key components of any health system aiming to ensure quality data. In Ogun State, Nigeria, as of 2017, the average annual reporting and timeliness rates of data reports was 40% and 31% respectively among the 20 Local Government Areas (LGA). In 2018, Management Sciences for Health began implementing a seven-step approach to address this challenge, with the aim of getting the timeliness and reporting rates above the 90% national target. Working with the State team, we adopted the following steps: established a data control room to track reporting and timeliness rates and other data quality issues; trained the control room team on the use of District Health Information Software v.2 (DHIS2) to download and track data; divided LGAs among control room members for better accountability; shared daily reporting with LGAs and stakeholders from 8th to 14th of each month; rewarded/celebrated best performing LGA each quarter; presented a letter from the Permanent Secretary of the Ministry of Health to the best performing LGA over the past year; and, supported cleaning and validation of the DHIS2 data reports and having a health facility registry. The results show a steady increase from 2018 through 2023 with the average reporting and timeliness rates increasing from 40% and 31% to 71% and 65% respectively. There was a slight dip in 2021 due to the migration to DHIS2. While the combined effect of the seven-step approach appears to have yielded good results, more study is required to ascertain which of the steps are the most critical and whether the intervention can be sustainably supported by the State. In conclusion, MSH implementation in Ogun State has led to a steady increase in reporting rate and timeliness, although the state still falls slightly below the national target of 90%. However, a dip in 2021 was due to the migration from DHIS version 2013 to 2019, affecting reporting rates and timeliness. Further cleaning on DHIS is needed to remove duplicate and non-functional facilities, which also affect reporting rates.

8058

ENHANCING WEEKLY EPIDEMIOLOGICAL SURVEILLANCE DATA COMPLETENESS ACROSS KARAMOJA REGION OF UGANDA: A QUALITY IMPROVEMENT APPROACH

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In Uganda's Karamoja region, a review of key malaria indicators revealed significant incompleteness in the weekly epidemiological surveillance report (HMIS 033B), particularly in the commodity section, which is crucial for malaria tracking at health facility and district levels. At baseline in week 40 of 2023, HMIS 033B report completeness was only 67%, well below the required 95% completeness. To address data quality issues, the PMI Uganda Malaria Reduction Activity (PMI MRA) conducted a desk analysis of the report, focusing on completeness, consistency, accuracy, and integrity. Further inquiry revealed inadequate knowledge among health workers on how to complete the HMIS 033B and an unclear understanding of roles regarding who should fill which report section and when. Consequently, PMI MRA worked with Karamoja's 9 district local governments using a systematic quality improvement approach, including regular monitoring, mentorship, data validation, and joint support supervision of malaria activities at the health facility level, along with weekly desk-based generation of malaria indicator dashboards. Forty-two district health technical resource persons were trained in constructing and using malaria surveillance charts and filling the HMIS 033B report, who subsequently trained 448 health facility workers, followed by continuous monthly coaching, monitoring, and supervision for 6 months. The reports also helped district health teams and leadership identify 60 overstocked and 7 stocked out facilities for appropriate commodity redistribution. The proportion of completed HMIS 033B reports improved from 67% in week 40 of 2023 to 97% in week 10 of 2024, following intense data quality checks, and emphasizing completing reports during performance review meetings. Intense data quality improvement efforts in response to incomplete reporting resulted in improvements in reporting rates and data use in Karamoja region.

8059

SOCIODEMOGRAPHIC STUDIES AND THE SPATIAL DISTRIBUTION OF MALARIA EPISODES IN DANGASSA, KATI DISTRICT FROM 2014 TO 2016

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One of the main characteristics of malaria epidemiology is its heterogeneity in malaria-endemic areas, especially in semi-urban areas such as Dangassa in Mali. This study evaluates the risk factors associated with the occurrence of multiple episodes of malaria in Dangassa from 2014 to 2016 and their spatial distribution. This was a longitudinal study with the ICEMR1 cohort in Dangassa from 2014 to 2016. In the study, participants were malaria-free during the cross-sectional round and were followed according to the occurrence of malaria episodes between the passages. The risk of multiple episodes was determined by ordinal logistic regression with SPSS 25.0 software. Arc-GIS version 10.2 software was used to analyze the spatial distribution of malaria episodes. The risk of a high number of malaria episodes was higher in children aged 5 to 9 years compared to those under 5 years of age (OR=1.33(1.06; 1.66). This risk was greater during periods of high transmission OR=2.05(1.74; 2.42) and varied by year (lower in 2016) OR= 2.69 (2.21; 3.3) and 2.93(2.44; 3.52). The malaria episodes were scattered throughout the village with a high concentration to the west

where the Niger River passes about 4 km away. Our results showed that there would likely be malaria transmission hotspots in Dangassa and that vulnerability related to malaria occurrence was higher among children aged 5 to 9 years compared to those less than 5 years of age.

8060

IMPROVING MALARIA EPIDEMIC SURVEILLANCE IN UGANDA'S WEST NILE REGION THROUGH HEALTH WORKER CAPACITY STRENGTHENING AND REUSABLE MALARIA SURVEILLANCE CHARTS

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Malaria remains a significant public health challenge in Uganda, with varying prevalence rates across high-burden regions, namely: 22% in West Nile, 34% in Karamoja, 21% in Busoga, 13% in Lango, and 12% in Acholi (Malaria Indicator Survey, 2019). In West Nile, there was limited monitoring and tracking of malaria cases between July and September 2022, with weekly epidemiological surveillance reporting (HMIS 033B) consistently at 78%, just below the 82% annual national target in financial year 2022/2023 (UMRESP 2020-2025). To strengthen surveillance in the region, reusable malaria surveillance boards were procured and distributed to all 13 district health offices, 358 health facilities, and two emergency operation centers. Additionally, 279 health workers were trained-including district health officers, biostatisticians, HMIS focal persons, malaria focal persons, district medicines management supervisors, and surveillance focal persons to construct, plot and update, interpret, and use the charts to monitor weekly malaria case trends, set incidence thresholds, and trigger epidemic alerts and response. Of the 378 malaria surveillance charts distributed in health facilities across the region, 94 in six districts successfully plotted and constructed the malaria normal channel charts after training. As a result, the weekly epidemiological surveillance reporting rates increased by 16%, from 76% in week 1 to 92% in week 9 of 2024, indicating improved reporting in the region. Given that malaria epidemics are often localized, the surveillance charts prove most effective when completed and interpreted at the health facility level. Using malaria epidemiological surveillance charts is critical for enhancing the weekly epidemiological surveillance reporting rate and triggering rapid response.

8061

INTEGRATION OF COMMUNITY DATA WITH ROUTINE HEALTH FACILITY DATA TO GENERATE INSIGHTS INTO MALARIA EPIDEMIOLOGY AND SERVICE DELIVERY IN BUIKWE DISTRICT IN UGANDA

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While routine surveillance is a key component in control, prevention and elimination of diseases, use of this data for decision making is still limited. This study sought to understand how data from community and health facility-based systems in Buikwe district, Uganda, can be utilized to better-inform decision making. The study reviewed analyzed monthly outpatient and community data from Buikwe district for the period Jan - Aug 2023 to assess service uptake, malaria testing rates, number of confirmed malaria cases, and crude incidence for this period. Completeness of data from health facilities was high with over 90% of the expected reports submitted monthly, however, community data completeness was lower ranging from 33% (Feb) to 75% (Jul) of expected reports submitted. Monthly data trends showed that, as the number of confirmed malaria cases seen at the community increased, the number of confirmed cases seen at the health facilities reduced. At the community, there was 349% increase in the number of cases in May 23 compared those seen Aug 23, while a 114% decrease in the number of confirmed cases was seen at health facilities in the same period. Similar observations are seen with results for crude malaria incidences. Diagnosing malaria at community level reduced the number of cases seen at health facilities. Solely using health facility data to monitor trends in malaria cases could have led to misinterpretation of the prevailing situation. This study showed that combining health facility-based and community surveillance data can provide a more holistic picture of the malaria situation in a given geography.

8062

DIGITALIZATION THROUGH DHIS2 TRACKER PROGRAMS AT HOUSEHOLD AND INDIVIDUAL LEVELS FOR 2023 SEASONAL MALARIA CHEMOPREVENTION CAMPAIGNS IN CÔTE D'IVOIRE

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The PMI Stop Djekoidjo project, funded by the U.S. President's Malaria Initiative, supported the Ivorian Ministry of Health's National Malaria Control Program (NMCP) to launch its first seasonal malaria chemoprevention (SMC) campaign in two health districts in 2023. The NMCP DHIS2 instance, separate from the national Health Management Information System, was used to digitally collect and analyze the campaign data. The goal was to ensure the availability of data to enable course correction during the campaign, reduce workload burden on health workers and community health workers (CHWs), and minimize the data quality issues experienced in previous campaigns using paper-based tools. Data collection tools were first configured to work with DHIS2 Tracker and indicators to monitor performance within a DHIS2 dashboard were created. User acceptance testing was then conducted, and necessary corrections were made to the data collection tools and the dashboard based on feedback. Supervisors, district management teams, and CHWs were trained on the collection of household-level data using a QR code using tablets equipped with the DHIS2 Android Capture application. Training also included conducting analyses and data visualizations within the DHIS2 dashboard. During the SMC campaign itself, data were entered after scanning unique QR codes, which households received during registration. Using QR codes provided instantaneous information to health workers and CHWs than searching children in a register that would take on average five minutes. Digitization of data allowed for more efficient data entry and an overall faster campaign, since data entry took less time per household. Data were submitted every day, allowing near real-time monitoring across the entire campaign. The first and second cycles of the SMC campaign covered 86% and 90% of eligible children, respectively, who received tablets of sulfadoxine-pyrimethamine+amodiaquine (SPAQ). This digitization provided improved data quality, ease of coverage rates monitoring, and reduction of workload burden on health workers and CHWs.

8063

STREAMLINING THE MEDICINE REGISTRATION SYSTEM TO IMPROVE ACCESS TO QUALITY MALARIA COMMODITIES IN MADAGASCAR, 2018 - 2024

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Strengthening the essential medicine registration system is critical to improving availability of malaria commodities in Madagascar. Registration of antimalarial commodities funded by donors to allow their importation and presence on the market has typically taken at least six months, compromising their availability. To address this, the U.S. Agency for International Development (USAID)-funded IMPACT program began supporting the Malagasy Ministry of Public Health (MOPH) in 2019 to harmonize the Madagascar Medicines Regulatory Authority (AMM) market authorization (MA) process, by applying a quality assurance system for the Madagascar Central Medical Store (SALAMA) and donors to prequalify vendors. In 2021, a multi-stakeholder registration committee was established by the AMM to analyze pending dossiers and clear the backlog of MA requests submitted by SALAMA and donors. Monthly meetings have been organized since 2022 with the committee to evaluate the dossiers and grant MA letters for products that fulfill the criteria to be registered. From 2018 to 2024, 91 dossiers of MA requests were submitted to the AMM for malaria medicines, and after technical assessment by the committee, 76 (84%) of the dossiers met the requirements to be assessed for MA. Sixty of the 76 (79%) received MA, and MA requests were processed (dossiers reviewed and, if approved, MA letters issued), on average, in a period of two months (an estimated four months less than before the IMPACT program) from receipt of dossier and payment for combinations of artemether-lumefantrine, artesunate-amodiaquine, and sulfadoxine-pyrimethamine. Implementing a harmonized system of prequalification of and MA processes for malaria commodities streamlines their registration, thereby helping facilitate their availability on the market and ensure quality. Harmonized and streamlined review processes for registration of malaria products is a key strategy to strengthen the medicine regulatory system and improve access to safe, quality antimalarial products, and can be considered for scale up in other low- and-middle income countries.

8064

ESTABLISHING ROBUST, OPEN, ACCESSIBLE BIOINFORMATICS TOOLS FOR MALARIA GENOMIC DATA ANALYSIS AND REPORTING, IMPLEMENTED IN THE TERRA CLOUD-BASED ANALYSIS PLATFORM

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Bioinformatic analysis capacity remains a significant challenge in advancing the implementation and impact of malaria genomic surveillance. Here we share progress in developing validated genomic data analysis tools (workflows) to serve common use cases for Plasmodium falciparum (Pf), and the implementation of these workflows in Terra, a secure, user-friendly, open access, cloud-based data analysis platform. We describe the development of a workflow for high confidence SNP variant calling from short read whole genome sequence data, using the current gold standard genomic analysis toolkit (GATK 4.5.0) and state-of-the-art methods in alignment (BWA-MEM2), variant calling (HaplotypeCaller with De Bruijn graphs), and filtration (GATK VETS). The variant filtration process leverages the MalariaGEN Pf7 data resource, which provides broad representation of global Pf genetic diversity to optimize filter correctness, and has been validated against well characterized samples, including the Pf genetic crosses datasets. Openly accessible in the Terra cloud platform, this workflow offers robust whole genome variant calling regardless of local compute infrastructure or computational expertise. It is part of a larger data analysis ecosystem being developed to provide accessible and reliable tools and support for the malaria genomics community. Additional workflows currently available in Terra will also be featured, including SNP-based drug resistance determination and genetic relatedness inference from short read sequence data, deconvolution of polygenomic infections and hrp-2/3 deletion determination from long read data, and denoising and analysis of amplicon sequence data. We also show the application of these tools to the analysis of Pf genomic surveillance data from Senegal, including local workflow development, data analysis, and NMCP reporting. Practical considerations for the use of these tools and of the Terra platform by the malaria genomics community will also be covered.

8065

COMPARATIVE ANALYSIS OF INDIVIDUAL-BASED MALARIA MODELS: CHARACTERIZING MODEL BEHAVIOR FOR ENHANCED CONFIDENCE IN MODEL-INFORMED DECISION MAKING

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Mathematical models are increasingly used to support global and national malaria policy decision making. It is unclear how the use of different models may affect supporting model evidence for decision making, however, no exhaustive comparison of model behavior, including perturbations, exists. We use three widely used individual-based models of malaria to characterize model behavior and compare relationships in outcome measures across varying age groups at equilibrium or after perturbations that approximate common interventions used (preventive therapies, vector control, and vaccination). The models were aligned as much as possible on critical input parameters, such as transmission intensity, case management, and diagnostic performance while maintaining structural model differences. The models produce daily, monthly, and yearly clinical outcomes by flexible age groups as well as indicators of transmission for varying scenarios. We describe the relationships between transmission intensity, prevalence, and clinical or severe incidence, in specific age groups or trends by age. While these epidemiological relationships were generally similar across the models at equilibrium and under perturbation, differences were apparent, for extreme levels of low or high transmission, by disease outcome, and for perturbations affecting immunity acquisition. The results support transparent and improved understandings of performance and behavior of the three models assessed. Ultimately this type of comparison increases confidence of model users and decision makers in the modeling results.

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EVALUATING SUB-NATIONAL TAILORING OF MALARIA INTERVENTIONS

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In an environment of limited financial resources for malaria control, directing those resources in the most cost-effective way to maximize reductions

in malaria burden is critical. As a result, data-driven sub-national tailoring (SNT) of malaria interventions has become a key component of developing national strategies and applying for funding from the Global Fund (GF) and other funders. While this process is increasingly driven by funding organizations, the World Health Organization, and partners, it requires strong country leadership and ownership to be truly successful. Country programs also need guidance on how best to implement SNT under the current funding conditions. We completed an in-depth assessment of the effectiveness of the SNT process conducted for the past two GF cycles in seven countries (Central African Republic, Democratic Republic of the Congo, Ethiopia, The Gambia, Nigeria, Senegal, and Zambia) to understand key challenges, gaps, and best practices. We first created a conceptual framework to identify key steps in the SNT process, including improving surveillance data quality, creating a repository of intervention and related data, convening a technical working group, conducting stratification and intervention targeting based on country-defined criteria, obtaining adequate funding, and implementing and evaluating the SNT plan outcomes with allocated funding. For each country we reviewed and collated data on each of these steps from the two most recent GF grant cycles (6 and 7), national strategic and operational plans, intervention coverage, and routine malaria surveillance data. In addition, we conducted 25 in-depth interviews with key national malaria program and partner organization staff to document perspectives of challenges and bottlenecks encountered and successes achieved. We present results of this analysis where a systems approach was used to characterize factors associated with a successful SNT process, focusing on efficiency, equity, country ownership and value for money. Both country specific and cross-country themes will be presented.

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RAPID MOLECULAR MONITORING OF *KELCH13* OF *PLASMODIUM FALCIPARUM* SHOWS LOW DIVERSITY AND LACK OF ARTEMISININ RESISTANCE-ASSOCIATED MUTATIONS ON BIOKO ISLAND, EQUATORIAL GUINEA

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In 2023, the Bioko Island Malaria Elimination Project (BIMEP) conducted their annual malaria indicator survey (MIS) on Bioko Island (BI), Equatorial Guinea, revealing 12.9% *Plasmodium* species (Pspp) prevalence by RDT over all age groups. As BIMEP pushes towards pre-elimination, monitoring malaria for drug resistance markers, including low parasite density infections, becomes a high priority. With the aim of developing a pre-screening workflow to monitor for drug resistance markers, we analyzed 1,500 dried blood spot samples collected from individuals with positive (n=1400) and negative (n=100) RDTs for the presence of malaria parasites. Utilizing PlasmoPod, a novel, cartridge-based, rapid PCR diagnostic device, samples were tested in the research laboratory on BI, for the presence of Pspp using 18S rDNA/rRNA RT-qPCR. Further, a subset (n=209) was assessed by qPCR for *kelch13* mutations R561H, M579I and C580Y in the propeller region, signals known to be associated with artemisinin resistance in SE Asia. No resistant mutations were found at target sites among these samples. Nanopore sequences from the 2023 MIS are being generated and analyzed on BI providing more detail on currently circulating variations in drug resistance sites of the *kelch13* propeller region. Analysis of *P. falciparum* sequence data from the 2019 MIS (n=90) show nucleotide diversity in the *kelch13* coding region to be low (π = 0.001 ± 0.0001). While most mutations occur in the coiled-coil-containing and BTB (Bric-a-brac, Tramtrack and Broad complex) domains, some SNPs appear in the propeller region. However, these are not known to be associated with resistance, but are common alleles appearing in African isolates. As BI transitions to a low-transmission area, BIMEP will need to conduct continuous surveillance to monitor the potential expansion of drug-resistant strains due to antimalarial-related selective pressure. Employing a qPCR-based screening protocol locally for key *kelch13* mutations with Plasmopod, improves cost-efficiency without compromising PCR accuracy and allows for close, rapid monitoring of *P. falciparum* strains.

8068

ASSESSEMENT OF QUALITÉ OF MALARIA CASE MANAGEMENT AND PREVENTION USING MICROSTRATIFICATION METHOD

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Although there has been a 10% drop in incidence over the past 5 years despite the multitude of interventions implemented to reduce malaria burden, malaria remains the leading cause of mortality in Burkina Faso, accounting for 14% of deaths in 2022. In 2023, the NMCP carried out a microstratification analysis with the aim to assess the quality of malaria services. A two-prong approach was used to carryout this assessment as guided by WHO. Firstly, 17 indicators for malaria management and prevention services were calculated using routine data from health facilities. Secondly, using this 17 indicators, 4 composite indicators were generated to mesure management of uncomplicated malaria, management of malaria (uncomplicated and complicated), routine prevention interventions and a composite indicator of overall malaria program performance. All indicators were then classified into low, medium and high performance. Overall, all the health facilties (3843) were included, analysis of the 4 composite indicators showed that : 13% had a high performance for the management of uncomplicated malaria, 24% for the implementation of routine preventive services, 19% for the total composite indicator. Data on the management of severe malaria were not collected in the health information system. Among the 12 simple indicators, the one with the best performance was the rate of treatment of uncomplicated malaria with an ACT, with a high performance for 27% of health facilities. Prevention through the distribution of LLINS to children under 5 had the lowest performance, with 8% of health facilities with high performance.According to our analysis, the quality of malaria case management and prevention service provision in health facilities faces challenges. These results are in line with those of the SARA survey carried out in 2018, which highlighted the challenges of implementing malaria treatment guidelines. The implementation of routine microstratification analysis using routine data and using the results to inform the targeting of interventions such as supportive supervision to health facilities will greatly improve the quality of service

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ADVANCING EARLY WARNING SYSTEMS FOR MALARIA, PROGRESS, CHALLENGES, AND FUTURE DIRECTIONS

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Malaria early warning systems (EWS) are predictive tools that often use climatic and environmental variables to forecast malaria risk and trigger timely interventions. Despite their potential benefits, the development and implementation of EWS for malaria face significant challenges and limitations**.** We reviewed the current status of EWS for malaria, including their settings, methods, performance, actions, and evaluation. We conducted a comprehensive literature search using keywords related to EWS and malaria in various databases and registers. We included primary research and programmatic reports focused on developing and implementing EWS for malaria. We extracted and synthesized data on the characteristics, outcomes, and experiences of EWS for malaria. After reviewing 5,535 records, we identified 30 studies from 16 countries that met our inclusion criteria. The studies varied in their transmission settings, from pre-elimination to unstable, and their purposes, ranging from outbreak detection to resource allocation. The studies employed

various statistical and machine-learning models to forecast malaria cases, often incorporating environmental covariates such as rainfall and temperature. The most common mode used is the time series model. The performance of the models was assessed using measures such as the Akaike Information Criterion(AIC), Root Mean Square Error (RMSE), and adjusted R squared(R^2). The studies reported actions and responses triggered by EWS predictions, such as vector control, case management, and health education. The lack of standardized criteria and methodologies limited the evaluation of EWS impact. This review provides a comprehensive overview of the current status of EWS for malaria, highlighting the progress, challenges, and gaps in the field. The review informs and guides policymakers, researchers, and practitioners in enhancing EWS and malaria control strategies. The review also underscores the need for further research on the integration, sustainability, and evaluation of EWS for malaria, especially in light of ongoing climate change**.**

8070

STRAIN-TRANSCENDING ANTI-AMA1 HUMAN MONOCLONAL ANTIBODIES NEUTRALIZE MALARIA PARASITES INDEPENDENT OF DIRECT RON2L RECEPTOR BLOCKADE

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Malaria remains one of the most fatal and prevalent infectious diseases globally. Apical membrane antigen 1 (AMA1) is a promising vaccine and therapeutic antibody target to prevent blood-stage malaria infection. However, AMA1 alleles in endemic areas are highly polymorphic. These polymorphisms serve as an immune evasion strategy to circumvent strain-transcending protection, preventing the development of effective strain-transcending vaccines based on AMA1. AMA1 interacts with rhoptry neck protein 2 (RON2) during merozoite invasion into red blood cells, and this essential interaction is conserved among apicomplexan parasites. While extensive research has focused on antibodies that neutralize parasite growth by disrupting the direct interaction between AMA1 and RON2, no monoclonal antibodies have yet been identified that neutralize parasites through alternative mechanisms. In this study, we investigated a panel of naturally acquired human monoclonal antibodies (hmAbs) specific to AMA1, derived from individuals living in malaria-endemic areas. Our approach utilized structural biology and biophysical tools, along with parasite growth inhibition assays. We evaluated the specificity and binding kinetics of human antibodies using enzyme-linked immunosorbent assay and biolayer interferometry. Epitope binning experiments revealed that two potent neutralizing hmAbs engage AMA1 without disrupting RON2 binding. Co-crystal structures of AMA1 with these neutralizing hmAbs were determined, revealing novel and distinct conformational epitopes. One of the hmAbs neutralized diverse parasite strains, and the combination of these hmAbs showed synergistic enhancement of parasite neutralizing activity. Importantly, this work underscores the significance of neutralization mechanisms for AMA1 hmAbs that are independent of RON2 blockade. These findings highlight a novel, strain-transcending surface targeted by naturally acquired human antibodies that hold promise for the development of broadly protective vaccines and therapeutics.

8071

PRE-CLINICAL STUDY ON VIRAL-VECTORED *PLASMODIUM FALCIPARUM* MULTISTAGE VACCINE EFFECTIVE BOTH FOR PROTECTION AND TRANSMISSION-BLOCKADE IN RHESUS PRIMATES

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We have established an innovative and efficacious vaccine platform (m8Δ/AAV1) that consists of two viral vectors. The m8Δ/AAV-based malaria vaccine is based on a proven viral-vectored vaccine platform, consisting of a highly attenuated vaccinia strain; LC16m8Δ (m8Δ), and adeno-associated virus type1 (AAV1) expressing *P. falciparum* Pfs25-PfCSP fusion protein. The vaccine named m8Δ/AAV1-Pf(s25-CSP) is specifically designed to synergize with the WHO Expanded Program on Immunization (EPI) for infants. A heterologous m8Δ-prime/AAV1-boost immunization regimen has successfully been proven to be highly effective both for protection and transmission blocking in a murine model. Crucially, this activity is long-lasting in comparison with other anti-malarial vaccines tested in the same assays.The present study addressed its safety and vaccine efficacy to a non-human primate model. Four rhesus monkeys were immunized with a heterologous m8Δ-prime/AAV1-boost regimen. The immunized monkeys induced high PfCSP- and Pfs25-specific IgG antibody titers. Remarkably, the persistence of vaccine-induced immune responses were over 6 months and additionally provided *in vitro* sporozoite neutralizing activity against transgenic PfCSP/Pb sporozoites and transmission-blocking efficacy against transgenic Pfs25/Pb. Thus, our vaccine has extensive high-quality pre-clinical data and clear efficacy with a robust antibody response and substantial efficacy against malaria's pre-erythrocytic and sexual stages in non-human primates. Our vaccine would be worth proceeding to a clinical trial as a novel alternative to Protein-in-Adjuvant vaccines such as RTS, S and R21.

8072

R21/MATRIX-M™PHASE III TRIAL: FURTHER FOLLOW-UP AND ASSESSMENT OF AN ADDITIONAL BOOSTER DOSE

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R21/Matrix-M™ received WHO and several national approvals for use in African children using a four-dose regime in 2023. Deployment of this vaccine is expected from May 2024. Due to the low-cost per dose ($3.9) and a manufacturing commitment from Serum Institute of India Pvt. Ltd (SIIPL) of up to 200 million doses annually, all of the target population, comprising at least 40 million children per year in sub-Saharan Africa, should soon receive R21/Matrix-M™, significantly reducing malaria morbidity and mortality. The phase III trial of R21/Matrix-M™ is continuing, not only assessing long-term safety and efficacy but also the potential added value of additional annual or biennial boosters to maintain efficacy

in childhood. Participants in the malaria vaccine group were further randomised to receive an additional zero, one or two annual or biennial R21/Matrix-M™ boosters, resulting in them receiving a total of four, five or six doses of R21/Matrix-M™. Prior to this, participants aged 5-36 months had received 3 doses, 4 weeks apart, followed by a booster dose a year later of either R21/Matrix-M™ or a control vaccine. At 24 months following the primary series of vaccinations, evaluation of time to first clinical malaria episode demonstrated vaccine efficacy (VE) of 73% [70-76] at the seasonal administration sites with VE of 77% [72-81] in 5-17 month olds. VE was similar on assessment of multiple malaria episodes: 71% [68-74], and 75% [70-79] in the younger age group. R21/Matrix-M™ also demonstrated significant efficacy against severe malaria: 18 episodes were recorded at 18 months of follow-up across all sites and VE was 62% [6-85]. Further safety and efficacy data from the third year of follow-up will be presented, with the impact on vaccine efficacy of an additional booster dose following a third malaria season. These results all contribute to the growing body of data on R21/Matrix-M™ which will assist policy-makers in judging the optimal use of this low-cost, widely-accessible and high-impact vaccine.

8073

STRUCTURE GUIDED DESIGN OF A MRNA VACCINE TARGETING APICAL MEMBRANE ANTIGEN 1 IN PLASMODIUM FALCIPARUM

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Previous clinical trials of vaccines targeting apical membrane antigen 1 (AMA1) in *P. falciparum* suffer from low induction of neutralizing antibodies against parasites homologous to the vaccine and offer almost no protection against heterologous parasites. While AMA1 is highly immunogenic, many of the antibodies induced by AMA1 immunization target non-neutralizing and polymorphic epitopes. We employed a stepwise approach to engineer an AMA1 vaccine capable of overcoming these limitations. *In vitro* results show that elimination of AMA1 domain 3 from the vaccine construct may focus the immune response on more neutralizing epitopes on domains 1 and 2 (D12). A *baculovirus* expressed AMA1 (D12) vaccine provides near complete protection of mice challenged with lethal *P. yoelii* parasites. Next, we show that production of this AMA1 (D12) construct in a mRNA LNP platform produces higher antibody titers, more avid antibodies and a higher proportion of mouse IgG2a/IgG1 antibodies than an Addavax adjuvanted protein vaccine. Membrane anchoring this mRNA AMA1(D12) construct induces even higher antibody titers and more avid antibodies than the previous secreted mRNA construct. Interestingly, introduction of the transmembrane region (TM) appears to focus the immune response on the apical end of AMA1, where most known neutralizing monoclonal antibodies bind. While highly neutralizing against homologous parasites, this AMA1(D12)-TM mRNA vaccine still suffers from low *in vitro* efficacy against heterologous parasites. To develop a more conserved vaccine, we designed a fusion protein of the AMA1(D12)-TM construct fused to the RON2L peptide, the parasite derived binding partner of AMA1. Immunization with the AMA1(D12)-RON2L-TM construct enhances the production of cross neutralizing antibodies against heterologous parasites. We have developed a *P. berghei Pf* AMA1 RON2L model to test this vaccine. Currently, we are employing glycoengineering to introduce novel N-glycosylation sites on our construct to further direct the immune response to conserved, neutralizing epitopes.

8074

SAFETY OF THE RTS,S/AS01$_E$ MALARIA VACCINE ONE YEAR AFTER THE PRIMARY VACCINATION IN REAL-LIFE SETTINGS IN THREE SUB-SAHARAN AFRICAN COUNTRIES: INTERIM RESULTS

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In 2021, WHO recommended the use of the RTS,S/AS01$_E$ malaria vaccine for the prevention of *Plasmodium falciparum* malaria in children living in regions with moderate to high malaria transmission. In the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP), a surveillance study (EPI-MAL-003, NCT03855995) is conducted in Ghana, Kenya and Malawi with the main objective to evaluate the safety signals described in the RTS,S phase 3 trial (NCT00866619). This study includes a prospective cohort event monitoring (home visits, outpatient visits and hospitalizations) in exposed clusters where the RTS,S/AS01$_E$ vaccine was introduced compared to unexposed clusters where the vaccine was not offered. Incidence rates (IR) of malaria, meningitis and mortality were monitored in children under 5 years old. RTS,S/AS01$_E$ vaccinated children in exposed clusters were compared to unvaccinated children in unexposed clusters. We report the safety outcomes one year after the 3-dose primary vaccination. This interim analysis (IA) included 44,912 children uniformly distributed between exposed and unexposed clusters. The primary RTS,S/AS01$_E$ vaccination coverage was 85% in the exposed clusters. IR per 100,000 person-years (PY) of etiology-confirmed meningitis were similar in vaccinated (4.1, 95% confidence interval [CI]: 0.1-23.0) and unvaccinated children (4.0, 95% CI: 0.1-22.6), with IR ratio (IRR) of 1.02 (95% CI: 0.06-16.29, p=0.990). There were 3 cases of cerebral malaria in vaccinated and 2 cases in unvaccinated children (IRR: 1.53, 95% CI: 0.26-9.15, p=0.642). IR per 100,000 PY of all-cause mortality were 659.7 (95% CI: 561.5-770.3) in vaccinated vs 724.5 (95% CI: 622.3-838.8) in unvaccinated children and with similar IR in both genders. Overall, the RTS,S/AS01$_E$ vaccine was not associated with any safety signals previously observed in the phase 3 study, using an at-risk period of one year after the primary vaccination, which confirms the MVIP IA results. Meningitis and cerebral malaria were rare and distributed equally among vaccinated and unvaccinated children. Mortality rates were comparable between boys and girls.

8075

OFF-TARGET ANTIBODY RESPONSES TO BLOOD STAGE ANTIGENS ARE ASSOCIATED WITH CROSS-REACTIVE ANTIBODIES TO THE MAJOR AND MINOR REPEATS OF THE *PLASMODIUM FALCIPARUM* CIRCUMSPOROZOITE PROTEIN IN AFRICAN CHILDREN PARTICIPATING IN THE RTS,S VACCINE TRIALS

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Malaria remains a major global health issue, with the largest disease burden caused by *Plasmodium falciparum* (*Pf*), predominantly in children from sub-Saharan Africa. Current malaria vaccines are partially effective and their correlates of protection are not fully understood. Thus, further studies focusing on the mechanisms mediating potent immune responses are warranted to inform next generation vaccines. RTS,S/AS01 is the most advanced malaria vaccine and targets the pre-erythrocytic stage of *Pf*

by presenting a truncated form of the circumsporozoite protein (*Pf*CSP) composed of 18.5 NANP major repeats and the C-terminal domain. We previously reported that an off-target antibody response to blood-stage antigens is associated with *Pf*CSP reactivity and an estimated lower incidence of clinical malaria in a fraction of vaccinated African children during the RTS,S/AS01 phase 3 trial. To gain further insights of this phenomenon as a potential correlate of protection, we selected 60 RTS,S vaccinees displaying equivalent *Pf*CSP IgG antibody levels and differential off-target profiles. Competition ELISA experiments to MSP5, one of the most relevant off-target antigens previously identified by us, showed an abrogation of antibody signals in presence of *Pf*CSP, confirming the recognition of a common epitope. Binding experiments to *Pf*CSP truncated proteins revealed that individuals with high off-target scores presented a superior CSP_{NANP}/CSP_{Cterm} IgG antibody ratio. Surprisingly, a strong decrease of the avidity index to CSP_{NANP} was detected in those individuals presenting the lowest off-target scores. Notably, ELISA experiments using overlapping peptides encompassing the *Pf*CSP sequence revealed that plasma from donors with high off-target scores were enriched in antibodies recognizing the N-terminal junction of *Pf*CSP. Therefore, high off-target profiles in RTS,S vaccinees are associated with a strong cross-reactivity to CSP major and minor repeats.

8076

GENOTYPIC INFECTION ENDPOINT ANALYSIS TO UNDERSTAND EFFICACY AND ESCAPE POTENTIAL OF THE MALARIA MONOCLONAL ANTIBODY CIS43LS

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The development of malaria infection-blocking monoclonal antibodies (mAbs) has advanced rapidly in recent years. Several mAb candidates have entered field trials to validate safety and efficacy characteristics established in controlled infection experiments. Field trial efficacy measurement typically uses blood microscopy or qPCR to determine parasite presence/absence in study subjects sampled at regular time points after administration of the study agent or placebo. Time to first malaria infection is then compared between study arms. There is clear potential to enhance efficacy measurement and characterize intervention outcomes in greater detail by using genotypic endpoints that specify which strains are circulating among infected study subjects and whether parasite genetic polymorphisms may contribute to present or future intervention escape. This work applies high-sensitivity antigen genotyping to longitudinally track strain diversity in all *P. falciparum* malaria infections detected among the study subjects of a recent phase 2 trial assessing low and high-dose applications of the mAb CIS43LS. Our genotyping results distinguish several events of recrudescence from uncleared baseline infection, amending original efficacy interpretations based on binary endpoints. We observe dose-dependent reductions in strain diversity within individual subjects and discuss new ways to quantify efficacy using metrics based on complexity of infection (COI; number of strains per infection) and molecular force of infection (molFOI; number of newly acquired strains over time). We also observe significant nucleotide and structural variation in the circumsporozoite protein (CSP) N-terminus and in CSP regions flanking the CIS43LS epitope. The observed polymorphisms are not correlated to study arm and thus unlikely associated with antibody escape. Our work demonstrates the value of complementing current trial designs with genotypic endpoints and also highlights various methodological innovations we have applied to boost assay sensitivity and integrate false-positive detection in a high-throughput context.

8077

COMPARATIVE IMMUNOGENICITY OF THE R21/MATRIX-M MALARIA VACCINE ACROSS AGE GROUPS AND GEOGRAPHIES

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The R21 vaccine was recommended for use by the World Health Organisation in 2023 for the prevention of malaria in children aged 5-36 months. Transmission of the causative pathogen, *Plasmodium falciparum* is not limited to children. Malaria elimination therefore cannot succeed without global eradication of the disease, necessitating vaccination of all age groups. An understanding of vaccine efficacy in older age groups and across geographies is vital in tackling the disease. Immunoglobulin G (IgG) levels specific to the R21 vaccine central repeat region (NANP) have been shown to broadly correlate with vaccine-induced protection. Here, we will show immunogenicity data for the R21 malaria vaccine across different age groups and geographic regions, offering insights into its potential as a universal malaria vaccine. The analysis will compare IgG antibody responses to four constituents of the R21 malaria vaccine, utilizing data from clinical trials conducted across four countries with distinct malaria endemicity profiles. The studies include three age groups: adults, children, and infants in studies conducted in the UK, Thailand, Kenya, Mali, Burkina Faso, Uganda, and The Gambia. Each trial administered three doses of the R21 vaccine with Matrix M adjuvant, one month apart. The objective was to analyse and compare the immunogenicity of the vaccine between these cohorts at baseline and post-vaccination, by assessing antibody responses measured by a validated multiplexed ELISA-based assay to four constituents of the R21/Matrix-M vaccine; Hepatitis B surface antigen, the central NANP repeat, full length R21 construct, and the C-terminus region. The standardisation of data across different cohorts for this comparative analysis involved the validation of the multiplex ELISA, ensuring consistency and accuracy in the interpretation of the immunogenicity results across the cohorts.

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R21/MATRIX-M MALARIA VACCINE PHASE 3 CLINICAL TRIAL IMMUNOGENICITY

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R21/Matrix-M pre-erythrocytic malaria vaccine, a circumsporozoite protein-based nanoparticle with no surface-exposed hepatitis B antigen, was recommended for use by WHO in October 2023, and prequalified in December 2023 following Phase 3 clinical trial efficacy estimates in 5-36 month olds of 75% in seasonal malaria transmission sites and 68% in 'standard' perennial malaria transmission sites. In this Phase 3 efficacy trial, 4800 children aged 5-36 months were enrolled in 5 sites in 4 African countries. Seasonal sites included Burkina Faso and Mali, and standard sites included Burkina Faso, Tanzania and Kenya. Children were randomised 2:1 to receive 3 doses of R21 or a control (Rabies) vaccine in the primary series, plus a booster dose 1 year after the primary series. Fifty per cent (2400) infants were enrolled into an immunogenicity cohort. IgG antibodies specific to the central repeat region of R21 (NANP) have been shown to broadly correlate with vaccine-induced protection. Over 12 months, higher NANP-specific IgG was observed in the younger children (5-17 month age group) compared with older children (18-36 month age group). This younger age group also had higher 12-month vaccine efficacy on time to first clinical malaria episode at both seasonal and standard sites: 79% [95% CI 73-84] p<0.001 at seasonal sites, and 75% [65-83] p<0.001 at standard sites. Here, we report updated data on vaccine-elicited IgG from the immunogenicity cohort post booster dose to four R21 antigens: NANP, C-terminal, full length R21 vaccine construct, as well as the vaccine backbone, Hepatitis B surface antigen using Meso Scale Discovery (MSD). We observe geographical, age and sex variation in vaccine-elicited antibodies before and after primary series and booster dose administration. We also observe differences between sites in rates of decay of NANP-specific antibodies after primary series vaccinations.

8079

A CONJUGATED PFS230D1 VACCINE INDUCES ANTIBODIES THAT DIRECTLY PREVENT FERTILIZATION AND COMPLEMENT ENHANCES NEUTRALIZATION

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Malaria imposes a global public health burden. The delivery of the WHO-approved malaria vaccines, RTS,S/AS01 and R21/Matrix-M, which reduce human infection and associated clinical disease, will aid in the control of the global disease burden. Development of a combination vaccine that also disrupts mosquito infection and subsequent transmission events holds even greater promise to control disease. We developed a conjugated Pfs230D1 vaccine that forms nanoparticles which induce antibodies that block mosquito transmission, including in humans. In preclinical studies conducted in rhesus monkeys, conjugated Pfs230D1 formulated with various adjuvants (Alhydrogel, GLA-LSQ, GLA-SE, and AS01) induced varied immunological responses; conjugated Pfs230D1/AS01 induced one of the most robust antibody responses. Transcriptome profiling of fine needle aspirates of draining lymph nodes revealed the induction of blood transcription modules related to antibody production including enrichment in monocytes, neutrophils, and TLR and inflammatory signaling, among other unique adaptive responses. Next, we examined the role of antibodies and complement in preventing parasite development within the mosquito. Antibodies against Pfs230D1 generated in rabbits, rhesus, and human volunteers blocked mosquito infectivity in the absence of complement, indicating disruption of a protein-protein interaction required for sexual development. Subcellular localization of Pfs230 which forms a complex with the glycosylphosphatidylinositol anchored Pfs48/45 on the gamete surface demonstrated that Pfs230D1 and Pfs48/45 domain 3 (D3) are in close proximity to each other by fluorescence resonance energy transfer, even though Pfs48/45D3 specific antibodies only block fertilization independent of complement. Pfs230D1 appears to be a critical transmission blocking vaccine component, as antibodies prevent fertilization alone with enhanced neutralization activity by complement, which together increase the duration of killing and wholistically limit vaccine selection.

8080

FORCED DEGRADATION STUDIES WITH CONJUGATED PFS230D1-EPA DRUG PRODUCT PROVIDE A BASIS FOR EVALUATING ACCELERATED STABILITY

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Malaria is a life-threatening disease that affects 249 million people each year. Currently, two WHO-approved vaccines are indicated to prevent clinical disease and target pre-erythrocytic stages of the *Plasmodium* parasite. Development of a transmission-blocking vaccine (TBV) that targets sexual stages in mosquitoes may prevent spread of infection within a community. Combining an effective TBV with a current vaccine would form a promising multi-stage vaccine for use in control and elimination efforts. The leading TBV candidate is a conjugated nanoparticle called Pfs230D1(M)-EPA; in a Phase 2 safety and immunogenicity trial in Mali (NCT03917654), Pfs230D1-EPA formulated with AS01 induced high levels of antibodies with functional activity, and conferred significant reduction (>75%) in mosquito infection. In anticipation of phase 3 clinical trials and integration into a multi-stage vaccine, evaluation of unformulated Pfs230D1-EPA drug product (DP) stability is critical. To this end, forced degradation studies of conjugated Pfs230D1-EPA DP (heating at 80°C for 15 minutes) have shown a significant loss of functional activity (assessed by standard membrane feeding assay) following immunization of mice with mixtures of denatured and non-denatured Pfs230D1-EPA DP. No marked change was observed in the solubility while significant biophysical changes in the secondary structure were observed by circular dichroism (CD) spectra that were effectively replicated in assays to evaluate binding using Pfs230D1 conformation-dependent mAbs. Next, we determined significant changes could be determined in the CD spectra using mixtures of force degraded and non-degraded DP (0:100 to 25:75 with increments of 5%). We aim to correlate the statistical changes in CD spectra to corresponding changes in ELISA titration curves using conformation-dependent mAbs. Subsequently, the CD spectra and/or an ELISA may be used to evaluate changes in conjugated Pfs230D1-EPA DP in an accelerated stability following WHO guidelines (40°C for 14 days, and 2 - 8°C and 25°C for 6 months).

8081

DESIGN, CHARACTERIZATION, AND EFFICACY OF TWO UNIQUE MRNA-BASED BLOOD-STAGE MALARIA VACCINES

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The rapid deployment of COVID mRNA vaccines represents a significant achievement. The mRNA platform has several advantages over recombinant antigen formulations, including ease of construction and scalability. mRNA-lipid nanoparticles (LNPs) can be easily modified to deliver antigen to both exogenous and endogenous processing pathways to drive broad humoral and cellular immunity. Here, we evaluate the mRNA platform

for delivery of a blood-stage malaria vaccine. Using the *Plasmodium yoelii* model, we focused on the 19-kDa fragment of merozoite surface protein 1 ($MSP1_{19}$) fused to merozoite surface protein 8 (MSP8). Two EGF-like domains within $MSP1_{19}$ are the target of neutralizing antibodies, although T cell recognition of $MSP1_{19}$ is weak. We previously reported that fusion of recombinant $MSP1_{19}$ to MSP8 provided strong MSP8-specific CD4+ T cell help for production of merozoite neutralizing antibodies. Immunization with r*Py*MSP1/8 formulated with Quil A adjuvant afforded significant protection against lethal *P. yoelii* 17XL malaria. We designed a mRNA vaccine construct that targeted *Py*MSP1/8 for secretion (*Py*MSP1/8-sec). The mRNA was encapsulated into LNPs and outbred mice were immunized three times at a 3-week interval. Comparator mice were immunized with r*Py*MSP1/8 formulated in Quil A adjuvant. The *Py*MSP1/8-sec mRNA vaccine induced high titers of antigen-specific antibodies, significantly higher than those induced by the recombinant antigen formulation. Two weeks following the final immunization, mice were challenged with *P. yoelii* 17XL parasitized RBCs. The *Py*MSP1/8-sec vaccine was remarkably protective; all mice survived an otherwise lethal infection, and 5/10 immunized animals did not develop detectable blood-stage parasitemia. We designed a second *Py*MSP1/8 mRNA-based vaccine (*Py*MSP1/8-mem) that encodes a GPI anchor signal sequence and demonstrated successful expression of *Py*MSP1/8 on the surface of transfected cells. Studies are ongoing to compare the immunogenicity and efficacy of secreted versus membrane-bound *Py*MSP1/8 to inform related work focused on *Plasmodium falciparum*.

8082

INTRODUCTION OF MALARIA VACCINE IN BURKINA FASO: LESSONS LEARNED

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In October 2021, the World Health Organization recommended RTS,S/AS01 vaccine as a new way for the prevention of malaria. Burkina Faso made the critical decision to introduce the malaria vaccine into its vaccination program, declared interest in roll-out to GAVI and finalized its implementation plan in January 2023. A Malaria Vaccine Introduction Committee was created to spearhead and monitor the introduction, which was occurred on February 5th, 2024. The target population for this vaccine is children aged 5 to 23 months with a vaccination schedule of the first three doses administered at 5, 6, and 7 months, followed by the 4th dose at 15 months. We conducted a comprehensive review of the vaccine introduction process using the WHO's Malaria Vaccine Introduction Readiness Assessment tools. We also analyzed through relevant documents several areas such as planning, training communication, logistic. It took 12-month from December 2022 to January 2023 to introduce the RTS,S/AS01 malaria vaccine. The process began with a strong commitment from the country's top government officials. Ten months before the scheduled introduction, 31% of the preparation activities were completed. By the six-month, the completion rate of all activities required had increased (78%) with the establishment of technical groups. A month ahead of schedule, communication activities, were not conducted due to funding constraints. This led to the postponement of the introduction by 10 days. A month after the introduction, districts with proactive awareness campaigns among community leaders achieved high coverage rates (>90%), while those without had lower coverage rates (<50%), despite the security context.Burkina Faso introduction of the RTS,S/AS01 vaccine demonstrates a commitment to reducing malaria mortality. Lessons learned from this process include the importance of establishing technical working groups, ensuring timely funding for communication activities, and actively involving relevant stakeholders from the outset. Moving forward, these insights guide future vaccine introductions, ensuring a more successful rollout process

8083

FUNCTIONAL EFFICACY OF NANOPARTICLE CONJUGATED *PLASMODIUM VIVAX* CIRCUMSPOROZOITE PROTEIN SUBDOMAIN VACCINE

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A vaccine against vivax malaria is a high priority, due to its global prevalence, relapse, and its socio-economic burden. The circumsporozoite protein (CSP) is the most abundant molecule on the surface of *Plasmodium* sporozoites and is considered a leading pre-erythrocytic stage vaccine candidate. CSP is essential for sporozoite gliding motility, cell traversal activity and entry into the liver parenchyma. Anti-CSP antibodies can prevent sporozoite migration and infection of hepatocytes. The immunodominant central repeat region of CSP is considered important target of protection that is observed with CSP vaccines. Inhibitory monoclonal antibodies specific to the dominant Bc epitopes of two *P. vivax* CSP repeats (VK210 and VK247) show no cross reactivity with the different *P. vivax* variants. Therefore, this dimorphism represents a challenge to developing a broadly neutralizing strain transcending CSP-based vaccine targeting primarily the repeat region. This study aims at exploring the flanking N- and C-terminal domains of PvCSP for induction of broadly neutralizing inhibitory antibodies. Mice were immunized with different recombinant CSP subunits formulated with CpG-1018 as adjuvant and surface conjugated to PLGA nanoparticles and the immunogenicity was evaluated. NP conjugated rCSP subunit formulations induced high titer antibodies to the respective rCSP antigens that could recognize the native antigen on the sporozoite. Preliminary studies revealed that the antibodies produced by NP conjugated rPvCSP sub-domains showed inhibition of transgenic *P. berghei* sporozoites expressing PvCSP liver stage development *in vitro*.

8084

DIRECT SKIN FEEDING ASSAY IN MALARIA TRANSMISSION BLOCKING VACCINE STUDIES - STANDARDIZATION, SAFETY, TOLERANCE, AND SCALABILITY FOR USE IN PHASE 2 AND PHASE 3 CLINICAL TRIALS

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Malaria Transmission Blocking Vaccines (TBVs) are vaccines designed to reduce the number of infected mosquitoes circulating in a community by blocking the sexual stages of the *Plasmodium* parasite from developing within mosquitoes. For decades, the Standard Membrane Feeding Assay has been the gold standard for measuring activity of these vaccines; however, this assay requires cultured *Plasmodium* parasites to test sera, is time consuming and has relatively low throughput. Logistically this poses many issues for large scale clinical trials and due to the intricacies of performing the assay, oftentimes it isn't conducive to tight timelines where the quick turnaround of results is needed for decision making. Consequently, the Direct Skin Feeding (DSF) and Direct Membrane Feeding (DMFA) Assays are the preferred assays in the field. However, DMFA has its own limitations, and its set-up and execution can be challenging in a field setting. Because of this the DSF has become the leading assay for use in TBV studies as there are fewer limitations to performing them and is the assay closest to mimicking what is naturally seen in the field. Here we will show over 10 years of safety data from over 34,000 DSFs performed across multiple study sites in Mali. We will evaluate acceptability and tolerance of the assay looking at study withdrawal and refusal rates as well as adverse events across studies. We will compare assay logistics and data from recent studies that paired DMFA and DSF and highlight the

reasons DSF is the superior assay. We will also discuss the steps taken to standardize the DSF assay for use in a Phase 2 multi-component vaccine trial in Mali, and what this means in terms of scalability (colony mosquito production and post -feed processing). Lastly, we will discuss how we propose to transfer the assay to multiple sites across Africa and how this assay will be implemented in a multisite Phase 3 clinical trial.

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COMPARABILITY OF THE STANDARD MEMBRANE FEEDING ASSAY (SMFA) ACROSS DIFFERENT VACCINE STUDIES, STUDY SITES, AND TIME

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The Standard Membrane Feeding Assay (SMFA) is utilized widely to assess the efficacy of malaria transmission blocking vaccines (TBV). The assay is performed by feeding cultured *P. falciparum* gametocyte parasites to *Anopheles* mosquitoes in the presence of test sera and measuring the resulting midgut oocyst infections against a naïve control. The activity of vaccine-induced antibodies to prevent mosquito infection can be expressed as both transmission reducing activity (TRA) where the percent reduction in oocyst count per mosquito against the naïve control is calculated and transmission blocking activity (TBA) where the percent reduction in infection prevalence against the naïve control is calculated. Here we assemble data from the comparator arms of several recent TBV studies (Pfs230D1-EPA and Pfs25-EPA in alhydrogel, Pfs230D1-EPA in AS01 in adults, Pfs230D1-EPA in AS01 in a community setting and Pfs230D1-EPA in Matrix M) to assess the variability in the baseline/control values of SMFAs performed on individuals residing in malaria endemic areas. TRA and TBA data for each study were assembled along with attributes of sites, demographics of study population, and month and year of study in order to examine these control data to determine what differences in the baseline data exist. A total of 681 samples from 289 participants were analyzed using Generalized Estimating Equation (GEE) models fitted with offsets for the number of samples each individual contributed to the analysis. Results of individual variability, within study and cross study variability will be contrasted for both TRA and TBA.

8086

IMMUNOGENICITY OF A *PLASMODIUM VIVAX* BLOOD STAGE NANOPARTICLE VACCINE

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The *Plasmodium vivax* Duffy binding protein (DBP) is essential for invasion of human reticulocytes during blood stage infection and development. Region II of DBP (DBPII), contains the critical residues important for binding to its cognate receptor, the Duffy antigen receptor for chemokines (DARC), during the invasion process. Naturally acquired anti-DBPII antibodies block *P. vivax* merozoites invasion of reticulocytes and are associated with protection against disease. These features of DBPII makes it a prime target for vaccine mediated immunity against blood stage vivax malaria. Despite its functional role in the invasion process, allelic variation in dominant B-cell epitopes may complicate vaccine efficacy. An engineered rDBPII based protein, DEKnull-2, with altered variant Bc epitopes, retains conserved, neutralizing epitopes and is reactive with long-term memBc and stable binding inhibitory antibodies from natural *P. vivax* infections. Challenges with conventional vaccines such as low immunogenicity, instability, and the need for multiple doses, are limitations to vaccine efficacy. Innovative formulations and technologies such as nanoparticle vaccines (NPV) show great potential as an alternative to conventional sub-unit vaccines. In this study, the immunogenicity of a rDBPII based NPV was evaluated in BALB/c mice. The vaccine was highly immunogenic in mice, eliciting antibodies reactive with variant DBPII alleles and recognize native DBP on merozoites. Ongoing studies are evaluating the vaccine induced antibodies for inhibition erythrocyte invasion by transgenic *P. knowlesi merozoites* expressing *P. vivax* DBP *in vitro.* Data obtained from this study will determine the suitability of NPVs as a delivery system for a DBP based vaccine compared to traditional subunit vaccine formulations.

8087

NOVEL ASSAY PREDICTS STANDARD MEMBRANE FEEDING RESULTS FOR MALARIA TRANSMISSION BLOCKING VACCINE PFS230D1-EPA/AS01

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In 2024, malaria affects half the global population, with ~250 million cases and more than 600,000 deaths annually. Resistance to drugs and insecticides has made effective vaccines crucial. Transmission-blocking vaccines (TBVs) like Pfs230-EPA are designed to stop malaria transmission through mosquitoes and are moving towards Phase 3 trials. Traditional mosquito-based assays such as the Standard Membrane Feeding Assay (SMFA) are low-throughout, labor-intensive, and limited in detection range, prompting the need for new assays to measure vaccine-induced immune responses that correlate to efficacy. This necessitates the development of cost-effective, scalable tests for large-scale trials. We developed a competitive ELISA (cELISA) platform using human monoclonal antibodies (hmAbs) isolated from Malian adults vaccinated with Pfs230D1-EPA. The assay incorporates single-chain variable fragments that block functional epitopes to quantify levels of antibody (Ab) that react to epitopes targeted by functional hmAbs. A pilot study was run to analyze 185 serum samples collected during a Pfs230D1-EPA/AS01 trial that compared efficacies of full and fractional dosing regimens delivered in a Month 0-1-6-17 schedule. Samples collected 3 months post doses 3 and 4 were assessed in five novel epitope-specific cELISAs that measured different Ab parameters (total IgG, IgG1, IgG3, IgG4, c1q). Immune responses were evaluated for their ability to predict SMFA mosquito assay endpoints. Ab responses for standard ELISA and cELISA (total IgG, IgG1, IgG3, c1q) were significantly higher in the full versus fractional dose group post-dose 3, while all Ab responses were similar between groups post-dose 4. Multivariate logistic regression analysis showed significant relationships to SMFA results for cELISA total IgG and IgG1 assays. Receiver Operator Curve analysis confirmed the strong predictive value of the standard ELISA as well as cELISA total IgG and IgG1 assays for SMFA results, with AUC over 75% at both study time points. These findings lay the foundation for novel assays to assess Ab activity and durability induced by Pfs230D1 in large-scale trials.

8088

ABUNDANT NON-NEUTRALIZING, SYNERGIZING IGG LINEAGES PLAY A CRUCIAL PROTECTIVE ROLE IN MALARIA-NAÏVE UNITED KINGDOM ADULTS VACCINATED WITH BLOOD-STAGE VACCINE CANDIDATE RH5.1/AS01$_B$

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Reticulocyte Binding Protein Homologue 5 (RH5) is a *P. falciparum* merozoite surface protein that has low polymorphism frequencies and is an

essential component of a non-redundant erythrocyte invasion pathway. The Draper Laboratory (Oxford) clinically tested RH5.1, an engineered variant of RH5, with $AS01_B$ adjuvant (GSK) to induce long-lasting, protective antibody titers. In this study, we evaluated United Kingdom malaria-naïve adult volunteers (n=5) who received three monthly doses of the RH5.1/$AS01_B$ vaccine and subsequently demonstrated significant reductions in parasite multiplication rate (NCT02927145). Recombinant monoclonal antibodies (mAbs) derived from RH5-specific B cell receptors (BCRs) of volunteers were discovered that neutralize merozoite invasion *in vitro*. In comparison, polyclonal plasma IgG of volunteers exhibited an average neutralizing potency ~10-fold greater than that of mAbs cloned from B cells, highlighting a disconnect between the BCR and circulating IgG repertoires. To address this, we completed high-throughput BCR sequencing coupled with plasma IgG proteomics, followed by subsequent recombinant mAb expression and functional characterization. In four of five donors, the most abundant RH5.1-specific plasma IgG lineage is non-neutralizing *in vitro*, targeting epitopes like the N-terminus, while lower abundance lineages exhibit neutralizing properties. In one donor, all top six lineages (~59% relative abundance) target non-neutralizing epitopes. To explore the contributions of individual mAbs within a polyclonal setting, we generated an artificial plasma IgG repertoire of one donor by pooling together 22 recombinant mAbs at relative abundances (~72% relative abundance total) and evaluated them in an *in vitro* parasite growth inhibition assay. By systematically removing mAbs from this repertoire, we uncovered a synergistic relationship between two mAbs that alone are non-neutralizing. The ability of non-neutralizing antibodies to synergize with each other alongside neutralizing mAbs may reduce the burden of high antibody titers, influencing future RH5 vaccine engineering efforts.

8089

ELICITATION OF POTENT LIVER-STAGE IMMUNITY BY NANOPARTICLE IMMUNOGENS DISPLAYING *PLASMODIUM FALCIPARUM* CSP-DERIVED ANTIGENS

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The circumsporozoite protein (CSP) of *Plasmodium falciparum* is the major surface antigen of the sporozoite stage, and is the target of two WHO-recommended vaccines, RTS,S/AS01 and R21/Matrix-M. Though these vaccines offer promise for reducing malaria burden, their rapidly waning antibody titers may affect long-term efficacy. Recent studies have elucidated structures of epitopes not included in RTS,S or R21 that target the junctional NPDP motif and NVDP minor repeat motifs of the CSP repeat region, and the addition of these epitopes may improve long-term potency of CSP-based vaccines. Here, we first stabilized full-length CSP by mutating a proteolytic cleavage site. We then produced a shortened version, named SAmut-5/3-CSP, that displays the 3D7 strain "junctional" region as its repeat region, conjugated it to protein nanoparticles of various valencies, and found that our conjugate to a computationally designed nanoparticle, I53-50, offered the greatest protection against challenge. We also tested genetic fusions of the junctional region, major repeats, and the CSP C-terminal domain (CTD) to I53-50, and compared these to an RTS,S-like benchmark, RT-I53-50. We found that though our immunogens exhibited greater responses toward the junctional region, immunogens with higher major repeat content were associated with improved protection in a transgenic parasite challenge model, with RT-I53-50 being the most protective. To further improve on these constructs, we evaluated I53-50 immunogens that displayed non-native repeat cadences [e.g., $(NANPNVDP)_9$]. These immunogens showed improved cross-reactivity toward junctional region epitopes, but again did not outperform RT-I53-50 liver burden reduction after challenge. Finally, we performed experiments that compared RT-I53-50 to R21 in a head-to-head challenge study and we observed equivalent reductions in liver burden after 3 immunizations. However, subsequent experiments with a titrated, 2-dose regimen showed that R21 was slightly superior. Overall our results support further development of CSP-based vaccines on our clinically validated I53-50 nanoparticle platform.

8090

ASSESSMENT OF THE BURDEN AND RISK OF TYPHOID FEVER USING AVAILABLE DATA TO INFORM VACCINE INTRODUCTION IN RWANDA

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Since 2018, WHO has recommended typhoid conjugate vaccine (TCV) for use in typhoid-endemic countries, prioritizing those with high disease burden or a high burden of antimicrobial resistance. However, the burden of typhoid fever is often unknown due to poor surveillance. To address this challenge, we piloted the Burden and Risk Assessment of Typhoid (BRAT) framework, a tool developed by CDC, WHO and typhoid experts, to systematically collect and interpret available typhoid data from 2018–2022 in Rwanda. We identified incidence, outbreak, and risk factor data through a desk review and collected prevalence, antimicrobial resistance (AMR), and intestinal perforation data from 13 health facilities, including at least one facility per province. We identified 290 *S.* Typhi isolates from patients in > 18 of Rwanda's 30 districts, with four districts accounting for 45% of *S.* Typhi isolates, indicating geographic variation. Overall, 40%–65% of isolates were resistant to at least one first-line antimicrobial (ampicillin, chloramphenicol, cotrimoxazole), while <40% were resistant to second-line antimicrobials (fluoroquinolones and third-generation cephalosporins). Resistance to fluoroquinolones, the antimicrobials of choice in Rwanda, increased from 38% in 2018 to 70% in 2022. Twenty-four percent of isolates were resistant to all first-line drugs, and no isolates were resistant to all first- and second-line drugs. A total of 360 cases of intestinal perforation were reported, of which 26% were diagnosed as typhoid-associated and resided in > 20 districts. Nationally, 56% of households had access to basic water and 57% had access to basic sanitation. No incidence or outbreak data were found. Using the BRAT framework, we rated the likely burden for prevalence and intestinal perforation as moderate, AMR as high, and WASH risk factors as high at the national level. We determined that typhoid fever is endemic in Rwanda, documented increased antimicrobial resistance and potentially unrecognized typhoid outbreaks. We conclude that Rwanda meets the criteria for moderate evidence to support TCV introduction.

8091

AEROMONAS HYDROPHILA AS A CAUSE OF ACUTE DIARRHEA FROM WESTERN AND COASTAL REGIONS IN KENYA

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Aeromonas hydrophila group are emerging pathogens that cause gastroenteritis. Nonetheless *Aeromonas spp* can also cause wound infections and septicemia in humans in both developing and developed countries. The reservoirs include, aquatic environment, stored drinking and sewage water and in raw milk, vegetables and meat (food products). This

study tested stool samples for *Aeromonas hydrophila* group and associated phenotypic antibiotic resistance profiles. *Aeromonas hydrophila* group was isolated from stool samples collected from an ongoing case (symptomatic)-control (asymptomatic) diarrheal study. Standard microbiological culture and biochemical tests were performed, followed by identification and antimicrobial susceptibility testing using NC 66 panels and ascertained using the Microscan Walkaway 40 Plus automated identification platform. The drug susceptibility results were interpreted using the CLSI guidelines. According to the study, there were significantly more *Aeromonas hydrophila* isolates in symptomatic individuals (15/19; 79%) than in asymptomatic subjects (4/19; 21%; p=0.01). The isolates were resistant to trimethoprim/sulfamethoxazole 9/19 (47%), amoxicillin/k clauvanate 7/19 (37%), ampicillin sulbactam 5/19 (26%), aztreonam 5/19 (26%), cefepime 2/19 (11%), ceftazidime 2/19 (11%), cefoperazone 2/19 (10%) and meropenem 1/19 (5%). All isolates were susceptible to gentamicin, levofloxacin and piperacillin/tazobactam. The isolation of *Aeromonas hydrophila* is indicative that it may be a potential pathogen that causes acute diarrhea. The isolates were also found to be more resistant to the sulfonamide and beta lactams hence possible transfer to other gut pathogens or normal flora leading to increased antimicrobial resistance.

8092

PHENOTYPIC RESISTANCE OF CIPROFLOXACIN AND AZITHROMYCIN RESISTANT *CAMPYLOBACTER* SP. ISOLATES FROM PERU TO AN EXTENDED PANEL OF ANTIBIOTICS

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Antimicriobial resistance jeopardizes the effectiveness of prevention and treatment of an increasingly wide range of infections caused by viruses, bacteria, fungi, and parasites. In 2017, the WHO published a list of bacteria with high antimicrobial resistance. *Campylobacter* was included in this list as a high-priority pathogen due to its progressive, alarming, and high resistance to fluoroquinolones worldwide. During the years 2021, 2022, and 2023, a cohort study was conducted in children aged zero to two years in the city of Iquitos, Peru, with the aim of estimating the disease burden and transmission dynamics. Additionally, it aimed to evaluate antibiotic resistance attributable in Campylobacter in humans and livestock. Stool samples were collected from participants once a month and whenever they had diarrhea. Campylobacter culture was performed on every stool sample and antibiotic resistance was tested using traditional Kirby-Bauer methods. A total of 997 *Campylobacter* spp. strains were isolated, of which 8% (83 strains) were resistant to Azithromycin, 59.3% (591 strains) showed resistance to Ciprofloxacin, and 7.3% (73 strains) were resistant to both. For the strains resistant to both antibiotics, an extended antibiogram battery was performed, consisting of Clindamycin, Fosfomycin, Ampicillin, Tigecycline, and an Azithromycin E-Test. Resistance to Clindamycin was 100%, as well as the Azithromycin E-test. Resistance to Ampicillin was 74% to Ampicillin, 41% to Fosfomycin, and finally Tigecycline proved to be 100% sensitive. This extended, nontraditional antibiogram panel will be useful to evaluate potential alternative antibiotics when Azithromycin and Ciprofloxacin show phenotypic resistance.

8093

APPLICATION OF THE RAPID DIAGNOSTIC TEST BASED ON LOOP-MEDIATED ISOTHERMAL AMPLIFICATION (RLDT) FOR *SHIGELLA* AND ENTEROTOXIGENIC *ESCHERICHIA COLI* (ETEC) DETECTION IN CHILDHOOD DIARRHEA IN BURKINA FASO

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Developing countries face major challenges in diagnosing and monitoring enteric infections, particularly shigellosis and ETEC diarrhoea. The lack of rapid, accessible, and sensitive diagnostic tools complicates the timely identification and management of these infections, exacerbating their impact on public health. In response to this pressing need, the application of the RLDT has emerged as a promising solution. This study aimed to compare the performance of RLDT with conventional culture methods for detecting of cases of Shigella and ETEC.This study focuses on the implementation and efficacy of the RLDT for detection of *Shigella* and ETEC in a cohort of children under the age of five living in the peri-urban area of Ouagadougou, Burkina Faso, shedding light on its potential to address diagnostic challenges in resource-limited settings. To enable comparison with RLDT-*Shigella* results, conventional culture methods were employed to isolate *Shigella* strains from stool samples. However, since culture alone proved inadequate for detecting ETEC, multiplex PCR was used to identify ETEC toxin genes in a subset of *Escherichia coli* colonies. Of the 165 samples analysed for ETEC, 24.9% were positive by the RLDT compared with 4.2% by culture followed by PCR. The distribution of ETEC toxins by the RLDT was 17.6% for heat-stable enterotoxin porcine (STp), 11.5% for heat-labile enterotoxin (LT) and 8.5% for heat-stable enterotoxin human (STh). From the 263 samples tested for *Shigella*, the RLDT showed a positivity rate of 44.8% compared with 23.2% using culture. Since RLDT is more sensitive than culture, when comparing the RLDT with culture, the sensitivity and specificity for *Shigella* were determined to be 93.44% and 69.8%, respectively, while for ETEC, they were 83.7% and 77.9%, respectively.These results highlight the significant underdiagnoses of *Shigella* and ETEC by bacterial culture-dependent tools and demonstrate the potential of RLDT to improve the estimation of the burden of enteric disease. This method could guide future efforts to prevent and control enteric bacterial infections in children under five years of age in Burkina Faso.

8094

ASSOCIATION OF THE HUNGER SEASON AND MALNUTRITION WITH DIARRHEA ETIOLOGY AND POOR OUTCOMES AMONG CHILDREN HOSPITALIZED WITH DIARRHEA IN HAYDOM, TANZANIA

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Children from agrarian communities in low resource settings with one annual harvest are at risk for malnutrition during the pre-harvest hunger season. Preliminary data was analyzed on 423 children (females: n=185, mean age: 14 months ± 10 months) hospitalized with diarrheal illness at Haydom Lutheran Hospital in Haydom, Tanzania from September

2022-March 2024. Of the 101 acutely malnourished children, 52 were severely (mid upper arm circumference (MUAC) <11.5 cm, weight for height/length z score (WHZ/WLZ) <-3, or bilaterial pitting edema) and 49 were moderately (MUAC ≥11.5 but <12.5 cm or WHZ/WLZ ≥ -3 but <-2) malnourished. Log binomial regressions adjusted for sex and season examined associations between malnutrition, season of admission, diarrheal etiology, and poor outcomes (death or 90-day re-hospitalization). Children with acute malnutrition and diarrhea were 1.74 (RR: 1.74, CI: 0.99, 3.08) times more likely to have a poor outcome, 1.57 (RR: 1.57, CI: 1.01, 2.44) times more likely to have *Shigella* attributable diarrhea (Ct<29.8) and 49% (RR: 0.51; CI: 0.27, 0.94) less likely to have rotavirus attributable diarrhea (Ct<31.8) compared to children with diarrhea but without acute malnutrition. Children admitted with diarrhea during the hunger season (November-March) were 1.28 (RR: 1.28, CI: 0.91, 1.80) times more likely to be malnourished, 2.11 (RR: 2.11, CI: 1.35, 3.29) times more likely to have *Shigella* attributable diarrhea, and were 71% (RR: 0.29, CI: 0.17, 0.52) less likely to have rotavirus attributable diarrhea compared to children admitted during the non-hunger season (April-October). There was no association between hospital admission season and poor outcomes. Rotavirus exhibited seasonality from August-November, while *Shigella* and acute malnutrition tracked closely together throughout the year, peaking from November-June. There was no association between pathogen attributable diarrhea and poor outcomes. Acute malnutrition, not hospital admission season, was a risk factor for poor outcomes, which may underscore the need for vigilant nutrition interventions both during and outside the hunger season.

8095

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY ON THE EFFICACY AND SAFETY OF CAMPETEC HYPERIMMUNE BOVINE COLOSTRUM (HBC) FOR THE PREVENTION OF *CAMPYLOBACTER*-MEDIATED DIARRHEAL DISEASES

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Campylobacter causes significant diarrheal disease morbidity in children in low- and middle-income countries, travelers, and deployed military, and is a major cause of foodborne illness worldwide. Growing antibiotic resistance of *Campylobacter* makes improved prevention and control measures imperative. Given the prolonged and expensive nature of vaccine development, passive prophylaxis using oral administration of Hyperimmune Bovine Colostrum (HBC) was explored. CampETEC HBC is derived from cows immunized with a *C. jejuni* HS23/36 capsule polysaccharide (CPS) conjugated to CfaEB, a recombinant fusion protein of the major tip adhesin and subunit of CFA/I from enterotoxigenic *Escherichia coli*. CampETEC contains a high concentration of CPS-specific IgG which bind to HS23/36+ *C. jejuni* strains. Protective efficacy of CampETEC HBC was evaluated following a challenge with *C. jejuni* strain CG8421 (serotype HS23/36) in a randomized, double-blind, placebo-controlled, human infection model. Twenty-seven eligible participants were admitted to the inpatient facility and randomly assigned to receive 1g of CampETEC HBC or placebo (milk powder) thrice daily before meals. After 2 days of product consumption, participants were challenged with 1.67 x 10^5 colony-forming units of *C. jejuni*; they were monitored clinically and continued the CampETEC HBC for an additional 5 days. All participants were treated with azithromycin and ciprofloxacin when they met campylobacteriosis criteria or prior to discharge. CampETEC HBC was well-tolerated by participants, with no moderate or severe product-related adverse events. Study data remain blinded. Preliminarily, 17 of 27 (63%) met criteria for campylobacteriosis; 14 (52%) with moderate-severe diarrhea and 3 (11%) with fever and other symptoms. Twelve participants (71%) with campylobacteriosis required early treatment. Fever 100.8°F was present in 9 (33%) participants. Stool culture data aligned with clinical findings. Final determination of campylobacteriosis will be adjudicated by an independent committee. The protective efficacy of the CampETEC HBC will be determined upon unblinding.

8096

GENOMIC SURVEILLANCE OF ANTIMICROBIAL RESISTANCE IN CHILDREN WITH DIARRHEA AT A COMMUNITY-LEVEL HEALTH FACILITY IN MALI

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Diarrheal diseases are amongst the most common causes of death in children in Africa. The treatment of diarrhea caused by *Enterobacteria* are often comprised by the emergence of drug resistant strains. Antimicrobial resistance (AMR) remains one of the biggest threats to global health and specially to resource limited countries such as Mali. The extent of AMR burden at the community level is not known. To better gain insights on the extent of AMR at the community health center level, we have performed a whole genome and metagenomic sequencing respectively on isolated bacteria and uncultured stools samples from children with diarrhea. Antibiotics sensitivity tests were performed, and phenotypic data were used to select samples. Genomic and metagenomic analyses have been carried out to detect AMR genes, virulence factors as well as unculturable pathogens. Our results indicate that multi-drug resistant bacteria, mainly *Salmonella* and *E. coli* are circulating at the community level. More importantly, *Enterobacteriaceae* carrying New Delhi metallo-β-lactamase genes (NDM) associated with carbapenem resistance were detected at the community level. Mobile genetic elements harboring AMR genes were detected suggesting them as potential drivers of the spread of AMR genes. We are analyzing metagenomic sequence data to better capture unculturable bacteria that might be involved in the pathogenesis of diarrhea in children. In addition, analyses are underway to fully characterize the pattern of transmission of AMR genes. Our results will inform healthcare workers and policy makers on a rational use of antibiotics.

8097

INTESTINAL MICROBIOME AND IMPLICATIONS ON MATERNAL HEALTH AND BIRTH OUTCOMES

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Unfavorable birth outcomes, such as low birth weight and preterm birth, can have detrimental impacts on a child's prognosis and later development. This concern is greatest in low-middle income countries in Asia and sub-Saharah Africa where pre-term birth rates are highest and there are less resources for post-natal care. Despite the need, there is still a lack in understanding what maternal factors contribute to these outcomes. Using randomly selected mother-child dyads from the Global Network Maternal Neonatal Health (MNH) registry in the Tangail district of Bangladesh, potential causes of unfavorable birth outcomes were investigated. It was found that in a sub-cohort of 376 mother-child dyads, elevated inflammatory cytokines (i.e. CRP and AGP) during the first trimester were correlated with preterm birth (OR = 2.23; 95% CI: 1.03, 5.16). Additionally, presence of aEPEC was significantly associated with increased odds of preterm birth (OR = 2.36; 95% CI: 1.21, 4.57), and higher loads of aEPEC were associated with increased odds of preterm birth (OR = 0.92 ;95% CI: 0.86, 0.98). When these models were adjusted for elevated AGP, the

strength of association was slightly attenuated. It may be hypothesized that elevated AGP captures a history of enteropathogenic infection or colonization in very early pregnancy. To further understand how the intestinal environment influences maternal health and birth outcomes, 16s sequencing was performed on 368 maternal stool samples from the same sub-cohort. Microbiome diversity, community composition, and multivariate analysis were performed. With this data, the correlation between intestinal microbiome, maternal health, and birth outcomes were evaluated.

8098

ISOLATION AND GENOMIC CHARACTERIZATION OF *CAMPYLOBACTER* SPECIES AND IDENTIFICATION OF ANTIBIOTIC RESISTANT *ESCHERICHIA COLI* AND *KLEBSIELLA PNEUMONIA FROM ZIMBABWE*

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During a study to determine reservoirs of *Campylobacter* in Zimbabwe, stool samples from symptomatic and asymptomatic children and mothers were grown in selective Campylobacter media. In addition to isolating *Campylobacter* species, we identified multiple significantly antibiotic resistant *Escherichia coli* and *Klebsiella pneumoniae* strains. We report on genomic characterization and antimicrobial susceptibility of the isolated strains from a region where few genomic sequences are known. Samples were plated on mCCDA plates in microaerophilic conditions at 42ºC to enrich for *Campylobacter spp*. Putative *Campylobacter* were isolated and sequenced via a combination of Oxford Nanopore Technologies (ONT) long read sequencing and Illumina short read sequencing. Assembled genomes were profiled using MLST typing, genomic distance with Mashtree. Antimicrobial resistance (AMR) gene profiles and select virulence genes and serotypes were identified using abricate, ECTyper, and Kleborate. We identified and sequenced 40 *Campylobacter* isolates; 28 *C. jejuni*, 10 *C. coli*, and 2 other. In addition, isolates of *E. coli* (n=41) and *K. pneumoniae* (n=14) grew on Campylobacter selective media, which included cefoperazone. *E.coli* isolates had predicted encoding of antimicrobial resistance genes (ARG) including TEM-1, TEM-141, CTX-M, and beta lactamase. *K. pneumoniae* was classified via Kleborate with resistance to yersiniabactin, colibactin or both, with evidence of ARG transfer via the genes AGly, Phe, Tet, TMT, Bla, and BlaESBL. Comparison to previously published genomes, the Campylobacter isolates sequenced in this study represent novel populations with significant genetic distance from existing resources. Genomic analysis of *E. coli* and *K. pneumoniae* also suggest that strains are distinct from most sequenced clinical isolates and align with relatively few genome sequences derived from Africa. This study contributes to our understanding of *Campylobacter spp*., *E. coli*, and *K. pneumoniae* genome characteristics in Zimbabwe and contributes to our understanding of antimicrobial resistance patterns in the region.

8099

PATHOGENS CAUSING DIARRHEA IN CHILDREN UNDER FIVE AMONG A VACCINATED POPULATION IN COASTAL GHANA

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Diarrhoea remains a leading cause of morbidity and mortality globally. Rotavirus A vaccine was introduced almost 20 years ago to reduce the incidence of diarrhoea among children under five years. Since Ghana adopted the rotavirus A vaccine in 2012, coverage has been very high, 94% in 2022, yet diarrhoea still persists with a prevalence of 13% in under-fives. We conducted a pilot study to assess the possible pathogens causing diarrhea in under-fives in a high prevalent coastal district in Ghana. A case was an under-five confirmed with diarrhoea. Hospitalized diarrhoea cases(38) in Anloga district over an 8-month period were tested. Information on immunization status, WASH practices, and socio-demographics was also obtained. We extracted total nucleic acid of their stool samples. Pathogen detection was performed using quantitative PCR with customized TaqMan Array cards identifying 23 pathogens (10bacteria, 6parasites and 7viruses). Findings were presented in tables and charts. Median age was 21.5(IQR:30,12)months, 55.3%(21/38) with being male. Fully vaccinated were 97.4%(37/38). Diarrhoea pathogens were found in 94.7%(36/38). Of the 23 pathogens tested, 15 were identified. More viruses were identified (71.4%, 5/7) than bacteria (70%, 7/10). Rotavirus A was found in 5.3%(2/38). Other viruses identified were Saprovirus (23.7%, 9/38); Norovirus(26.3%, 10/38); bacteria pathogens identified included: Shigella/ Enteroinvasive Escherichia coli 50%(19/38); Enterotoxigenic Escherichia coli(23.7%, 9/38); Enteroaggregative Escherichia coli(52.6%, 20/38). Almost all (97.4%, 37/38) had access to improved water sources, Hand washing practices among caregivers was poor (28.9%, 11/38) and most children 89%(30/38) did not use household toilet facility. Vaccination was high. Aside known pathogens (Rotavirus A), other diarrhoea pathogens are present. WASH practices were poor. Interventions to improve WASH practices mainly handwashing among caregivers and child use of household toilets are needed. Long term recommendations could consider diarrhoea vaccines which target other pathogens in addition to Rotavirus A.

8100

USING A VACCINATION REGISTER TO MINIMIZE THE RISK OF MISCLASSIFICATION OF CHOLERA VACCINATION STATUS IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Oral cholera vaccines (OCV) are a key component of the global cholera control strategy. Today, none of the available vaccines have gone through Phase III clinical trials and all have been licensed (and WHO approved) based on immunological bridging studies. Gold-standard field clinical efficacy studies are ethically and logistically challenging with the current vaccine landscape. Phase IV observational studies, like case-control and case-cohort studies, have and will likely continue to serve as the primary source of new data on protection from these and newer OCVs though they are often challenged by misclassification of vaccination status, due to social desirability- and recall bias, and unreliable records. In Uvira, a cholera-endemic city of ~315,000 inhabitants in the eastern DR Congo, one dose of Euvichol-plus was administered to individuals ≥12 months old during a vaccination campaign in December 2023/January 2024. As part of a vaccine impact evaluation in Uvira, we implemented a paper-based vaccine register to record data on all vaccine recipients. We used artificial intelligence algorithms and developed a custom data validation pipeline to digitalize the paper-registers to allow for the validation of vaccination status in participants of cholera vaccine studies. We also conducted a representative household survey 2 months post-vaccination to estimate the vaccination coverage and to compare to the register. We recorded 250,102 vaccine recipients, yielding an estimated administrative vaccination coverage of 79.3% compared to 72.5% coverage measured in the survey.

We are finalizing the data validation at the time of writing this abstract. We will present estimates of the true vaccine coverage in the population based on both the survey and register data using a latent class model and will quantify the biases related to self-reporting vaccination status. We expect the results from our study to provide important and actionable insights for future observational field studies of vaccines, like OCV.

8101

USING CLINICAL PREDICTION TO IDENTIFY CHOLERA IN SEVERELY DEHYDRATED CHILDREN WITH DIARRHEA

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Cholera remains an important cause of infectious disease deaths, primarily through severe dehydration due to acute watery diarrhea. Because of the lack of reliable diagnostic testing in low and middle-income countries (LMICs), the World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) and the Global Task Force on Cholera Control (GTFCC) provide antibiotic prescribing guidelines based primarily on symptom presentation. However, severe dehydration can occur with other enteric pathogens. Our goal was to develop a clinical prediction rule to identify severely dehydrated children with cholera. We used clinical and demographic data from the Global Enteric Multicenter Study (GEMS) of the incidence, etiology, and outcome of moderate-to-severe diarrhea (MSD) among children aged 0-59 months to build predictive models to identify severely dehydrated children (as defined by the IMCI and GTFCC guidelines) with MSD attributable to cholera. We screened variables using random forests, and assessed predictive performance with random forest regression and logistic regression using 5-fold cross-validation. External validation via additional prospective data is pending Fall 2024. Of the 2,284 children randomly selected for qPCR testing and classified as severely dehydrated, 101 (4.4%) had MSD attributable to cholera. Top predictors ranked from most predictive included age (months), mid-upper arm circumference (MUAC), respiratory rate per minute, axillary temperature, and if the child is currently breastfed. We were able to achieve an area under the receiver operating curve (AUC, discriminative performance) of 0.69 (95% CI: 0.65, 0.73) with only 2 predictive variables (age, MUAC), and AUC of 0.83 (95% CI: 0.80, 0.85) with 10 predictor variables. Our findings indicate that clinical prediction rules may help identify children suffering severe dehydrating diarrhea as a result of cholera. Antibiotics are indicated and efficacious for children with cholera and MSD. Improved targeting of cholera diagnostics and antibiotic usage has the potential to aid patient outcomes and stewardship of limited resources.

8102

SHIGELLA SPECIFIC DIARRHEAL BURDEN OVER A DECADE IN THE GAMBIA

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The Gambia participated as study site of the Enterics for Global Health (EFGH) *Shigella* Surveillance study (August 2022-December 2024), Vaccine Impact on Diarrhea in Africa (VIDA, 2015-2018) and Global Enteric Multicentre Study (GEMS, 2007-2011). This abstract presents the burden of *Shigella* spp. in young children spanning over a decade in The Gambia. VIDA and GEMS enrolled children aged 0-59 months with medically-attended acute moderate-to-severe diarrhea (MSD) while EFGH enrolled children aged 6-35 months with medically-attended acute diarrhea. *Shigella* spp. was detected by microbiological culture and TaqMan assay (qPCR). In all three studies, Population Enumeration and Health Care Utilization Surveys were done to estimate population-based *Shigella* spp. incidence. Among diarrhea cases, *Shigella* isolation by culture was 116/1029 (11.3%), 217/1678 (12.9%) and 90/929 (9.7%) from GEMS, VIDA and EFGH respectively. *Shigella* spp. detection by qPCR from GEMS, VIDA and EFGH was 36.9%, 45.9% and 33.0%, respectively. *Shigella* spp. incidence per 100-child years by qPCR in 0-11, 12-23 and 24-59 months was 1.0, 6.5 and 0.7 respectively in GEMS; 3.4, 8.8 and 2.1 in VIDA, and 36.9 in 6-35 month-olds in EFGH. The highest incidence was observed in 6-35 month-olds and peaked in toddlers (12-23 months) in all three studies. Attributable shigellosis was high in the rainy season (June to October). *Shigella flexneri* was the leading serogroup in GEMS, VIDA and EFGH, accounting for 69.0%, 67.6% and 57.3% of isolates, respectively, followed by *S. sonnei* (20.7%, 18.2%, 36.9%). The most prevalent *S. flexneri* serotypes were 1b, 2a, 6, 3a and 4a in all three studies. *Shigella* spp. is a significant diarrhea pathogen in The Gambia in EFGH and the second most common in GEMS and VIDA. The highest incidence was amongst 6 to 35 month-old children. *Shigella* spp. peaked in the rainy season. *S. flexneri* and *S. sonnei* serogroups accounted for >90% shigellosis. Quadrivalent *Shigella* vaccines could be an important preventive measure in The Gambia in addition to improved hygiene practices.

8103

ENTERIC PATHOGEN PREVALENCE, INCIDENCE AND CLEARANCE RATES, AND SHEDDING INTENSITY IN URBAN KENYAN INFANTS FROM MOLECULAR TESTING OF SEQUENTIAL FECAL SAMPLES

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Prior studies have highlighted a high burden of enteric infection in infants living in low- to middle-income countries, but there is a dearth of information on the incidence and clearance of symptomatic and asymptomatic enteric infections in this susceptible population. This information is imperative for improving modeling efforts aimed at determining the relative importance of transmission pathways as well as for intervention assessments. Additionally, is it not known how various pathogens lead to diarrheal symptoms. This study's goals were two-fold. First, we aimed to estimate prevalence, 2-week incidence, and clearance rates, as well as shedding intensity for 19 types of enteric pathogens in infants 0-12 months of age living in urban settings in Kenya. Second, we investigated whether shedding intensity of these pathogens was predictive of caregiver-reported infant diarrhea. To achieve these goals, a total of 266 infants in Nairobi and Kisumu were recruited into the PATHOME study. For each infant, 5 fecal samples were taken over the course of 14 days and analyzed via TaqMan Array cards for 23 indicator genes of 19 viral, bacterial, and protozoan pathogens. Infant diarrhea was assessed using a 14-day caregiver self-report calendar. Point prevalence and 2-week incidence rates were estimated for each pathogen. Clearance rates for the more prevalent pathogens were estimated via accelerated failure time models. Using complete data from 133 Nairobi infants, prevalence and incidence was found to vary widely across pathogens, age groups, and neighborhood SES, with prevalence rates as high as 0.75 and incidence rates as high as 0.45. Median clearance rates for pathogens ranged from 4 days (Shigella) to 9 (Salmonella). Ct values patterns over 14 day periods were examined, shedding light on the natural history of infections. Using XGBoosting with SMOTE upsampling, pathogens' Ct

values marginally improved predicting diarrhea ±1 day from models only using age, achieving an F1 score of 0.745. Forthcoming data from an additional 133 Kisumu infants will bolster strength of these observations.

8104

ASSEMBLY AND PERFORMANCE OF A CHOLERA RAPID DIAGNOSTIC TEST PROTOTYPE THAT DETECTS BOTH *VIBRIO CHOLERAE* AND BACTERIOPHAGE

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Virulent bacteriophage are associated with compromised performance of cholera rapid diagnostic tests (RDTs). We hypothesized that an enhanced cholera RDT that detects the common virulent bacteriophage ICP1 might serve as a proxy for pathogen detection when the phage are present. We previously developed a monoclonal antibody (mAb) to the ICP1 major capsid protein and demonstrated target specificity. However, the approach for the RDT design (single versus duel mAb sandwich for ICP1) and assembly were outstanding. Our objective herein is to demonstrate a proof of concept for the design and assembly on an RDT that targets both a bacterial pathogen and associated virulent bacteriophage. Candidate mAbs were expanded to increase design options and evaluated by immuno-assays (ELISA; western blot). A subset of mAbs were selected for gold conjugation and printing on the RDT. The limit of detection (LOD) of prototype RDTs were determined in diarrheal stools with and without the addition of ICP1. Three mAb candidates were developed and evaluated for the capsid decoration protein (GP123) and tail fiber protein (GP93), and the prior mAb for the major capsid protein (Gp122). A single mAb sandwich RDT prototype for Gp122 was able to detect ICP1; RDTs with mAbs to GP123 and GP93 failed to detect ICP1 in single or dual sandwich configurations. Biologically meaningful LODs for ICP1 were achieved only with boiling of stool with ICP1; electron microscopy demonstrated increased epitope availability after boiling. In this study, we demonstrate a proof of concept for an RDT that can detect a virulent bacteriophage as a proxy for pathogen detection. Preparation by boiling the substrate increased the limit of detection, however further optimization is required before scaled implementation.

8105

INTEGRATION OF ANTIMICROBIAL RESISTANCE DIAGNOSTICS IN BOKÉ REGIONAL HOSPITAL LABORATORY: GUINEA, JULY-DECEMBER 2023.

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According to WHO, 1.27 million deaths worldwide in 2019 were attributable to multidrug-resistant bacteria. However, hospital laboratories in Guinea are facing major challenges in detecting antimicrobial resistance (AMR). This abstract describes the steps involved in integrating AMR detection into the essential activities of the Boké Regional Hospital Laboratory in Guinea. Between July and December 2023, we conducted the following to introduce AMR testing at the Boké Regional Laboratory: assessment using an adapted WHO Stepwise Laboratory Quality Improvement Process Towards Accreditation Checklist (SLIPTA); training and mentorship of two bacteriology technicians on AMR detection, provision of laboratory equipment, reagents and consumables; and external quality assessment. Performance data were collected and analyzed to describe the effectiveness of the integration. Means and proportions were calculated using Excel (2013). The laboratory scored an average of 72% across 11 quality indicators assessed in the adapted SLIPTA tool. After training, theorical and practical performance of the technicians improved from 40% to 63% and from 28% to 75%, respectively. Accuracy for bacterial culture and microscopy reached 83% and 50%, respectively. From July to December 2023, 85 public health samples were received, and pathogens were isolated in 29 (34.1%) samples. 28 were pathogens under surveillance., *E. coli* was the most prevalent pathogen identified (n=17, 60.7%). Additionally, 25 (89.3%) of the isolated pathogens showed AMR. AMR prevalence was 16.2% for Ofloxacin, 16.2% for Imipenem, 11.8% for Tobramycin, 10.3% for Ciprofloxacin, 10.3% for Ampicillin, 8.8% for Ceftazidime and (8.8% for Gentamicin.This study highlights the effectiveness of training and mentorship on improving integration of AMR detection into clinical testing in a hospital laboratory setting. The obtained results are crucial for raising awareness among authorities and the population about AMR as a public health issue and for serving as a model for expansion to other healthcare facilities.

8106

INITIAL ISOLATION AND WHOLE GENOME SEQUENCING OF *CORYNEBACTERIUM HINDLERAE* IN ISIOLO, KENYA.

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Corynebacteria, also known as Coryneforms, are a diverse group of gram-positive bacilli with a high G+C content in their genomes. Once dismissed as contaminants, recent research has indicated them as opportunistic pathogens, particularly in immunocompromised individuals and nosocomial infections. *Corynebacterium hindlerae*, a relatively recent addition to the genus, has garnered attention due to its isolation from only clinical sources. This study focuses on the isolation and genomic characterisation of *C. hindlerae* from an unexpected source - *Hyalomma truncatum* ticks collected from cattle in Isiolo County, Kenya. This marks the first reported instance of *C. hindlerae* in Kenya and from a non-human host. The isolation was guided by 16S rRNA metagenomics analysis of tick homogenates. It was identified from a pool of 8 ticks. The homogenate was cultured on 5% Sheep Blood Agar to obtain pure cultures of the bacterium. Following DNA extraction, libraries were prepared using the Illumina Nextera XT DNA Library Preparation Kit. Sequencing was performed on an Illumina MiSeq platform. Reads were filtered and trimmed using BBduk. Kraken2 and PubMLST were used for speciation. *De novo* assembly and annotation were performed in Unicycler and Prokka respectively. A genome map was then drawn using Proksee. Read mapping onto a reference genome using BBmap revealed that the sequenced genome had a coverage of 95.92% and an average depth of 15X. This isolation of *C. hindlerae* highlights the potential role of ticks in the circulation of emerging bacterial pathogens. *C. hindlerae* has so far only been isolated from humans in two different continents, its isolation from ticks in Africa suggests that the bacterium may be more diversely distributed. This points to a pressing need for further research to determine its ecological niche, transmission dynamics, pathogenicity, and potential public health risks.

8107

DIAGNOSTIC PERFORMANCE OF ANTIGEN F1-BASED RAPID DIAGNOSTIC TEST AT THE BEDSIDE ON-SITE AND AT REFERENCE LABORATORY FOR BUBONIC PLAGUE IN HIGH ENDEMIC SETTINGS IN MADAGASCAR

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Madagascar contributes >80% of global plague cases. Plague occurs seasonally in rural areas in the central highland during August-April. Early detection and treatment in the community prevents death. As per national guidelines, an antigen-based rapid diagnostic test (F1RDT) is routinely used at peripheral health centres and confirmed at the central reference laboratory (RL) by culture and qPCR (gold standard, GS). As part of the IMASOY trial (NCT04110340), we assessed the performance of F1RDT for bubonic plague conducted on-site before treatment (D1) and at the RL vs GS in 45 healthcare centres. Serology was also tested on D1, 11, 21 on blood samples. F1RDT performance was assessed against two GSs (culture and qPCR regardless of serology (GS1); and culture, qPCR and serology (GS2)) in 441 suspected bubonic cases: 59% male, 41% female, median age 12 years (range 0-72). Among them, 192 (44%) were confirmed bubonic cases with GS1 and 220 (50%) with GS2. Serology data were available for 426 participants and identified 28 (7%) additional cases (seroconversion or 4-fold titre increase).The sensitivity (Se), specificity (Sp), positive (PPV) and negative predictive value (NPV) of the on-site F1RDT against GS1 (%, 95% CI) were 93.8 (89.3, 96.7), 73.5 (67.6, 78.9), 73.2 (67.2, 78.6) and 93.8 (89.5, 96.8) respectively, and 89.1 (84.2, 92.9), 77.0 (70.8, 82.4), 79.7 (74.1, 84.5) and 87.4 (81.9, 91.8) respectively against GS2. The Se, Sp, PPV and NPV of the F1RDT at RL against GS1 were 92.2 (87.4, 95.6), 97.6 (94.8, 99.1), 96.7 (93.0, 98.8) and 94.2 (90.6, 96.7) respectively, and 82.3 (76.6, 87.1), 99.1 (96.7, 99.9), 98.9 (96.1, 99.9) and 84.6 (79.6, 88.8) respectively against GS2. The head-to-head comparison of the F1RDT on-site and at RL showed agreement (83%) with a Phi coefficient of 0.666. There was no apparent difference in performance of F1RDT by age (<15, ≥15 years). Current practice of combining on-site testing of suspected bubonic plague with F1RDT and confirmatory tests at RL is effective in identifying plague. Serology would identify few more but it would not be feasible in routine practice.

8108

VARIATIONS IN NASOPHARYNGEAL MICROBIOTA ACCORDING TO COVID-19 SEVERITY STATES

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Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, is affected by a variety of factors. Evidence suggests a relationship between COVID-19 and the nasopharyngeal microbiota. This study compares the diversity and taxonomic composition of the nasopharyngeal microbiota with clinical outcomes of COVID-19. A descriptive and comparative study was performed on patients classified into four groups according to their disease severity. For each study group, 26 patients were recruited: patients hospitalized in the intensive care unit (G1), hospitalized in regular hospitalization wards (G2), those without hospitalization and with mild or no symptoms with SARS-CoV-2 (G3), and healthy patients (G4). SARS-CoV-2 was tested on all patients using RT-PCR. The nasopharyngeal microbiota was characterized by PCR, targeting 13 genera of bacteria. Some bacteria were significantly more frequent in hospitalized patients (G1, G2) compared to the non-hospitalized patients (G3 y G4). This is the case with *Lactobacillus* (G1=96.2% of cases, G2=92.3%, G3=23.1%, G4=15.4%). Similarly, *Prevotella* (G1=96.2%, G2=80.8%, G3=3.8%, G4=23.1%). In the same way, *Veillonella* (G1=92.3%, G2=96.2%, G3=7.7%, G4=11.5%) presented a similar distribution. However, some bacteria were detected more frequently in healthy and asymptomatic subjects, such as Others Bacteroidetes (OB) and Others Firmicutes (OF). Similarly, relative abundance shows similar results to percentage frequency. There are several alterations in the nasopharyngeal microbiome associated with SARS-CoV-2 infection status and disease severity, reported in this study. The presence of *Lactobacillus*, *Prevotella*, *Veillonella*, and the Proteobacteria division were higher in critical and hospitalized patients, compared to asymptomatic and healthy subjects. On the other hand, others Bacteroidetes and species of Firmicutes were predominant in the groups of asymptomatic and healthy subjects. The nasopharyngeal microbiota should be studied in the future as a therapeutic, diagnostic, and prognostic tool in COVID-19.

8109

MOLECULAR DIAGNOSIS OF *SHIGELLA* SPP. IN CHILDREN WITHOUT CLINICAL SYMPTOMS IN A RURAL AND URBAN AREA OF NORTHERN PERU

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According to the World Health Organization (WHO), *Shigella* spp. infection is, in general, the most common cause of dysentery and the second most common cause of diarrhea. Bacterial dysentery due to *Shigella* spp. is an important morbidity and mortality cause, which accounts for 188 million diarrhea or dysentery cases caused annually by *Shigella* spp. around the world and 164,000 deaths related to this pathogen. In low- and middle-income countries, the most affected population is children under five years old. The purpose of this study is to assess the prevalence of *Shigella* spp. and determine the factors related to school-age children from urban and rural communities of the department of Cajamarca in Peru. Descriptive, cross-sectional study with a chunk sampling based on convenience. The study was conducted in 4-to-14-year-old children 14-year-old children from the districts of Baños del Inca (Urban zone) and San Pablo (Rural zone) in Cajamarca. Amplification by PCR assay for the detection of *Shigella* spp. was carried out using the primers and conditions previously described. The prevalence of *Shigella* spp. was 9.1% in the rural community and 3.6% in the urban community. It was found that the consumption of salads (p=0.24) and handwashing before eating (p=0.008) were factors associated to *Shigella* spp. infection. This study found a higher prevalence of *Shigella* spp. in the rural community and, therefore, we suggest implementing interventions to prevent the infection by this gastrointestinal bacterium It was found that a higher prevalence of *Shigella* spp. in the rural community in school-age children. Despite their healthy lifestyles, such as washing their hands before eating and after using the bathroom, they may be infected by this bacterium. In addition, in rural communities, all infected individuals lack sanitary facilities, so some intervention strategies could be recommended.

8110

A MULTIPLEX REAL-TIME PCR ASSAY FOR DETECTION OF THE FOUR MAIN CAUSES OF BACTERIAL MENINGITIS

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Strengthening diagnostic capabilities and monitoring circulating pathogens are essential to effectively combat meningitis. Current multiplex assays cannot detect all four WHO priority pathogens for meningitis diagnosis, i.e. *Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae* and *Streptococcus agalactiae*. This work developed multiplex real time PCR assay capable of simultaneously detecting these pathogens. A total of 45 DNA test samples were used, including appropriate specimens from the National Collection of Type Cultures (NCTC). Specific real-time PCR primers and probes targeting *sodC*, to detect *N. meningitidis, dmsA* for *H. influenzae, SP2020* for *S. pneumoniae*, and *cfb* for *S. agalactiae* were tested individually (monoplex) and in combination (multiplex). Standard curves were generated using tenfold dilutions of DNA extracted from reference DNA samples and the limit of detection (LLD), slope, intercept and R2 were determined. In addition, sensitivity, specificity, and positive/negative predictive value (PPV/NPV) of the multiplex assays were calculated. The monoplex and multiplex real-time PCR assays showed the same sensitivity, specificity, PPV and NPV for each of the four bacterial species, indicating that multiplexing did not alter individual assay performance. The assay sensitivities were all 100%, with specificities between 91.7% (*sodC*) and 100%, PPVs were between 72.7% (*sodC*) and 100%. All NPVs were 100%. The multiplex assay showed high efficiency and robust amplification for each target genes. The LLD ranged from 2 (*S. pneumoniae*) to 66 (*H. influenzae*) genome copies/µl. The multiplex assay showed good performance for rapid and accurate detection of meningitis associated bacteria. This test has application for improved diagnosis of meningitis, particularly for group B Streptococci, which remains underdiagnosed in LMIC. However, field validation with clinical specimens is required before implementation.

8111

EFFICACY OF MACOZINONE AND SUTEZOLID AGAINST *MYCOBACTERIUM LEPRAE*

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Mycobacterium leprae (M. leprae), the principal etiological agent of Hansen's disease infects the peripheral nerves, mucous membranes, and skin. The present anti-leprosy multi-drug therapy (MDT) requires prolonged treatment duration (6 to 24 months), and has unpleasant side-effects: causing reduced compliance, increasing the risk of relapse, transmission opportunities, and drug resistance. Therefore, there is a clear need to explore new therapeutic interventions against leprosy, which can effectively shorten treatment duration, without increasing adverse reactions. To test the efficacy of Macozinone and Sutezolid against *M. leprae* in vitro as well as in the mouse foot pad (MFP) model. *M. leprae*, freshly harvested from nude mouse foot pads (FP) were incubated at 33ºC with Macozinone and Sutezolid at different concentrations, Radiorespirometry (RR) assay was used to determine bacterial β-oxidation rate as a measure of viability. Mouse bone marrow derived macrophages were infected with *M. leprae* and were treated with different drug concentrations. The cells were lysed and RR was performed on released *M.* leprae to measure bacterial *viability.* To evaluate the efficacy of Macozinone and Sutezolid against *M. leprae* in vivo, athymic nude mice hind FP were inoculated with $3x10^7$ *M. leprae* and infection was allowed to progress for 2 months. Then drugs were administered by gavage as either a single dose, 5 daily doses or 20 doses (5x4weeks). FPs were harvested one month post-treatment and *M. leprae* viability determined by measuring normalized expression of *esxA* transcripts. Results show that Macozinone and Sutezolid are effective against *M. leprae* both in vitro (axenic and intracellular) and in vivo (MFP). Therefore, Macozinone and Sutezolid, having different modes of action, should be tested in combination with other first and second line drugs to explore new shorter treatment regimens for leprosy.

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DETECTING NOVEL MECHANISMS OF CARBAPENEM RESISTANCE: AN INNOVATIVE SCREENING SYSTEM IN LIMA, PERU

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The global spread of Carbapenem Resistant Klebsiella pneumoniae (CRKP) presents a severe public health threat, yet research on the genetic mechanisms of carbapenem resistance, particularly in developing nations, remains limited. Robust screening strategies are therefore urgently needed to address this issue. We implemented a high-throughput, novel screening strategy to detect novel carbapenem resistance mechanisms in Lima, Peru. Over 3 years, 200 000 isolates were screened by the regional reference laboratory. Antimicrobial susceptibility was assessed using Kirby-Bauer disc diffusion, and Minimum Inhibitory Concentration testing was conducted with VITEK® 2. Carbapenem-resistant isolates then underwent immunoassay screening (OKNVI Resist-5, Blue-Carba). We identified 3 CRKP isolates from 3 different patients which exhibited carbapenem resistance, but with no known carbapenemases on immunoassay. These isolates were whole genome sequenced (WGS) using Oxford Nanopore Technology. Bioinformatic analysis utilised Resistance Gene Identifier v6.0.3 and Comprehensive Antibiotic Resistance Database v3.2.8. WGS identified OXA-1, SHV-11, Mdtq, LptD, OmpK37, KpnH, KpnG, and marA resistance genes; none individually known to be associated with high level carbapenem resistance. Notably, although all 3 samples were genotypically identical, 2 isolates showed low level resistance, potentially explained by the antimicrobial resistance gene combinations identified. However, 1 isolate exhibited unexplained high-level resistance. WGS of these strains with unexplained carbapenem resistance, identified by our screening strategy, revealed a combination of beta-lactamase genes, and the Mdtq porin. Mdtq has not been previously associated with high-level carbapenem resistance, but could partially explain our findings. We anticipate that as combined genotypic and phenotypic testing among gram negative bacteria gains prominence, treatment dilemmas will increasingly arise due to genotype-phenotype differences.

8113

EXPLORING POTENTIAL ASSOCIATION BETWEEN LOW BODY MASS INDEX AND MID-UPPER ARM CIRCUMFERENCE WITH LEPROSY: A CASE-CONTROL STUDY IN ADDIS ABABA, ETHIOPIA

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Leprosy is classified as a neglected tropical disease (NTD) that affects about 200,000 annually. Factors associated with poverty, like undernutrition, have been associated with leprosy, but research is limited on the extent of this association. We aimed to determine if low body mass index (BMI) and low mid-upper arm circumference was more common in those with leprosy compared to controls in Addis Ababa, Ethiopia. Individuals attending the outpatient clinics at ALERT hospital in Addis Ababa, Ethiopia were recruited and evaluated for the case control study. Leprosy cases, diagnosed within 1 year, were recruited through convenience sampling of the leprosy clinic within ALERT while controls were recruited from neighboring clinics within the hospital. Controls were tested for antibodies against PGL1, phenoglycolipid-1, a specific *Mycobacterium leprae* antigen, and were included in this study if they tested negative. Height, weight and mid-upper arm circumference (MUAC) were measured and body mass index (BMI), calculated. An analysis was conducted to test the association between BMI and MUAC and leprosy, controlling for age, sex, and education level (as an indicator of socioeconomic status). There were 201 controls and 61cases; 56% were females. Univariate analysis showed that a MUAC less than or equal to 22cm was associated with leprosy [OR = 3.85, 95% CI (1.80, 8.26)] while an underweight BMI, defined by a BMI < 18.5, was not significantly associated, although had a high odds ratio [OR = 2.19, 95% CI (0.87, 5.42)]. A stepwise regression was then conducted to control for factors such as age, sex, and education status (as an indicator for SES), and found MUAC to still be significantly associated with leprosy [aOR = 2.46, 95% CI (1.01, 5.99)]. This study demonstrated the association with undernutrition, adding to the body of knowledge on the likely contribution of low nutrition to the development of disease. Further research, such as longitudinal studies and mechanistic studies, can help elucidate the role of poor nutrition and determine interventions that could potentially prevent clinical disease in at risk individuals.

8114

SEROPOSITIVITY TO IGG ANTIBODY OF *RICKETTSIA SPP*. IN A ENDEMIC AREA OF SOUTHEAST MEXICO

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Rickettsioses are tick-borne diseases caused by Gram-negative intracellular bacteria of the genus *Rickettsia.* The state of Yucatan has had a history of rickettsial diseases with the presence of *R. rickettsii* and *R. parkeri* both belonging to the spotted fever group (SFG) and *R. typhi* from the typhus group (TG). Seroprevalence in the states is 5.6% of SFG (*R. akari).* Yucatán has experienced urban growth which contributes to deforestation in areas with wildlife that is an important host for the transmission of this group of diseases. The present study aims to identify IgG antibodies to Rickettsia in participants of three geographic regions of Yucatan. Serum samples were collected from 60 participants. The IgG antibody titers were determined by indirect immunofluorescence assay (IFA), slides were fixed with antigens of *R. typhi* (TG), *R. rickettsii*, *R. parkeri*, and *R. conorii (SFG),* positive results were considered as titers IgG 1:64. For 60 participants 55% were female, 22% were older than 65 year the mean age was 51.4 (+16.16). 75% of participants were seropositive for *Rickettsia spp*., 17% (10/60) were seropositive for *R. typhi*, 15% (9/60) for *R. rickettsii*, 15% (9/60) for *R. parkeri* and 14% (8/60) for *R. conorii*,17% (10/60) presented cross-reaction between SFG and TG and 12% (7/60) cross-reaction between SFG. In t student test mean age was significantly difference between positive and negative patients ($p<0.001$). Chi-square test of independence reveals no significant differences in seropositivity for *Rickettsia spp* by gender ($p=0.635$). These preliminary results indicate high seropositivity to Rickettsia *spp*. in a representative sample of three geographic regions of Yucatan, which contrasts with previous investigations where the estimated seroprevalence in the state is 5.6%. Epidemiological studies of rickettsiosis are relevant because the changes in the ecosystem in recent decades as a result of human activity may impact the observed increase. A study with a larger sample size is important to determine the current seroprevalence.

8115

EVALUATION OF AN ELECTRICITY-INDEPENDENT METHOD FOR IS2404 LOOP-MEDIATED ISOTHERMAL AMPLIFICATION (LAMP) DIAGNOSIS OF BURULI ULCER IN RESOURCE LIMITED SETTING

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Buruli ulcer (BU) is a devastating necrotic skin disease. PCR, recommended for confirmation of BU by WHO, requires an equipped laboratory, which often delay timely diagnosis and treatment of BU patients in remote settings. This study aims to evaluate a simple rapid syringe DNA extraction method (SM) in comparison with an elaborate conventional DNA extraction method (CM) followed by loop mediated isothermal amplification (LAMP) assay targeting IS*2404* for the detection of MU, either using a pocket warmer (pw) or a heat block (hb) for incubation. Secondly, we aim to also explore the diagnostic workflow for BU at a community-based health centre in an endemic area in rural Ghana as an example of a potential target setting, using interviews with researchers and health care workers (HCWs). A protocol using SM for DNA extraction followed by IS*2404* PCR (IS*2404* PCR^{SM}) was able to identify MU DNA in 73 out of 83 BU clinical specimens submitted for diagnosis. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of IS*2404* PCR^{SM} were 90.12%, 100%, 100% and 65.21% respectively, as compared to the reference standard IS*2404* PCR in combination with a standard extraction protocol for mycobacterial DNA. Evaluation of the LAMP assay on 64 SM DNA extracts showed a sensitivity, specificity, PPV and NPV of 83.6%, 100%, 100% and 50%, respectively, using either pocket warmer (pwLAMP SM) or heat block (hbLAMP SM) for incubation of the reaction, as compared to the same reference standard. In terms of the limit of detection, the pwLAMP^{SM} could detect 30 copies of the IS*2404* target. Interviews confirmed that a diagnosis at the PoC, in addition to screening based on clinical criteria, would be advantageous to prevent delays and loss to follow-up. The high diagnostic and analytic accuracy of the pwLAMP, evaluated by us in combination with the SM, supports its potential use for the rapid detection of MU in suspected BU samples at the community or primary health care level without reliable electricity supply. Further optimization needs include a lysis buffer, evaluation directly at the PoC and other sites and assessing staff training requirements.

8116

POOR WASH, UNDERNUTRITION, AND FOOD INSECURITY IS ASSOCIATED WITH ANTI-PGL1 POSITIVITY, MARKER OF LEPROSY INFECTION, IN ADDIS ABABA, ETHIOPIA

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Given stagnant global leprosy cases, more needs to be done for elimination and halting local transmission. The use of anti-PGL1, a specific IgM antibody to *Mycobacterium leprae* infection, can identify individuals exposed to infection at increased risk of developing disease and identify factors related to infection. We conducted a cross-sectional study to determine the prevalence of anti-phenoglycolipid-1 (PGL1) seropositivity among communities near the ALL-African Leprosy, Tuberculosis Rehabilitation Center (ALERT),a former leprosy hospital, and to identify factors associated with seropositivity. Individuals without a present or past history of leprosy were recruited from the outpatient clinics at ALERT hospital from May till December 2023. A questionnaire about sociodemographic, environmental (WASH), and nutritional factors was administered. Height, weight, and mid-upper arm circumference (MUAC) were measured and blood samples tested for anti-PGL1 IgM using a point-of-care lateral flow (ML Flow). Of the 319 participants, 36.8% (n=118) were positive for anti-PGL1 IgM. The majority of participants had improved water sources and sanitation facilities, however 71% reported sharing toilets with other household. Among the study population, 6.6% were categorized as underweight(BMI<18.5), and 12% had low MUAC (< 22 cm). Factors associated with positive PGL-1 IgM included owning agriculture land (aOR 2.95, 95% CI [1.22: 7.51]), unimproved bathing water source (aOR 3.85, 95% CI [1.57: 10.2]) , dirt floors (aOR 1.64, 95% CI [0.97: 2.77]; p=0.065), lower MUAC (< 22 cm) (aOR 1.98, 95% CI [0.97:4.09) and a higher frequency of not eating for an entire day within the past year (aOR 1.77, 95% CI[0.95: 3.29];p=0.071), controlling for age, sex, source of income and education. Our study identified a high prevalence of PGL1-IgM in community members that highlights the likelihood of occult transmission in this region. Associated environmental and nutritional factors also show the likely roles of both the environment and the host in the exposure-infection-disease model in leprosy and should be further investigated.

8117

EPIDEMIOLOGICAL FACTORS ASSOCIATED WITH *MYCOBACTERIUM LEPRAE* SEROPOSITIVITY AND HISTORY OF HANSEN'S DISEASE IN A HIGHLY ENDEMIC AREA OF MINAS GERAIS, BRAZIL

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Many of Hansen's disease (leprosy) endemic areas are also endemic to helminth infections and studies have shown associations of helminths and mycobacterial infections. Therefore, we assessed the overlap of *Mycobacterium leprae* infection (as measured by antibodies to the LID-1 antigen) and Hansen's disease (HD) with parasitic infections. Children and adults were recruited from high-endemic municipalities in eastern Minas Gerais, Brazil, enrolled, and blood taken by fingerstick. A multiplexed bead assay (MBA) tested for antibodies and questionnaires on demographics and infection history were administered. Data were analyzed multivariable logistical regression with both anti-LID-1 antibody and history of HD as outcomes in separate models. Exposures in the analysis included history of parasites (both antibody results and self-reports) and several pertinent socio-demographics like area of residence (i.e. urban vs. rural). Of 1311 enrollees, 72 (5.5%) reported a history of HD, 94 (7.2%) positive for anti-LID-1, 836 (63.8%) reported having parasitic diseases in the past, 153 (11.7%) tested positive for SEA antibody, and 69 (5.3%) for NIE antibody. There was an association between rural residence and history of HD (aOR, 1.97, CI: 1.14 – 3.38) as well as rural residence and anti-LID-1 positivity (aOR 1.79, CI: 1.07- 3.38). While not statistically significant, there was a positive association between anti-LID-1 and strongyloides serology (aOR 1.57, CI: 0.69-3.57), and a negative one with SEA antibodies (aOR 0.79, CI: 0.38 - 1.61). This differed for those with a history of HD where SEA antibodies was positively associated (aOR 1.26, CI: 0.63-2.50); and NIE seroreactivity negatively associated (aOR, 0.40, CI: 0.09-1.70). There were no statistically significant associations with reported history of parasite infections and either anti-LID-1 or past HD. While we did not find a significant overlap for these infections, we did find statistical significance related to residency in rural places and both anti-LID-1 antibody and history of HD. This suggests an epidemiologic connection with rural residence and HD and deserves further investigation.

8118

SEASONALITY AND ENVIRONMENTAL ASSOCIATION OF MELIOIDOSIS IN NORTHERN VIETNAM

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Burkholderia pseudomallei is the causative bacterium of melioidosis, a potentially fatal disease primarily affecting people in the tropics and sub-tropics. This bacterium is environmentally mediated, infecting hosts through contact with contaminated soil and water. *B. pseudomallei* is endemic across Southeast Asia. Vietnam has a high hospital burden of melioidosis in its central region. Despite the history in Central Vietnam and the endemicity in nearby Thailand, melioidosis is not a nationally reportable disease and little is known regarding epidemiology of melioidosis in Northern Vietnam. The objective of this study is to investigate melioidosis distribution, associated environmental and geographic conditions, and determine its seasonality in Northern Vietnam. An ELISA assay with high specificity and selectivity for the detection of *B. pseudomallei* exposure was used to determine melioidosis seroprevalence from febrile patients of unknown cause reporting to hospital (2020-2023). Case data were aggregated to commune (sub-district) for spatial Bayes rate smoothing, local Moran's I, and spatial regression. A presence/absence analysis was performed to elucidate the relationship between environmental/physical conditions and seroprevalence. Blood culturing and WGS of a subset of patient samples was performed. A phylogenetic analysis revealed close genetic relationships between the isolated species, all of which persist in similar environments as *B. pseudomallei*. This study found that *B. pseudomallei* exposure was identified in all six provinces but spatially clustered. Seroprevalence was related to established soil conditions associated with *B. pseudomallei* persistence and increased cropland. A relationship between seasonality and melioidosis seropositivity was established, with the wet season having high seroreactivity. Healthcare accessibility was impactful to the melioidosis seropositivity, indicating that an improvement in public health surveillance regionally would be beneficial. Isolation of genetically similar opportunistic pathogens can be useful for informing clinicians.

8119

ECOLOGY AND EPIDEMIOLOGY OF *SARCINA TROGLODYTAE*, A NOVEL BACTERIUM ASSOCIATED WITH A LETHAL DISEASE IN CHIMPANZEES (*PAN TROGLODYTES*) IN SIERRA LEONE

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Bacteria of the genus Sarcina (family Clostridiaceae) have been associated with gastrointestinal disease in animals, including humans, since 1842. Although commonly thought to be opportunistic pathogens associated with delayed gastric emptying, evidence is emerging that, like the genus Clostridium, Sarcina consists of a diverse complex of species, some of which may be frank pathogens. Recently, a novel species, Sarcina troglodytae, was identified and epidemiologically associated with epizootic neurologic and gastroenteric syndrome (ENGS), a lethal disease of chimpanzees that has killed at least 56 chimpanzees at a sanctuary in Sierra Leone since 2005. Here, we describe the isolation of S. troglodytae from the brain of an affected chimpanzee and determined viable in vitro growth conditions allowing for further species characterization and elucidation of fermentation byproduct(s) with potential clinical relevance. Additionally, we have developed a species-specific diagnostic PCR which we used to test fecal and environmental samples from chimpanzees in sanctuaries and the wild. Our results demonstrate that S. troglodytae is more prevalent in sanctuary chimpanzees in the affected population in Sierra Leone than elsewhere where, to our knowledge, ENGS has not been observed. We also detected S. troglodytae in environmental samples, primarily soil, which combined with evidence of sporulation in vitro suggests a potential environmental reservoir. Reports in the literature of similar Sarcina-associated pathology in humans and other animals have increased dramatically in the last 15 years, suggesting that bacteria in this genus may be responsible for more morbidity and mortality than is generally appreciated. Clinicians, researchers, conservation biologists, and public health officials should consider certain members of the genus Sarcina to be potential pathogens of interest.

8120

OUTCOME AND PREDICTORS OF MORTALITY AMONG NEWBORNS WITH SEPSIS IN FOUR HEALTH FACILITIES IN MALI A COHORT STUDY

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Neonatal sepsis is a is a major cause of neonatal mortality and morbidity. No prospective study has been conducted on the survival of newborns with sepsis in Mali. This study aims to analyze the survival of newborns with sepsis and assess possible predictors of mortality in four health facilities in Mali.A prospective cohort study was conducted among neonates diagnosed with sepsis in four health facilities in two regions of Mali from December 2022 to January 2023. The data were analyzed using R software version 4.3.1. Kaplan-Meier estimators with log-rant test were used to estimate the survival time of the neonates. Bivariate and multivariate Cox proportional hazards models were used to show associations between possible predictors and survival time. Variables which p value < 0.05 in multivariable analysis were declared as statistically significant predictors of mortality.The study involved 152 neonates with their respective mothers. The median age of the mothers was 28 years [22-34], and for neonates, it was 2 days [2-8]. Male sex represented (74) 48% of the total. The neonates were followed for a median of 4 days [4-6]. Of the total, (62) 40% were mothers with positive sepsis. The survival rate at 15 days was 63% (50-79). At the end of this follow up 33 (21%) of the neonates died, with incidence of 21.30 per 100 neonates admitted with sepsis. Prematurity [P = 0.001, AHR = 8.81, 95% CI: (1.79, 43.26)], male sex [P = 0.02, AHR = 2.32, 95% CI: (1.08, 4.98)], admission in the hospital [P = 0.02, AHR = 2.48, 95% CI: (1.09, 5.96)], were the independent predictors of mortality among neonates admitted with neonatal sepsis**.**It is important to note that this conclusion is based on objective data analysis and not subjective evaluations. The risk of mortality was high among neonates with sepsis. The prematurity, sex male and the admission in the hospital were identified as predictors of mortality. The intervention focusing on the predictive factors identified could have an effect on mortality.

8121

INFLUENCE OF HIV INFECTION ON COMMON BACTERIA CAUSING SEPSIS AND ASSOCIATED SUSCEPTIBILITY PATTERNS IN CHILDREN AT A PEDIATRIC HOSPITAL IN ZAMBIA

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Sepsis, a condition of global public health concern, is a major cause of morbidity and mortality. There is a rise in antimicrobial resistant (AMR) bacteria attributed to sepsis. This study aims to determine the etiology and antibiotic resistance patterns among children admitted with clinical features suggestive of sepsis at Arthur Davison Children's Hospital (ADCH) in Ndola, Zambia and assess the influence of HIV infection on sepsis etiology. This is an ongoing prospective longitudinal study of children aged 2 years admitted at ADCH with clinical sepsis defined as the presence of 2 of the following conditions: temperature 38.0°C, respiratory rate ≥20/minute, and pulse ≥90/minute. Blood collected from each participant is inoculated into BACTEC culture bottles and incubated for 5 to 7 days. Positive cultures are inoculated onto culture media for subculture followed by species identification and antibiotic susceptibility testing. Ethical clearance and approval has been granted by the Tropical Diseases Research Centre ethics committee (TDRC-EC 092/07/23) and National Health Research Authority. Of the 95 participants (63.3% of 150 target sample size) of who have been recruited, 44.2% (42/95) are females and the mean age at admission is 9.8 (SD 6.8) months. About 30.5% (29/95) have had positive blood cultures and 17/29 are probable (true) pathogens with *Staphylococcus aureus* being the most common (10/17). About 6/17 of the true pathogenic bacteria isolated were Gram negative rods (GNR) *(*2 *Klebsiella pneumoniae,* 2 *Pseudomonas aeruginosa,* 1 *Escherichia coli* and 1 *Yersinia pestis*). Approximately 60% of the *S. aureus* isolates were methicillin-resistant (MRSA); multidrug resistance (MDR) was noted in *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. Analysis of association with HIV status is ongoing.*S. aureus* is a common cause of pediatric sepsis and is resistant to penicillins, the first line agent along with gentamicin. Similarly, all GNRs isolated were MDR so strengthening microbiology laboratory capacity is needed and the use of more potent antibiotics such as clindamycin should be encouraged in a low resource setting like ADCH.

8122

AUSTRIAN SYNDROM : A RARE CASE REPORT

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Austrian syndrom is a rare and fatal triad of pneumonia, meningitis and endocarditis caused by streptococcus pneumoniae, with a mortality rate of 60%. Pneumococcus is responsible for less than 3% of native valve endocarditis, but causes rapid valve destruction. A few published cases of austrian syndrome were confirmed by blood cultures.we report a case of austrian syndrome in a 59-year-old patient with a history of arterial hypertension on angiotensin-2 receptor antagonist therapy for five years, presenting with prolonged fever associated with loss of conscience without respiratory or cardiac signs, in whom purulent bacterial meningitis with positive gram stain, infective endocarditis with mitral and aortic localization and interstitial pneumonitis were demonstrated with negative blood cultures. Although the mortality rate is very high, early management aof austrian syndrome can improve the patient's quality of life

8123

WHOLE GENOME SEQUENCING OF EXTENSIVELY DRUG-RESISTANT *ENTEROBACTER HORMAECHEI* CLINICAL ISOLATES FROM A SECONDARY HOSPITAL IN MOROCCO WITH *HSV* AND *NDM* CARBAPENEMASE GENES

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The *Enterobacter cloacae* complex (*Ecc*) comprises enteric Gram-negative bacteria responsible for nosocomial outbreaks, primarily affecting immunocompromised patients. These infections are often fatal due to the high-level multidrug resistance of *Ecc* isolates. Despite their clinical significance, little is known about their virulence and pathogenicity. To understand the patterns and mechanisms of antibiotic resistance in three carbapenem-resistant bacterial isolates (EC254, EC256, EC83) selected from a biobank at a hospital in Agadir, genomic DNA was extracted and sequenced using the Illumina MiSeq platform. Hybrid assembly was utilized with Unicycler v0.4.2, and annotation was done via PATRIC version 3.6.6. Resistome and plasmid analyses were conducted using CARD and Plasmid Finder 2.0, respectively. Phylogenetic analyses were performed using MEGA version 10.1.7. The Genome sizes were 4.88Mb (EC83), 5.28Mb (EC256), and 5.29Mb (EC254). BLASTn alignment analysis using the *16S rRNA* gene showed high similarity to *Enterobacter hormaechei* subsp. *xiangfangensis* strain 10-17, with 99.2% and 100% identity for EC83 and both EC254/EC256, respectively. Multilocus Sequence Typing (MLST) (*dnaA*, *fusA*, *gyrB*, *leuS*, *pyrG*, *rplB*, *rpoB*) was assigned as follows: 49/20/19/44/*/24/32 for EC83 and 10/21/9/44/*/4/32 for both EC254 and EC256. Annotation of the assembled genomes indicated the presence of various antimicrobial resistance genes to aminoglycosides, β-lactams, fosfomycin, macrolides, sulfonamides, and fluoroquinolones. Notably, the strain EC83 was identified to carry seven main carbapenemase genes (*SHV-64, TEM-1*, *NDM-1*, *ACT-20*, *CMY-4*, *OXA-1*, and *OXA-48*). For EC254-EC256, five main carbapenemase genes were identified (*CTX-M-15*, *TEM-1*, *ACT-25*, *OXA-1*, and *OXA-48*). Plasmid detection revealed the presence of at least two large (~400 kb total) incompatibility group plasmids belonging to *IncF*, *IncH*, and *IncI1*. Phylogenetic analysis showed that EC254, EC256, and EC83 are closely related. The study generated draft genome sequences that provide valuable information for tracking antibiotic resistance in nosocomial outbreaks.

8124

SUCCESSFUL APPLICATIONS OF PHAGE THERAPY TO OVERCOME MULTIDRUG RESISTANT BACTERIAL INFECTIONS

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Abstract: Antimicrobial resistance (AMR) is a growing threat for public health around the globe. This threat is currently more pronounced due to ad libitum use of antibiotics. The selection pressure generated by the overuse of antibiotics has led to the rapid spread of AMR in our environment. Additionally, recent overuse of antibiotics during the COVID-19 pandemic has exacerbated these circumstances. Currently, conditions are so unmanageable that an alternative treatment must be developed and implemented. Phages are the most abundant biomolecules on the surface of the earth and a natural predator for bacteria, regardless of whether those bacteria are susceptible or resistant to conventional antibiotics. In this regard, a properly formulated phage mixture would be highly effective for overcoming the AMR problem for any class of bacteria. Unfortunately, two of the hindrances related for rapid implementation of phage therapy are associated with (i) host specificity of phage against the targeted bacteria and (ii) development of phage resistant bacteria during phage therapy. Recently, in our lab we have developed a rapid phage screening system to overcome both problems. This system allowed us to implement the phage therapy and successfully overcome several MDR bacterial infections in humans. In each case, using the system to evaluate the bacteriolytic nature of phages in a liquid environment, we were able to generate an effective therapeutic phage mixture. This liquid-based assay system allowed for the real-time evaluation of the kinetics of bacterial growth and the development of phage resistance over the course of the observation. Additionally, the system was also used for monitoring phage-bacterial interactions in the presence of antibiotics and the subsequent changes in the antibiotic resistance patterns of MDR bacteria under the selective pressure of the lytic phages. The details of the selection and characterization of the phages for these treatments along with treatment outcomes will be described in this presentation.

8125

BURKHOLDERIA PSEUDOMALLEI: A NEGLECTED 'NEGLECTED TROPICAL DISEASE'?

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Neglected tropical diseases (NTDs) are a group of preventable and treatable diseases caused by a range of pathogens, each capable of causing significant morbidity and mortality. Over the years, the list of NTDs has grown. However, *Burkholderia pseudomallei* has not been included thus far. *B. pseudomallei* is a gram-negative, soil-dwelling bacteria which is the causative agent of melioidosis. It is endemic in tropical and subtropical regions with a higher incidence in low-income settings. Infection can cause severe health complications, such as pneumonia, sepsis and multi-organ abscesses. An extensive review of published cases and publicly available information was conducted to identify reoccurring presenting symptoms, comorbidities, average time to diagnosis and treatment outcomes. A meta-analysis was carried out and a literature summary table was constructed. Results showed delays in diagnosis frequently occurred due to the resemblance of symptoms to other conditions, coupled with the similarity of *Burkholderia* organisms to *Pseudomonas* in laboratory settings, thereby predisposing to misidentification. No single presenting symptom was indicative of melioidosis, suggesting a strong clinical suspicion is required to help with prompt diagnosis. Therefore, it is essential for healthcare workers to have awareness of disease and specific areas of endemicity. Approximately 165,000 individuals are diagnosed with melioidosis each year, with an estimated 89,000 deaths. This represents a higher disease burden and greater mortality rate than many other recognised NTDs, such as dengue and leptospirosis. Although *B. pseudomallei* is not formally recognised as a NTD, the case studies examined in this investigation

demonstrate that melioidosis is a major global health concern. The addition of *B. pseudomallei* on the NTD list would significantly increase awareness amongst healthcare professionals, and drive crucial research, leading to improved diagnostic tools, surveillance, treatment, and patient care.

8126

GENOTYPIC AND PHENOTYPIC PROFILES OF ANTIMICROBIAL RESISTANCE IN PATHOGENIC BACTERIA ISOLATED FROM SEPTICEMIC PATIENTS IN WESTERN KENYA

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Antimicrobial resistance (AMR) is a significant global health threat, causing approximately 700,000 deaths annually. Traditional phenotypic antimicrobial susceptibility testing (AST) methods are limited by delays and result in delayed treatment with appropriate antibiotic therapies. We compared phenotypic AST with whole genome sequencing (WGS) in septicemic patients. WHO-GLASS pathogenic bacteria were retrospectively analyzed (2022-2023) from Western and Lake region referral hospitals. BD Bactec9050 and BD Phoenix 100 facilitated blood culture incubation, identification, and AST. DNA extraction and WGS were performed using the Oxford Nanopore Technologies platform, with EDGE Bioinformatics for bacterial identification and abritAMR/RGI for AMR gene identification. Among 960 blood cultures, 12.8% (123) showed bacterial growth, with 17 pathogenic bacteria identified by BD Phoenix. There were 13 Gram-negative bacteria (4 *E. coli*, 8 *Salmonella typhi* and 1 *Salmonella spp*.), and 4 gram-positive bacteria (3 *Staphylococcus aureus*, 1 *Streptococcus pneumoniae*). WGS revealed discrepancies between phenotypic and genotypic identifications, identifying *S. typhi* as *S. typhimurium,* probably due to phenotypic similarities. Two *E. coli* isolates were phenotypically susceptible but interestingly, multidrug-resistant (MDR) efflux genes were detected by WGS. Salmonella isolates displayed resistance to various antibiotics with MDR efflux genes detected. Notably, Salmonella isolates clustered with *S. typhimurium* global sequences, confirming their misidentification by BD Phoenix. *S. aureus* exhibited resistance to several antibiotics, while *S. pneumoniae* was generally susceptible, although genotypic AMR was evident but could not be confirmed due to low reads. In conclusion, the study identified disparities in bacterial identification and AST between phenotypic and genotypic methods, emphasizing the importance of incorporating both techniques for accurate AMR prediction.

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INFORMING ECOLOGICAL NICHE MODELS OF *BACILLUS ANTHRACIS* WITH CONSTRAINED DIVERSITY INDICES AND PHYLOGENIES FOR TEXAS AND VIETNAM

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Ecological niche models (ENMs), including GARP, MaxEnt, Random Forest, and Boosted Regression Trees, are used to prediction the distribution of *Bacillus anthracis* from local to global scales. *Bacillus anthracis,* the bacterial cause of anthrax, has a near global distribution limited by specific soil and environmental conditions constraining its range. As a spore-former, *B. anthracis* can persist for years resulting in repeat outbreaks in areas meeting these ecological conditions. Phylogenetically, *B. anthracis* is divided into five major lineages and 12 to 19 sub-lineages (defined by single nucleotide repeats [SNPs]). Within these sub-lineages, *B. anthracis* can be differentiated into several genotypes using many typing systems, including variable number tandem repeats (VNTR) in a multi-locus VNTR analysis (MLVA) and core genome multi-locus strain typing (cgMLST). While cgMLST is promising for tracking evolution in local populations, a much smaller subset of strains has been whole genome sequenced, limiting cgMLST value in mapping *B. anthracis*. In contrast, available MLVA data reflect a larger population of *B. anthracis* strains in the global collection. Some studies informed ENMs with MLVA-specific sub-lineages and showed environmental and spatial differences. No models have examined which specific VNTRs differentiate spatially. Here, we use ENMs, MLVA-25 phylogenies, and constrained-Simpson Indices to model local patterns of *B. anthracis* lineages in Texas and Vietnam, two regions with endemic anthrax affecting animals and humans. This integrative approach improved model performance and better explained diffusion and evolutionary patterns on both landscapes and across a diversity of sub-lineages.

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SEROEPIDEMIOLOGY OF TRACHOMA IN A LOW PREVALENCE REGION RECEIVING ANNUAL MASS AZITHROMYCIN DISTRIBUTION IN MARADI, NIGER

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Trachoma programs use the indicator trachomatous inflammation-follicular (TF) to monitor indication for and response to treatment for trachoma at the community level. Alternative indicators, including serologic responses, are increasingly being evaluated for trachoma surveillance. We evaluated seroprevalence to IgG antibody responses to the Pgp3 antigen in two districts in Maradi, Niger thought to have low TF prevalence. Data were collected as part of the baseline assessment of the Azithromycin Reduction to Reach Elimination of Trachoma (ARRET) trial in September 2021. A random sample of 80 communities were selected from Mayahi and Guidan Roumdji districts, both of which had TF prevalence <20% at their most recent trachoma surveillance survey in 2018. A random sample of 50 children per community were sampled. We collected field grades, conjunctival swabs for processing PCR for ocular *Chlamydia trachomatis*, and dried blood spots for serologic assessment. The most recent mass drug administration prior to sample collection was in March 2020, 18 months prior. Of 3,994 children sampled in 80 communities, 49% were female and median age was 4 years. Overall TF prevalence was 4.6% (95% CI 3.5 to 5.8%) and trachomatous inflammation-intense (TI) prevalence was 0.6% (95% 0.3 to 0.9%). The prevalence of ocular chlamydia was 0.03% (95% CI 0.08%). Seroprevalence with Pgp3 was 6.3% (95% CI 5.5 to 7.1%) in 1-9-year-olds and 3.7% (95% CI 2.9 to 4.4%) in 1-5-year-olds. TF and Pgp3 seroprevalence were more strongly correlated in 1-5-year-olds (correlation coefficient 0.29) compared to 1-9-year-olds (correlation coefficient 0.09). In this low trachoma prevalence setting in Niger, serologic responses to Pgp3 were consistent with little ongoing transmission of *C. trachomatis*.

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THE RE-EMERGENCE OF TRACHOMA INFECTION AMONG CHILDREN IN KONGWA DISTRICT, TANZANIA, POSES A THREAT TO YEARS OF PROGRESS

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Kongwa District, historically burdened by high trachoma prevalence, witnessed a notable decline from 60% in 1986 to 10% in 2010, further plummeting to less than 5% in 2019 before resurging in late 2020 despite the implementation of SAFE intervention measures. By 2021, the Trachomatous follicular prevalence reported to be 7.1% higher than the

reported baseline. To explore predictors for this resurgence, we conducted a cross-sectional study from January to June 2022 among children aged 1-9 in five villages. Enrolling 247 participants, aligned with the Kongwa Trachoma community outreach program, we managed to obtain clinical data on the disease. Most participants (57.5%) were aged 1-5, with only 22.7% of the school age children enrolled in primary school. While 99.2% had pit latrines, 52.5% reported poor water quality and infrastructure and 47% use open field for waste disposal near household. Univariate analysis revealed risks including larger household size, lack of face washing with soap, poor water quality, and open field waste disposal. Multivariate analysis identified household size (AOR 17.5, 95% CI: 5.5-54.9), absence of face washing with soap (AOR 13.69, 95% CI: 3.5-36.0), and improper waste disposal (AOR 17.9, 95% CI: 4.4-73.5) as continuous risk factors for trachoma infection. Despite SAFE intervention, sustained exposure to risky behaviours and environments perpetuates reinfection. In previous years, absence of pit latrines and distance to water sources were mitigated through a national campaign, suggesting potential for similar strategies to influence hygiene and waste management behaviours. Therefore, our findings have a potential to inform key actors on the need for sustainable approaches in trachoma elimination interventions and further research in other endemic areas.

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THE ROLE OF ANTIBODY DATA FOR IMPROVED UNDERSTANDING OF RECRUDESCENT ACTIVE TRACHOMA IN NEBBI DISTRICT OF UGANDA

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Uganda has progressed towards elimination of trachoma with 92% of 61 endemic evaluation units (EU) having attained trachomatous inflammation—follicular (TF) prevalence of <5%. However, trachoma remains persistent or recrudescent in five districts. Nebbi district was recrudescent after a trachoma surveillance survey (TSS) in 2019 reported a TF prevalence >5%. After restarting MDA, Nebbi had a TF prevalence <5% during next impact survey. At a subsequent TSS in 2023, we included serological testing into standard surveys to evaluate evidence of community transmission of ocular chlamydia. Dried blood spots (DBS) were taken from 1-9-year-olds and tested for antibodies to the *Chlamydia trachomatis* antigen Pgp3 using a lateral flow assay (LFA). Analysis was undertaken to estimate the prevalence of TF, TT, pgp3 antibody (seroprevalence), and pgp3 seroconversion rate (SCR) per 100 children per year. In Nebbi East, 1400 children 1-9 years were examined, of whom 1119 were sampled for DBS; and 1490 adults ≥15 years were examined. In Nebbi West, 1273 children 1-9 years were examined, of whom 1199 were sampled for DBS; and 1530 adults ≥15 years were examined. In Nebbi East children aged 1-9 years had a TF prevalence of 1.9% (95% CI [confidence interval] 1.0-2.7), seroprevalence of 8.2 %(95% CI 6.0-10.9), and SCR of 2.0 (95% CI 1.5-2.8). In children aged 1-5 years the seroprevalence was 4.1% (95% CI 2.5-6.5), and SCR was 1.3 (95% CI 0.8-2.2). In Nebbi West children 1-9 years had a TF prevalence of 1.0% (95% CI 0.3-1.9), seroprevalence of 7.6% (95% CI 5.5-9.9) and SCR of 1.7 (95% CI 1.2-2.3). In children 1-5 years, the seroprevalence was 4.6% (95% CI 3.1-6.6) while the SCR was 1.6 (95% CI 1.1-2.3). Among people ≥15 years, TT prevalence was 0.18% and 0.25% in Nebbi East and Nebbi West, respectively. The trachoma seroprevalence and seroconversion rates in both EUs are consistent with the TF prevalence of <5% reported in Nebbi East and Nebbi West. Based on these findings, on-going community transmission of ocular chlamydia is unlikely.

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SOCIAL-ECONOMIC AND CULTURAL PRACTICES INFLUENCING TRACHOMA TRANSMISSION AMONG RESIDENTS IN NORTHERN KENYA

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Trachoma is a neglected tropical illness caused by Chlamydia trachomatis. It is a leading cause of avoidable blindness. It creates a severe public health challenge in Kenya's northern region. The problem is widespread, with Turkana being one of the places with the highest trachoma prevalence due to the area being socio-economically disadvantaged. The study employed a descriptive cross-sectional design, recognizing the qualitative nature of the investigation. The results from the study captured a prevalence of 46.8% for trachoma within the past year from a sample size of 444. Based on the binary logistic regression analysis conducted sex, settlement type and occupation were significantly associated with disease transmission in the multivariable level. The qualitative analysis revealed that cultural practices were associated with Trachoma Transmission in Turkana West sub-County. These were inclusive associated with water access, prioritization of animals over household chores, water scarcity had a significant impact on bathing frequency among children, disorganization on waste disposal and unawareness of water treatment methods and poor hygiene practices. The prevalence of Trachoma in Turkana west subcounty is relatively high as such the need for immediate interventions that focus immediate healthcare service delivery, community sensitization and interventions to increase the access of water. They relate with other studies conducted in Baringo and Ethiopia. The recommendation from the findings would be to develop policies like Tailored Education programs, Water and sanitation infrastructure investment and cross-border collaboration.

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RESULTS FROM TRACHOMA PREVALENCE SURVEYS IN SENEGAL AS IT NEARS ELIMINATION

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Senegal is a country at the extreme west of Africa with a climate varying from desert in the north to tropical savannah in the south. In 2000, a national trachoma prevalence survey revealed that trachoma was a public health problem in 6/8 regions included in the survey; two regions were not included due to insecurity. In 2004-2021, district -level trachoma baseline surveys were conducted in 69/79 districts. Following these surveys, Senegal's National Eye Health Program scaled up the SAFE strategy (Surgery, Antibiotics, Facial cleanliness, Environmental improvement) where warranted. Trachoma impact surveys (TIS) and surveillance surveys (TSS) have been conducted in all endemic districts. This presentation will present results from trachoma prevalence survey and outline the last steps the country must take to eliminate trachoma. The surveys used a two-stage cluster random sampling design for each evaluation unit (EU). An EU corresponded to one or more health districts (HD) or a proportion

of an HD. In each EU, a list of villages was made and 30 systematically selected using probability proportional to size. In selected households, all consenting individuals aged ≥1 year had their eyelids examined. Trachomatous inflammation—follicular (TF) prevalence was calculated for children aged 1-9 years; trachomatous trichiasis (TT) prevalence was calculated for adults aged ≥15 years. From 2014, surveys were carried out with GTMP or Tropical Data support. District-level baseline mapping initially indicated that 27 districts had TF≥5%; remapping in 8 districts showed TF<5%. A total of 46 districts had TT ≥0.2%. TIS were completed between 2014-2018; all but 5 districts showed that TF had fallen to <5% after SAFE strategy implementation. In those 5 districts, additional years of SAFE were conducted and upon 2nd TIS, TF was <5%. TSS were conducted between 2017-2021; TF remained <5% in all districts. However, TT remains a public health problem in 4 HD/7 EU. Senegal has made great progress towards the elimination of trachoma as a public health problem. However, continued TT case-finding and management are required for elimination validation.

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INTER-LABORATORY VALIDATION OF A MULTIPLEX BEAD ASSAY USING A CHIMERIC MONOCLONAL ANTIBODY AGAINST PGP3

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A multiplex bead assay (MBA) that tests for antibodies against the *Chlamydia trachomatis* (Ct) antigen Pgp3 is used for population level serosurveillance for trachoma, the leading infectious cause of blindness. CDC laboratories generated a human/mouse chimeric monoclonal antibody (mAb) against Pgp3 that was used for the inter-laboratory validation of the assay. CDC and three external laboratories, two of which use different MBA protocols than CDC, ran a standard curve (with a typical linear range between 15.6 - 16,000 ng/mL depending on instrument type) along with 3 spiked "unknowns" (high, medium, and low concentrations of mAb) on 3 to 5 different days. Testing was performed by 5 different operators and on 3 different instrument types, giving 7 unique laboratory/operator/instrument conditions for assessment. Values for unknowns were interpolated into concentrations based on each laboratory's standard curve to estimate test accuracy (interpolated value / known value x 100) and inter-laboratory precision (%CV of interpolated values on plates run between different labs). While the absolute median fluorescence intensity signal varied across labs due to the different assay conditions and instruments used, the concentrations interpolated from the standard curve showed accuracy for all medium and low positive unknowns within 80—120% (the acceptable range for accuracy) in each setting. The high positive sample was within range for accuracy in 4/7 conditions. The inter-lab precision of interpolated concentrations for medium and low positive samples was <5% and the high positive sample was 20.6%. While accurate quantitation of antibody levels is not necessary for prevalence studies—the intended use case of the Pgp3 MBA—these results show the Pgp3 MBA is a robust assay with high reproducibility across different laboratories, assay conditions and instruments. The data also point toward the Pgp3 mAb is a useful reagent for inter-laboratory standardization, and generating similar control reagents may be useful for the growing field of serosurveillance more generally.

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A NOVEL BEHAVIOR APPROACH TO SUPPORT ELIMINATION OF TRACHOMA IN NOMADIC POPULATIONS

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Impact assessments conducted between 2012 - 2022 by the Tanzania Neglected Tropical Disease (NTD) Control Program revealed that nine nomadic councils in Arusha, Manyara, Dodoma and Rukwa regions had persistent or recrudescent high prevalence of Trachoma Follicular (TF). Another assessment supported by the Ministry of Health (MoH) and Helen Keller International (2016-2018) revealed overall lower uptake of the National Sanitation Campaign in nomadic communities. These results prompted development of a more holistic approach to implementing the Surgery, Antibiotics, facial cleanliness and environmental improvement (SAFE) strategy for trachoma, with a renewed focus on face cleanliness and environmental improvement (F&E). In 2020, Helen Keller supported the MOH to create innovative interventions to influence the F&E behaviors in these nomadic populations. One of the interventions identified and tested in seven wards of Ngorongoro district for twelve months included promoting the use of games and activity books in primary schools to enhance learning hygiene behaviors and sanitation practices. This intervention was assessed through key informant interviews and observations. Findings indicated that this school-based gaming approach had successful results including: the activation of school-based WASH clubs (SWASH Clubs) which excited and engaged the students, increased understanding of trachoma and its association with poor hygiene and sanitation by students, and creation and use of local waste bins to encourage hygiene and cleanliness in schools. Overall, there was an increased number of handwashing facilities at schools and improved personal hygiene among students participating in SWASH clubs. These interventions were well received by the students, and led to reduction of absenteeism, improved use of toilets, and improvement of hygiene and sanitation practices in the households of students. These results support the need for interventions targeting nomadic populations to include innovative approaches that engage communities in new ways to achieve the greatest impact.

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PATHWAYS TO PROGRESS: ENHANCING INFECTIOUS DISEASE DETECTION IN THE PERUVIAN AMAZON

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Loreto, Peru, annually reports one of the highest rates of infectious diseases in Peru, and it continues to be the site of the discovery of novel agents of infectious diseases. Because of this plethora of tropical infectious illnesses, Iquitos has become the base for many international infectious diseases research programs, including the Etiology of Acute Febrile Illness in the Peruvian Amazon as determined by modular formatted quantitative PCR: A Protocol for RIVERA, a Health Facility-Based Case-Control Study. This study aims to establish a stable annual surveillance system over four years (2021-2023) for 32 pathogens that cause acute febrile illness using the TaqMan Array Cards. This sub-analysis of the RIVERA study aimed to identify the time and method of delivery of qPCR-based results to enrolled patients. Until December 2023, the study enrolled over 1600 cases through facility-based surveillance and 1600 community-based controls. After enrollment, 51% (1588/3362) of participants received test results between days 2 and 4. Results were delivered both in digital and printed formats.

For the remaining 49% (1545/3362) of participants, the delivery timeline was extended between day 5 to day 10. Results are also systematically distributed to the respective epidemiology departments within each health center. Comprehensive documentation of these actions is diligently maintained, capturing pertinent details such as the date of dissemination, personnel involved, and the results delivery method. Through meticulous sample collection and efficient result delivery processes, the study underscores the importance of timely information dissemination for effective disease management. This concerted effort not only enhances healthcare services but also signifies a significant step towards combating emerging diseases in the region, ultimately improving public health outcomes in Iquitos.

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DEVELOPMENT, IMPLEMENTATION, AND CLINICAL VALIDATION OF AN ISOTHERMAL CAS12A BASED QUANTITATIVE ASSAY FOR CONGENITAL CYTOMEGALOVIRUS VIRAL LOAD DETERMINATION

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Congenital CMV (cCMV) is the leading cause of nongenetic infant hearing loss and accounts for more cases of life-long disabilities than more commonly known conditions. In West Africa, the prevalence of CMV is largely unknown due to resource limitations reducing capacity to perform laboratory tests. For the United States, there's evidence suggesting the cost effectiveness of universal cCMV screening though only one state (MN) has a program so far. Thus, there's a need for low-cost, non-laborious, sensitive assays to enable CMV research in low- and middle-income countries (LMIC) and decrease barriers to universal testing in high-income countries (HIC). We developed a quick, isothermal DNA quantitative assay that spans the entire sample collection to result pipeline. This platform utilizes a novel extraction method, HUDSON (Heating Unextracted Diagnostic Samples to Obliterate Nucleases) with isothermal amplification (recombinase polymerase amplification, RPA) and detection (CRISPR/Cas12a). We clinically validated this assay using a Sierra Leonean infant cohort and started implementation through laboratory capacity building efforts at the Kenema Government Hospital (KGH). Cost analysis shows reduction of price and time to obtain a result (40 minutes incubation compared to 65 minutes with PCR); and minimal use of extracted sample (2µL) allows for triplicate testing. Limit of detection and quantification (LOD/LOQ) is $10^{2.5}$IU/mL via fluorescence reader. RPA/Cas12a viral load determination from CMV-exposed infant saliva samples is not statistically different from PCR results (paired t-test, p=0.7692, N=101). HUDSON extraction is successful in serum and saliva samples, and compatible with subsequent DNA detection. Initial implementation involved evaluating assay performance in a low-resourced laboratory (KGH) using lateral flow output, which had an LOD of 10^{5}IU/mL. This novel isothermal DNA assay increases the capacity of a low-resourced laboratory for determining viral loads of suspected cCMV cases and/or CMV clinical research by providing results in less time, lower temperatures, and less costs per sample compared to PCR.

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SCARCE FOLLOW UP AFTER A LATE DIAGNOSIS: A SURVEY OF KEY STEPS IN CLINICAL CARE AMONG PATIENTS WITH CHRONIC TRYPANOSOMA CRUZI INFECTION IN BOGOTÁ, COLOMBIA

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For people with chronic *Trypanosoma cruzi* infection (cTCI) in endemic countries, receiving proper clinical care is challenging. In Colombia, a country with universal health care coverage, most people with cTCI live now in urban centers with no vector transmission and theoretically easier access to health care services. We surveyed *T. cruzi* seropositive individuals living in Bogotá who participated in observational or interventional studies at a referral center for cardiovascular disease since 2016. The aim was to describe key steps of clinical care in diagnosing, stratifying risk, or treating patients with cTCI. From 152 eligible participants, 102 were contacted and 96 gave consent to participate. The mean age was 61.5 years; 51 were women, 67.8% had chronic Chagas cardiomyopathy (CCC) and 24 participated in randomized trials. Age at cTCI diagnosis was 51.4 years (54 for those with CCC versus 46 for CCC-free participants, p<0,001). Fifty (52.1%) participants were diagnosed incidentally: 39 as blood donors, 10 after a family member was diagnosed and 1 after an occupational health assessment. The other 46 were diagnosed after cardiac manifestations suggesting CCC: 17 because of heart failure and 14 for arrythmias/sudden cardiac death. No participants diagnosed with cTCI had gastrointestinal complaints. Risk of CCC was stratified using ECG in 87 participants (95% among those with CCC and 80% for CCC-free, p=0.021) and echocardiogram in 77 (87% with CCC and 64% for CCC-free, p=0.008). Of 27 reporting trypanocidal therapy, 20 (74%) had it as part of interventional studies (Median time diagnosis-to-treatment 4[IQR 3-12] months). Regarding follow-up, 64 participants reported visits at least once a year, whereas 32 (16 with CCC) had none or just occasional visits. In this small series from a referral center in Bogotá, cTCI diagnosis is usually made decades late and, unacceptably, often when cardiac involvement is present. Despite the use of risk stratification tools upon cTCI diagnosis, many patients, even those with CCC, are not properly followed. It is imperative to promote an earlier diagnosis and timely follow-up for those at risk or with cTCI.

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COMPLICATED SPINAL CYSTIC ECHINOCOCCOSIS SUCCESSFULLY TREATED WITH SURGERY: 10-YEAR FOLLOW-UP

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Spinal Cystic Echinococcosis (CE) is a devastating form of *Echinococcus granulosus* infection, with a poor prognosis due to the infiltrative growth of the parasite larva in the bone, as no cleavage plan exists. Surgery is the standard treatment, but complete resection of infiltrating cysts remains difficult and recurrence is the rule. We report a case of vertebral and paravertebral Cystic Echinococcosis, successfully treated with sequential surgery. A 47 y.o. woman from Italy sought medical attention for the onset of dorsal-lumbar pain, lower limb paraesthesia and claudication. A CT scan of the spine showed a hypodense fluid-filled mass in the paravertebral and retroperitoneal space at D12-L1 level, measuring 9x9x5 cm. The mass infiltrated the iliopsoas muscle and was adjacent to the aortic wall. Destruction of the D12-L1 intervertebral disc was noted, with osteolysis of the adjacent vertebras and extension into the vertebral canal. Differential diagnosis included vertebral osteomyelitis and spinal Cystic Echinococcosis. Serology for Cystic Echinococcosis (Western blot) was positive. In October 2012, a posterior surgical decompression by laminectomy, intradural lavage with hypertonic saline and stabilization was performed. The next month, a second intervention was performed to remove all the pathologic tissue and for cage positioning. Pathological examination confirmed *E.*

granulosus infection. The patient recovered after surgery and is still disease-free after 10 years. While this outcome is exceptional for spinal CE, it shows that successful management is possible in a referral center.

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HIGH PREVALENCE OF UNDIAGNOSED ACUTE FEBRILE ILLNESS IN THE PERUVIAN AMAZON

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The Peruvian Amazon has a heavy burden of arbovirus infections and is an important location to maintain vigilance for early detection of emerging pathogens. The Abbott Pandemic Defense Coalition (APDC) and Universidad Peruana Cayetano Heredia (UPCH) are conducting acute febrile illness (AFI) surveillance in hospitals and health centres in Iquitos city and San Lorenzo region screening with (rapid diagnostic test) RDTs for malaria, COVID-19, and dengue. Between September 2023 and April 2024, 608 participants were enrolled in the study with a confirmed diagnosis for 129 (21.22%) participants including malaria 54 (8.88%), COVID-19 21 (3.45%), and dengue 52 (8.55%) single infections. We report a high prevalence of undiagnosed cases of febrile illness of 78.78% (n=479). Overall, 50.82% (309/608) were female and had a median age of 27.02 years old (IQR: 12.75 - 41.31 years old). The participants with and without a confirmed diagnosis did not differentiate relative to sex and age. However, we report that there is an association between the reported occupation and the diagnosis status by Fisher's exact test (p=0.023). The undiagnosed group did report working proportionately more on wildlife (2.33% vs 0.21%) and farming (9.30% vs 2.51%) in comparison to the group with a confirmed diagnosis while the latter had other non-health-related occupations (29.46% vs 40.08%). Additionally, the confirmed cases shared a triad of general symptoms: sickness, fever/chills, and headache, and had a disease-specific pattern of specific symptoms. The commonly screened diseases have an undifferentiated clinical manifestation making a clinical diagnosis troublesome and thus there is a high burden of febrile cases with unknown etiology. It is important to have the capacity to study unknown cases with next-generation sequencing, particularly those with unusual or serious clinical manifestations, as part of surveillance for the detection of emerging pathogens.

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MALARIA RETINOPATHY IS ASSOCIATED WITH WORSE LONG-TERM COGNITION IN UGANDAN CHILDREN WITH SEVERE MALARIAL ANEMIA

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Severe malarial anemia (SMA) and cerebral malaria (CM) due to *Plasmodium falciparum* are both associated with long-term neurocognitive impairment (NCI) in children. Malaria retinopathy is an important clinical feature of CM, caused by sequestration of parasitized erythrocytes in retinal blood vessels, reflecting sequestration in the vasculature of the brain. However, long-term NCI in children with CM does not correlate with malaria retinopathy. The presence of retinopathy in children with SMA has rarely been evaluated, and the association of retinopathy in SMA with long-term NCI is not known. We evaluated the association of malaria retinopathy with long-term cognitive outcomes (overall cognition, attention, and associative memory) among children ages 6 months to 4 years with CM (n=41) or SMA (n=101). Malaria retinopathy was assessed by medical officers on admission and cognitive outcomes were measured one year after admission. On admission, 7.2% of children with SMA and 45% of children with CM exhibited retinopathy. In children with SMA, retinopathy was associated with worse overall cognition ($p<0.001$) but was unrelated to attention or associative memory ($p=0.67$ and $p=0.53$, respectively). In children with CM, retinopathy was not associated with overall cognition or associative memory ($p=0.94$ and $p=0.71$, respectively), but was associated with better attention scores ($p=0.04$). Among children with SMA, neither continuous *P. falciparum* histidine-rich protein-2 (*Pf*HRP2) level nor *Pf*HRP2 level >1700 ng/mL was associated with overall cognition or attention, but both were associated with worse associative memory ($p=0.01$ and $p=0.02$, respectively), while in children with CM, neither *Pf*HRP2 level nor level >1700 ng/mL was associated with any cognitive outcomes. Scores in overall cognition were lower in children with CM or SMA, irrespective of retinopathy, than in 108 asymptomatic community children. The study findings suggest that sequestration of *P. falciparum*-infected erythrocytes occurs in the brain vasculature of a subset of children with SMA and is strongly associated with worse long-term cognition in these children.

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SAFETY, IMMUNOGENICITY AND EFFICACY OF THE SHIGELLA VACCINE - A SYSTEMATIC REVIEW

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Shigella infections present a significant global health challenge, especially in low- and middle-income countries where antimicrobial resistance is increasing. Vaccination is a promising approach to address this threat, but the immunogenicity, efficacy, and safety of Shigella vaccines undergoing phase 1 and phase 2 trials require thorough evaluation. This systematic review aims to assess the effectiveness and safety of Shigella vaccines. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, experimental trials comparing Shigella vaccines with placebo or other vaccines in adults and children were included.Five trials were included, two of which used oral and three parenteral vaccines. Adverse events were lower with oral vaccines as compared to parenteral ones. Comparison of ZF0901 (bivalent Shigella conjugate vaccine) with the existing approved HIB vaccination as a control showed no significant adverse events linked to vaccinations after half, one, or two doses. In all three age groups, similar rates of adverse events were seen at each injection, with fever accounting for most of these occurrences.Regarding immunogenicity, the ZF0901 vaccine caused a statistically significant increase in type-specific IgG antibodies against S. flexneri 2a and S. sonnei 30 days after immunization in all vaccine groups, regardless of the amount or number of injections. More than half of the recipients exhibited >4-fold seroconversion across all age categories. No substantial dose impact between 10 µg and 5 µg was detected. Likewise, SF2a-TT15 (Monovalent vaccine) was compared with and without alum A single injection of non-adjuvanted 10 µg oligosaccharide resulted in a 27-fold increase in IgG GMT (5080 vs 189) vs the non-adjuvanted 2 µg oligosaccharide dose, which showed a 5-fold increase (1411 vs 283) compared to baseline. The existing data from included trials provide promising and interesting results regarding the efficacy, safety and immunogenicity of the Shigella vaccines. However, data from phase 3 trials is needed to develop recommendations for use in public health.

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CLINICO-EPIDEMIOLOGICAL STUDY OF SNAKEBITE: AN AUDIT OF THIRTEEN YEARS DATA FROM A COMMUNITY-BASED TREATMENT CENTRE OF EASTERN NEPAL

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Snakebite envenomation is a global public health concern, especially in tropical and subtropical regions where venomous snakes are endemic. We describe the demography, clinical presentation, management and prevalence of traditional practices for snake bites in eastern Nepal. This study involves 13,825 patients who received snakebite treatment in Damak Red Cross Snakebite Treatment Centre (DRSTC) situated in eastern Nepal, over a period of thirteen years (2008-2021). The median age of the victims was 29 years (IQR: 18-43) with farming and agriculture (39.53%) being the most affected occupation. Most snake bite incidents occurred outdoors, notably during the monsoon season (61.72%). Cobras (Naja spp.) were the predominant species identified, often resulting in lower limb bites (69.24%). Most patients were asymptomatic. The predominant symptom was pain at the bite site (14.2%). Local remedies like application of chili powder and tourniquets were common (91.7%) and 0.8% of victims consulted traditional healers prior to seeking treatment at DRSTC. Antivenom was infused for 3.25% of victims. Motorcycles (57.9%) were the primary mode of transport and significantly decreased time in reaching healthcare centres in comparison to other means ($p<0.001$). We conclude that Snakebites are a common problem in eastern Nepal. Tourniquet application as a part of first aid is common. Neurotoxic envenomation, inflicted by common cobra predominates in this region.

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IDENTIFYING ADDITIONAL RISK FACTORS FOR DEVELOPING CHRONIC KIDNEY DISEASE

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Chronic Kidney Disease(CKD) is an increasing global problem with significant morbidity and mortality. Immigrants to the United States frequently work in hot environments without sufficient access to water, and often have poorly controlled diabetes (DM) and /or hypertension (HTN), all possible risk factors for the development of CKD. All patients seen in a clinic for the uninsured by 1 provider during a 4 month period with either a reduced glomerular filtration rate (eGFR) and/or proteinuria (albumin-to-creatinine ratio ACR), were interviewed for current and past hot occupational environments and the availability of water. Fifty patients were evaluated; 28 were female, 6 were aged 30-40 years old (yo), 13 40-50 yo, 17 50-60 yo, 13 60-70 yo, 1 70-80 yo. Twenty-five patients had DM, 41 had HTN, 19 patients had both DM and HTN. Thirty-five had worked in a hot environment, 27 did not have any or easy access to water, including 1 person who worked in a cold environment, 24 patients worked in both a hot environment and did not have access to water. Twenty-six had a lowered eGFR, 10 sufficient to diagnose CKD, including 2 who were in kidney failure (<15), 26 patients had both lowered eGFR and moderate to severe proteinuria. Two patients were from Africa, 3 from the Caribbean, 45 from the Americas. Patients arrived in the US from the 1960s to the 2020s, the majority in the 2000s. Examining the 30-40 year old cohort, 4 were female, 1 had both DM and HTN, 4 worked in a hot environment, 3 did not have water, 2 had both a low eGFR and proteinuria, all 6 were from C Am, 2 arrived in the 2000s, 2 in the 2010s, 1 in the 2020s. Females were more common than males, the youngest cohort had the worst eGFR, and none had worked as migrants. Patients frequently are asked their current job but not always asked their current or past working conditions. Asking a patient their current and past work environment and their current/past access to water, can help identify those who may need additional occupational counseling for cooling and rest breaks and a need for increased water intake, evaluation and monitoring to prevent or identify CKD, and the risks of heat stress.

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DISCORDANCE BETWEEN IMMUNIZATION HISTORY AND SEROLOGIC IMMUNITY TO VACCINE-PREVENTABLE INFECTIONS AMONG ASYLUM SEEKERS IN THE US

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In the past year, nearly 2 million people have entered the US through irregular routes of migration, most to seek asylum. Outbreaks of vaccine-preventable infections, such as measles and varicella, have been reported in migrant shelters across the US. We sought to determine the susceptibility of this population to vaccine-preventable infections. We conducted a cross-sectional study of unhoused asylum seekers in New York City from January 1- November 30, 2023. We measured serologic evidence of immunity against varicella, measles, mumps, rubella, hepatitis A, and hepatitis B. We used multivariable logistic regression to determine the adjusted odds ratio (aOR) for susceptibility. In the subset of individuals who provided written vaccine records from their countries of origin, we analyzed their vaccination history and evaluated for discordance between reported vaccination history and serologic immunity. Among 1147 people (53.2% female, median age 13), nearly one-third were susceptible to measles(26.9%, 95% CI: 24.3-29.5%), varicella (32.0%, 95% CI: 29.3-34.8%), and hepatitis A (32.0%, 95% CI: 29.3-34.8%). Almost half were susceptible to hepatitis B (41.6%, 95% CI: 38.7-44.5%). Susceptibility to measles was more likely in children (aOR 1.69, 95%CI: 1.24- 2.30) and adolescents (aOR 2.10, 95%CI: 1.37-3.19) compared with adults. Susceptibility to varicella was more likely in children (aOR 9.85, 95%CI: 6.81-14.59) and adolescents (aOR 4.90, 95%CI: 3.02-8.01) compared with adults and in men (aOR 1.35, 95%CI: 1.02-1.78) compared with women. We found that 195 people (17.0%) provided documented completion of the two-dose MMR vaccine series in their country of origin, of whom 53 (27.2%) did not have serologic evidence of immunity against measles. People with discordant vaccine records and immunity were most commonly from Ecuador (35.9%), Colombia (26.4%), and Venezuela (15.1%). In summary, a high number of unhoused asylum seekers are not immune to vaccine-preventable infections. People with documented history of vaccination against measles prior to entering the US were no more likely to have serologic evidence of immunity against measles.

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STRENGTHENING INTEGRATED COMMUNITY CASE MANAGEMENT COMMODITY AVAILABILITY IN UGANDA

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The Integrated Community Case Management (iCCM) program is a key strategy for delivering life-saving interventions for malaria, pneumonia and diarrhoea to populations with poor access to health services mainly targeting children under 5 years of age. The program has been implemented in Uganda since 2010, reaching 70% of districts by 2023 though Village Health Teams (VHTs). However, stagnation in achieving malaria testing and treatment targets at the community level has been noted due to frequent stockouts of commodities, hindering its effectiveness. To address this issue, the Ministry of Health, in partnership with PACE and

PATH-PMI Insight, conducted a Landscape Assessment to investigate iCCM commodity stockouts in Uganda. A mixed-methods approach was utilized, involving forty in-depth interviews conducted at national, district, and health facility levels, alongside eight focus group discussions with VHTs. Inductive qualitative analysis using QSR International's NVivo software explored community-level barriers to iCCM stock availability. Document review offered insights into VHT service provision, while District Health Information System (DHIS2) data analysis using STATA version 14 assessed commodity stockouts. Additionally, a design workshop engaged key stakeholders to craft intervention strategies. Stockouts of key commodities such as ACTs, ORS+ Zinc, and Amoxicillin were prevalent. The proportion of villages with ACT stockouts increased from 52.6% in 2020 to 62.9% in September 2023. DHIS2 data for 2023 revealed significant stockouts of iCCM commodities, with 62.9% of villages experiencing stockouts. Challenges in the commodities supply chain were identified at various levels, including national, district, health facility, and community levels. Key reasons for stockouts included governance issues, management challenges, human resource constraints, and data quality gaps indicating a systemic issue. Strengthening iCCM stock availability requires government leadership, civil society engagement, reliable medicine supply, and improved governance.

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THE PREDICTIVE VALUE OF SIRS AND Q-SOFA SCORES AS MEASURES OF SEPSIS SEVERITY AMONG PATIENTS IN A PRIVATE HOSPITAL IN LAGOS, NIGERIA: RESULTS FROM THE R JOLAD SEPSIS STUDY

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In sepsis, systemic inflammatory response syndrome (SIRS) and quick Sepsis-related Organ Failure Assessment (qSOFA) scores are used to screen patients and predict mortality in sepsis. Studies have documented their predictive value, notably in high-income countries. There is little data on their efficacy in low-resource, high-malaria settings. This study evaluated SIRS and qSOFA for septic patient screening at a Lagos, Nigeria, private hospital. A sepsis registry was established at R-Jolad Hospital. Septic patients meeting at least two SIRS criteria were enrolled in the registry. Data on qSOFA scores generated from the vital signs, patient disposition, malaria co-infection, and management, including the use of vasopressors and mortality outcomes were recorded. Frequencies, chi-square tests, and regression analyses were used to assess the relationship between these outcomes and the SIRS and qSOFA scores.230 sepsis patients aged ≥ 18 were enrolled from September 2023 to April 2024. 57.8% were outpatients, 41.8% emergencies, and 0.4% admitted. Fifty percent of enrolled patients met two SIRS criteria, 42.7% met three, and 7% met four. The average qSOFA score was 0.9 (SD ±0.6). 77.6% of 215 hospitalized patients were discharged, 11.2% were referred, 6.8% were discharged against medical recommendation, and 4.4% died in hospital. SIRS and qSOFA did not significantly affect patient disposition, vasopressor use, or hospital stay. 74.3% of patients had malaria co-infection, of which 10.3% and 1.2% had qSOFA scores of 2 and 3. 48.5% of this group met 2 SIRS criteria, 42.7% met 3, and 8.2% met 4. The qSOFA score may better screen for severe illness in malaria-endemic areas than SIRS. In our resource-constrained environment, neither SIRS nor qSOFA accurately predicted the severity of sepsis or the likely final disposition of admitted patients. Though half of patients enrolled in the registry presented with an SIRS score >2, the majority were discharged. Further studies are required to determine a suitable sepsis clinical severity score in similar environments with high endemic malaria transmission.

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CLINICAL PRESENTATION OF ACUTE ARBOVIRAL INFECTIONS DURING THE 2023 OUTBREAK IN THE TIRS PROJECT COHORT

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Aedes borne diseases (ABD) are caused by viral infections transmitted to humans through bites of infected Aedes aegypti. The increase in the incidence and geographical distribution of ABDs is a major public health problem in the Region of the Americas. The year 2023 had the highest historical record of dengue cases in the continent, with more than 4.1 million new infections. Mexico was within the regions with the highest cumulative incidence and both total number and severe number of cases. Within the country, Yucatan state reported 19% of Mexico's cases. The aim of this study was to describe the clinical characteristics of the ABD cases from the last active surveillance season during the outbreak (July-December 2023) in the TIRS trial cohort of ~4600 children aged 2-15 at enrollment in Merida, Yucatán, Mexico. Through household visits, phone calls, phone messages and a toll-free line, 822 reports of potential ABD symptoms were observed. Of these, 558 (68%) were considered suspected ABD cases. A total of 488 participants provided a blood sample. From these, 310 cases were detected (64% attack rate) by PCR or IgM results. Dengue represented 82% of the cases (n=254), followed by Zika 12% (n=37) and coinfections 6% (n=19). Patients with confirmed ABD were slightly older than the negatives but there were no significant differences between age nor sex. The clinical presentation of the cases was diverse, with fever (100%), headache (79.8%-84.6%) and myalgia (78.9-84.6%) as the most common signs/symptoms reported regardless the diagnosis. A total of 15 patients presented alarm signs and were referred to ER consultation. No ABD severe cases were observed. All the patients recovered satisfactorily. These results describe the variable array of symptoms involved in DENV infections and reinforce the importance of strengthened surveillance and laboratory diagnosis to detect silent ZIKV transmission during a DENV outbreak.

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ASSESSMENT OF HOME BASED RAPID DIAGNOSTIC TESTING UPTAKE TOWARDS INCREASING COMMUNITY-BASED ACCESS TO CARE IN KENYA, SOUTH AFRICA, AND ZAMBIA

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Rapid diagnostic tests (RDTs) offer a cost-effective solution for early disease detection, public health screening, and surveillance; however, their uptake remains sub-optimal. We sought community members' perspectives on the distribution and administration of RDTs to increase testing and treatment uptake for health priorities. In this qualitative study, we conducted 60 in-depth interviews and 11 focus group discussions with community members in rural and urban settings in Kenya, South Africa, and Zambia. Interviewers collected written informed consent and audio-recorded interviews. They distilled key information in structured memos capturing context, perspectives, and recommendations. We conducted rapid thematic analyses using analytic memos and debriefs with country research teams. All participants prioritized HIV, TB, and malaria for rapid testing. South African participants wanted to self-test for malaria in facility-based settings due to low confidence in interpreting results. All participants had a strong preference for home delivery of RDTs and medication by CHWs, despite concerns of increased workload. Though most were confident

about self-testing, participants generally preferred having a CHW present for pre-/post-test counseling, consultation, and linkage to treatment and prevention. Kenyan participants had mixed feelings about HIV self-testing at home due to perceived need for counseling and medical attention. If unfacilitated self-testing, participants preferred audio-visual demonstrations and pictorial brochures to follow at their own pace. If reactive, participants preferred phone consultation with a professional healthcare worker to get personalized advice on medication, lifestyle, and being fast-tracked for medicine pick-ups at a private pharmacy or health facility. A non-reactive result could prompt online information seeking or care-seeking if feeling unwell. Convenience, access, easy-to-follow instructions and personalized guidance through testing and accessing care pathways should be prioritized for the implementation of RDTs.

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HIGH-RISK *APOL1* VARIANTS ARE ASSOCIATED WITH REDUCED LONG-TERM SURVIVAL FOLLOWING SEVERE MALARIA

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Acute kidney injury (AKI) is an emerging complication of clinical importance occurring in 24-59% of children hospitalized with severe malaria. Survivors of AKI are at increased risk of post discharge mortality and chronic kidney disease (CKD). High-risk variants in the apolipoprotein-L1 (*APOL1*) gene account for ~70% of increased risk of kidney disease in people of African descent. G1 and G2 variants of *APOL1* are protective against African trypanosomiasis but confer increased risk of kidney disease. We hypothesized that children with severe malaria, subsequently at risk for AKI, and who carry high-risk *APOL1* variants have increased risk of long-term mortality and CKD. Analysis is nested in an established prospective cohort study of children under 5 years hospitalized with severe malaria at 2 sites in Uganda. Array genotyping determined *APOL1* status of 564 children. Children were followed for 1 year then recontacted and consented to kidney function assessment at 4-9 years using serum creatinine and urine albumin to creatinine ratio using the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. G1 frequency was 7.4% and G2 frequency was 8.9%. 2.7% (15/564) of children were considered high-risk if they have 2 *APOL1* risk variants (G1G1/G1G2/G2G2). There was no difference in age, sex, patient characteristics, or disease severity at presentation (p>0.05 for all) between kidney risk groups. In-hospital mortality was 20% in the high-risk group (3/15) versus 6.9% (38/549) in the low-risk group (p=0.088). All-cause mortality among children at 4-9 years was 58.3% (7/12) versus 19.4% (85/438), corresponding to a hazard ratio of 3.71 (95% CI 1.72 - 8.03, p=0.001). Among surviving children, with long-term follow-up available, the odds of CKD was 3.70 times higher among children with high-risk *APOL1* (95% CI 0.40 - 33.74, p=0.247). There were no differences in mean eGFR or specific KDIGO CKD risk categories (p>0.05) between kidney risk groups. Efforts to validate mortality risk among children with high-risk *APOL1* variants living in malaria endemic regions are ongoing.

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POSTMORTEM CHARACTERIZATION OF GASTROSCHISIS ASSOCIATED UNDER-5 DEATHS IN MOZAMBIQUE: INSIGHTS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS)

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The Child Health and Mortality Prevention Surveillance (CHAMPS) Network performs advanced minimally invasive tissue sampling (MITS) postmortem techniques in deceased children, providing a unique opportunity to investigate in depth causes of death (CoD), including rare conditions like gastroschisis, in Africa and South Asia. Gastroschisis is a congenital malformation associated with increased risk of mortality in settings with limited resources for prenatal diagnosis and surgical intervention. Here we present CHAMPS CoD findings in children who died from gastroschisis in Mozambique (Manhiça and Quelimane). A panel of multidisciplinary specialists reviews MITS pathology and microbiology results together with clinical records and verbal autopsy to determine the immediate, underlying, and comorbid CoD using ICD-10 codes. Of 1312 cases DeCoded betwen 2016 and 2022, 1.4% (n=19) had gastroschisis as the underlying CoD. All but one start with were perinatal deaths: 2 stillbirths (10.5%), 3 deaths in less than 24 hours (15.8%), and 13 deaths between 1-7 days (68.4%). The non-perinatal death e was 47-month-old child born with gastroschisis and submitted to sugery three days post-birth who developed postosurgery complications (rectovaginal fistula) and died due to sepsis. The immediate CoD among those cases were sepsis (47.4%), pneumonia (10.5%), peritonitis (5.3%), hyaline membrane disease (5.3%), and intrauterine hypoxia (5.3%). *Klebsiella pneumoniae* (44%), *Escherichia coli*, and *Pseudomonas aeruginosa* (11%) were the main etiology of sepsis. The maternal conditions grastroschisis-associated were young maternal age (15.8%), HIV exposure (5.3%), pre-term rupture of membranes (5.3%), chorioamnionitis (5.3%), twin pregnancy (5.3%), and maternal anaemia (5.3%). Our findings provided a snapshot of the impact of a rare condiction in the early child mortality in Mozambique, calling for the urgent need of improving antenatal care including ultrasound check and surgical capacities and improve targeted infection control and clinical management in high-risk groups

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IMPORTANCE OF CLINICAL EXPERTISE IN DIAGNOSIS OF LEPROSY AND AMERICAN CUTANEOUS LEISHMANIASIS: INSIGHTS FROM CLINICAL PROFILES IN EASTERN MINAS GERAIS, BRAZIL

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Leprosy and American Cutaneous Leishmaniasis (ACL) are neglected tropical diseases (NTDs) with considerable prevalence and morbidity rates in Brazil. Conventional laboratory techniques for leprosy exhibit suboptimal sensitivity, leaving diagnosis to the clinical assessment of physicians, often a challenging task. Similarly, clinical examination for ACL lacks sensitivity and specificity, leading to underdiagnosis and delayed treatment. Furthermore, the broad spectrum of immune responses leads to a diverse array of clinical presentations. We present, therefore, four cases of these two NTDs

from eastern Minas Gerais, Brazil, demonstrating the diversity of clinical presentations making diagnosis challenging. Two individuals diagnosed with MB leprosy exhibited disparate disease phenotypes. One patient initially presented with right forearm pain and neural thickening, subsequently developing hypochromic skin lesions with sensory deficits several years later. The second patient manifested hypochromic patches with sensory loss. Notably, while the bacilloscopic index for this individual was negative, suggestive biopsy findings confirmed the clinical suspicion. For the ACL cases, one patient displayed suspicion of cutaneous involvement with a localized lesion, while the other exhibited cutaneous involvement with a localized lesion and reactive lymphadenitis in the adjacent region. The inconclusive diagnosis in the latter ACL suspect was attributed to a negative parasitological examination. Subsequently, a lesion sample was obtained for molecular diagnosis (PCR). Accessibility to this diagnostic tool posed challenges in patients' cities, far from reference centers. Therefore, the development of rapid diagnostic tests holds promise for accurately diagnosing infections with reduced technological complexity, facilitating effective control of new cases and highlighting the critical need for improved diagnostic methods. Moreover, enhancing physicians' training to recognize clinical cases without reliable tests is imperative for timely intervention and management.

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RENIN RELEASE IS ASSOCIATED WITH ACUTE KIDNEY INJURY AND PREDICTS MORTALITY IN CHILDREN WITH SEVERE MALARIA

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Renin has been identified as a biomarker of acute kidney injury (AKI) in critical illness. In a two-site prospective cohort study, we assessed plasma renin levels in 594 children with severe malaria (SM). Community children renin levels were used to establish a population reference with the 99th percentile as the cut-off for elevated renin. The mean age of children was 2.1 years and 44.3% were female. Children with SM had substantially higher renin levels than community children, with 26.9% of children with SM having elevated renin. We compared the relationship between elevated renin with clinical complications of SM and mortality. Children were separated into two groups, those who met a specific research definition of SM (n=275) and children who did not (n=319). Irrespective of SM definition, children with elevated BUN and acidosis were more likely to have elevated renin ($p<0.001$). In the subset of children who did not meet the specific definition of SM, complications related to volume status (shock, cold peripheries, vomiting) metabolic complications (severe AKI, hyponatremia) and hematologic complications (severe anemia, blackwater fever) were strongly associated with elevated renin ($p<0.001$ for all except hyponatremia and vomiting, $p=0.001$ for both). In addition, elevated renin was associated with increased mortality irrespective of malaria definition after adjusting for age, sex, site and the presence of severe AKI at enrollment ($p=0.002$). We evaluated pathways of host response in both groups of children. While significant in both groups of SM, markers of kidney injury, stress and hemolysis were more strongly associated with elevated renin in children who did not meet a specific definition of malaria. Together, these findings suggest that elevated renin is a shared biomarker of mortality in children with SM. However, the pathways of renin induction may vary depending on the underlying cause of illness and may be affected by the timing that children seek care and by pretreatment with antimalarials. Additional studies are needed to understand whether interventions targeting renin could be beneficial in SM.

8153

SEVERE AND FATAL LASSA FEVER - OBSERVATIONS IN 19 ICU PATIENTS TREATED IN NIGERIA

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Lassa fever (LF) is a viral hemorrhagic fever (VHF) classified as priority disease by WHO. Due to the high case fatality rate, lack of adequate vaccine and treatment, urgent improvement of the therapy is needed. The pathophysiology of LF is poorly understood and complicated by biosafety restrictions. After extensive capacity building and employment of a glovebox laboratory setup and point-of-care devices we here characterized 19 cases of severe Lassa fever patients admitted to the intensive care unit (ICU) of the VHF isolation ward at Irrua Specialist Teaching Hospital in Edo State, Nigeria. Cases were recruited during the current seasonal outbreak between January and April 2024. All cases had RT-PCR confirmed LF. The mean age was 40.7 years and 36% were female. Eight (42%) of the 19 cases died during admission. The most frequently observed severe complication was hepatitis. Acute liver failure was rare and mainly occurred in advanced stages. Acute kidney injury (AKI) was common, often requiring hemodialysis. Relevant hemorrhage was not observed commonly. However, upon ultrasonography, we consistently noted pleural effusions in severe and fatal patients resulting in respiratory insufficiency. In some cases, this could be attributed to hypervolemia in the case of AKI with reduced urinary output. However, in most cases, patients were hypovolemic. Coagulation parameters were usually only mildly deranged until late stage, when we observed thrombocyte dysfunction and DIC. We thus conclude that the picture of severe and fatal LF is hallmarked by hepatitis, AKI and pleural effusions, most likely due to vascular leak syndrome. In two patients we noted secondary bacterial sepsis due to *E. coli* and *K. pneumoniae* with highly elevated Il-6, procalcitonin and C-reactive protein results compared to other cases, further indicating that not hyperinflammation and viral sepsis, but vascular leak drives pathophysiology in LF. We henceforth recommend case management and research for LF focuses on host-directed therapies to address vascular leak and improvement of coagulopathy to enable invasive drainage of effusions to aid the compromised respiration.

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ASSOCIATION OF DENGUE VIRUS SEROTYPES AND THE CLINICAL SEVERITY OR MORTALITY IN TAIWAN'S LARGEST DENGUE OUTBREAK

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Dengue virus serotype 2 (DENV-2) was the major serotype in the 2015 dengue outbreak in Taiwan, while DENV-1 and DENV-3 were dominant between 2005 and 2014. We aimed to investigate whether DENV-2 contributed to disease severity and mortality in the outbreak in Kaohsiung city, Taiwan. We collected serum samples from dengue patients to detect the presence of DENV and determine the serotypes by using quantitative reverse transcription-polymerase chain reaction. Our cohorts comprised 105 DENV-1-infected cases and 1,550 DENV-2-infected cases. Demographic data, DENV serotype, and comorbidities were covariates for univariate and multivariate analyses to explore the association with severity and mortality. The results suggested that DENV-1 persisted and circulated, while DENV-2 was dominant during the dengue outbreak that occurred

between September and December 2015. However, DENV-2 did not directly contribute to either severity or mortality. Aged patients and patients with diabetes mellitus (DM) or moderate to severe chronic kidney disease (CKD) had a higher risk of developing severe dengue. The mortality of dengue patients was related to a higher Charlson comorbidity index score and severe dengue. Among DENV-2-infected patients and older patients, preexisting anti-dengue IgG, DM, and moderate to severe CKD were associated with severe dengue. Moreover, female sex and severe dengue were associated with a significantly higher risk of death. Our findings highlight the importance of timely serological testing in elderly patients to identify potential secondary infections and focus on the meticulous management of elderly patients with DM or moderate to severe CKD to reduce dengue-related death.

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SEPSIS ENDOTYPES IDENTIFIED BY HOST GENE EXPRESSION ACROSS GLOBAL COHORTS

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Sepsis is a global health priority accounting for 47 million deaths in 2017. The signs and symptoms of sepsis are highly variable and the failure to develop effective therapeutics is attributed to clinical and immunological heterogeneity. Disease endotypes defined by shared phenotypes have shown promise for precision medicine approaches that address complicating heterogeneity in sepsis. The human host response to infection is highly sensitive and specific, enabling the use of gene expression measures in blood to delineate patient endotypes. There is an urgent need to characterize sepsis endotypes in diverse populations to facilitate new and better prognostic and therapeutic solutions in low- and middle-income countries that carry the greatest burden for sepsis. Here we analyze host gene expression in a prospective multi-site international sepsis cohort (n=494) in West Africa (Ghana), Southeast Asia (Cambodia), and the United States (North Carolina) as part of the Austere environments Consortium for Enhanced Sepsis Outcomes (ACESO). We employ soft-clustering decomposition of host RNA sequencing data to identify discrete and overlapping clusters within high-dimensional gene expression data. We identify four sepsis subtypes differentiated by 28-day mortality. A low mortality "immunocompetent" group is specified by features that describe the adaptive immune system. In contrast, three high mortality groups show elevated clinical severity. The "immunosuppressed" group members show signs of a dysfunctional immune response, the "acute-inflammation" group is set apart by molecular features of the innate immune response, while the "immunometabolic" group is characterized by metabolic pathways such as heme biosynthesis. Using latent space exploration techniques with these data and public datasets we further describe the cell type-specific molecular phenotypes that underly these endotypes including a dysregulated myeloid compartment shared between sepsis and COVID-19. Taken together our data supports endotype-driven immunotherapeutic interventions for sepsis and identifies biomarkers that predict outcomes.

8156

INTEGRATED SEROLOGICAL SURVEILLANCE FOR MULTIPLE INFECTIOUS DISEASES IN VANUATU

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Vanuatu's population is at risk of neglected tropical diseases (NTDs) and vaccine-preventable diseases (VPDs). Serological surveys that measure the prevalence of antibodies are a strategy for monitoring current or past exposure to infectious pathogens. Integrated serosurveillance using novel multi-bead assays that can detect ~100 different disease-specific antibodies from a single dried blood spot, and has the potential to provide information on the distribution of a wide range of infections, including estimating vaccine coverage.Between 2021 and 2023, we conducted integrated serological surveys to assess the seroprevalence of IgG antibodies against multiple VPDs, NTDs, and other infectious diseases in 92 villages in Vanuatu's Tafea, Sanma and Shefa provinces. After obtaining informed consent, approximately 2000 participants aged >1 year of age provided a finger prick blood sample to prepare a dried blood spot (DSB) that was analysed using the Luminex technology. Seroprevalence was defined as the proportion of patients with positive IgG results in DBS specimens. Here, we report the overall estimated cluster-adjusted seroprevalence in 501 participants across Sanma (N=245), Tafea (N=243) and Shefa (N=13). Seroprevalence of *Chlamydia trachomatis* was 28.6% by pgp3 (95%CI 23.0-35.0%) and 12.6% (95%CI 9.3-16.8%) by CT694; *Brugia malayi* 3.6%, (95%CI 1.0-11.9%) and *Wuchereria bancrofti* 3.3% (95% CI 1.8-5.9%). Seroprevalence of measles was 35.6% (95%CI 27.6-22.5%), rubella 72.7% (95%CI 61.7-81.5%), tetanus toxoid 76.7% (95%CI 64.6-85.6%), and diphtheria toxoid 57.2% (95%CI 44.9-68.7%). The seroprevalence of SARS-CoV-2 spike protein was 29.9% (95%CI 17.8-45.6%). An additional 648 samples are being analysed and will be presented. Our preliminary results provide a promising measure of effective population-level immunity and exposure to multiple infectious diseases, with the advantage of being cost-effective, scalable, acceptable, and able to target hard-to-reach and high-risk populations. Additional analysis by age groups has been conducted, and comparisons with national immunisation coverage surveys are pending.

8157

OVERCOMING DIAGNOSTIC CHALLENGES WITH ACUTE FEBRILE ILLNESS IN NIGERIA: WHAT CAN WE LEARN FROM THE SURVEILLANCE OF AFI AETIOLOGIES IN NIGERIA (SAFIAN) STUDY?

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Undiagnosed acute febrile illness (AFI) is a serious public health concern, with cases often remaining undiagnosed, or misdiagnosed and treated as malaria. Insufficient laboratory capacity for routine diagnosis is a common limitation for timely and accurate diagnosis of the cause of AFI. We established a hospital-based surveillance study to generate data to support

decisions on which pathogens should be prioritized for routine screening. In this presentation we aim to assess the operational lessons learned to improve AFI diagnosis and surveillance. The Surveillance of AFI Aetiologies in Nigeria (SAFIAN) study introduced a new technology, TaqMan Array Card (TAC) to screen patients presenting with AFI for 25 pathogens at two tertiary hospitals in Nigeria, expanding the hospital's diagnostic capacity. TAC is an efficient and accurate multiplex PCR allowing for simultaneous testing of multiple pathogens. RedCap was used to collect medical record abstraction and patient self-reported demographic and risk behaviors. We trained hospital clinical and laboratory staff and provided regular technical assistance to resolve issues. Study teams monitored supply management; reagents required frequent replenishments since they had a shorter shelf-life than the study length, and TAC required repeated runs for failed samples due to routine laboratory issues; 15.1% (114/754) of samples were repeated, along with 12.3% (15 of 122) of cards. The procurement process for the TAC-specific supplies was complex, expensive and lengthy. Efficient study operations management was critical to track RedCap data management issues and resolve in real time. Steady communication and regular monitoring were key to addressing critical study issues. Lessons learned highlight the importance of integrating innovative diagnostic tools and training in laboratory practices. Strengthening laboratory capabilities and adopting advanced diagnostic methodologies are crucial for enhancing public health responses to AFIs in Nigeria, but this will require sustainable investment in diagnostic infrastructure.

8158

A CASE OF PRE-EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN KWAZULU-NATAL, SOUTH AFRICA

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A 35-year-old man from KwaZulu-Natal, South Africa with HIV [CD4 unknown; viral load 6,368,115 copies/mL (6 months prior), improved to 283,791 copies/mL (3 months prior)] and presumptive treatment for pulmonary & extrapulmonary multi-drug-resistant (MDR) tuberculosis (TB) with left neck TB abscess status-post abscess aspiration (3 months prior), presented to clinic for follow-up. He received 3 months of presumptive MDR-TB treatment and felt overall well and in good health. He reported unintentional 14 kg weight gain over 3 months. He denied fever, chills, weight loss, cough, hemoptysis. He was adherent to medications and TB clinic appointments. He was generally well-appearing, in no acute distress. He was afebrile. He weighed 83 kg. Skin exam revealed a left neck 3-cm length healed, clean, dry scar. The remainder of his exam including pulmonary exam was normal. GeneXpert testing of sputum culture (on initial presentation): *Mycobacterium tuberculosis* with Rifampicin resistance. A recent chest X-ray demonstrated left-sided nodular lesion (2 cm) and few, scattered sub-cm calcifications bilaterally. The chest X-ray was improved his prior chest X-ray 3 months prior, demonstrating scattered infiltrates, nodules, and calcifications bilaterally. His sputum culture (on initial presentation) later resulted with *M. tuberculosis*: *Resistant* - Isoniazid (INH), Rifampin, Fluoroquinolones, Second-line injectables. His prior left neck abscess aspirate culture (on initial presentation), later demonstrated growth of *M. tuberculosis*: *Resistant* - INH, Rifampin, Fluoroquinolones, Second-line injectables. For the management of at minimum pre-extensively drug-resistant TB, he was to restart/continue linezolid for 1 year; start delamanid for 0.5-1 year; continue bedaquiline for 1 year; stop ethambutol, pyrazinamide, and high-dose isoniazid. Levofloxacin was continued given patient's overall clinical improvement with monitoring. Also, the plan was to add clofazimine and terizidone for 18 months. This is a challenging case of diagnosed pre-XDR TB, which has a nuanced and complex management that providers should recognize and understand.

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IMPLEMENTING NEUROCOGNITIVE ASSESSMENT TOOLS - A PILOT STUDY COMPARING NEUROCOGNITIVE FUNCTION OF EBOLA SURVIVORS WITH NON-INFECTED CONTROLS IN SIERRA LEONE

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Neurocognitive issues often follow viral infections, both acute and chronic including mental illness, hearing loss, and depression. The Ebola virus (EBOV) continues to pose a significant global health threat, notably highlighted by the 2013-2016 West African outbreak, which infected over 28,600 people and claimed more than 11,300 lives, surpassing previous outbreaks combined. Consequently, an estimated 17,000 West Africans are now EVD survivors. These survivors seem to suffer from a variety of post-Ebola sequelae, which is now characterized as Post-Ebola Syndrome (PES). PES encompasses a range of persistent health issues, including rheumatologic, ophthalmologic, psychologic, and neurologic conditions. In a study conducted in Eastern Sierra Leone, EVD survivors were found to be significantly more likely than age- and sex-matched controls to report difficulties such as sleep disturbances (14.2% vs 1.6%, p<.001), depression (12.5% vs 2.7%, p<.001), anxiety (8.9% vs 3.2%, p<.001), and hallucinations (11.3% vs 1.6%, p<.001), 2.5 years post-recovery. To delve deeper into these discrepancies, we conducted a pilot study involving 50 adult participants, split evenly between EVD survivors and matched controls. Employing Neurocognitive Assessment tools, we evaluated specific types of neurocognitive dysfunction approximately eight years after EVD recovery. Participants underwent a battery of validated neurocognitive tests covering processing speed, attention, executive functioning, and memory domains. Using linear regression and controlling for the effects of age, sex, and education, the group of EVD survivors performed significantly worse than controls on measures of attention (β=.32, p=.01), executive functioning (β =-.38, p=.01), and immediate memory (β =-.29, p=.04). There was no notable group difference observed in delayed memory recall (β=.14, p=.34). These initial findings are instrumental in deepening our comprehension of neurocognitive impairment among adult EVD survivors and elucidating the true impact of PES on this population.

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DISCREPANCY ANALYSIS BY USING DATA QUALITY ASSESSMENT AT COMMUNITY LEVEL IN RWANDA

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Introduction:since 2013, malaria data reported through rwanda routine under the health information system. however prior supervisory assessments have revealed concerns regarding the accuracy and reliability of aggregated data from public health facilities across the country. system. Methods:This study was conducted in two districts such as Rulindo and Gisagara, under six health facilities, with 12 cells covered 24 villages. data were collected from January to March 2023. the key indicators such as malaria cases, RDT test and acts based on SISCom were compared to the same indicators based on records from chws data reported through the system for the same time period. We used T-test for data analysis.Result: In rulindo district, the malaria cases reported in the system out of chws data we found 3.0% (52/50) and acts reported in the system out of CHWs data were 1.0% (51/50) both level of discrepancy was acceptable, contrary to RDT reported into the system out of CHWs data 13.0% (52/40) where the level of discrepancy is not acceptable. Although, in Huye district, the malaria cases reported in the system out of CHWs data was 0.2% (1544/1539), ACT reported in the system out of CHWs data was 0.2% (1544/1537) and RDT reported in the system out of CHWs data were 0.2% (1543/1537), all discrepancies were acceptable.Conclusion:Our study found non significant different in the discrepancies observed for malaria indicators such as

malaria case,RDT and ACT within the system is acceptable based on WHO, there is a significant different for ACTs with P=0.0026 in the discrepancies observed in Rulindo district.However,discrepancy was increased for RDT reported both in the system and CHWs. Thus, we suggest that the improvement in working conditions for CHWs ,to respect malaria data validation meeting before reporting system.

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MOLECULAR DETECTION AND SEQUENCING OF GENES ENCODING THE PREDICTED AMIDASE, NADH UBIQUINONE OXIDOREDUCTASE AND SODIUM NEUROTRANSMITTER SYMPORTER ENZYMES IN *ONCHOCERCA VOLVULUS* PARASITE

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Current evidence shows that mass drug administration of ivermectin alone may not be sufficient to achieve elimination of transmission of onchocerciasis by 2030 in some highly endemic foci. Drug repurposing may offer a cheaper and faster route of new drug development considering the ambitious timelines for elimination championed by the World Health Organization. However, there is insufficient knowledge on the metabolism and chokepoint metabolic enzymes which could serve as targets for repurposed drugs. This study set out to identify and sequence three previously predicted genes encoding amidase, NADH ubiquinone oxidoreductase and Sodium symporter in the *Onchocerca volvulus*, the causative agent of onchocerciasis. These potentially chokepoint enzymes are predicted to be encoded in the genome of the worm and may be inhibited by analgesics and other existing drugs. Briefly, extracted DNA from the parasites was amplified using the Proflex PCR system. The PCR products were visualized using gel electrophoresis and then sequenced via Sanger sequencing. The sequences were then compared with the predicted sequences. The amino acid sequences of the sequenced genes were determined using the Expasy translate tool and SWISS model was used to create the 3-dimensional alpha folding structures. Clustal Omega was used to determine the similarity between the enzymes in the parasite and other species. It was confirmed that the previously predicted genes encoding the three enzymes were present in the genome of adult *O. volvulus* parasite. The sequences of the genes amplified in this study were 100% identical to the sequences predicted previously and available in GenBank. From the 3-dimensional alpha fold structure of the proteins, we inferred that *O. volvulus* amidase is a single-pass membrane protein whilst NADH ubiquinone oxidoreductase and Sodium neurotransmitter symporter are multi-pass membrane proteins with roles in transport across the membranes Sequence analysis showed high similarity with *O. ochengi* for amidase and NADH ubiquinone oxidoreductase, and with *Caenorhabditis elegans* for sodium neurotransmitter symporter.

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INFECTION STAGE L3 OF *LOA LOA* AS POTENTIAL TARGET FOR PROTECTIVE IMMUNITY

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Loa loa is a neglected filarial which has drawn attention this last thirty years. This is due to its negative impact on the WHO control program on mass chemotherapy in region where this filarial is co-endemic with *O. volvulus* or *W. bancrofti*, also a reduced life span has been observe in these area with individual carrying high density of *L. loa* microfilaria. Previous studies have shown that *L. loa* L3 might be linked to concomitant immunity. In order to search for potentiel protective molecule. L3 were harvest from natural infected *Chrysop* in different village of endemic region of Gabon and L3 isolated according to modified Baerman technique. The immunogenicity of L3 extract was evaluate after a separation by SDS-PAGE and probe by western blot with IgG1 and IgG4 of individual infected or exposed to *L. loa* from endemic country. In parallel to these experiments, *Brugia pahangi* adult extract was digested with *N-glycanase* or not digested. These extract were also probe with the IgG1 and 4 of the same individuals. Primers were designed from *B. pahangi ALT*-1, *ALT*-2 and *chitinase* genes follow by PCR using *L. loa* DNA as template. The result show that both IgG1 and IgG4 react with different L2 antigen with different molecular weight (from 8-110 kDa and 10-100 kDa respectively). The adult *B. pahangi* extract react with the same probe whether de glycosylated or not, suggesting that the reactivity is linked to peptide backbone. The amplification: using *L. loa* DNA as a template generate amplicon with size of 1200 bp for both *ALT*-1 and *ALT*-2 a supplementary band of 600 bp for *ALT*-2 while primers from chitinase generate amplicon of 1500 bp.Our results suggested that the natural *L. loa* L3 are immunogenic. The cross reactivity observe between *L. loa* and Lymphatic filarial is Linked to peptide backone. The amplicon generated with lymphatic filarial show the existence of homologue antigens for *ALT*-1,-2 and *chitinase* in *L. loa*. The extension of these homologies will be clarified after the ongoing sequencing of these amplicons.

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INFLAMMATION AND FIBRINOLYSIS IN LOIASIS PATIENTS BEFORE AND AFTER IVERMECTIN TREATMENT: POTENTIAL MECHANISM UNDER POST-IVERMECTIN SEVERE ADVERSE EVENTS

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Loiasis is often regarded as a relatively benign disease, but recent evidence suggests an association with excess mortality. In addition, there have been documented instances of thrombosis and micro-emboli formation in capillary vessels, both spontaneously and as part of post-ivermectin serious adverse events (SAEs). However, the hemostatic profile of individuals with loiasis has never been studied. A biological pilot study was conducted in a rural area of Cameroon to assess the impact of loiasis and the treatment with ivermectin on hematological, hemostatic, and biochemical blood parameters. A total of 38 adult participants were enrolled and categorized into four balanced groups based on their *Loa loa* microfilarial densities (Group A (N=10): 0 mf/ml, Group B (N=11) : 20-4160 mf/ml, Group C (N=7): 5380-19,580 mf/ml, Group D (N=10): 21,300-39,870 mf/ml). Subsequently, the 18 microfilaremic patients from groups B and C received ivermectin treatment. At baseline, no significant differences in hemostasis and inflammation parameters were found among the groups. However, a positive correlation was observed between microfilarial densities and granulocyte ($p=0.012$) as well as eosinophil ($p<0.001$) counts. Four days off treatment, a significant increase in D-dimer levels, from 725 ng/mL to 1276 ng/mL ($p=0.024$), was recorded. Prothrombin fragment 1+2 levels rose from 315 to 435 pmol/L, but this difference was not statistically significant ($p=0.313$). C-reactive protein, fibrinogen, and alpha-1-globulin levels also showed significant increases. Eosinophil counts markedly increased from 225/µL to 1807/µL ($p<0.001$). Ivermectin treatment appeared to induce inflammation and pronounced fibrinolysis, indicative of coagulation activation. These preliminary findings shed light on potential biological mechanisms underlying SAEs following ivermectin treatment in loiasis. Further comprehensive studies investigating the hemostatic profile in loiasis are warranted for a better understanding of this complex disease and its management.

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IMPACT OF THE FILARIAL INFECTIONS *ONCOCECA VOLVULUS, LOA LOA* AND *MANSONELLA PERSTANS* ON THE METABOLIC PROFILE OF LEAN, OVERWEIGHT AND OBESE INDIVIDUALS IN CAMEROON (FIMMIP)

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Type 2 diabetes is among the ten leading causes of death as identified by the WHO in 2019 with the prognosis that type 2 diabetes prevalence will increase the strongest in sub-Saharan Africa reaching an 134% increase by 2045. The FIMMIP study was designed to investigate the impact of filarial infections on metabolic diseases in rural Cameroon. In this open label pilot trial, 1619 participants infected with the filarial nematodes *Onchocerca volvulus* (n=359)*, Loa loa* (n=54)*, Mansonella perstans* (n=117), multiple filarial species (n=165) or filariae-free endemic participants (n=924), being lean (BMI <25), overweight (BMI 25-30) or obese (BMI ≥30) were analysed for their parasitological, anthropomorphic and metabolic profile. Filariae-infected participants had significantly reduced levels of circulating liver enzymes (ALP, ALT, AST and γGT) as well as increased markers associated with kidney health (urine microalbumin, serum creatinine). Similarly, C-reactive protein, a marker associated with obesity-derived inflammation, was significantly reduced in filariasis patients. Strikingly, glycated hemoglobin (HbA1c) values were significantly reduced in filariasis patients and diabetes prevalence (HbA1c >48 mmol/mol Hb) was 2.3 times lower in the filariasis patients (31% vs. 13.4%). Furthermore, comparing the impact of *O. volvulus, L. loa* and *M. perstans* infection indicated filarial-species dependent differences with *M. perstans* infections inducing the strongest beneficial impact on liver enzymes, CRP levels, kidney markers, and lowest rate of diabetes prevalence (9.4%). Ongoing analyses include multiplex assays to assess the immunological profile, insulin and adipokine levels as well as the comparison of the metabolic and immunological profile 12 and 18 months following doxycycline treatment in *O. volvulus* and *M. perstans*-infected participants. Taken together, our study suggests that filarial infections improve metabolic parameters and protect against the development of type 2 diabetes with *M. perstans* infected individuals showing the most striking effects.

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DOXYCYCLINE TREATMENT REDUCES IMMUNE ACTIVATION OF CD4$^+$ T CELLS AS WELL AS CLINICAL SIGNS OF INFLAMMATION IN PATIENTS WITH FILARIAL LYMPHEDEMA IN TANZANIA

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Filarial lymphedema (LE) is caused by chronic infection with *Wuchereria bancrofti* (WB), a mosquito-borne nematode. Around 51 million people worldwide are infected with WB, and 15 million suffer from filarial LE. As part of an ongoing clinical trial to test the efficacy of doxycycline, people were recruited in Tanzania as part of the TAKeOFF-LEDoxy-trial. Four hundred and twenty participants were randomized to receive either doxycycline, 100 mg or 200 mg per day, or placebo for 6 weeks. The average age of the participants was 51 years and 67% were female. In addition to clinical characteristics, immunological aspects of the different treatment groups were measured at baseline, end of doxycycline treatment (day 42) and after 6 and 24 months in a subgroup of participants. In total, whole blood from 42 patients was analyzed for the presence of regulatory T cells (Tregs) and immune activation markers (CD38/HLADR) on CD4$^+$ T cells. All 42 participants were recruited in the dry season, the 6-month visit took place in the rainy season, and the 24-month visit took place in the dry season. In terms of immune parameters, the values for all treatment groups on day 42 were comparable to the baseline results of CD38$^+$/HLADR$^+$ and regulatory CD4$^+$ T cells. In contrast, the 6-month visit showed a significant increase in immune activation parameters and a decrease in Tregs for participants of the placebo group, but not for the doxycycline 200mg group. Interestingly, these results were consistent with the clinical data, as after 6 months the placebo group had a significantly higher number of individuals with acute adenolymphadenitis (ADL), an acute clinical manifestation characterized by recurrent attacks of fever that is associated with inflammation caused by secondary bacterial infection that enter the body via wounds and damaged skin. This difference resolved at subsequent visits, most likely due to the effect of intensive and regular hygiene training, which prevented wounds, inflammation and with that progression of LE in all treatment groups. Similar to those clinical findings at 24 months, all groups showed reduced immune activation.

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EVALUATION OF THE BIOLOGICAL ACTIVITY OF CHEMICAL CONSTITUENTS FROM THE STEMBARK OF *KIGELIA AFRICANA*, A CAMEROONIAN MEDICINAL PLANT, AGAINST *ONCHOCERCA OCHENGI* PARASITES

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Onchocerciasis is the second leading infectious cause of blindness, with about 21 million people infected and 120 million persons at risk of infection worldwide. It is caused in man by the filarial worm, *Onchocerca volvulus*. For over 30 years, Mass treatment with ivermectin has been the mainstay control/elimination strategy for this disease. In recent years, moxidectin has been approved for the treatment of onchocerciasis. Both drugs are only effective against the microfilarial form of *O. volvulus*, but not the adult worms which may live for upto 15 years in patients. Also, the emergence of resistance to ivermectin in parasitic nematodes of veterinary importance raises serious concerns that this may extend to the human *O. volvulus.* Therefore, the search for new and highly effective filariacides is imperative. About 50 % of drugs used in modern medicine are of plant origin and about 80 % of Africa's population relies on medicinal plants for their health needs. *Kigelia africana* is described in the Cameroon national herbarium and is used locally to treat skin diseases including onchodermatitis, a symptom of onchocerciasis. To investigate the potential of *Kigelia africana,* fractions (hexane-ethyl acetate 10 %, hexane-ethyl acetate 25 %, and ethyl acetate 100 %) were extracted and pure compounds (lapachol, 2-(1-hydroxyethyl-2-acetylnaphtho [2,3-b] furan-4,9-dione and 2-acetyl-naphto [2,3-b]furan-4,9-dione) were isolated from the stembark of this plant against *Onchocerca ochengi*, a bovine onchocerciasis parasite closely related to *O. volvulus*. The pure compounds belong to the quinone class. The hexane-ethyl acetate 25 % fraction showed the best activity, having a 100 % inhibition at a concentration of 125 µg/ml meanwhile, all the pure compounds were found to be very active, showing complete inhibition at a concentration of 5 µg/ml. All the tested fractions and pure compounds showed varying degrees of toxicity on the monkey epithelial cells which served as hosts for the filarial parasites. These findings open new avenues on research and development of new therapeutic agents for the treatment of onchocerciasis.

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EVALUATION OF SLASH AND CLEAR COMMUNITY-DIRECTED ONCHOCERCIASIS VECTOR CONTROL INTERVENTION IN THE TROPICAL RAINFOREST OF LIBERIA

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Onchocerciasis is caused by a parasitic worm known as *Onchocerca volvulus* that is transmitted by repeated bites of *Simulium* blackflies. Onchocerciasis programs rely on mass drug administration of ivermectin, which may be insufficient to eliminate the parasite. Slash and clear (S&C) is the removal of trailing vegetation to which blackfly larvae attach. It has significantly reduced *Simulium damnosum* sp. biting rates in some settings. We evaluated the effectiveness of S&C in reducing the biting rate of *Simulium yahense* in the tropical rainforest of Liberia. We identified two comparable control (Baila) and intervention (Gargar) sites along River St. John in Bong County. Baseline fly collection was conducted by human landing catching for 7 days at each site followed by S&C at the intervention site in November 2022. Flies were then collected 2 times per week from December 2022 until November 2023 at both sites. Daily biting rates (DBR) were calculated by dividing the number of flies collected by number of days of collection. Independent sample T-tests were used to show differences in DBR at control and intervention sites. After S&C, DBR progressively decreased at the intervention site, with a significant difference from baseline at 4 months post S&C ($p < 0.05$), while in the control site there was an initial increase in DBR followed by a downward trend over the same period. There was a maximum reduction from baseline of 79% at 4 months post S&C compared to an increase of 7% at the control site, which is significant ($p<0.05$). By 7 months post S&C, daily biting rates at both sites returned to baseline levels, after which the Gargar (intervention) site DBR increased until again falling below pre-S&C levels while the Baila (control) site DBR steadily increased until plateauing. The change in biting rate at the intervention site was not as pronounced, time to decline was slower, and suppression was not as sustained as what was reported in savanna grassland settings. Adjusting the timing and frequency of S&C is planned to evaluate these differences. S&C is a low-cost, community-directed intervention that may reduce *S. yahense* biting rates in Liberia.

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PARASITOLOGICAL INDICATORS SUGGESTS THAT ONCHOCERCIASIS MIGHT LIKELY NEVER BEEN ELIMINATED IN THE YABASSI HEALTH DISTRICT (LITTORAL REGION, CAMEROON) USING IVERMECTIN SOLELY: URGENT NEED OF COMPLEMENTARY INTERVENTIONS

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Ivermectin has been the mainstay of the control of onchocerciasis through annual mass administration under community directives. This strategy has been successful in transmission elimination of onchocerciasis in certain foci in Africa, leading to the shift of the paradigm of the fight against onchocerciasis from control to elimination. Despite this sustained effort, hotspots for transmission of the infection have been identified in certain foci, as it was the case in 2015 in the Yabassi Health District where onchocerciasis was still meso-endemic after more than 15 years of uninterrupted ivermectin based-mass treatments. This study therefore aimed to assess prevalence and intensity of *Onchocerca volvulus* infection in the Yabassi Health District after 10 additional annual rounds of mass drug administration. A cross-sectional survey was therefore conducted in first- and second-line communities of the Yabassi Health District. All volunteers aged 5 years and above underwent clinical and parasitological examinations. Two skin snips were collected from the posterior iliac crest of each participant using a 2mm corneoscleral Hold-type punch and examined for *O. volvulus* microfilaridermia. Of the 572 enrollees, 181 (31.6%; 95% CI: 28.0% - 35.6%) presented with microfilariae under the skin, with the mean microfilarial density estimated at 8.13 (standard deviation, SD: 34.5) mf/ss. In the sentinel communities visited in 2015, *O. volvulus* parasitological indicators remained unchanged, from 43.8% (95% CI: 37.7% - 50.1%) to 38.8% (95% CI: 33.0% - 45.0%), after 10 additional yearly rounds of uninterrupted treatment with ivermectin (Chi-square: 1.49; df: 1; *p*: 0.222). These results indicate that ivermectin solely might not be enough to eliminate transmission of onchocerciasis as predicted by mathematical models, and call for introduction of targeted complementary/alternative interventions to accelerate the elimination of this debilitating disease.

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REBOUND IN PREVALENCE AND INTENSITY OF ONCHOCERCA VOLVULUS INFECTION FIVE YEARS AFTER CESSATION OF ALTERNATIVE TREATMENT STRATEGIES IN THE MASSANGAM HEALTH DISTRICT, WEST REGION, CAMEROON: NEED FOR COORDINATED AND SUSTAINED EFFORTS

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The control of onchocerciasis currently relies on yearly distribution of ivermectin to at-risk populations. To tackle onchocerciasis in hotspots and achieve elimination of transmission, several complementary/alternative strategies (biannual ivermectin, doxycycline-based test-and-treat and vector control) have been implemented in Massangam Health District (HD), and short-term impact evaluation showed significant reductions in the endemicity levels in three focal hotspot communities (Makouopsap, Makankoun, and Njinja-Njingouet). Since this three-years pilot initiative stopped, this study therefore aimed to assess the situation of onchocerciasis in the focal hotspot communities five years after the cessation of alternative strategies. A quantitative cross-sectional survey was conducted in December 2023 in the three focal hotspot communities. Participants underwent a comprehensive assessment that involved interviews, clinical examinations and skin snipping to establish *Onchocerca volvulus* microfilaridermia. The overall prevalence of *O. volvulus* infection in the three focal communities was 18.8% (95% CI: 13.8-24.3), the highest prevalence (30.8%) being found in the community Makankoun. The intensity of infection was 3.136 (standard deviation, SD: 19.3099) mf/ss, ranging from 5.218 mf/ss (Mankakoum community) to 2.840 mf/ss (Njinja-Njingouet community). The parasitological indicators significantly increased five years after the cessation of Alternative Treatment Strategies (ATS) in all three focal communities ($\chi^2 = 4.18$; df = 2; $p = 0.0409$) compared with their baseline levels (end of ATS implementation). These findings indicate a rebound in onchocerciasis transmission and underscore the need for coordinated and

sustained efforts, which can be implemented in a transmission zone as recommended by the WHO, to achieve the elimination goals outlined in the 2021-2030 roadmap to end the neglect and achieved SDGs.

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ADMINISTRATION OF THE SUPERVISOR'S COVERAGE TOOL TO ASSESS THERAPEUTIC COVERAGES OF MASS DRUG ADMINISTRATION FOR ELIMINATION OF NEGLECTED TROPICAL DISEASES IN 3 LGAS OF AKWA IBOM STATE, NIGERIA

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Between June and July 2023, mass drug administration (MDA) for the control and elimination of schistosomiasis (SCH), onchocerciasis (oncho), and lymphatic filariasis (LF) were conducted in 15 SCH endemic LGAs, 4 oncho endemic LGAs, and 1 LF endemic LGA in Akwa Ibom state, Nigeria. Directly following the MDA, the WHO's Supervisors Coverage Tool (SCT) was administered in 3 LGAs (Ibeno, Udung Uko and Ini) to ascertain the status of the SCH, LF and Oncho therapeutic coverage rates following the MDA, identify gaps in treatment, and inform an action plan to emergent and reported challenges. The SCT followed the approved WHO methodology, including training activities, a survey using an open data kit, and the WHO Decision Rule guide to determine coverage. The result of the SCT indicated the status of the MDA as well as the treatment coverage in the 3 LGAs and recommended actions to improve NTD programming in the state. The main gaps identified during the SCT were (1) the absence of target individuals during MDA implementation, (2) issues of over/underreporting, and (3) Praziquantel/drug paucity. These gaps could be addressed by adjusting the timing of MDA delivery in the communities to conduct MDAs in the morning and evening when the majority of families are in the house, increased advocacy to the key stakeholders and/or training to the medicine distributors and supervisors, and improved coordination between stakeholders.

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MANAGEMENT PRACTICES AND THEIR ASSOCIATED FACTORS AMONG LYMPHOEDEMA PATIENTS ATTENDING LYMPHOEDEMA CLINICS IN SELECTED ENDEMIC DISTRICTS FOR LYMPHATIC FILARIASIS IN SRI LANKA

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<Lymphatic filariasis is one of the main causes of lymphoedema in tropical endemic countries. Sri Lanka reports around 500-900 lymphoedema patients annually despite validation as eliminating the disease in 2016. Majority of new patients reported are in the early stages. Good management practices can prevent disease progression to disabling complications. Therefore, this study was conducted to determine factors associated with morbidity management practices among lymphoedema patients attending lymphoedema clinics in three filariasis endemic districts in Sri Lanka. This was a clinic-based cross-sectional study conducted among 405 lymphoedema patients selected through consecutive sampling. A pre-tested interviewer-administered questionnaire was used to collect data. The chi-square test was used to determine the association of all factors with the practices of lymphoedema management. The sample consisted of 51.4% of males, 88.1% had unilateral lymphoedema and 58.5% were in the early stages. The knowledge of skincare (58.6%), compression (74.9%) and management of acute attacks (64.2%) was good among most patients. The attitude was good among 94.1%. More than half the patients had good practice in skincare, use of topical antibiotics, elevation, wearing comfortable footwear and compression. Age and civil status were associated with the practice of exercise (P<0.05) and elevation (P<0.01). Level of education and income were associated with all practices (P<0.001) except skincare. Having a good knowledge of the same practice showed a statistically significant association in the practice of hygiene and skin care (P<0.001), footwear (P=0.001) and compression (P<0.001). Good attitudes were significantly associated with the practice of elevation (P<0.001). Quality of life was associated with all practices (P<0.001). Awareness programs should be organized for patients and health staff to improve practices. Prospective studies with control groups would establish the impact of interventions of morbidity management practices.>

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ADAPTIVE BASKET TRIAL TO ASSESS THE EFFICACY AND SAFETY OF OXFENDAZOLE AS PAN-NEMATODE CANDIDATE IN ONCHOCERCIASIS, LOIASIS, MANSONELLOSIS AND TRICHURIASIS PATIENTS

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Oxfendazole is a broad-spectrum veterinary anthelmintic that offers a number of advantages that are desirable for a new anthelmintic agent for human use. The safety and broad spectrum efficacy of oxfendazole are consistently demonstrated in intestinal helminth infections in animals, as well as tissue-dwelling larval cestode and trematode infections in diverse animal species. First-in-human safety and pharmacokinetic data have shown its safety in humans at acceptable exposure. In experimental filarial infections, oxfendazole acts against adult worms, but not the microfilarial stage, which is expected to prevent microfilariae-induced adverse events in onchocerciasis and loiasis patients. Thus, oxfendazole represents a promising candidate to expand the limited portfolio of anthelmintic drugs available. A field-applicable formulation for early studies in infected patients was developed and confirmed its safety and tolerability via the EU HELP consortium. Via EU EDCTP3 funding, the eWHORM consortium is now conducting a "basket trial" approach for the first time in NTDs, assessing efficacy and safety in onchocerciasis, loiasis, mansonellosis and trichuriasis patients at the same time in four sub-Saharan African countries. To harmonize procedures among different study sites and diseases, a master protocol was developed and data simulations were used to design this adaptive basket trial, which includes an interim analysis six months after oxfendazole treatment. Based on the results from the interim analyses, midcourse adaptions will drop non-efficacious treatment arms and allocate additional study participants to the efficacious treatment arms or initiate a new treatment arm. This patient centric approach allows for the first time not only the inclusion of co-infected patients, but at the same time to detect country-specific differences in efficacy. Such an adaptive basket trial design avoids costly repetitions, allows quicker decisions and expedites drugs to market. The eWHORM consortium aims to provide the proof of concept of oxfendazole as pan-nematode drug candidate for future registration studies.

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RESULTS OF STOP TREATMENT ASSESSMENTS FOR ONCHOCERCIASIS IN SEVEN DISTRICTS OF LOWER MADI MID NORTH FOCUS, UGANDA

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In Uganda, onchocerciasis was initially reported in 17 foci. The largest of these foci, the Madi Mid North (MMN) focus, comprising 11 districts and one city in northern Uganda bordering the Republic of South Sudan, is one of two foci where mass drug administration (MDA) with ivermectin remains ongoing. In 2019, the Uganda Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) classified MMN as "transmission suspected interrupted" after the focus passed initial entomological and epidemiological sentinel site assessments. Stop-MDA entomological (2021-2023) and epidemiological (2023) assessments were conducted in the seven southernmost districts of MMN that are thought to be at lower risk of reintroduction of onchocerciasis as they do not share a border with South Sudan. None of the 3,499 blood samples from children under 10 years of age tested positive (95% upper confidence limit [UCL] <0.001) for Ov16 antibodies by ELISA, and none of the 293 pools of 19,537 collected *Simulium* black flies caught were positive for parasite O-150 DNA (95% UCI, 0.2/2000) by PCR, thus meeting WHO stop-MDA criteria of <0.1% Ov16 prevalence and <1/2000 infective black flies with 95% confidence. Based on this evidence, the UOEEAC recommended in August 2023 to halt MDA and begin post-treatment surveillance (PTS) in the seven districts of lower MMN with a population of 1,121,520 people—the single largest stop-MDA recommendation in the history of Uganda's onchocerciasis elimination program. PTS will continue until transmission elimination is achieved in the entire MMN cross-border focus.

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BARRIERS TO MORBIDITY MANAGEMENT AND DISABILITY PREVENTION (MMDP) CARE IN BENISHANGUL GUMUZ REGION, ETHIOPIA

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Despite achievements in scaling up preventive measures in lymphatic filariasis (LF) endemic regions in Ethiopia, access to lymphedema and hydrocele care remains low in many areas. This assessment evaluated areas previously targeted for LF morbidity management and disability prevention (MMDP) service provision and explored barriers to MMDP services. A modified Direct Inspection Protocol (DIP) and Hydrocele Surgery Facility Assessment Tool (HSFAT) were conducted in three woredas of Benishangul Gumuz Region in March 2024 across 6 health facilities, 2 hospitals, and 8 health posts. Key informant interviews (KIIs) were held with patients, service providers, program officers and managers and Community-Based Health Insurance (CBHI) Officers. The average DIP score was 61%, with 2 facilities only slightly below the 75% benchmark. While health facility staff were able to correctly identify aspects of MMDP care in the DIP, KIIs reported lack of adequate MMDP knowledge and skills arising from poor continuity of training, staff turnover/workload, and lack of job aids and guidelines. While Ethiopia has integrated MMDP indicators into the health system database, half of facilities and both hospitals showed weak documentation of MMDP in registration books and patient charts. Use of Ethiopia's CBHI benefit package was weak and non-standardized in the woredas visited. Few facilities provide services for MMDP through CBHI for those enrolled. Affected persons are often obliged to pay high costs out of pocket for hydrocelectomies and medicines. However, both hospitals generally possessed the infrastructure, capacity, and supplies needed for hydrocele surgery. Findings in Benishangul Gumuz highlight the need for strengthened integration of MMDP case management in CBHI and improving overall implementation of CBHI as a strategy for sustainable financing, universal health coverage and equity. To further scale up and enhance accessibility, affordability, and service quality for MMDP services, strengthened integration and ownership, as well as financial, technical, and logistical support are needed.

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PROGRAMMATIC IMPLEMENTATION OF THE TRIPLE DRUG MASS DRUG ADMINISTRATION FOR LYMPHATIC FILARIASIS ELIMINATION IN HAITI

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Haiti is one of four countries in the Americas endemic for lymphatic filariasis (LF). Haiti recently adopted the WHO-recommended triple drug strategy for mass drug administration (MDA) using ivermectin, diethylcarbamazine, and albendazole (IDA) to accelerate elimination of LF. We report on program results for the first Haitian commune implementing IDA MDA. In September 2023, Le Ministère de la Santé Publique et de la Population (MSPP) conducted a 10-day MDA campaign using IDA in Limonade, a semi-urban commune in the North department. A one-month community mobilization and sensitization preceded the MDA. Trained community drug distributers distributed IDA to all eligible individuals through door-to-door and fixed posts. School-aged children were reached either at home or in schools. All MDA participants were dosed by weight. Adverse events were managed at local health facilities. Treatment data were recorded electronically and monitored daily. Among 60,815 inhabitants living in Limonade, 45,568 (74.9%) were offered the medications and 45,265 (74.4%) swallowed them. Of people accepting treatment, 98.6% reported being residents of Limonade and 1.4% were from neighboring communes. Treatment coverage was similar among females (47.1%) and males (52.9%). One third of the people treated were school-aged children. Overall, 0.7% (n=303) of people offered treatment refused the MDA. Most common reasons for refusal were fear of side events and the desire to take pills at home. A total of 23,061 (50.9%) people were treated via door-to-door approach, 17,990 (39.7%) in fixed posts, and 4,214 (9.3%) in schools. Mop-up treatments were given to 1,845 (4%) out of all people treated. Only 44 (0.1%) people reported an adverse event, usually (nausea or headache); no serious adverse events were reported following treatment. The high coverage and overall success of IDA MDA in Limonade demonstrates its feasibility in other Haitian communes. The challenges and successes in Limonade can serve as a blueprint for scale-up in all endemic communes and in other country LF elimination programs.

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THE HEALTH AND WELLNESS IMPACT OF HOPE GROUPS FOR PEOPLE WITH LYMPHATIC FILARIASIS IN EBONYI STATE, NIGERIA: PATIENT DATA AT BASELINE

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Lymphatic filariasis (LF) is a chronic disease that is highly stigmatized in Nigeria, the third most LF-endemic country globally by prevalent case count. The Carter Center has used "Hope Groups," nurse-led support groups, in Plateau and Nasarawa states of Nigeria since 2003 to provide ongoing support to people living with LF as part of morbidity management and disability prevention (MMDP). We aim to evaluate the impact of this program on a cohort of adult LF cases as it is newly introduced in Ebonyi state, Nigeria. Baseline data were collected on demographics, physical manifestation of LF, disability status (WHO Disability Assessment Schedule [WHODAS] 12-item tool), depression status (Patient Health Questionnaire [PHQ]-9 tool, social support (Oslo social support scale), and perceived stigma. Of 197 total participants, 67.5% were male. Sixty-nine (35%) had hydrocele and 128 (65%) had lymphedema, of which 43 (33.3%) had ulcer complications and 27 (21.1%) had fungal infection from lymphedema. Disability scores were moderate, averaging 35.7 (sd 13.5) on a scale from 12 (mild) to 60 (extreme). PHQ-9 scores indicated poor depression status in the cohort; 95% met the criterion for depression requiring mental health care referral (score 10+) and 71% met the criterion for severe depression (scores 20-27). Disconcertingly, 57% of the participants reported considering self-harm nearly every day in the prior two weeks. Most participants (59%) reported poor social support (Oslo support score 3-8), 27% had moderate support (scores 9-11), and only 13% reported strong support (scores 12-14). Most (68%) also responded in the affirmative to all three dichotomous stigma questions. Based on the high PHQ-9 scores, additional support is needed beyond the initial Hope Group plan. The intervention will incorporate WHO's Mental Health Gap Action Program (mhGAP) training for the Hope Group facilitators to enhance care.

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MASS SURGERY WEEKS FOR TREATMENT OF HYDROCELE DUE TO LYMPHATIC FILARIASIS IN PLATEAU AND NASARAWA STATES, CENTRAL NIGERIA, 2020 - 2021

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Lymphatic filariasis (LF) is a neglected tropical disease with high burden in Nigeria. Despite significant progress in interrupting transmission, people with past lymphatic damage from LF can continue to suffer severe morbidity. Hydrocele is a common manifestation which can require surgery to treat, but sufferers often live in areas with limited access to surgeons. We report the results of a program of mass surgery weeks (MSW) between 2020 and 2021 supported by the Carter Center to provide hydrocelectomy services to men with filarial scrotal hydrocele in Plateau and Nasarawa states in central Nigeria. Patients were mobilized to five general hospitals by Local Integrated Health Team members in the catchment areas using their patient line-listings, which included telephone numbers. Patients were pre-screened on arrival at the hospitals for hydrocele surgery eligibility by physical examination and ultrasound. Approved patients had the hydrocelectomy surgical procedure and postoperative follow-up explained to them. In general, the operation was performed under local anesthesia using lignocaine infiltration of the scrotal skin and spermatic cord. If general anesthesia was needed, intravenous ketamine was administered with local lignocaine. The technique used was making a vertical (median raphe) skin incision to deliver the sac for hydrocelectomy, or making oblique incision along the affected groin down to the spermatic cord for hernia. Local general practitioners supervised by two urologists performed 492 surgical repairs (hydrocele 430; hernia 62) in 378 men over seven MSW in five semi-urban Nigerian community hospitals with excellent outcomes. Postoperative complications were uncommon among the 93% who returned for recommended follow-up, including hematoma (1%) and infection (2%). MSW can be a safe and effective method of delivering LF morbidity management in remote areas if candidates are preoperatively screened and surgeons are supervised by qualified urologists.

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DETERMINING THE FUNCTION OF AN APICOPLAST-LOCALIZED GTPASE IN *TOXOPLASMA GONDII*

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The apicomplexan phylum contains a diverse group of obligate intracellular parasites which are the causative agents of medically relevant diseases including malaria and toxoplasmosis. Many of these parasites contain a four-membraned non-photosynthetic plastid organelle, termed the apicoplast, which produces several essential metabolites that the parasite cannot scavenge from the host. As loss of the apicoplast is lethal to the parasite, characterization of apicoplast proteins provides valuable insight into novel pathways of apicoplast biology which can be targeted for therapeutic intervention. While the apicoplast genome encodes multiple proteins, most apicoplast-localized proteins are nuclear encoded and trafficked to the apicoplast. Despite their importance, many apicoplast proteins remain uncharacterized. Our lab has identified a homolog of a prokaryotic translational GTPase(trGTPase) BipA in *Toxoplasma gondii*, termed TgBipA. Based on high-throughput proteomic and genomic screens, this protein is predicted to localize to the apicoplast and be essential for parasite survival. Through immunofluorescence assays, we demonstrate that TgBipA is in fact localized to the apicoplast lumen. To investigate the function of this protein, we created a TgBipA inducible knockout (KO) line using Cre recombinase-based methodology. TgBipA KO parasites do not form plaques indicating an essential role for TgBipA in parasite growth. 72 hours after TgBipA KO, 50% of parasites do not contain an identifiable ring-shaped apicoplast and nuclear-encoded apicoplast proteins are found in vesicular structures in the parasite cytosol. Ultrastructure expansion microscopy reveals a shrunken apicoplast prior to dissolution. Taken together, this data shows that TgBipA is essential for apicoplast upkeep. Our future goal is to examine the mechanistic role of TgBipA by mutating conserved residues found to be essential for GTP hydrolysis and ribosome binding in BipA and determining if these mutants are sufficient to rescue a wildtype TgBipA KO, providing valuable insight into the functional domains of TgBipA and its role as a potential trGTPase.

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COMPARISON OF CARDIAC FIBROSIS CAUSED BY *TRYPANOSOMA CRUZI* IN THE CHRONIC PHASE IN IN VIVO MODELS OF MICE (BALB/C, SWISS), AND *CAVIA PORCELLUS*

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Chagas disease, caused by *Trypanosoma cruzi*, necessitates effective animal models for study. This research evaluates Balb/C mice, Swiss mice, and guinea pigs (*Cavia porcellus*) for their utility in modeling Chagas disease's cardiac aspects. We compared parasitological, histopathological, and immunological responses among these models after infecting them with *T. cruzi*. Balb/C and Swiss mice showed higher parasitemia and more significant electrocardiographic changes compared to guinea pigs, indicating greater susceptibility to *T. cruzi*. Histopathological analysis confirmed more extensive cardiac fibrosis in these mice. Swiss mice, in particular, demonstrated heightened susceptibility and severe clinical signs, suggesting they may serve as more relevant models for studying human Chagas disease. This study highlights Swiss mice's potential as suitable models for investigating Chagas disease pathogenesis and testing new treatments due to their pronounced response to *T. cruzi* infection.

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SUCCESSFUL REPURPOSING OF FDA-APPROVED DRUGS AGAINST *LEISHMANIA* PARASITES PREVIOUSLY PREDICTED THROUGH A MACHINE LEARNING APPROACH

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Drug repurposing holds significant promise in the search for new treatments against Neglected Tropical Diseases, as it drastically reduces cost and time through the drug discovery process. In previously published work, we developed a Machine Learning (ML) pipeline to repurpose FDA-approved drugs against Leishmaniases. We herein provide validation of such approach through *in vitro* experiments, evaluating the antileishmanial effects of 10 ML-predicted drug candidates. We assessed the activity of these drugs against promastigotes from two strains of *L. infantum* and one of *Leishmania major*, each associated with distinct clinical manifestations, using an MTT assay. Among them, 5 molecules exhibited an effect against the *Leishmania* strains, including Acebutolol, Prilocaine, and Phenylephrine, newly identified in this study, with IC50 values ranging from 67 to 200 µg/mL. Dibucaine and Domperidone demonstrated potent activity, consistent with previous *in vivo* studies. None of the 5 compounds displayed notable cytotoxic effects on THP-1 derived macrophages. Intracellular *L. major* forms were also susceptible to these compounds, displaying enhanced IC50 values compared to those observed against the promastigotes. Notably, Dibucaine and Domperidone showed IC50 values < 2 µg/mL, comparable to Amphotericin B. Acebutolol, Prilocaine, and Phenylephrine exhibited IC50 values ranging from 17 to 57 µg/mL. Additionally, all compounds demonstrated satisfactory to high selectivity indexes. Our previously established Computer-Aided repositioning pipelines identified Dibucaine and Domperidone as promising candidates, reinforcing prior *in vivo* findings. In conclusion, this study brings confirmation of the potential of Dibucaine and Domperidone as promising candidates through *in vitro* tests against two prevalent *Leishmania* species in Africa and the Middle East, reinforcing previous *in silico* and *in vivo* findings. More importantly, we herein uncovered Acebutolol, Prilocaine and Phenylephrine as novel drug candidates against Leishmaniases, underscoring the relevance of our computational approach and warranting further investigation.

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CONSIDERATION OF FEXINIDAZOLE AS A NOVEL TREATMENT OPTION FOR RHODESIENSE-HUMAN AFRICAN TRYPANOSOMIASIS

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Human African Trypanosomiasis (HAT) is caused by the protozoan parasites *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense*. It is endemic in 36 sub-Saharan African countries and efforts for elimination are ongoing. Treatment options have been unchanged for decades until the new drug fexinidazole was included in the 2019 WHO interim guidelines for the treatment of gambiense HAT. Fexinidazole has antitrypanosomal activity against both *T.b. rhodesiense* and *T.b. gambiense*. Therefore, fexinidazole is now being considered as a treatment option for rhodesiense HAT for patients >6 years or >20kg. Fexinidazole is an oral medication and has fewer adverse effects than currently recommended treatment options, although vomiting and nausea can be significant. Risk of relapse in patients with gambiense HAT is higher after fexinidazole compared to nifurtimox-eflornithine combination therapy. Data on the efficacy of fexinidazole in rhodesiense HAT are limited. Preliminary data from an unpublished clinical trial on the efficacy and safety of fexinidazole in patients with rhodesiense HAT show positive outcomes, although with a small sample size. Patients treated with fexinidazole should be monitored closely for relapse. The US Food and Drug Administration (FDA) approved fexinidazole for treatment of gambiense HAT in 2023. The European Medicines Agency (EMA) approved fexinidazole for use in the treatment of rhodesiense HAT in 2023. Current treatment guidelines for HAT were reviewed by WHO in February 2024 and updated WHO guidelines to expand fexinidazole use in HAT treatment are in development. Fexinidazole is available in the US by contacting Sanofi Customer Service or Medical Affairs at 1-800-372-6634 or customersupport@sanofi.com. In nonendemic countries outside the US, it may be obtained for compassionate use from WHO. WHO continues to track cases closely as elimination efforts are ongoing. US physicians are encouraged to discuss management of patients with suspected HAT with subject matter experts at Centers for Disease Control and Prevention who can provide treatment guidance and report confirmed cases to WHO.

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CLINICAL PRESENTATION AND MANAGEMENT OF CUTANEOUS LEISHMANIASIS AMONG NEWLY ARRIVED AFGHAN EVACUEE CHILDREN

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In 2021, over 80,000 Afghan citizens were evacuated to the U.S., half of them children. As part of a larger retrospective cross-sectional analysis of all pediatric Afghan evacuees referred for care at an urban quaternary children's hospital and associated community hospital system between 08/2021 and 02/2022, we identified children diagnosed with complex cutaneous leishmaniasis (CL). Children were referred for management by physicians on a military base and in the emergency department due to concern for complex CL (i.e. lesions in areas at high risk of mucosal involvement, multiple or large lesions). The majority of these children presented for a joint dermatology/infectious diseases clinic, which was cross-referenced for inclusion. Chart reviews were conducted by study clinicians and abstracted into a REDCap database. Of 477 children in the larger study, nine cases of complex CL were identified. The age range was 11 months to eight years. Eight cases (89%) were female. Seven children (78%) had facial lesions. Seven (78%) had PCR positivity. *Leishmania tropica* was the most commonly identified species (56%). One child was diagnosed with leishmaniasis recidivans (presumed *L. tropica*) based on morphologic characteristics, history of previous intralesional

therapy, and positive PCR (speciation unable to be performed). Treatment was chosen based on patient's clinical presentation, social factors, and available resources. Two children were treated with fluconazole for presumed *L. major*, two with miltefosine, and one with LAmB, all (56%) with good responses to therapy. Three children (33%) were resettled before initiating treatment. One child (11%) was lost to follow up prior to diagnostic testing or treatment. The number of children identified likely represents an underestimation of total cases of CL. It is likely that some cases were misdiagnosed as impetigo and simple cases were not referred to subspecialty care. This case series highlights both the challenge of recognizing unfamiliar diseases and the difficulty of connecting evacuee children to subspecialty care and ensuring appropriate follow-up.

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TARGET-BASED 6-5 FUSED RING HETEROCYCLIC SCAFFOLDS DISPLAY BROAD ANTIPARASITIC POTENCY *IN VITRO*

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Malaria, leishmaniasis, and African trypanosomiasis are protozoan diseases, which represent major global health problems, mainly in developing countries; however, the development of drug resistance coupled with the toxicity of current treatments has held up their management. The implication of certain enzymes (dihydrofolate reductase [DHFR]) or proteins (potassium channels) in the pathogenesis of these protozoan diseases is undeniable. In this study, a series of three DHFR inhibitors (6-5 fused heterocyclic derivatives X, Y, and Z) and one K+ channel blocker (E4031) were screened for their inhibitory effects on *Leishmania donovani*, *Plasmodium falciparum*, and *Trypanosoma brucei*. A resazurin assay was used to assess the antitrypanosomal and antileishmanial effects of the test compounds, whereas the antiplasmodial activity was evaluated through the SYBR Green I assay. Moreover, the cytotoxicity of the test compounds was evaluated in Vero, Raw 264.7, and HepG-2 cells using a resazurin-based assay, while their pharmacokinetic properties were predicted using the online tool, pkCSM. As a result, compound Y exhibited selective (selectivity index range: from 2.69 to >61.4; Vero, Raw 264.7, and HepG-2 cells) and broad-spectrum antiprotozoal activity against *L. donovani* promastigotes (IC_{50}: 12.4 µM), amastigotes (IC_{50}: 4.28 µM), *P. falciparum* (IC_{50}: 0.028 µM) and *T. brucei* brucei (IC_{50}: 0.81 µM). In addition, compound X inhibited the growth of *P. falciparum* (IC_{50}: 0.0052 µM) and *T. brucei* brucei (IC_{50}: 6.49 µM). *In silico* screening of the active antiprotozoal compounds demonstrated positive drug likeness scores, as none of the criteria for Lipinski's rule were violated by these compounds. However, in-depth pharmacokinetic and mechanistic studies are warranted to support the discovery of novel antiprotozoal agents against malaria, leishmaniasis, and African trypanosomiasis by repurposing K+ channel blockers and DHFR inhibitors.

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IMMUNOMODULATION EFFECT OF HOOKWORM PROTEINS ON CHRONIC CHAGASIC LIVER MODELS

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Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, affects nearly 7 million people globally. Its chronic stage often induces inflammatory cardiac and digestive immunity, posing significant challenges for treatment. Unfortunately, patients with Chronic Chagas disease lack a definitive cure, relying instead on managing symptoms with drugs like Benznidazole and Nifurtimox which have serious side effects of toxicity. Given the liver's pivotal role in drug metabolism and parasite control, understanding hepatic immunity in Chronic Chagasic models is imperative. In this context, exploring immunomodulatory strategies becomes paramount. Hookworm-derived recombinant proteins, AIP-1 and AIP-2, have demonstrated efficacy in reducing inflammation in mouse models of inflammatory diseases, including cardiac inflammation due to *T. cruzi* infection. We previously showed that both AIP-1 and AIP-2 reduced inflammatory cell infiltrate into the heart and decreased several inflammatory cytokines including IFNγ and IL-6. Here we evaluated the impact of these two proteins on liver inflammation. Female BALB/c mice were infected with bioluminescent *T. cruzi* H1 strain trypomastigotes for 70 days. Following infection, mice received a seven-day treatment regimen of 1mg/kg AIP-1 or AIP-2 protein via intraperitoneal injection. Control groups remained untreated or received a 14-day regimen of 25mg/kg aspirin in their drinking water. At 84 days post-infection, samples of hepatic tissue were collected for comprehensive evaluation. Both AIP-1 and AIP-2 significantly reduced pSTAT3 levels in the liver, indicating the reduced inflammation pathway. We will discuss further the immunomodulatory effects of AIP-1 and AIP-2 specifically on hepatic immunity in a mouse model of Chronic *T. cruzi* infection.

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IMPROVED TREATMENT OUTCOME FOLLOWING THE USE OF A WOUND DRESSINGS IN CUTANEOUS LEISHMANIASIS LESIONS

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Leishmaniasis, caused by *Leishmania* parasites, is a neglected tropical disease and Cutaneous Leishmaniasis (CL) is the most common form. Despite the associated toxicity and adverse effects, Meglumine antimoniate (MA) remains the first-choice treatment in Brazil, pressing the need for the development of better alternatives. Bacterial Nanocellulose (BNC), a biocompatible nanomaterial, has unique properties regarding wound healing. In a previous study, we showed that use of topical BNC + systemic MA significantly increased the cure rate of CL patients, compared to treatment with MA alone. Herein, we performed a study comparing the use of wound dressings, BNC or placebo, in CL caused by *Leishmania braziliensis, versus* use of systemic MA alone. We show that patients that made use of topical wound dressings (BNC or placebo) showed improved cure rates and a decreased need for rescue treatment, compared to patients treated with systemic MA alone. Of note, time-to-cure was significantly improved with the use of a wound dressing (BNC or placebo). Assessment of the immune response showed that patients treated with wound dressings displayed a downmodulation in the production of immune mediators, in comparison to those treated with MA alone, particularly in inflammatory mediators such as IL-1. This study shows that topical application of a wound dressing, in addition to the standard systemic use of MA, can improve chemotherapy outcome in CL caused by *L. braziliensis*.

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IMPROVING THE LEISHMANICIDAL ACTIVITY OF MILTEFOSINE USING SPRAYABLE DRESSINGS BASED ON NANOFIBERS OF PVP/TETRONIC®/CYCLODEXTRINS

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Miltefosine (MF) is a well-known amphiphilic zwitterionic alkylphospholipid used in clinic for the treatment of leishmaniasis. This pathology is a neglected tropical disease, caused by *Leishmania species* and transmitted by the bite of sandflies. Leishmaniasis presents different clinical forms, of which the cutaneous one is the most prevalent. Despite being the only oral antileishmanial drug, MF is restricted by dose-limiting gastrointestinal side effects, a high cost compared to other drugs, teratogenicity, and potential of drug resistance due to long treatment duration. Currently, the development of effective therapies against leishmaniasis is of utmost importance. Our approach to the improvement of the leishmanicidal activity of MF has been its formulation in the form of sprayable dressings, based on submicrometric fibers of MF with polyvinylpyrrolidone (PVP), a biocompatible hydrophilic polymer. The fibers are produced by solution blow spinning, (SBS) an emerging method for the manufacturing of non-woven materials made of nanometric fibers. Cyclodextrins (CDs), which have demonstrated to reduce the hygroscopicity of PVP and to improve its stability, have been also incorporated in the formulation, along with Tetronic® 1307, an amphiphilic block copolymer that improves the antileishmanial action of MF. The release profile of the drug from the fibers was tested to correlate the performance with the composition, degree of functionalization and morphology of the material. The cytotoxicity on macrophages and the antileishmanial (*Leishmania major*) activity were evaluated to assess the biological and therapeutic effects of these new formulations of MF. Therefore, in addition to the possible oral and intravenous administrations, our results prove the effectiveness of this new in-situ delivery of MF on affected areas such as skin lesions of cutaneous leishmaniasis.

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A VALID 96-WELL-PLATE-ENZYMATIC ASSAY FOR *LEISHMANIA* METHYLTHIOADENOSINE PHOSPHORYLASE MTAP PROTEIN, A CANDIDATE DRUG TARGET

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The Leishmania infantum methylthioadenosine phosphorylase (LiMTAP) protein is the unique enzyme capable of metabolizing the MTA. Identified as highly druggable by the Tropical Disease Research database, it has ~35% identity to the human MTAP (huMTAP), so considered as a Leishmania drug target. We previously cloned and expressed the protein as a bacterial recombinant. Our goal is to develop a feasible, rapid, and coupled-enzyme assay in a format of 96-well-plate for the MTAPase activity. The test is critical for biochemical studies e.g. kinetic experiments to determine enzyme parameters, and biochemical screenings to discover Leishmania inhibitors. Thus, we used the plasmid constructs to purify the recombinant LiMTAP on Nickel based columns and developed an LiMTAPase 96-well plate assay. Based on our previous established tube-assay in crude extracts and on published work on huMTAP, we varied the reaction volume [50-100µl], temperature [25-37°C], time [0-180min], MTA concentrations [0-250µM], and DMSO rates [0-10%]. Enzymatic activity was monitored at 305nm based on a reference curve generated from the adenine conversion using 2 commercial xanthine oxidase (XO) sources [MedChemExpress and Sigma] and various concentrations [0.08-0.4 units per reaction]. Reaction mixtures contained 10ng/µl LiMTAP, 50mM potassium phosphate (pH7.4). We found experimental conditions to be highly reproducible using an MTA concentration range of [75-150µM], 5-10 % DMSO percentage, between 90-120 minutes, in 100 µl. We used MTAPase kinetics to determine Michaelis Menten kinetic parameters to select for the best XO. We found comparable Kcat mean value (Vmax/[LiMTAP]) of ~4.5 min-1, when we considered the conditions where the XO conversion rates were comparable. In conclusion, we have developed effective conditions to set a miniaturized LiMTAP biochemical assay adapted for multiple and single points enzymatic tests. Currently, a cost-effectiveness comparison is ongoing to further improve the assay for the screenings of novel inhibitors of this protein, and thus accelerating discovery of promising anti-Leishmania molecules.

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OPTIMIZING THE MULTI-FACETED PIPELINE OF AI-BASED DRUG DISCOVERY AGAINST INFECTIOUS DISEASES

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Artificial Intelligence (AI) has now gained a wide interest in the field of drug discovery due to the increasing availability of large datasets useful in training AI models to predict properties and activities of chemical compounds, and design novel drug candidates. The AI-based pipeline encompasses: the dataset, the model and the prediction task as main components. The present work is focused on optimizing the different components of such a pipeline towards providing robust predictive tools of chemical compound activities against five infectious diseases, including Malaria, AIDS, Tuberculosis and Trypanosomiases.For each disease of interest, we retrieved bioassays datasets from the PubChem database. All datasets are highly imbalanced towards the inactive class. Data balancing was applied to all datasets through targeted strategies in order to identify optimal ratios. We used different molecular fingerprints and graph-convolution methods to encode the chemical structures from these libraries. Then, we trained two Machine Learning (ML) and four Deep Learning (DL) algorithms to assess the anti-pathogen potential of chemical entities. Investigating the impact of the data imbalance on the ML and DL models performances demonstrated a consensus ratio of 1:9 as optimal across all simulations. Among the evaluated models, Random Forest (RF), Multi-Layer Perceptron (MLP), Graph Convolution Network (GCN) and Attentive Fingerprint (AFP) demonstrated the best performances on specific datasets, and were optimized through hyperparameter tuning. At this stage, we identified the optimal balancing ratio and predictive model for each dataset. We then assessed the generalization power of each model to unseen data (external validation). Although no particular model could exhibit optimal performances on all datasets, MLP provided a superior ability to accurately identify the active molecules, with the best trade-off between the True Positive and False Positive rates. We aim at further automating the optimized pathogen-specific pipelines on our open source platform https://cidalsdb.streamlit.app/ for use by the scientific community.

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FEXINIDAZOLE IN PATIENTS WITH HUMAN AFRICAN TRYPANOSOMIASIS DUE TO *TRYPANOSOMA BRUCEI RHODESIENSE,* TOWARDS AN ARSENIC FREE FIRST LINE THERAPY

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Rhodesiense human African trypanosomiasis (r-HAT) is the zoonotic, acute, and fatal form of sleeping sickness in Eastern Africa. To date neurotoxic melarsoprol is the only drug available for treatment of the advanced meningo-encephalitic stage. A new oral treatment could simplify HAT elimination as proposed by the World Health Organization. In 2022, a clinical trial to test fexinidazole, a new, safer, highly effective, short-course treatment, was completed in Malawi and Uganda for r-HAT as an alternative to the toxic existing treatment. Fexinidazole has now received a positive scientific opinion from the European Medicines Agency to treat both forms of HAT, first the chronic *gambiense* form in 2018 and in 2023 the acute *rhodesiense* HAT. The last trial for the clinical development of fexinidazole for HAT was designed as a single arm benchmark study comparing observed to unacceptable fatality rates at the end of hospitalization, due to the low number of detected r-HAT cases. The principal endpoint was defined as an unacceptable attributable fatality rate equal or greater than 8.5% . Additional study objectives were treatment failure (including relapses) or deaths at the end of hospitalization or during 12 months follow-up, and safety, pharmacokinetics, and molecular assessments. The sample size, defined according to the principal objective was of 34 evaluable patients in advanced stage complemented by the available number of patients in early stage. The primary efficacy result was achieved, with no related deaths during hospitalisation: 0 C.I. (0.0-8.43%) in any of the 45 patients who were included, of which 34 were evaluable in the advanced stage of illness. Safety was acceptable; one patient relapsed. Full results will be communicated during the presentation, including all secondary endpoints and safety data. After its addition to the treatment arsenal for gambiense HAT, fexinidazole has now been shown to be a good first-line treatment alternative to replace melarsoprol and suramin for the oral treatment of both stages of r-HAT.

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IN VITRO EVALUATION OF THE ANTI AMOEBIC ACTIVITY OF BENZOTHIAZOLE BT3 AGAINST *ENTAMOEBA HISTOLYTICA*

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Due to the side effects of the available anti-amebic drugs, it is necessary to seek new compounds. Since previous studies have demonstrated the anti-parasitic activity of benzothiazoles, the aim of the current contribution was to evaluate the *in vitro* effect of BT3 (4-[5-(trifluoromethyl)-1,3-benzothiazol-2-yl] benzoic acid) against *Entamoeba histolytica* and during the interactions of the amoebae with hamster neutrophils (a model of susceptibility). *E. histolytica* trophozoites were treated with different concentrations of BT3 for 5 h and viability was examined by using the WST-1 reagent. The 50% inhibitory concentration (IC_{50}) was obtained by linear regression between the concentration of the compound and the percentage of inhibition. The cytotoxicity of BT3 was assessed on the Vero cell line. Additionally, determination was made of ROS production with a 2', 7'-dichlorodihydrofluorescein (DCF) ROS Assay Kit (Ab238535, Abcam, Cambridge, UK) and of NO production with a NO Assay Kit (Ab272517, Abcam, Cambridge, UK), based on the conventional Griess method. The *in vitro* results showed that the viability of trophozoites treated with BT3 was significantly decreased in a dose dependent manner, while BT3 did not show any cytotoxic effect on the Vero cell line. The IC_{50} of BT3 was 117.5 µM at 5 h. The test compound triggered the production of reactive oxygen species and nitric oxide by the neutrophils. These prooxidant species, which were found in the supernatant of amoebae-neutrophils interactions, could possibly contribute to amoebic damage.

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FACTORS ASSOCIATED WITH RELAPSE IN VISCERAL LEISHMANIASIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS USING THE INFECTIOUS DISEASES DATA OBSERVATORY DATA PLATFORM

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A significant geographical variation is observed in the efficacy of existing drugs used for treating visceral leishmaniasis (VL). Elucidating factors that explain some of this variation can provide valuable insights regarding treatment response across different endemic settings. An individual patient data meta-analysis (IPD-MA) using data from 33 studies (published 2000-19) was therefore undertaken to explore the predictors of relapse using hierarchical logistic regression models fitted separately by geographical region. Of the 9,353 patients included, 5,924 (63.3%) were from the Indian sub-continent (ISC), 2,929 (31.3%) from Eastern Africa (EA), 377 (4.0%) from Brazil and 123 (1.3%) from Greece. Treatment administered included: miltefosine (n=2,109, 22.5%), pentavalent antimony (n=1,871, 20.0%), amphotericin B deoxycholate (n=2,669, 28.5%), liposomal amphotericin B (n=485, 5.2%), paromomycin (n=712, 7.6%), a combination of these drugs (n=977, 10.4%), or other (n=530, 5.7%). Overall, 4.0% (376/9,353) of patients relapsed following initial treatment response: 4.4% (260/5924) in the ISC and 3.3% (97/2929) in EA. In a multivariable model from the ISC that included age, sex and treatment, age <15y was the only factor associated with an increased relapse risk (adjusted odds ratio (AOR) [95% confidence interval (CI)]: 1.6 [1.2-2.0]; reference ≥15y]. In EA, variables associated with increased relapse risk in a multivariable model that included age, sex, anaemia (defined using WHO's age and sex specific threshold) and treatment included: male sex (AOR: 3.4 [1.5-7.8]), age<5y (AOR: 5.9 [1.9-18.4]) and 5-15y (AOR: 3.3 [1.3-8.0] (reference ≥15y), and severe anaemia at presentation (AOR: 2.8 [1.4-5.3]). This IPD-MA demonstrates young age, male sex, and severe baseline anaemia are predictors of relapse; potentially explaining some of the observed heterogeneity in treatment response. Studies in this IPD-MA often excluded patients with complicated disease and pregnant/lactating women which could have potentially biased the conclusions. Further work is underway to assess the factors associated with all-cause mortality.

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LEVERAGING MACHINE LEARNING (ML) AND DEEP LEARNING (DL) MODELS FOR DRUG REPURPOSING: A SUCCESSFUL CASE STUDY ON LEISHMANIA PARASITES

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Computer-Aided Drug Discovery has gained momentum with recent advances in data analysis and artificial intelligence (AI). In this context, disposing of reliable datasets is of utmost importance. We herein report our efforts in collating targeted and manually curated datasets and the implementation of highly reliable AI models in the frame of Ligand-Based Drug Discovery against COVID-19 and Leishmaniases, among others. Extensive literature search for biologically active or inactive molecules was backed-up with data retrieval from PubChem and other chemical databases. For each pathogen, manually curated datasets of up to 4,000 molecules could be consolidated. Then, we implemented 4 machine learning (ML) and 4 deep learning (DL) algorithms that were trained and optimized on both disease-specific datasets. Our results highlighted the importance of injecting literature-issued data points within larger screening datasets towards obtaining optimal performances of the ML and DL models. Interestingly, ML models exhibited the highest scores (accuracy>0.85 and ROC-AUC>0.90), across all simulations as compared to DL models. Nonetheless, through external validation (unseen data) on the FDA-approved drugs, DL algorithms demonstrated higher generalization power and accurate activity predictions with True Positive rates>50%.As an ultimate validation of our approach, we used the Leishmania-specific models herein optimized (RF, MLP & GCN) to select the most potentially active compounds within the FDA-approved drugs. We opted for molecules commonly predicted as active by all 3 models with>80% confidence. Out of 71 predicted molecules, 21 were previously described in the literature as antileishmanial agents. Out of the remaining 50, 10 drugs have never been described before; and were thus purchased towards their validation as effectors on Leishmania parasites in vitro. The present research leverages the potential of AI within a data-driven approach that capitalizes on the team's expertise in Computer-Aided Drug Discovery to deliver an optimal strategy for a cost-effective therapeutics discovery against infectious diseases.

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EVALUATION OF TCNMT OF NOVEL IN-SILICO INHIBITORS AGAINST *TRYPANOSOMA CRUZI* N-MYRISTOYLTRANSFERASE

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Chagas disease (CD) is caused by the protozoan parasite *Trypanosoma cruzi.* Although originally endemic to South and Central America, the disease prevalence has increased in non-endemic regions such as the United States, Europe, Japan, and Australia. CD is hard to detect during the acute phase, progressing to the chronic phase, where it may cause damage to organs such as the heart and digestive system. Current standard serologic diagnostics lack enough sensitivity and specificity. In addition, treatment is long, with a high rate of adverse effects in patients. N-myristoylation is a posttranslational modification of proteins that is specific to the alpha-amino group of an N-terminal glycine residue and catalyzed by N-myristoyl transferase (NMT). It is known to play a role in cellular regulation and signal transduction in eukaryotes and parasite survival. NMT has been shown to be a chemotherapeutic target candidate in other protozoan parasites close to the *T. cruzi* family, such as *Plasmodium falciparum, Leishmania donovani,* and, more closely, *T. brucei*. In our study, it was purified the recombinant NMT enzyme from *T. cruzi* (TcNMT) and tested against newly designed in silico NMT inhibitors. First, we isolated the gDNA from *T. cruzi* CL-Brener strain parasites, followed by PCR to obtain the gene that codes for TcNMT. Subsequently, it was cloned into a pET15b expression plasmid. The recombinant protein 6xHis-TcNMT (TcNMT) in Rossetta-gami cells. The recombinant enzyme TcNMT was purified by affinity, ion exchange, and size exclusion chromatography. Next, the enzymatic activity of the recombinant TcNMT was characterized, followed by the evaluation of the inhibitors DA, QU, and DI. We also assessed the cellular cytotoxicity of our inhibitors in human cardiomyocytes AC16; the compounds the DA, QU, and DI showed an IC50 of 23.6 µM, 34.5 µM and 18.6 µM, respectively. Currently, we are assessing the efficacy of the inhibitors against intracellular amastigotes at 24, 48, and 72 hours after treatment, monitoring the infection in the Bio Tek Cytation 7.

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HEAT SHOCK PROTEIN TCJ2: A NOVEL MRNA VACCINE CANDIDATE FOR CHAGAS DISEASE IDENTIFIED THROUGH IMMUNOPEPTIDOMICS

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Globally around 6-7 million people are infected with the protozoan parasite *Trypanosoma cruzi*, the causative agent of Chagas disease. A subset of these people has the risk of developing cardiomyopathy as a symptom of chronic Chagas disease. Efforts to develop prophylactic and therapeutic vaccines against *T. cruzi* infection are ongoing, but no vaccine is currently available to prevent or treat Chagas disease. Developing effective vaccines requires targeting parasitic antigens presented on major histocompatibility complex-I (MHC-I) molecules, which can stimulate *T. cruzi*-specific CD8+ cytotoxic T cells and eliminate infected cells. However, no systematic screening has been done to evaluate which antigen targets are presented by *T. cruzi* - infected cells during natural infection and can be detected by antigen-specific CD8+ T cells. In our study, we employed mass spectrometry-based immunopeptidomics to analyze which *T. cruzi* peptides were presented on MHC-I of infected host cells. From dozens of *T. cruzi* peptides that were identified, multiple peptides from duplicate experiments traced back to Tcj2, which is a trypanosome chaperone protein and member of the DnaJ (heat shock protein 40) family. Protein sequence identity analysis showed that Tcj2 was very conserved between different *T. cruzi* strains, while human and mouse orthologs showed considerable differences. Next, an mRNA construct encoding for Tcj2 protein was developed and showed translation of Tcj2 protein *in vitro*. When Tcj2 mRNA was formulated into LNPs and tested as an mRNA vaccine candidate in mice, it induced cytotoxic CD8+ T cells, along with a Th1-skewed humoral antibody response. Splenocytes of Tcj2-immunized mice showed a much stronger reduction in replication of *T. cruzi* in an *in vitro* co-culture with *T. cruzi* infected cells, compared to co-cultures with splenocytes from naïve mice, demonstrating the protective potential of Tcj2 as a vaccine target. Our findings demonstrate the potential of immunopeptidomics to identify new vaccine targets for Chagas disease, and revealed Tcj2 as a promising new mRNA vaccine candidate.

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IMMUNOTHERAPY WITH TSA-1 C4 COMBINED WITH BZN INDUCES DIVERGENT IMMUNE RESPONSE BUT CONFERS PROTECTION AGAINST TRYPANOSOMA CRUZI INFECTION

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Chagas disease, caused by *Trypanosoma cruzi*, affects 6-7 million people worldwide. The infection progress to chronic chagasic cardiomyopathy in

30% of patients driving death by cardiac failure. The current treatments induce side effects and have poor efficacy during the chronic phase. Here, we propose the evaluation of TSA-1.C4 and the adjuvant TLR-4 agonist plus a low dose of BNZ. According to our data, Balb/c mice showed a protective effect mediated by a reduced peripheral blood parasitemia, and prevention of cardiac inflammation was observed in TSA-1.C4+TLR-4 agonist+Low BNZ treated mice. In addition, significant IFNy+CD4+ producing T cells, IL-2 and IL-4 cytokines were observed in vaccine-linked chemotherapy treated mice. This is the first report demonstrating the beneficial effect of a vaccine-linked chemotherapy formulated with the recombinant TSA-1.C4 protein and TLR-4 agonist adjuvant and all these results suggests a promising therapeutic option for further studies.

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VALIDATION OF *TRYPANOSOMA CRUZI* MULTI-EPITOPE RECOMBINANT PROTEIN IN INDIVIDUALS WITH HLA-A*02 ALLELE AS A HUMAN CHAGAS DISEASE VACCINE CANDIDATE

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Chagas disease is the most significant neglected tropical disease affecting individuals in the Americas, caused by the protozoan *Trypanosoma cruzi.* Available drugs are toxic and ineffective in chronic phase and the development of a Chagas disease vaccine is hampered by the complexity of parasite and HLA polymorphisms. Epitope-specific $CD8^+$ T cells are necessary to confer a robust immune response and protection against intracellular parasites such as *T. cruzi* by producing IFN-γ and perforin. Thus, the antigen(s) for the development of a Chagas vaccine or immunotherapy must include $CD8^+$ T cell epitopes. In this study, we aimed to develop a multi-epitope recombinant protein as a novel human vaccine for Chagas disease. Sixteen database programs were used to predict *de novo* 40 potential epitopes for HLA-A*02:01. Nine out of 40 predicted epitopes were able to elicit IFN-γ in PBMC from chagasic patients. Molecular docking revealed a good binding affinity among the epitopes with diverse HLA molecules. A recombinant multi-epitope protein including nine nonamers *T. cruzi* $CD8^+$ epitopes was expressed and able to recall an antigen-specific immune response in *ex-vivo* assay using PBMCs from chagasic patients with HLA-A*02 allele.

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IMPACT OF MALNUTRITION ON THE EFFICACY OF LMCEN-/- VACCINE

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Globally, malnutrition is the most frequent cause of immunodeficiency and significant risk factor for the development of visceral leishmaniasis. The susceptibility to and severity of *Leishmania* infection can be altered by the host's body weight and serum levels of micronutrients. In murine models, malnutrition leads to failure of the draining lymph node and a reduction in the number of immune cells that prevent the dissemination of *Leishmania*. However, there is a gap in our understanding of how malnutrition affects the development of a specific immune response to a *Leishmania* vaccine. Our laboratory has developed a promising *Leishmania major* live attenuated vaccine with a Centrin gene-knockout (*LmCen*$^{-/-}$), which has been shown to be safe and efficacious against *Leishmania donovani* and *L. major* challenges in animal models of visceral leishmaniasis and cutaneous leishmaniasis respectively. Nevertheless, how malnutrition affects the immune response to *LmCen*$^{-/-}$ vaccine remains unknown. This study aimed to determine whether the efficacy of the *LmCen*$^{-/-}$ vaccine is abrogated in the malnourished host. We used a murine model of malnutrition to assess the *LmCen*$^{-/-}$ vaccine's efficacy in both well-nourished (WN) and poly nutrients-deficient (PND) mice. The control mice group (WN) received a diet of normal mouse chow containing 17% protein, 100 ppm iron, and 30 ppm zinc. The test mice group (PND) received a chow with decreased protein (3%), iron (10 ppm), and zinc (1 ppm). Mice are fed with WN or PND diets, 4 weeks before the start of immunizations and throughout the challenge with *L. donovani*. We evaluated whether malnutrition status has a significant impact on neutrophils, macrophages, and dendritic cellularity at the local and systemic levels. In addition, we assessed the nutritional markers in the lymph node barrier and splenocytes. Results from the series of experiments assessing how malnutrition affects Leishmania burden and whether it abrogates LmCen-/- vaccine efficacy will be presented.

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FACTORS AFFECTING COMMUNITY DIRECTED INTERVENTION VOLUNTEERS' PERFORMANCE IN ONCHOCERCIASIS AND LYMPHATIC FILARIASIS ELIMINATION PROGRAMS, ETHIOPIA

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In Ethiopia, the onchocerciasis program started with control in 2001 and shifted to elimination in 2012. The lymphatic filariasis (LF) program began in 2009. The Carter Center was significant in integrating the community-directed treatment with ivermectin/albendazole (CDTI/A) approach into the primary health care system throughout RB/LF endemic areas in the country. Over 500,000 community drug distributors (CDDs) and community supervisors (CSs) work for the CDTI/A program in Ethiopia, but their level of quality, commitment, and dedication varies. To monitor the program, we conducted a desk review and a mixed-methods cross-sectional community-based study. We randomly selected two kebeles from 12 woredas from seven regions. Then, we randomly selected CDDs in these selected kebeles, resulting in 402 samples. We also conducted 44 key informant interviews and 24 focus group discussions in all targeted kebeles. Consistent with qualitative data, the CDD to population ratio of 1:67 among surveyed CDDs is below the national standard of 1:50. High attrition has led to few active CDDs/CSs in most woredas in Amhara, Gambela, and Benishangul Gumuz regions. These woredas have substandard recruitment and selection processes. Per national guidelines, CDDs should be chosen by community members, but 46% of surveyed CDDs were appointed by kebele leaders. Moreover, 55% of CDDs received only 1-2 hours of training before their last MDA round while half a day is recommended. Qualitative data indicated that pastoral/agro-pastoral areas have tried to improve MDA coverage by directly involving health professionals rather than community volunteers and recruiting more male CDDs to combat high attrition rates for female CDDs. Training and recruitment practices that do not align with national recommendations may contribute to CDD attrition in some parts of Ethiopia. We should evaluate different modes of CDD recruitment, provide quality CDD training, and consider targeted recruitment strategies in pastoralist areas with high attrition rates, particularly for female CDDs.

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IMPACT OF MASS DRUG ADMINISTRATION FOR LYMPHATIC FILARIASIS AND YAWS ELIMINATION ON ATTENDANCES FOR SKIN DISEASE IN RURAL HEALTH CENTERS IN WEST NEW BRITAIN PROVINCE, PAPUA NEW GUINEA

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Papua New Guinea (PNG) is highly endemic for lymphatic filariasis (LF) and yaws. Other skin diseases such as scabies, crusted scabies, fungal and bacterial infections are some of the most common reasons for visits to rural health centers (HCs) in PNG. Recently, PNG started mass drug administration (MDA) to eliminate lymphatic filariasis (LF) and yaws and control scabies and STH with ivermectin, diethylcarbamazine, albendazole (IDA), followed by azithromycin. West New Britain Province (WNBP) in PNG is the first province to receive MDA with IDA and azithromycin, which began in December 2023. Using the PNG National Health Information System (NHIS), we show a significant drop in HC visits for skin diseases and yaws-like lesions two months following MDA compared to the previous six months before MDA. For the 23 HCs reporting complete records in the NHIS for the periods mentioned above, pre-MDA HC visits for all skin diseases excluding yaws-like lesions had a median = 63 (48, 93 IQR) that declined to a median = 42 (26, 55 IQR, p<0.001 Wilcoxon rank-sum test) post-MDA. For yaws-like lesions, there was a median of 24 (13, 30 IQR) visits pre-MDA that declined to a median = 12 (6, 17 IQR, p<0.001) post-MDA. There were no significant changes in non-skin disease HC visits during this period (pre-MDA median = 501 (337,693 IQR) versus post-MDA median = 493 (400,733 IQR, p=0.41). These results show that MDA with IDA and azithromycin can dramatically reduce the burden of skin diseases seen at HCs, with benefits beyond treatment for LF and yaws alone, and that significant decreases in HC visits for skin disease are detectable shortly after MDA. These effects could increase treatment acceptability within the health system and help sustain the high drug coverage in the population necessary to achieve elimination targets for LF and yaws. We will continue to conduct active surveillance of skin-neglected tropical diseases in WNBP to see how long the reduction in HC visits persists after MDA and better evaluate participants' perceptions of the MDA program.

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EMPOWERING YOUTH AGAINST LYMPHATIC FILARIASIS: A GAME-CHANGING APPROACH TO URBAN DRUG COMPLIANCE

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Lymphatic Filariasis (LF) is a significant public health challenge in India, accounting for 43% of global infections. Across 339 endemic districts, approximately 650 million people are at risk. Mass drug administration (MDA) targets 402 million individuals annually for directly observed therapy (DOT). While rural DOT rates have improved from 18% in 2018 to 49% in 2023, urban areas struggle, with only 33% DOT rate in 2023 due to limited number of drug administrators (DAs), residents' unavailability during work hours, low risk perception and limited interface with the DAs. Within urban areas, the assessments have shown poor DOT among youth aged 18-23 years, and among individuals with higher education. Youth, comprising 12% of the total population, offer a potential solution. Engaging youth volunteers from the National Service Scheme during the 2023 MDA increased DOT from 34% to 43% in urban areas. Leveraging this, the Department of Higher Education sensitized nearly 3 million university students across five states namely Uttar Pradesh, Bihar, Jharkhand, Odisha and Chhattisgarh during the Feb 2024 MDA. During Feb 2024 MDA, booths were placed in 343 colleges across 67 districts of 5 states. The records showed 49% college going students consumed filaria prevention drugs at dedicated booths. Further assessment revealed 81% of youth consumed filaria prevention drugs during the Feb 2024 MDA, with 65% consuming at booths and 35% at home. More than 64% students informed about MDA at their home and reported that their parents or siblings consumed anti-LF drugs. Odds of DOT were over 5 times higher (OR: 5.4, p:0.00, 95% CI: 3.1-9.3) when youth received LF/MDA information and over 9 times higher (OR: 9.9, p:0.00, 95% CI: 4.2-23.1) with the knowledge of preventive drug consumption. These findings indicate the potential of youth-focused interventions to significantly improve urban DOT rates when coupled with comprehensive information dissemination about MDA. Implementing activities such as interactive campaigns, social media challenges, and recognition programs to motivate youth involvement can yield encouraging results in elimination efforts.

8201

PARTICIPATORY ACTION RESEARCH TO ENHANCE EQUITABLE HEALTH SEEKING FOR PERSONS AFFECTED BY SKIN NTDS IN LIBERIA

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Persons affected by skin neglected tropical diseases (NTDs) often experience barriers toseeking timely, quality care across their care - seeking journey. The literature predominantlyfocuses on curative care, with little emphasis on holistic care (such as physical rehabilitationand psychosocial support). Spiritual beliefs about the causation of NTDs impact both ability toperceive the need to seek care. Health workers, friends, and family can stigmatise personsaffected, impeding their treatment, participation and inclusion. We sought to understand howan intervention bundle influences the health-seeking pathway of persons affected by skin NTDsusing the Levesque Pathway. REDRESS centred lived experience within intervention design.Persons affected, informal providers and health actors co-developed a bundle of interventionswhich sought to strengthen person-centred integrated case management for skin NTDs.To understand the impact of such health systems reform on the lived experience of personsaffected, we used a series of participatory methods including photovoice (20), focus groupdiscussions (6) and in-depth interviews (12) to document their health seeking journey from thedemand side.Many participants expressed pain, discomfort, and difficulties managing their conditions,particularly at baseline. They experienced stigma and neglect and were not included indecision-making relating to their health. Health-seeking journeys often oscillated betweentraditional and formal practices. Barriers to their ability to seek and reach care, includingdistance, poor roads, cost of transportation persisted throughout the intervention period. PeerSupport Groups impacted their mental wellbeing through mutual experience-sharing. Familyand community support enabled healthcare seeking. Support from family and friends and peersupport groups are key to engagement of persons affected by stigmatising diseases, particularlyin remote rural settings. We find using a person-centred approach for integrated casemanagement strengthens engagement across the patient pathway, promoting their participationand inclusion.

8202

THREE GEOSPATIAL APPROACHES OFFER INSIGHTS INTO PLANNING EFFECTIVE MDAS FOR NTDS IN WEST AFRICA

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Effective mass drug administration (MDA) is the cornerstone of preventive chemotherapy (PC) neglected tropical disease (NTD) programs. USAID's Act to End NTDs | West program supports Ministries of Health to eliminate or control five PC NTDs across 11 West African countries by assisting with MDAs and disease specific assessments. Coverage evaluation surveys (CES) are used to validate treatment coverage shortly after MDA. Non-treated populations (MDA eligible people in endemic districts who do not participate in the most recent treatment campaign) are of concern as they may enable ongoing transmission of infection. If these populations can be identified, programs can take more precise actions to identify and target them for treatment. Geospatial patterns of non-treated populations are identified by mapping CES data from five surveys (29,501 MDA-eligible respondents) conducted in 16 districts (879 villages) across Niger, Senegal, and Sierra Leone. Clusters of sampled villages with high rates of non-treatment are identified on the maps, as well as locations where disproportionately more men (or women) were not treated. Further, a geospatial analysis describing the travel time between households and health facilities was conducted, and the results are used as a proxy to measure village remoteness. The geospatial maps reveal clusters of high levels of non-treatment associated with remote populations in Sierra Leone and with mobile populations in both Senegal and Niger. One district-level map reveals a distinct pattern of high non-treatment villages located along district administrative boundaries. This research shows how conducting geospatial analyses of varying complexity can be used to refine NTD MDA programs. During program planning, GIS-generated travel time maps could support programs to ensure areas physically more remote from the health system receive additional support in subsequent rounds of MDA. During program evaluation, maps provide crucial insights into the effectiveness of interventions, enabling adjustments to improve microplanning ultimately contributing to the successful elimination or control of NTDs.

8203

ROLES OF COMMUNITY DRUG DISTRIBUTORS FOLLOWING THE HALT OF MASS DRUG ADMINISTRATION FOR ONCHOCERCIASIS IN UGANDA

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Mass drug administration (MDA) with ivermectin is key to onchocerciasis elimination. In Uganda, community drug distributors (CDDs), typically volunteers selected by other community members, mobilize communities for MDA, increase disease awareness, and distribute and report treatments. At peak in 2009, The Carter Center trained 77,600 CDDs in Uganda, but as transmission is interrupted, MDA is no longer required. We conducted a mixed methods, cross-sectional study in late 2023 to describe the involvement of former CDDs in other community health and development activities in formerly endemic foci that have stopped MDA. We randomly selected two subcounties per district and two parishes per subcounty, then surveyed ~162 former CDDs from the parish rosters. Twenty-two focus group discussions, 33 in-depth interviews, and 90 key informant interviews were also conducted. About 78% of 1,580 surveyed former CDDs reported that they had opportunities for service after MDA stopped, and 70.6% reported engaging in such health or development services. Nearly all (90%) felt their CDD service equipped them with skills for other service roles, and 94% reported increased interest in such work. Other activities they had performed included mosquito net distribution, health education and community sensitization, sanitation improvement, immunization, and integrated community case management. Of the 29.4% of former CDDs who did not engage in health and development after their CDD service, lack of opportunity stood as the primary barrier for 68%. The national and district Ministry of Health officers highlighted the value of CDDs' previous training and good reputations in their communities and reported integrating them where possible into health programs, though several noted that educational barriers and poor rosters of former CDDs can be practical limitations. Ultimately, this study has demonstrated that many former CDDs have been integrated into continued service activities in their communities when opportunities arose. Additional opportunities, cross-training, and improved documentation would help maximize their contributions.

8204

EFFECT OF MOBILE POPULATIONS ON STOPPING MDA FOR LYMPHATIC FILARIASIS/ONCHOCERCIASIS IN CROSS RIVER STATE

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The mobility of populations presents a significant challenge in reaching milestones to stop Lymphatic Filariasis (LF) and Onchocerciasis (OV) mass drug administration (MDA). These NTDs affect communities in remote or underserved areas where populations may be highly mobile due to factors like seasonal migration, economic opportunities, or displacement from conflict or environmental disasters. Nigeria, particularly Cross River State, borders Cameroon. In both 2019 and 2023, refugees camped in six LGAs (Aamkpa, Boki, Bakassi, Etung, Ogoja and Obanliku) in the state, staying in the camps with some later integrating into host communities. As of 2023, only Ogoja, and Etung LGAs continued to host refugees supported by UNHCR. Refugee camps often experience high population turnover as people arrive, depart, or move between camps. This mobility complicates efforts to track and treat individuals for LF and OV, as it may be challenging to ensure consistent coverage of MDA. This is further worsened by limited access to health facilities, constrained by logistical requirements or reluctance to seek medical care due to cultural or religious reasons. From 2020 till date, the state NTD program identified the LGAs and communities where refugee populations were located and collaborated with UNHCR and other International Organization to provide targeted treatments to these camps, this was further strengthened by continuous monitoring of MDA and use of members of refugees as medicines distributors (community implementers). As a result, 21,314 refugees were treated from 30,483 persons in 2020 for Oncho/LF MDA in five camps (Adagom 1, Adagom 3, Ukende, Agbokim, and Ajassor) across 2 LGAs (Ogoja and Etung), with 100% geographical coverage and 70% therapeutic coverage. The 2023 treatment was for OV only due to Implementation Units (IU) fulfillment of criterion to stop LF MDA (passed Transmission Assessment Survey TAS 1). A total of 14,804 refugees were treated, from 21,487 persons, in five camps across 2 LGAs thereby achieving 100% geographical coverage and 69% therapeutic coverage.

8205

ELIMINATING ONCHOCERCIASIS IN NIGERIA: SUCCESSES, FAILURES, AND LEARNINGS FROM CROSS RIVER STATE

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This paper explores past successes and failures of Onchocerciasis program in CRS and identifies few hypotheses on why the state is yet to reach elimination goal. Onchocerciasis prevalence mapping was completed in 1998, confirming that 15 of the 18 LGAs in CRS were endemic. After more than 20 years of Mass Drug Administration (MDA), CRS conducted epidemiological assessments in 2009, 2012, 2017 and 2023 to evaluate progress towards elimination. A 2017 assessment indicated the state had reached elimination target; 3,193 DBS samples collected in 2017, were analyzed in 2019, showing zero positive case. The NOEC recommended a repeat of the epidemiological assessment due to delays in completion of laboratory analysis. A repeat of the assessment in 2023 unexpectedly confirmed disease prevalence; 100 children aged 5-9 years of consenting parents/guardians were targeted in 34 purposively selected endemic communities; a total of 3,260 DBS samples were collected on labelled filter papers using sterile lancet needles to prick the children's fingers. The blood samples, spotted on the filter papers, and stacked onto pencil sticks, were allowed to dry completely before storage in humid-free bags packed with desiccants. Samples were analyzed using OV-16 ELISA serological test to determine presence of IgG4 antibodies. A total of 56 positive cases were found in 15 communities across 8 LGAs, resulting to 1.72% OV prevalence in the state. This result reveal evidence of ongoing OV transmission in CRS with the following hypothesis - ineffective MDA coverages formed reservoir for transmission; influx of refugees from endemic regions of Cameroun increased transmission rate and spread; populations living in hard-to-reach areas missed treatment during MDAs; there are cross border transmission from neighboring endemic communities; and there is change in vector distribution due to shifts in waterways and breeding sites over the years. Two years of additional MDA has been recommended. As we explore approaches to strengthen MDA to reach all vulnerable populations, it is crucial to consider factors like climate change and cross border movements in our future programming.

8206

LEAVING NO ONE BEHIND: STRENGTHENING MASS DRUG ADMINISTRATION CAMPAIGNS AGAINST NEGLECTED TROPICAL DISEASES THROUGH THE IMPLEMENTATION OF SUPERVISOR COVERAGE TOOL IN ANGOLA

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Mass Drug Administration (MDA) is one of the recommended public health strategies to control and eliminate preventive chemotherapy neglected tropical diseases (NTDs) in endemic regions. However, ensuring comprehensive coverage of target populations remains a challenge, particularly in resource-constrained settings and hard to reach populations. In Angola, improvement of campaigns reach has been the main focus of the Ministry of Health. In 2018, Supervisor Coverage Tool (SCT) started to be implemented alongside MDA campaigns to identify areas not reaching optimal treatment coverage thresholds. The main objective of the SCT is to identify areas not reaching optimal treatment coverage thresholds and to improve the coverage when the campaign is still ongoing. Trained supervisors used the results of the tool to direct mop-up activities to recover areas where individuals were missed, ensuring that no one is left behind. Data collected through the SCT is used to assess gaps in access, tailor outreach efforts, and optimize resource allocation for future campaigns. In 2024, SCT was implemented in 3 provinces, 13 municipalities and 52 villages. Implementation of the SCT in Angola has resulted recovering of more than 7,400 treatments during ongoing campaigns. The impact results on MDA coverage are being analyzed and will be presented. The tool has enhanced the accountability and efficiency of MDA campaigns, enabling health authorities to track and monitor adherence in real-time and adjust strategies as needed. The SCT proved to be of great support to improve MDA management and increase coverage of interventions. The tool is also used to inform ongoing campaign implementation and gaps encountered during campaigns, therefore contributing to continuously improving MDA planning and implementation.

8207

HYPERENDEMICITY OF SOIL-TRANSMITTED INFECTIONS IN CHILDREN OF THE HONDURAS TROPICAL RAINFOREST

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The Honduran Moskitia, located in the eastern region of the country, is one of the most isolated and remote geographies in Central America, as well as one of the last remaining tropical forests in the continent. Populated by Afro-Caribbean Garífuna and indigenous Miskito communities, La Moskitia inhabitants are plagued by poverty and lack of basic water and sanitation; situation conducive to intense transmission of soil-transmitted helminths (STH). According to the Ministry of Health, mass drug administration (MDA) is provided to schoolchildren twice a year, but the efficacy of this strategy is unknown. The present study aimed to undertake a rapid assessment of the prevalence of STH in a small group of schoolchildren living in the community of Kaukira in the Honduran Moskitia. The formol-ether concentration (FEC) technique was used to detect STH, and a qPCR was evaluated as a screening diagnostic tool. A total of 54 samples were analyzed by both FEC and qPCR. Two multiplex qPCR protocols were tested, each including specific primers and probes for STH identification. Following DNA detection, a spiking experiment was performed to assess the limit of detection of the qPCR for *A. lumbricoides* and *T. trichiura*. Using both methods, an overall STH prevalence of 98.2 % (CI 95%: 94.6-100%) was observed; the highest STH prevalence reported to date in Honduras. *T. trichiura* was the most prevalent parasite, followed by *A. lumbricoides, N. americanus, and S. stercoralis,* with prevalences of 92.6%, 57.4%, 37% and 7.4%, respectively. In comparison to the FEC, the qPCR demonstrated higher sensitivity, with the advantage of detecting *S. stercoralis*. The spiking experiment showed that the qPCR can detect 1 egg/100 mg of stool for both parasites. The findings of this study demonstrate that, despite undergoing bi-annual anthelminthic therapy, STH prevalence in this region is remarkably high. They also highlight that measuring achievement of the STH elimination target by 2030 requires the implementation of sensitive diagnostic techniques that allow effective surveillance, specially in regions where MDA is the single strategy for STH control.

8208

COMMUNITY LEADERS ACTION GROUP: A SOCIAL CATALYST TO INCREASE MASS DRUG ADMINISTRATION COVERAGE AND COMMUNITY SUPPORT FOR COMMUNITY-DIRECTED DISTRIBUTORS

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Onchocerciasis is a neglected tropical disease endemic in Nigeria for which a key intervention strategy is mass drug administration (MDA) with ivermectin. It is possible to interrupt transmission with 12-15 rounds of MDA; however, onchocerciasis transmission has persisted after 28 years of MDA in four districts of Edo and Enugu states, Nigeria. These two states have had low MDA coverage, with community leaders' disengagement from the MDA program having led to low community support and ownership and reduced support to community directed distributors (CDDs) of ivermectin. This study examined the impact of the "Community Leaders Action Group" (CLAG) innovation, where committed community leaders were trained to engage non-committed leaders in both their own and nearby communities to step up support for the CDDs and MDA. CLAG members acted as social catalysts to improve incentives to CDDs. Forty community leaders with histories of supporting CDDs were engaged and asked to encourage other leaders to follow suit. We reviewed reported MDA coverage data from the treatment rounds before and after the CLAG intervention in the study area, in November 2021 and December 2022, respectively. Results showed significant increase in proportion of communities offering incentives to support CDDs from 370 communities (36.3%) before CLAGs to 580 (56.9%) after ($p<0.001$). Surveys of CDDs showed that community support to CDDs (financial or gifts) increased from 616 CDDs (34.8%) to 882 CDDs (49.9%). Fewer communities had inadequate (<65%) therapeutic coverage after CLAGs (249 communities, 24.4%) than before (417 communities, 40.9%), a 40.3% risk reduction (95% confidence interval [CI] 31.9-47.6%). CLAGs remain active and reported coverage rates have remained >65% for the two years after the study. CLAGs were successful in engaging community leaders and improving MDA delivery in these Nigerian districts with persistent onchocerciasis. We recommend the CLAG training in all endemic communities to improve ownership and sustainability of NTD elimination efforts and accelerate progress toward disease elimination.

8209

A PROGRAMMATIC OVERVIEW OF THE GULF SOUTH VECTOR EDUCATIONAL CENTERS FOR TRAINING, OUTREACH, AND RESOURCES (VECTOR) COLLABORATIVE

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Vector-borne diseases have increased in the past two decades at rates beyond what current infrastructure can manage. To protect public health, we must increase and strengthen our front-line defenses, which are mosquito abatement districts and public health workers. This is particularly important in the Gulf South of the United States because of its intersection of health and economic disparities with a climate that is susceptible to vectors and pathogens. The Gulf South Vector Education Center for Training, Outreach, and Resources (Gulf South VECTOR) was funded in 2023 by the Centers for Disease Control and Prevention (NC50CK000638). This is a regional partnership of public and private organizations led by the City of New Orleans Mosquito, Termite, and Rodent Control Board, Louisiana, United States. The goal of this project is to strengthen partnerships across public and private sectors. The Gulf South VECTOR Collaborative will coordinate training and evaluation of pest management, vector control districts, public health, sanitary, and animal health professionals in these fields to achieve an integrated workforce to mitigate community vector-borne disease risk in the Gulf Coast region of the United States. The project will aim to address critical gaps in information exchange, resources, infrastructure, evaluation methods, and training standards. Specifically, this project will train and evaluate students and professionals. We will create and test educational content that highlights procedural best practices. The core curriculum will be standardized and replicated across the region, and will be offered to students, working professionals, and trainees across audiences with diverse backgrounds. This project will break down silos and promote interdisciplinary training and create partnerships through regional and national cooperation that is desperately needed to build resiliency and protect people and animals from vector-borne disease. A summary of the progress will be presented.

8210

OSELTAMIVIR, A NON-METRONIDAZOLE CLASS OF COMPOUND, AFFECTS RAFT ASSEMBLY, VESICLE BIOGENESIS, AND HOST-PARASITE INTERACTIONS BY *GIARDIA*

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Giardia lamblia is a protozoan parasite responsible for intestinal illness, worldwide. Symptoms of giardiasis include diarrhea, abdominal pain, and malnutrition in children. Metronidazole is a common treatment for giardiasis, but toxicity and resistance has been reported. Being a non-invasive parasite, the mechanisms by which *Giardia* causes infection are unclear. Recent reports have suggested that *Giardia* releases nanoscale lipid particles, called extracellular vesicles (EVs). EVs exist as two subtypes: microvesicles (MVs) and exosomes (EXOs), both of which carry virulent factors that paralyze the host's immune defenses. We reported earlier that oseltamivir (Osm, Tamiflu®), an anti-viral compound, inhibits the attachment of trophozoites to intestinal epithelial cells and cyst production *in vitro*. Osm also disassembles giardial lipid rafts (LRs) and alters the production of EVs by *Giardia*. In the current study, we optimize the anti-*Giardia* activity by synthesis of Osm analogs. The analogs were evaluated for their inhibition of giardial growth, attachment to Caco-2 cells, cyst production, LR assembly, and EV biogenesis. LR assembly was assessed using confocal microscopy. EVs were isolated by ultracentrifugation (15,000 x g for MVs and 100,000 x g for EXOs), then EV size and concentration was assessed using nanoparticle tracking analysis. Four analogs were found to reduce the growth of trophozoites (IC_{50} ~30-50 μM), attachment (IC_{50} ~65-102 μM), cyst production (IC_{50} ~40-50 μM), LR assembly, and the EV production (~20 μM). Some compounds demonstrated selective activities on MVs and EXOs, suggesting that EV subtypes are structurally and functionally distinct. We found that the release of cytokines such as CCL20, CCL2, and PLAUR was reduced by our analogs, implicating that these compounds are effective in modulating the immune response by host cells. This is the first successful targeting of EVs and demonstration of the potential of EV production as a drug target. We propose that these synthetic Osm analogs should be effective in treating metronidazole-resistant giardiasis alone or in combination with other anti-giardial agents.

8211

TRUST IN THE HEALTHCARE SYSTEM AND NATIONAL CONTROL PROGRAMMES IN A RURAL SETTING IN CAMEROON: AN ECONOMIC EXPERIMENT

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Healthcare-seeking levels are low in the sub-Saharan Africa (SSA), where patients still confront weak health systems and face several barriers to access. This is partly why the current mainstay control of schistosomiasis and other neglected tropical diseases (NTDs) is based on community-targeted mass drug administration (MDA), irrespective of individual diagnosis. Asymmetry of information, such as the lack of trust, is a determining factor for healthcare behaviours and treatment compliance in rural SSA, and is influenced by interpersonal and institutional factors. We elicited trust among patients actively seeking care at health facilities and is the first study to compare it to trust levels measured among households eligible to receive MDA treatment through community outreach. We further analysed socio-economic and health predictors of trust, controlled by provider-specific characteristics. In the Bafia district (Cameroon), we recruited 108 adults eligible for MDA treatment and 11 MDA providers (January 2024); and 116 adults seeking care at district health facilities and 18 health providers (February 2024). We conducted a trust experiment where patients and providers received endowments and faced the decision to share them (or not) between one another in a three-stage economic experiment. We also conducted socio-economic questionnaires and interviews with clinical vignettes to assess providers' clinical competence on schistosomiasis and other common health issues. Results will be presented and discussed in the context of tackling NTDs where treatment coverage is a combined measure of MDA access and treatment compliance, with the latter likely driven by trust in the healthcare system and the effectiveness of such campaigns. Inadequate coverage translates to reduced effectiveness of control strategies, which perpetuates disease transmission and hinders the World Health Organization objective of eliminating the disease as a public health problem by 2030. This study sheds light on the relevance of trust in healthcare settings and parasitic helminth interventions, which has never been evaluated before.

8212

ENHANCING COMMUNITY LEADER ENGAGEMENT IN THE FIGHT AGAINST NTDS IN CAMEROON: UNDERSTANDING KEY DETERMINANTS

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Onchocerciasis, a neglected tropical disease, remains a significant public health challenge due to its persistence. Despite the implementation of community-based control strategies, certain community groups continue to remain uninvolved, presenting barriers to its elimination. There is an urgent need for a critical review of community health implementation principles to ensure consistent and active community participation. This study aimed at exploring the factors associated with the non-implication of community leaders in the fight against NTDs in Cameroon. We conducted a qualitative and descriptive study using a pre-designed interview guide. Focus groups involving community leaders from 32 hyperendemic communities across four regions were analyzed. Quantitative data were processed using SPSS, while Nvivo facilitated transcription and content analysis for qualitative data. Among the selected communities, community leaders included members of dialogue structures, traditional chiefs, and religious leaders. Knowledge about onchocerciasis remained limited and misconceptions negatively impacted awareness and communication related to Mectizan. Interestingly, in certain villages, leaders attributed onchocerciasis to supernatural causes. Although traditional authorities are aware of Mectizan as a treatment, they do not actively participate in its implementation. Additionally, feedback on program evolution is lacking, as well as an overview of the entire fight against NTDS, particularly onchocerciasis. Efforts to effectively engage community leaders in the fight against NTDs, especially onchocerciasis, require addressing misconceptions, enhancing awareness, and fostering active participation. Feedback mechanisms and comprehensive program evaluations are essential for successful elimination strategies.

8213

INTEGRATION OF HYGIENE MEASURES FOR LYMPHEDEMA MANAGEMENT INTO COMMUNITY HEALTH CENTERS' MINIMAL PACKAGE OF ACTIVITIES IN TWO RURAL SETTINGS, MALI

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Lymphedema (LE) impedes people from carrying out their daily activities, exacerbating poverty, social exclusion, and stigmatization. Evidence demonstrates the effectiveness of routine hygiene practices in managing LE. with a reported improvement of patient's living standards. To ensure sustainability of hygiene activities, we identified obstacles to integrating LE management into community health centers' minimal package of activities. A mixed-method study was conducted in the health districts of Kolondieba and Kolokani, enrolling LE patients involved in a doxycycline trial with hygiene care in both arms. A questionnaire was administrated to participants to identify barriers and facilitators to the integration of hygiene care into the minimal package of activities. Additionally, 24 in-depth interviews and 8 focus group discussions were conducted with patients and health workers. SPSS V26 and NVivo V14 were used for quantitative and qualitative data analysis respectively. In total, we enrolled 192 LEDoxy patients with mean age of 56±11 years and a sex ratio of 0.15. Most of the participants 83% (160/192) stated that they would like to have hygiene measures integrated into the minimal package of activities. Among the 35 obstacles to the integration reported, 14 (40%) and 11 (31%) respectively the poor quality of management and the lack of qualified health workers. Lack of resources for clinicians and patients/families, high cost of treatment at health centers and the low level of knowledge of the condition by health workers were the main obstacles reported by interviewees. Key reported integration facilitators include overcoming LE stigma, enhancing workforce capacity, promoting LE self-management and families' support. Resource scarcity, patients perceived low level of knowledge of the condition by heath workers, were identified as main barriers to hygiene measures integration

into community health centers' minimal package of activities in these rural settings. Overcoming these obstacles could help in implementing a sustainable integration system

8214

LEVERAGING FULL GEOGRAPHICAL COVERAGE APPROACH TO TRACHOMATOUS TRICHIASIS CASE FINDING AND MANAGEMENT WITH CATARACT TO SUSTAIN SERVICES IN TANZANIA

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Tanzania is one of the highest burden countries for trachoma. TT elimination program aims to provide sight saving surgeries to more than 48,000 people with Trachomatous Trichiasis in Tanzania. Neglected Tropical Disease Control Program of the Ministry of Health through collaboration with Helen Keller Int'l, Sightsavers International adapted Full Geographical Coverage Approach targeting all regions and districts with high endemicity of TT for case finding and organize surgical camps at the community level to offer treatment to confirmed cases. The approach focuses on leaving no one behind for case finding and management by ensuring it is reaching everywhere and everyone in the districts where the program is being implemented. Trained community case finders are used to identify, counsel, and refer people with TT for confirmatory screening and surgical care through surgical outreach camps. Initial screenings are conducted on a house-to-house basis using community case finders. Free surgeries are offered by qualified technical teams at health facilities within the targeted regions, thus ensuring easy access to care. The approach has proven efficiency in reaching all villages in each targeted districts resulting in high coverage of households and screening majority of marginalized population groups including women and disabled people living in remote areas and also experienced high acceptance rate of surgical services. The FGC approach was further leveraged with case finding of cataract cases in the same villages, using the same case finders and screening same population which was piloted in Mbarali district on Mbeya region and similarly witnessed high coverage in reaching the population for cataract case finding and treatment and demonstrated effectiveness in increasing the reach and highly contributing to saving many people from preventable blindness caused by Trachomatous Trichiasis and cataracts as well created sustainability in the service provision in the region.

8215

THE INFLUENCE OF RUMORS AND MISINFORMATION ON ONCHOCERCIASIS ELIMINATION - EVIDENCE FROM CROSS BORDER REGION OF MALI

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After more than 15 years of mass administration of ivermectin against onchocerciasis, Mali has succeeded in pre-stop survey of onchocerciasis in most areas except for the transmission zone KA05, a cross border area that includes three health districts. To inform the mass drug administration cycle in 2024, a study was carried out in February 2023 in 6 villages of KA05 using a mixed methods approach. This abstract will present the qualitative findings from 24 individual in-depth interviews (5 women and 19 men) and (10 focus group discussions (5 women's groups and 5 men's groups). Participants were 18 years and older and were purposively selected according to the following identities: gold miners, local community members, self-identified as never treated, people with high mobility, former community drug distributors and healthcare providers. Results showed that some participants believed that the existence of onchocerciasis in KA05 was "fake news" while others reported that onchocerciasis is the result of a "curse". Other rumors included the belief that it is only adult men who are at risk of contracting onchocerciasis while some participants believed that the tablets themselves distributed during MDA bring onchocerciasis to the communities. Themes related to side effects showed that some participants confused the side effects of praziquantel (used to treat schistosomiasis) with those of ivermectin, as the two campaigns have been conducted in close proximity in the past. Others refused the treatment out of fear of being skin snipped, as had been done in previous onchocerciasis detection campaigns. This research demonstrates the strength of rumors in KA05 communities in Mali and their potential for influence on people's acceptability of mass drug administration for onchocerciasis. Despite many years of mass drug administration in the region, it is clear from this research that new social mobilization approaches are needed. It is recommended that regular adaptations are made to health awareness and education messages to address misinformation and currently circulating rumors.

8216

THE THERAPEUTIC EFFICACY OF ALBENDAZOLE AND IVERMECTIN AGAINST SOIL-TRANSMITTED HELMINTH INFECTIONS IN RWANDA

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By 2030, WHO has set a new goal of eliminating soil-transmitted helminthiasis (STH) as a public health problem in 96 out of 101 countries (96%). To achieve this goal, the tools targeting both the agent and host must exhibit optimal efficacy and effectiveness. Rwanda's neglected tropical diseases (NTD) program has been implementing mass deworming campaigns in communities and schools since 2008. However, there is persistence of high prevalence of STH in many districts, with a high proportion of moderate to high intensity infections (MHI). The National NTD Program is currently conducting a community trial to *(1)* determine and quantify the force of each of the drivers behind that persistence of MHI in order to inform the design of proportional treatment, behavioral and water, sanitation and hygiene interventions; and *(2)* test different integrated interventions package to determine the most impactful package capable of accelerating the elimination of STH as a public health problem. Here we are presenting the findings of efficacy study. In November 2023, we performed efficacy testing of a single dose of albendazole chewable (400 mg) alone and a single dose of albendazole chewable (400 mg) combined with ivermectin 200 mcg/ kg body weight. Each treatment regimen was administered by directly observed therapy (DOT). Before administering medications, a stool sample was collected from each study subject and screened for helminth eggs using duplicate kato-katz technique and egg count was performed. On the 14th day after drug administration, a follow-up stool sample was analyzed. The results showed Trichuris Trichiura mean eggs per gram (EPG) reduction of 76% by ALB+IVM compared to 17% by ALB alone. The cure rate was 45% by combined treatment compared to 13% by ALB alone. These findings showed the superior therapeutic efficacy of albendazole when combined with ivermectin to treat Trichuris Trichiura. The same evidence was demonstrated in pemba island and Laos. The scale-up of this combination treatment should be piloted to inform the large scale-up in all districts endemic to Trichuris Trichiura.

8217

UNDERSTANDING PERCEPTIONS OF SCHISTOSOMIASIS AND ITS CONTROL AMONG HIGHLY ENDEMIC LAKESHORE COMMUNITIES IN MAYUGE; UGANDA

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Over 240 million people have schistosomiasis, of which the majority live in Africa. In Uganda, over 4 million people are infected, and 55% of the population is at risk. Praziquantel mass drug administration is the WHO-recommended control strategy, but coverage is often low. How perceptions of schistosomiasis shape prevention and treatment practices and their implications for control measures are not well understood. Rapid ethnographic appraisals were performed for six weeks using structured observations, transect walks, participant observation, sixty in-depth interviews, and 19 focus group discussions. Data were analyzed thematically using iterative categorization. Community members had varied perceptions about how one can catch and transmit schistosomiasis and these perceptions affect prevention and treatment practices. Observations revealed open defecation as a common practice, low latrine numbers, and all communities largely depend on lake water and contact it daily. Perceptions that a swollen stomach was a sign/symptom of '*ekidada'* (caused by witchcraft) resulted in some people rejecting free praziquantel in favour of herbal treatment from traditional healers at a fee. Others rejected praziquantel because of its perceived side effects. People who perceived that schistosomiasis is caught from drinking unboiled lake water did not seek to minimize skin contact with infected water sources. These findings exhibit knowledge gaps and misconceptions that impacted control, necessitating a contextualized health education programme, alongside MDA, and improved WASH practices. Therefore, we co-developed a set of interventions with community members and developed education messages tailored to community needs through community meetings, local radios, drama, posters/banners, videos and training VHTs for sustainability. These education programs have improved knowledge, led to reduced misperceptions, water processing, and increased demand for praziquantel. Therefore, working with the community to co-develop tailored education messages can lead to improved knowledge and prevention practices.

8218

OUTBREAK OF *PLASMODIUM VIVAX* INFECTION IN A NATIVE COMMUNITY OF CONDORCANQUI PROVINCE, AMAZONAS, PERU IN 2023

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Amazonas ranks as the second department in Peru with the highest incidence of malaria, affecting native communities within Condorcanqui province. In 2022, an increase in P. vivax cases (1,436) was reported, followed by P. falciparum cases (203). On June 6, 2023, the first seven malaria cases were detected within the native community of Alto Kashap and on June 9 the Condorcanqui Health Network coordinated an intervention to control the outbreak. The aim of this study was to describe the intervention during the malaria outbreak in Alto Kashap within the jurisdiction of the Atzakus Health Post, which provides coverage to 236 inhabitants. During the intervention, a total of 205 patients were evaluated. A total of 23 cases of P. vivax were diagnosed by microscopy, of which 15 were confirmed using qPCR. This revealed a positivity rate of 11.22% and an annual parasitic index of 83.03%, indicating a high risk of transmission in the area. Additionally, it was observed that 52.17% of the cases were men and more than 85% were under 27 years old. All positive patients were symptomatic and received on-site treatment, consisting of a seven-day course of chloroquine and primaquine, according to technical guidelines for malaria treatment in Peru. On the other hand, although the vector species was not identified during the intervention, outdoor residual spraying was carried out in all households (77) in the community as a preventive measure. In conclusion, the intervention played a critical role in the control of the malaria outbreak in Alto Kashap and contributed to the identification of housing and geographical factors involved in the transmission of the disease. These factors include the lack of basic services, such as limited access to drinking water, insufficient sanitation systems and limited medical care. Moreover, the community's proximity to the Kashap stream increases the risk of creating habitats conducive to vector proliferation. The study emphasizes the need for continuous research and coordinated efforts, as well as the implementation of new strategies to effectively control and mitigate the spread of malaria in other communities of Condorcanqui.

8219

GEOSPATIAL MODELLING TO PREDICT SOIL-TRANSMITTED HELMINTH RISK IN SCHOOLCHILDREN IN DAK LAK PROVINCE, VIETNAM

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Soil-transmitted helminth (STH) infections pose an ongoing public health problem in Vietnam despite long-running preventive chemotherapy (PC) programs. We used parasitological data (N=10,048) collected during a trial comparing the impact of school-based PC vs community-wide mass drug administration (MDA) on STHs in schoolchildren, in conjunction with open-source environmental and climatic data. We then conducted geospatial modelling to provide STH risk predictions at baseline (October 2019) and follow-up (November 2020) throughout Dak Lak province, Vietnam. Environmental and climate variables were selected through multivariate regression models that provided the lowest Akaike information criterion without co-linearity. Semi-variograms were then used to evaluate residual spatial autocorrelation and inform use of non-spatial or spatial risk prediction models to develop STH risk prediction maps for overall risk and risk of moderate-heavy intensity infections. The overall risk prediction maps demonstrated persisting STH hotspots in south and southeast corners of the province at baseline and follow-up. These hotspots were consistently demonstrated on risk prediction models stratified by control strategy (school-based PC vs community MDA). At baseline, there were considerable areas where the predicted moderate-heavy intensity infection risk was >2%, however at follow-up most of the province was predicted to have <2% moderate-heavy intensity infection. This analysis demonstrates that whilst the burden of STH infections, as measured by infection intensity, has reduced throughout the province, there remain persistent STH hotspots in the south and southeast of the province that require further evaluation for STHs and targeted interventions.

8220

ACCEPTABILITY OF INTEGRATED NEGLECTED TROPICAL DISEASES SURVEYS AND MASS DRUG ADMINISTRATION IN VANUATU

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Soil-transmitted helminths, scabies, and yaws are neglected tropical diseases (NTDs) endemic in Vanuatu. To control and eliminate these

diseases, the Vanuatu Ministry of Health implemented an integrated control program including mass drug administration (MDA) with albendazole, azithromycin and ivermectin. Community acceptability of integrated MDA was assessed between February 2023-April 2024 in a mixed-methods study that included questionnaires, focus group discussions with residents, and in-depth interviews with community leaders. Results of Tafea and Sanma province activities are presented here, while those for Shefa province are underway.

Questionnaire data revealed 88% (35/40) of respondents in Tafea and 91% (61/67) in Sanma recalled having received MDA. Predominant factors for residents' participation in MDA were prevention of intestinal worms (Tafea: 27%[15/56]; Sanma: 37%[39/105]) or skin infections (Tafea: 27%[15/56]; Sanma 38%[40/105]). Absenteeism and forgetfulness were the main reasons for not taking the medicines in both provinces. Most respondents were happy with the number of pills they took during the integrated MDA (Tafea: 86%[30/35]; Sanma 90%[55/61]), though fewer reported liking the taste (Tafea: 71%[25/35]; Sanma 48%[29/61]). A single visit (integrated MDA) was preferred to multiple visits by most respondents (Tafea: 79%[30/38]; Sanma 83%[55/65]). Qualitative findings confirmed that communities believed they had been suffering from multiple NTDs, and that the distribution of medication would reduce NTDs in their community. Misperceptions surrounding scabies were discovered during discussions, with some perceiving acid rain to be the cause of scabies. Participants expressed that sharing results of serosurveillance and stool sample analysis with the community would improve awareness of NTD causes and prevention mechanisms. In conclusion, this study suggests that the integrated MDA was acceptable to the community. Strategies to engage local communities in both awareness creation and medicine distribution can further improve participation of the communities and MDA acceptability.

8221

PILOTING INTEGRATION OF HUMAN, ANIMAL AND ENVIRONMENTAL ANTIMICROBIAL RESISTANCE (AMR) SURVEILLANCE TO MONITOR ESBL-PRODUCING *E. COLI* USING A ONE HEALTH APPROACH IN BANGLADESH

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One Health approaches have gained prominence in global antimicrobial resistance (AMR) surveillance but such approaches are currently limited in Bangladesh. We present a protocol and scoping results on integrated One Health (human, animal and environmental) AMR surveillance to monitor extended-spectrum β-lactamase (ESBL) producing *Escherichia coli* (Ec)) in Bangladesh. Our protocol uses the WHO integrated global surveillance on ESBL-Ec "One Health" approach (Tricycle protocol) for samples from Mymensingh and Chattogram metropolitan areas Bangladesh (July 2023 to December 2025). We will collect human (blood, n=2846 and rectal swabs of healthy pregnant women, n=120), environmental (wastewater, n=120) and animal (chicken caecum, n=240) samples to test and compare the prevalence of ESBL-Ec. Environmental and animal samples will be collected by icddr,b field team and human samples by IEDCR a government agency responsible for human AMR surveillance. Human samples will be tested in local medical college hospitals, animal samples in the central disease investigation laboratory of the Department of Livestock and environmental samples at icddr,b laboratory. The results will be in a single platform used by three labs to estimate the burden of ESBL- *Ec*. To date, we have conducted a preliminary environmental surveillance for ESBL-Ec along with physicochemical properties of wastewater and river water samples including community, hospital and poultry markets. We collected a total of 59 samples of wastewater, river water and drinking water from Mymensingh (n=24) and Chattogram (n=35). We detected ESBL-Ec in all wastewater and river water samples and *Ec* in 60% of drinking water samples in Chattogram. ESBL-Ec abundance was highest in poultry wastewater. ESBL-Ec counts were significantly correlated with all the physicochemical parameters ($p<0.05$). Integrated surveillance of AMR using a One Health approach can provide valuable insights when we have human, animal data to examine the sources and transmission routes of AMR organism. This information is crucial for designing effective interventions to address this global public health challenge.

8222

MOLECULAR CHARACTERIZATION OF EXTENDED SPECTRUM BETA LACTAMASE PRODUCING ESCHERICHIA COLI AMONG CHILDREN AND FARM ANIMALS IN AGOGO, ASANTE AKIM MUNICIPAL, GHANA

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ESBL-producing *Escherichia coli* are a growing global concern, particularly in sub-Saharan Africa, including Ghana. Overuse of antibiotics in healthcare and agriculture contributes to the prevalence of ESBL resistance in both humans and livestock. The prevalence of ESBL in *E. coli* across human, animal, and hospital settings underscores Ghana's one health challenge. This study in Agogo, Ghana, aims to comprehensively investigate ESBL-producing E. coli, including genetic diversity, transmission patterns, antimicrobial resistance, and virulence genes, employing a holistic one-health approach. This cross-sectional study was conducted from June to December 2019 in the Ashanti region of Ghana. Whole genome sequencing was performed on ESBL-producing *E. coli* isolates previously identified from children with and without diarrhoea below 5 years of age and farm animals from Agogo and its nearby communities. Raw reads were assembled using TORMES pipeline. Kraken2 was used for species classification, and ResFinder to screen for antibiotic resistance genes. MLST was conducted with PubMLST schemes, while SNPs were identified via SAMtools.This study sequenced 117 ESBL-producing *E. coli* genomes: 44 from healthy children, 30 from children with diarrhea, and 43 from animals. Among them, 55.6% were typed by MLST, with the rest yielding unknown profiles. The prevalent STs were ST-2 (23.1%), ST-8 (13.8%), and ST-535 (9.2%). Eight STs were shared between humans and animals. 47 antimicrobial resistance (AMR) genes were identified, with blaCTX-M-15 present in 87.0% of isolates. Additionally, 197 virulence genes were found, crucial for bacterial pathogenicity, including invasion, adhesion, biofilm formation, and secretion of toxins. In conclusion, we identified prevalent antimicrobial resistance genes such as blaCTX-M-15 and a myriad of virulence genes, indicating the potential for heightened pathogenicity. Shared sequence types between humans and animals indicates potential transmission. Further investigation into transmission dynamics is imperative to develop targeted interventions and mitigate the spread of resistant strains.

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DETECTION OF POTENTIAL ZOONOTIC PATHOGENS FROM BAT BLOOD SAMPLES COLLECTED IN BELIZE, CENTRAL AMERICA

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The Remote Emerging Disease Intelligence-NETwork (REDI-NET) is an expert Consortium engaged in emerging infectious disease surveillance efforts. We use Oxford Nanopore Technologies (ONT) Next-Generation Sequencing (NGS) technology for metagenomic sequencing of varied environmental, invertebrate, and non-human vertebrate sentinel sample types for rapid identification of microorganisms that may represent zoonotic spillover threats to humans. Here we report outcomes from NGS testing of 85 blood samples (FTA cards) taken from 18 bat species collected in 2019 at the Lamanai Archeological Reserve, Orange Walk District, Belize, as a part of a longitudinal ecological study of infection within and between members of the diverse bat community. Our sequencing outputs indicate the presence of 55 microorganisms previously documented to cause disease in humans across three major taxa groups: bacteria (52), eukaryotic parasites (helminths; 2), and fungi (1). All 18 bat species harbored at least one of these bacteria, while helminths were unique to Lasiurus ega and Sturnira parvidens, and fungi found only in Lasiurus ega bats. No known blood-borne pathogens or viruses were detected despite PCR positivity in some of the same samples. These results are intended to guide One Health efforts and public health decision-making in Belize, and highlight the need for further development of an optimized approach to pathogen surveillance in such sample types using NGS technology.

8224

DYNAMIC SURVEILLANCE OF MULTIDRUG-RESISTANT LARGE SPECTRUM B-LACTAMASE PRODUCING ENTEROBACTERIACEAE IN SEMI-URBAN POULTRY FARMS FOR PROSPECTIVE ZOONOTIC RISKS ASSESSMENT, ABIDJAN, CÔTE D'IVOIRE

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Zoonotic pathogens' surveillance is a global health issue, especially in Limited-and-Medium Income Countries. Among these infectious disease drivers, are Large Spectrum β-Lactamase producing Enteric bacteria that could spill over from poultry into humans, and as a result pose inherent health risks to domestic animals along with pathogen transmission in urban communities and hospitals. The current study therefore, aims at detecting reservoirs of these bacteria in semi-urban poultry farms for dynamic qualitative surveillance. For this pilot study over the 2023-year period, 40 faeces samples were collected from small scale poultry sites in Bingerville; a suburb of Abidjan. Then, bacteria were primarily seeded in physiological fluid before culture on selective agar Eosin Methylene Blue (EMB), isolation by Gram staining test, identification by Leminor serial tests, and antimicrobial susceptibility test using disk diffusion method as well as E-test, with both incubation temperatures 37°C, and 44°C to determine Inhibition Diameters and Minimum Inhibition Concentrations (EUCAST; CA-SFM 2021). Results showed 20 (50%) positive *Escherichia coli* culture, out of which 13 (65%) where Large Spectrum β-Lactamase producing enteric bacteria detected at 44°C, while 07 (35%) positive E. coli were detected as wild phenotype at 37°C. In conclusion, findings demonstrated a large amount of both Cephalosporinase, and Penicillinase enzyme producing bacteria circulating over the farming sites investigated. Current study, which is carried out yearly, is extended to nineteen (19) other sites for a successful implementation of integrated surveillance, and consequently contribute to curb emergence of zoonotic pathogens due to lack of hygiene, and biosecurity over small scale farms.

8225

SPILLOVER OF HIGH PATHOGENICITY AVIAN INFLUENZA A (H5N1) VIRUS IN INDIAN FLYING FOX (*PTEROPUS MEDIUS)* BATS IN BANGLADESH

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High pathogenicity avian influenza (HPAI) outbreaks raise concerns due to pandemic potential, socioeconomic impact, and wildlife conservation risks. Here, we report unusual mortality of Indian flying fox (*Pteropus medius)* bat populations due to spillover of H5N1viruses. We monitored house crow (*Corvus splendens*) mortality events in Dhaka city between 2017 and 2023. During investigation, we observed crows and Indian flying fox bats cohabiting in the same roost and occasionally observed dead bats in the affected roosts. We collected swab and tissue samples from dead crows and bats and tested for the presence of AIV matrix gene, followed by the H5, H7, and H9 subtyping using rRT-PCR. Aside from house crows, we found 11 Indian flying foxes infected with HPAI H5N1. We detected the H5N1 virus in tissue samples (trachea, kidney, liver, lungs, and brains) of these bats, indicate the systemic infection with H5N1 and could be the reason for the bats' mortality, and potential risk of HPAI viruses to mammalian hosts. Phylogenetic analysis revealed that bat sequences belonged to the 2.3.2.1a clade, closely related to sequences from house crows and ducks in Bangladesh. The 2.3.2.1a clade comprises two major lineages: G1 and G2 and the bat sequences cluster within the G2 lineage indicating continuing evolution that have resulted segregating multiple distinct subclusters in Bangladesh. We found bat H5N1 sequences contain several amino acid mutations and genetic markers of mammal adaptation. We report the first detection of HPAI H5N1 viruses in bats in Bangladesh, concurrent with H5N1 in sympatric wild birds. Our findings suggest acute disease caused by the virus as the likely cause of mortality events in bats cohabiting with infected crows. This underscores the potential of HPAI virus to cross host barriers and infect mammals, posing a significant public health concern for future pandemics if not controlled.

8226

SEROPREVALENCE OF BACTERIAL ZOONOSES IN A BIODIVERSITY HOTSPOT: A CROSS-SECTIONAL STUDY FROM MEGHALAYA, INDIA

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Zoonotic diseases (ZDs) remain a major global public health threat, with approximately 60% of infectious diseases considered to be of zoonotic origin. The northeast region (NER) of India, which is within the Indo-Burma biodiversity hotspot, is a region of concern for ZDs due to its unique ecology, cultural practices, dietary preferences (including bushmeat consumption), agricultural practices (slash-and-burn agriculture, mixed farming) and high animal-to-human ratio. However, the risk of ZDs is

largely undetected due to a paucity of infectious-disease surveillance. We conducted a population-based serosurvey in three ecologically distinct field sites of Meghalaya (a hilly, forested and predominantly tribal state in NER) to estimate the seroprevalence of three common bacterial ZDs: scrub typhus, leptospirosis, and brucellosis. A total of 1,328 participants from 30 village-clusters were included, using age-structured sampling; 1,307 (98.4%) provided blood samples. Serum samples were tested for pathogen-specific IgG using commercially-available immunoassays. Weighted seroprevalences were calculated using sampling weights that accounted for non-response. The overall (IgG) seroprevalences of *Orientia tsutsugamushi* (scrub typhus), *Leptospira* spp. and *Brucella* spp. were 12.1% (95% CI: 10.2-14.2%), 9.1% (95% CI: 7.4-11.2%) and 4.4% (95% CI: 3.2-6.1%), respectively. Village-level seroprevalence varied considerably: 0-43.9% for *Orientia* (intraclass correlation coefficient [ICC]: 0.214), 1-27.7% for *Leptospira* (ICC: 0.115) and 0-15.6% for *Brucella* (ICC: 0.182). The seroprevalences increased with increasing age ($P<0.001$ for *Orientia* and *Leptospira*, and $P=0.020$ for *Brucella*), and differed between males (15.4%) and females (10.2%) for *Orientia* ($P=0.001$), but not for *Leptospira* (8.1% vs. 9.6%, $P=0.419$) and *Brucella* (4.0% vs. 4.7%, $P=0.563$). The complex bio-socio-environmental drivers of ZD transmission need further exploration. Our findings highlight an under-reported burden of ZDs in Meghalaya and underscore the importance of heightened surveillance in areas with close human-animal contact.

8227

DETECTION OF *TRYPANOSOMA LEWISI* FROM *RATTUS RATTUS* AND *RATTUS NORVEGICUS* IN TOLIARA, ON THE SOUTHWESTERN COAST OF MADAGASCAR

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In the island of Madagascar, over the last two decades, different studies have described the presence of *Trypanosoma lewisi* infection in *Rattus rattus* in the central highlands and on the island's eastern cost. With the aim to update the parasite inventory in small mammals, we undertook the detection of *Trypanosoma* in rodents in the southwestern part of the island. For this preliminary study, rat trapping was carried out during transversal field trips at four sites (Amborogony, Maninday in town; and at two rural villages Andranomanintsy, Amboaboaka 45 km north of Toliara) in 2022 and 2023. For each captured rat, thin blood smears were prepared, stained with Giemsa and microscopy examined on site for *Trypanosoma* detection. Blood spots were collected on Whatmann 3MM CHR filter paper and sent to the Institut Pasteur de Madagascar for *Trypanosoma* identification by PCR. DNA was extracted with the Qiagen kit. Nested PCR was performed to amplify the *Trypanosoma rRNA* gene. The PCR products of positive samples were shipped to Genoscreen (Lille, France) for sequencing. The sequences obtained were analyzed on Geneious Prime to identify *Trypanosoma* species. In total, 173 small mammals including 144 *R. norvegicus,* 25 *R. rattus* and 4 *Mus musculus* were captured. Microscopically, *Trypanosoma* was found in seven rats [4.1%; 95% CI: 1.8-8.5%] (in one *R. rattus* and in 6 *R. norvegicus*). Additionally, PCR followed by sequencing confirmed that all of these infected rats harbored *T. lewisi.* Our results demonstrate for the first time the presence of *T. lewisi* in *R. rattus* and in *R. norvegicus* in the sub arid southwestern part of Madagascar. We plan to expand our investigation to type the population of *T. lewisi* that may infect small mammals living in forests in the island's southwestern areas.

8228

TICKS AND TICK-BORNE PATHOGENS IN GHANA: A SIGNIFICANT RISK OF ZOONOTIC PATHOGEN INFECTIONS

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Ticks and tick-borne diseases negatively impact human and livestock health. In Ghana, diverse tick species are present with the occurrence of tick-borne pathogens of zoonotic and veterinary importance. To reduce future human risk for tick-borne diseases, it is imperative to identify the variables influencing tick population dynamics and tick-borne pathogens. Therefore, the purpose of this study was to determine the relationship between season, climate variables, and land use on the prevalence of ticks and tick-borne pathogens in Ghana. In addition, we predict the likelihood of detecting zoonotic tick-borne pathogens in the nation. The data from tick collections done in 2020, 2022, and 2023 were geocoded and associated with available climate data from 2012-2022. Each data point was associated with its corresponding land use category label. All analyses were performed in R version 4.1.3. A total of 3864 ticks were collected with *A. variegatum* (49.25%) as the predominant species which was more likely to be abundant in the wet season (IRR=2.40, 95%CI=2.13-2.71, $p<0.001$). The overall prevalence of pathogens in all tick species was 56.24% with zoonotic tick-borne pathogens recorded as *R. africae* (34.76%), *R. aeschlimannii* (11.03%), *C. burnetii* (2.49%), *A. capra* (0.47%) and CCHFV (0.47%). *Rickettsia africae* was more likely to be detected in ticks sampled in the wet season (OR=3.50, 95%CI=2.57-4.81, $p<0.001$). It was also observed that precipitation (OR=106, 95%CI=0-172, $p<0.001$) was highly associated with tick pathogen positivity. Land use had a significant impact on the abundance of tick species and the distribution of identified pathogens. Using multivariable logistic models, we predict that there is an increased risk of detecting zoonotic tick-borne pathogens in Northern Ghana. Our research sheds light on the intricate relationship of climate and land use on the distribution and prevalence of ticks and tick-borne pathogens in Ghana and indicates the need for increased surveillance to develop efficient control and preventive strategies.

8229

DESCRIPTIVE ANALYSIS OF ZOONOSES ACQUIRED BY TRAVELERS RETURNING TO CANADA FROM 2013-2023

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Zoonoses account for the majority of established and emerging infectious diseases across the globe. Climate change has enhanced the burden of zoonoses due to vector range expansion. Globalization impacts travelers' potential for exposure to novel or rare pathogens and the introduction to an immunologically naïve population upon return. Understanding the zoonoses acquired abroad and imported into Canada is essential to inform effective public health guidance. This study aims to describe the travel-acquired zoonoses diagnosed in Canadian residents from 2013 to 2023 using data from the Canadian cohort of GeoSentinel, the Canadian Travel Medicine Network (CanTravNet). CanTravNet is comprised of 7 sites and is estimated to represent 15-20% of all ill travelers in Canada. For the purpose of this study, only patients who were residents of Canada at time of visit to a CanTravNet site were included. Zoonotic disease was defined as pathogens with a primary transmission route of direct or indirect animal or arthropod exposure. Among the 20,459 visits made to a CanTravNet

site from 2013-2023, preliminary results indicate that 12% (n= 2,392) resulted in at least one zoonotic diagnosis. Based on the available data, the proportion of zoonotic diagnoses increased over the study period from 9% in 2013 to 19% in 2023. Of the zoonoses diagnosed, the most frequent regions of acquisition were: Sub-Saharan Africa (37%), Central America (9%) and the Caribbean (9%). The majority (98%) of zoonoses diagnosed over the study period were vector-borne, specifically mosquito-borne (77%). Malaria and dengue were the top two zoonoses diagnosed every year of the analysis except in 2021 when filariasis replaced dengue. These preliminary findings suggest mosquito-borne diseases are the primary risk for zoonotic infections among Canadian travelers. As vectors continue to expand their range and the magnitude of vector-borne outbreaks increase, this risk is expected to increase. A better understanding of which zoonoses are acquired by Canadian travelers and from where, can help inform public health education and mitigate the risk of introducing novel pathogens into Canada.

8230

BABOON-HUMAN CONFLICT, COEXISTENCE AND COMMON BABOON MICROBIOME IN AL-BAHA REGION, SAUDI ARABIA

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Papio hamadryas existence in Al-Baha Region in areas of human proximity has been observed for several decades. Such coexistence has its impact on people health and finance. The goal was to investigate areas of hot spots conflicts between people and baboon. Our data showed that baboons occur on various districts of Al-Baha Regions with social, financial and ecological impact on people. Various number of divers microbes were detected in examined faecal samples. Further work is required to understand the relevance of microbes to the ecosystem and people in the rea.

8231

PLASMODIUM SPP. AND FILARIAL INFECTIONS IN MACAQUES IN BELITUNG DISTRICT, INDONESIA

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Until recently Belitung District in Indonesia was thought to be free of human malaria and to have eliminated lymphatic filariasis (LF) caused be *Brugia malayi* in humans by mass drug administration. Surveillance surveys showed later that *B. malayi* is still endemic in the area and that in some villages up to 5% of the adult residents are infected. *B. malayi* and *Plasmodium knowlesi* are mosquito transmitted, blood borne, pathogens that infect humans and macaques. Therefore, we decided to explore the role of macaques (*Macaca fascicularis*), that are abundant in Belitung, as a reservoir host for filarial and plasmodial parasites. We collected blood samples from 163 macaque in five different villages and tested the samples by real-time PCR for filarial and *Plasmodium* infection. Filarial and *Plasmodium* DNA was found in 30.1% and 79.8% of the samples, respectively. *B. malayi* DNA was detected in 13.5% of the macaques, while other filarial DNA was detected from a *Dirofilaria* species. Co-infections with both *Plasmodium* and filarial parasites were observed in 27% of the macaques, indicating that most macaques infected with filarial parasites were also infected with *Plasmodium* spp. Sanger sequencing of the partial plasmodial small subunit rRNA (SSUrRNA) gene region confirmed the presence of at least three different *Plasmodium* species: *P. knowlesi*, *P. cynomolgi* and *P. inui*. Population genomic studies have indicated that macaques and humans share the same *B. malayi* genomic profiles in Belitung. However, it is unclear whether *P. knowlesi* in macaques are transmitted to humans in this area. This study has shown that macaques in Belitung are infected with filarial and *Plasmodium* species that can infect humans. Further research will be needed to better understand the epidemiology of both infections in macaques and their potential role as a source for human infections. This information could inform strategies to prevent transmission of these zoonoses to humans.

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COMMUNITY PRACTICES CONTRIBUTING TO MAGNITUDE AND RECURRENCE OF ANTHRAX OUTBREAK IN MURANG'A COUNTY IN KENYA, FEBRUARY 2024

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Globally, Up to 100,000 Humans Get Infected with Anthrax Annually. Kenya Reports an Average of 10 Outbreaks Every Year. Murang'a County Has Had Recurrence of Anthrax With the Most Recent in February 2024 When County Health Department Reported 18 Suspected Human Cases That Were Linked to Cow That Had Died of Unknown Cause. The Magnitude of The Outbreak and the Drivers of Recurrence Were Unknown. We Sought to Characterize Anthrax Cases and Identify Possible Drivers of Recurrence in Murang'a. We Conducted Active Case Search in Health Facilities and in Community in February 14-21, 2024. Suspected Animal Case Was Sudden Death With Non-Clotting Bleeding from Body Orifices and Confirmed Case Was Positive for *Bacillus Anthracis* by Gram Stain. Suspect Human Case Was a Case With Painless Skin Lesion (Eschar) or Abdominal Pain and Diarhoea after Exposure to a Suspected Animal Case. Cases Were Interviewed and Data Collected Were Subjected to Descriptive Analysis. We Identified 14 Animals (13 Suspected and One Confirmed) With 8.8/100,000 Attack Rate and 71 Human Cases (22 From Health Records and 49 at the Community). Of those Interviewed, 62.7%(37/59) Had Gastrointestinal Form While the Cutaneous Was 52.5%(31/59) with One Community Death; Case Fatality Rate=1.4%(1/71). Attack Rate Among Humans Was 14.3/100,000 Population Contributed by Three Of Seven Sub Counties with Kigumo Sub County Recording 31.4/100,000 Population. The Age Group in Humans 10-19 Years Were the Majority at 23.9%(17/71). Of the Animal Cases, 85.7%(12/14) Were Buried Without Following Recommended Guidelines, 7.1%(1/14) Were Fed to Dogs and 7.1%(1/14) Was Consumed by Humans. Of the Respondents That Owned Livestock 82.4%(14/17) Would Neither Disinfect Slaughter Sites Nor Vaccinate Their Livestock. We Linked the Outbreak Among the Humans to Poor Handling and Consumption of Livestock Carcasses. Improper Disposal of Carcasses Leading of Environmental Contamination and Poor Attitude Towards Livestock Vaccination Could be Contributing to the Recurrence of Anthrax Outbreaks in Murang'a. We Recommend Enhanced Community Engagement on Handling of Anthrax Cases and Livestock Vaccination.

8233

AN ANALYSIS OF RICKETTSIAL INFECTIONS AMONG FEBRILE PATIENTS IN NIGERIA

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Rickettsial infections are underrecognized yet significant public health threats in Nigeria. Because Rickettsial infections are rarely diagnosed in Nigeria, our study offers a critical insight by reviewing confirmed cases to improve understanding of its symptoms, distribution and the factors influencing its transmission across different Nigerian regions. Data from 55 PCR-confirmed Rickettsial infection cases collected through the SAFIAN study from September 2023 to April 2024 were analyzed. Participants were recruited from Gwagwalada (Federal Capital Territory), a suburban area, and Irrua (Edo State), a rural setting. The analysis focused on patient

demographics, clinical symptoms, risk factors, and outcomes. Of the 55 cases analyzed, 76% (42 cases) were reported in suburban Gwagwalada, and 24% (13 cases) in rural Irrua. The affected individuals were predominantly females (53%), with ages ranging from 5 to 80 years (mean: 32 years, SD: 18.4). The symptom profile included fever (100%), headache (58%), nausea/vomiting (25%), abdominal pain (15%), diarrhea (12%), cough (18%), arthralgia (16%), muscle pain (13%), and infrequently, rash (2%) and unusual bleeding (4%). Environmental risk factors were prominent, with 35% of cases reporting contact with domestic animals, 10% recent visits to forested areas, 35% reporting recent insect bites, and 55% noting inadequate vector control measures. Participants with occupations associated with extended outdoor stays such as farmers, artisans, miners and traders accounted for 27% of the sample. There was PCR-confirmed coinfection with malaria in 27% of the sample. The mortality rate was approximately 6%. The study highlights a significant burden of Rickettsial infections in both rural and suburban settings of Nigeria, with a notable prevalence of infections in suburban areas adjacent to dense vegetation and domestic animal habitats. These findings emphasize the need for targeted surveillance, vector control, and community education to mitigate the risk of Rickettsial diseases and enhance public health outcomes in endemic regions.

8234

A ONE HEALTH APPROACH TO ASSESSMENT OF PATHOGEN EXPOSURE ACROSS INFORMAL SETTLEMENTS: APPLICATION OF BOOT SOCK SAMPLING AND SOURCE TRACKING METHODS

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Rapid urbanisation often results in informal settlements, lacking the infrastructure necessary for separating human and animal reservoirs of disease. A One Health approach to assessing pathogen exposure, and subsequent disease risk, requires reevaluating traditional methodological approaches. In the case of pathogen exposure via soil surfaces, grab sampling provide limited spatial representation, and may not accurately reflect pathogen transmission risk. In this study, we compared traditional grab sampling of soil with a novel bootsock method. The bootsock method is a composite technique used to capture microbial data, purported to better reflect human-pathogen interactions in real world environments. Bootsock sampling outperformed grab sampling in detecting *E. coli* in laboratory experiments and measuring average *E. coli* levels in field experiments within Fijian informal settlements. Power analysis suggested that bootsock sampling demonstrated spatial representation, allowing us to assess contamination on a settlement-level scale that was time and cost-effective. 16S amplicon sequencing data was collected over two years as part of the RISE (Revitalising Informal Settlements and their Environments) program to assess sources of microbial contribution in bootsock and grab samples from Fijian and Indonesian informal settlements. Sourcetracker analysis showed a significant dominance of animal fecal contributions over human feces. In Fijian soils, dog feces made up 7.8% of the predicted microbial contribution in bootsocks, compared to the 1.1% from human feces. In grab samples, dogs accounted for 4.8%, whereas human contributions were at 2.9%. In Indonesian soils, human fecal contributions were ~0.1% in bootsocks and 0% in grab samples, while duck feces accounted for up to 20% of microbial presence in bootsocks and 12% in grab samples. Overall, the application of the bootsock method demonstrably improved the assessment of enteropathogen contamination in soils, compared to grab sampling, highlighting the potential risk of human exposure to fecal pathogens associated with animals in soil environments.

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RAPID CLADE REPLACEMENT AND IMPACT OF VACCINE DEPLOYMENT IN THE SPATIOTEMPORAL CIRCULATION OF SARS-COV-2 VARIANTS IN SAO PAULO, BRAZIL

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Since 2021, the emergence of variants of concern (VOC) has led Brazil to experience record numbers of COVID-19 cases and deaths. The increased spread of the virus, combined with a low vaccination rate, has contributed to the emergence of new mutation that may enhance viral fitness leading to the disease persistence of the disease. Due to limitations in the real-time genomic monitoring of new variants in most Brazilian states, we aimed to investigate whether genomic surveillance, coupled with epidemiological data and spatiotemporal spread of SARS-CoV-2 variants in a smaller region, can reflect the progression of the pandemic at the national level. Our findings revealed three SARS-CoV-2 variant replacements in 2021 and early 2022, corresponding
to the introduction and rise in frequency of Gamma, Delta and Omicron variants, as indicated by peaks of the Effective Reproductive Number (Reff). These distinct clade replacements triggered two waves of COVID-19 cases, which were influenced by the increasing vaccine uptake over time. Our results indicated that the effectiveness of vaccination in preventing new cases during the Delta and Omicron circulation was six and eleven times higher, respectively, than during the period when Gamma was predominant, and it was highly efficient in reducing the number of deaths. Furthermore, we demonstrated that continuous genomic monitoring in a smaller region of Brazil can reflects the national trends in the spread and evolution of SARS-CoV-2.

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ASSESSING PYRAZINOIC ACID EFFLUX VELOCITY, UNVEILING THE IMPACT OF RV1258C AND RV0191 ON PYRAZINAMIDE RESISTANCE IN MYCOBACTERIUM TUBERCULOSIS

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Tuberculosis, predominantly caused by Mycobacterium tuberculosis, remains a significant global health concern due to the emergence of drug-resistant strains. Pyrazinamide is crucial in shortening the standard treatment duration from 9-12 months to six months. Resistance to this drug typically results from mutations in the pncA gene, impairing the pyrazinamidase enzyme required for converting pyrazinamide to its active form, pyrazinoic acid. Additionally, the role of efflux pumps in resistance, particularly in the absence of pncA mutations, is poorly understood and remains underexplored. This study aims to investigate the function of the efflux pumps Rv0191 and Rv1258c and their impact on pyrazinamide resistance. Specifically, we examine how these pumps alter the dynamics of pyrazinoic acid expulsion. To achieve this, we genetically engineered the modified H37Rv Mycobacterium tuberculosis by inactivating and suppressing both genes using the techniques of Oligonucleotide-mediated Recombineering followed by Bxb1 integrase Targeting (ORBIT), and CRISPR interference. Our results reveal that the two genes confer a unique efflux pattern for pyrazinoic acid in the modified strains over six days, differing significantly from the wild-type. Using linear regression, we observed statistically significant differences in the efflux profiles at

all evaluated time points (0-140 hours), with marked reductions in the genetically modified strains. A significant reduction in both the rate and quantity of pyrazinoic acid efflux was observed following the inactivation of both genes (p<0.0001) and when Rv1258c was suppressed (mRNA level 0.195, 95% CI 0.136 - 0.254, with a p=0.0037). Future work will assess the susceptibility of these strains to pyrazinamide and pyrazinoic acid. The discovery of two involved in pyrazinamide resistance suggests a In the near future, we will test the susceptibility to pyrazinamide and pyrazinoic acid. The identification of two efflux pumps involved suggests that resistance is multifactorial in nature, improving our understanding and informing future therapeutic treatment strategies against tuberculosis.

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THE DECEPTIVE LUNG: PULMONARY TUBERCULOSIS MIMICKING INTERSTITIAL LUNG DISEASE

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Tuberculosis (TB) can present as a variety of pulmonary manifestations, many of which are similar to other respiratory illnesses. We present a case of 25-year-old woman from rural North India presented with a one-month history of persistent intermittent fever, progressive shortness of breath, and dry cough. On admission, she had type 1 respiratory failure requiring noninvasive ventilation. High-resolution computed tomography (HRCT) of the chest was suggestive of diffuse ground-glass opacities and interstitial thickening, raising suspicions of ILD. She was worked up for connective tissue diseases and other causes of ILD, which were inconclusive. However, bronchoalveolar lavage (BAL) was done and BAL fluid GeneXpert PCR identified Mycobacterium tuberculosis without rifampicin resistance. The patient was diagnosed with pulmonary tuberculosis and initiated on anti-tubercular therapy. Subsequently there was dramatic clinical and radiological improvement. This case highlights the need of considering tuberculosis when making a differential diagnosis of unusual radiological findings, especially in TB-endemic areas. Early and accurate diagnosis is critical for commencing appropriate treatment and avoiding complications.

8238

SALIVA SAMPLE FOR WEEKLY SURVEILLANCE OF SARS-COV-2 IN A PERI-URBAN COMMUNITY STUDY IN LIMA-PERÚ

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Nasopharyngeal swab samples (NPS) and nasal swabs samples (NSS) have been the most common respiratory samples used to identify SARS-CoV-2 infections during the COVID-19 pandemic. However, some previous cross-sectional studies have shown that saliva could be used as an alternative sample for SARS-CoV-2 infection identification. This alternate approach may be particularly useful for longitudinal community-based surveillance studies that require frequent and repeated collection of respiratory samples. In this study, we evaluated the sensitivity and specificity of saliva samples (SLS) for detection of SARS-CoV-2 compared with NSS and NPS in a community-based cohort study conducted in San Juan de Lurigancho in Lima, Peru during 2021. We selected NPS, NSS and SLS samples (425 of each type) that were collected simultaneously on the same day on the same person from 132 participants (including 44 children and 88 adults), with or without respiratory symptoms, studied over a 2-month period. All samples were tested by RT-PCR at a research laboratory. Using NSS as reference, SLS had a sensitivity of 95%, specificity of 97% and agreement= 96.94%, with Kappa = 0.75 (CI95%: 0.62 - 0.88). Using NPS as reference, SLS had a sensitivity of 79%, specificity of 97% and agreement= 95.53%, with Kappa = 0.64 (CI95%: 0.50 - 0.79). We did not find differences in viral load between SLS and NSS (*p*= 0.22) or between SLS and NPS (*p*= 0.71). We conclude that SLS demonstrated excellent diagnostic performance and could be used for longitudinal surveillance of SARS-CoV-2 in both children and adults in community settings.

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PENICILLIN NON-SUSCEPTIBILITY IN PNEUMOCOCCAL CARRIAGE ISOLATES FROM PATIENTS WITH ACUTE RESPIRATORY ILLNESS IN KENYA, 2017 - 2020

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Vaccines can combat antimicrobial resistance (AMR). Penicillin non-susceptible pneumococcus is a global AMR threat. Kenya introduced 10-valent pneumococcal conjugate vaccine Synflorix™ (GlaxoSmithKline, $PCV10^{GSK}$) in 2011, and switched to Pneumosil™ (Serum Institute of India, $PCV10^{SII}$) in 2022. We examined penicillin non-susceptibility in pneumococci isolated from nasopharynxes of patients with acute respiratory illness (ARI) 6-9 years after $PCV10^{GSK}$ introduction. Nasopharyngeal swabs from patients meeting a standardized ARI case definition presenting to surveillance facilities in Kibera (Nairobi informal settlement) and Asembo (rural western Kenya) were cultured for pneumococci. Specimens with <10 colonies of any bacterial growth were excluded. Serotyped isolates were tested for susceptibility to penicillin (oral non-meningitis cutoff) by broth microdilution; intermediate or resistant results were classified as non-susceptible. We combined data from the two sites and described susceptibility of the isolates to penicillin and by PCV10 product. Among 3,905 ARI patients enrolled from January 2017 to April 2020, 1,807 (46.3%) were colonized with pneumococci; AMR data were available for 922 (51.0%) isolates, including 817 (88.7%) from Asembo. Penicillin non-susceptibility was observed in 85.7% (790) of all isolates, including 92.6% (263/284) of $PCV10^{GSK}$-type, 96.0% (243/253) of $PCV10^{SII}$-type, and 82.6% (519/628) of non-PCV10 serotypes. Among 271 non-susceptible PCV10-type isolates, 52.4% (142) are included in both $PCV10^{GSK}$ and $PCV10^{SII}$ (19F [n=64], 14 [n=39], 23F [n=25], 9V [n=7], 1 [n=6], 6B [n=1]), and 45.0% (122) in $PCV10^{SII}$ only (6A [n=96], 19A [n=26]). Among 519 non-susceptible non-PCV10 serotypes, the most common serotypes were 3 (n=64), 11A (n=53), 35B (n=44). We observed high penicillin non-susceptibility in pneumococcal carriage isolates, particularly among vaccine serotypes, in the context of a mature PCV program. The recently introduced $PCV10^{SII}$ that contains 6A may be useful in combating AMR.

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EXPLORING THE ASSOCIATION OF COMMUTING PATTERNS AND TUBERCULOSIS INCIDENCE IN LIMA, PERU: INSIGHTS FROM NETWORK ANALYSIS AND GENERALIZED ADDITIVE MODELS

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One-third of the population of Lima, Peru, lives in peripheral areas and relies on overcrowded public transportation for commuting, creating a suitable environment for TB transmission. To explore the association between commuting patterns and the cumulative incidence rate (CIR) of TB in Lima, the students and workers commuting flows were extracted from the 2017 National Census data and were analyzed using network analysis techniques. An analysis at a subregion level revealed that Central Lima was the only sub-region where the out-flow of commuters was less than the in-flow, coinciding with having the lowest CIR registered (88.53/100k ppl.). The remaining subregions exhibited the inverse commuting pattern, with Eastern Lima registering the highest CIR (131.91/100k ppl.). At a district

level, correlation analysis revealed a moderate positive association between certain centrality metrics of district importance in the commuting flows and the CIR. Notably, the out-degree centrality—the number of districts residents of a particular district commute to—in the students commuting flow was the one that showed the greatest association with the CIR (r = .55, 95% CI [.26, .74]). Next, we build generalized additive models (GAM) to model the district CIR as a function of the non-linear effects of poverty indices and pollutant concentration measures, and evaluate whether the addition of any of the centrality metrics improved model fit. The best-performing GAM according to the Akaike information criterion included the percentage of households with unsatisfied basic needs, the standardized CO concentration, and the intra-strength centrality (ISC)—the percentage of commuters that do not leave their district of residence—in the students commuting flow (P < .001). After adjusting for the other predictors, the ISC showed a positive non-linear association with the CIR with greater magnitude in the predictor's distribution tails. These findings highlight a relevant association between commuting patterns and TB incidence at a sub-region and district level in the province of Lima, Peru.

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EQUITABLE AND REAL-WORLD ASSESMENT OF TUBERCULOSIS CATASTROPHIC COSTS

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One of the 3 World Health Organization priorities for ending tuberculosis (TB) by 2035 is the elimination of catastrophic costs due to TB. These are defined as costs exceeding 20% of pre-illness household annual income, because these are usually too expensive for TB treatment completion to be affordable. Surveys of costs due to TB usually interview randomly-selected patients once during treatment, recording their costs from the previous 30 days and extrapolating these to their total illness duration. These surveys take more than an hour to complete, require specially trained researchers and inevitably exclude patients who could not afford to continue TB treatment. We developed and evaluated a more equitable approach that empowered TB program staff and/or community health workers to record patients' costs data cumulatively from the time of TB diagnosis, including the more vulnerable patients who could not complete TB treatment. In place of extrapolated estimations, we recorded data on all actual costs experienced throughout the TB illness. For 174 patients, our approach showed that pretreatment costs due to TB occurred over a median 30 (interquartile range, IQR=7-78) days. When pre-treatment costs were recently recalled, the median total was $437 (IQR=95-1450). These totals costs constituted lost income $202 (IQR=0-600), medical expenses $167 (IQR=50-640) and non-medical expenses $68 (IQR=0-110). During treatment, TB-related costs totaled a further $782 (IQR=210-3,200). Thus, pretreatment plus during treatment total household costs due to TB constituted a median 12% (IQR=5-29) of pre-illness annual household income (that was median $15,960 IQR=10,200-24,000). Consequently, 34% (IQR=27-41) of households experienced catastrophic costs due to TB. When pre-treatment costs were instead assessed by late recall at the end of treatment a median 184 (IQR=157-220) days later, these estimates were very similar (all p>0.1). Our approach empowered program staff to collect important data and ensured that data assessing catastrophic costs due to TB equitably included the most vulnerable patients for whom they have greatest importance.

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HOST IMMUNOTHROMBOSIS BIOMARKER ANALYSIS TO PREDICT COVID-19 CLINICAL OUTCOMES

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Strategies to improve clinical management identification of risk factors for severe COVID-19 patients are greatly needed. Hyperactivation and dysregulation of the hemostatic and immune systems contribute to the pathophysiology of COVID-19. In this study we analyzed a panel of soluble host immune markers from hospitalized COVID-19 patients (N=140) to identify a biomarker signature attributable to severe clinical presentation. For analysis, we included factors associated with immunothrombosis - Resistin, Myeloperoxidase (MPO), soluble Supression of tumorigenicity 2 (sST2), Tissue Factor (TF), Angiopoietin 2, Interleukin 8 (IL-8), Thrombomodulin, host cell-free DNA (h-cfDNA), and mitochondrial cell-free DNA (m-cfDNA). Plasma soluble biomarkers were analyzed by ELISA or Luminex assays. Cell free DNA measurements were obtained via quantitative PCR or fluorometry. Clinical biomarkers, obtained from patient chart review, included D-dimers, C-reactive protein (CRP), fibrinogen, ferritin, lactate dehydrogenase (LDH), white blood cell count (WBC), platelet count, and total neutrophils. We conducted binary logit analysis to predict the probability of either survival (N=97), death (N=20), or mechanical ventilation (N=22). Levels of h-cfDNA were higher in deceased versus survived patients (p=0.02) and in ventilated versus non-ventilated patients (p=0.0001). Levels of the neutrophil effector molecule, Resistin, were also higher in patients under mechanical ventilation (p=0.02). Our binary logit analysis also pointed to sex (males; p=0.04) and total neutrophil count (p=0.03) as predictive factors of a fatal outcome or ventilator use. In future studies, we will complement our analysis with supervised (Random Forest Analysis) and unsupervised machine learning approaches to identify patterns distinguishing the outcome models and incorporate additional biomarkers into our study. Our results indicate that neutrophil processes are at play in disease progression and that such biomarkers should be tested further to determine their suitability as a part of the standard clinical work up.

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RIFAMPIN HETERORESISTANCE, AN IMPORTANT KEY FACTOR TO CONSIDER IN THE TUBERCULOSIS DETECTION

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This study underscores the significance of identifying heteroresistant infections in comprehensive tuberculosis (TB) diagnostics, emphasizing the coexistence of drug-resistant and susceptible *Mycobacterium tuberculosis* (MTB) populations. A retrospective analysis of 2,916 MTB whole genomes, obtained from the Tuberculosis Group in Peru from 1999 to 2020 and analyzed using TBprofiler software, was conducted. Among these genomes, 39% exhibited at least one drug resistance, 18.8% were multidrug-resistant, 1.95% displayed mixed infections with different lineages, 4.7% were heteroresistant to at least one drug, and 0.75% were specifically heteroresistant to rifampin, comprising 22 isolates. The objective was to phenotypically and genotypically characterize clinical isolates identified as rifampin heteroresistant based on their whole-genome sequencing (WGS). Four rifampin-resistant (RR-MTB) and four sensitive MTB strains were cultured using the agar proportion method (APM) and test endpoint assay (TEMA) for minimum inhibitory concentration (MIC) determination. Three colonies from each MTB isolate were selected from 7H10 solid media in both the absence and presence of rifampin (1 µg/ml). MIC determination and sequencing of the *rpoB* gene were performed for each colony. Phenotypic analysis confirmed that all MTB isolates were

rifampin heteroresistant by APM; however, only one MTB isolate was categorized as RR-MTB by TEMA (MIC_RIF >1 µg/ml). Colony isolates from rifampin-free and rifampin-supplemented media showed different MIC values and *rpoB* SNPs, indicating selective growth of strains. Colonies from rifampin-supplemented media displayed high resistance (MIC >1 µg/ml) and mutations such as S450L, while those from rifampin-free media exhibited sensitivity (MIC < 1 µg/ml) with D435Y, L452P, and L430P mutations, and some retained the wild type. Among the tested sensitive strains, no mutations in the *rpoB* gene or variations in MIC were observed. This study confirmed the coexistence of both sensitive and resistant populations within the same clinical isolate, corroborating the WGS analysis.

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REDUCTIONS IN THE DETECTION OF POTENTIAL RESPIRATORY PATHOGENS DURING SARS-COV-2 PANDEMIC LOCKDOWN: EVIDENCE FROM TWO COHORT STUDIES IN LIMA, PERÚ

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During the COVID-19 pandemic, laboratory efforts mainly focused on detecting SARS-CoV-2 infections, rarely searching for other co-pathogens. The TrueMark™ Respiratory Panel 2.0 TaqMan Array Card (TAC) allows simultaneous detection of up to 41 pathogens, including SARS-CoV-2. We collected weekly nasopharyngeal samples (NPS), from household members enrolled in two cohorts in the same district in Lima, Peru, before (Dec-2019 to Mar-2020) and during the pandemic (Dec-2020 to Mar-2021). NPS were collected regardless of symptoms. A subset of NPS from both cohorts was selected for TAC analysis. The first group consisted of 58 NPS from the pandemic cohort 21 with positive to SARS-CoV-2 by RT-PCR, and 37 with respiratory symptoms and negative for SARS-CoV-2; the second group consisted of 18 NPS from the pre-pandemic cohort, paired with 18 NPS negative for SARS-CoV-2 from the pandemic group. We found a decline in the detection of 1 or more potential pathogens other than SARS-CoV-2 in the NPS from the pre-pandemic from 72.2% (13/18) to 29.3% (17/58) in the pandemic (p=0.002). In the pre-pandemic, the pathogens most commonly detected were human *Rhinovirus* (4/18; 22.2%), *H. influenzae* (4/18; 22.2%), *S. pneumoniae* (3/18; 16.7%), and *Moraxella catarrhalis* (3/18; 16.7%); while in the pandemic group, were human *Rhinovirus* (6/58; 10.3%), *S. pneumoniae* (3/58; 5.2%) and *Cytomegalovirus* (3/58; 5.2%). In the pandemic group, the detection of potential pathogens had a small decline from 32.4% in SARS-CoV-2 negative NPS (12/37) to 23.8% in SARS-CoV-2 positive NPS (5/21) (p>0.05). We found a higher detection of potential pathogens in NPS from participants ≤18 years of age (19/29, 65.5%, CI95%: 46.1-80.9) than in >18 years of age (11/47, 23.4%, CI95%: 13.3-37.9, p<0.005), suggesting that children were the main carriers. Our study indicates that the pandemic lockdown in Peru, that included 2 years of school closures, was associated with an important reduction in the detection of potential respiratory pathogens in the nasopharynges.

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RISK FACTORS FOR ILLNESS SEVERITY AMONG HOSPITALIZED CHILDREN <5 YEARS IN PERU, 2017—2018

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It is important to establish the timing, incidence, and clinical evolution of RSV among children under 5 years old, an RSV vaccine target group. We enrolled 489 children, of which 84% (411/489) had RNA or DNA from 1 or more pathogens identified. RSV was identified in 34% (165/489) of children; 74% (133/181) of children enrolled during April—June 2018 tested positive for RSV. Of all enrolled, 21% (103/489) required supplemental oxygen therapy, 47% of which tested positive for RSV. Infants under 1 year old were at greater risk for severe illness compared to children of 1 or more years old (PR: 2.36 [95% CI: 1.02-5.49], p=0.046). Children with laboratory-confirmed RSV illness (2.05 [1.44—2.94], p<0.001), household exposure to biomass fuel embers (3.16 [1.77—5.66], p<0.001), and neurological disease (3.32 [1.61—6.83], p<0.001) were at increased risk for severe illness as compared to children with other pathogens, without biomass fuel exposure, and without neurological disease, respectively. Among SARI cases, risk factors for severe illness were RSV illness, infancy, household biomass fuel exposure, and preexisting neurological disease. These findings may help to identify children disproportionately at risk for severe illness and guide clinical care and will help to prioritize future vaccination among risk groups which include military population.

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OUT-OF-SEASON RESPIRATORY VIRUS INFECTIONS DURING THE PANDEMIC PERIOD OF SARS-COV-2 TRANSMISSION IN BRAZIL

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Evidence from multiple countries suggests that the COVID-19 pandemic disrupted transmission of other respiratory viruses. We aimed to characterize respiratory virus transmission post the emergence of SARS-CoV-2 in a cohort in Salvador, Brazil, a region that typically experienced an annual peak of influenza in winter.From Nov2021 to Oct2022, we conducted biweekly household visits to screen individuals with respiratory symptoms in an urban informal settlement, in Salvador. Symptomatic individuals and their contacts underwent interviews and nasal swab collection. Virus identification was performed by RT-PCR or multiplex PCR to detect SARS-CoV-2, influenza (Flu), and respiratory syncytial virus (RSV), followed by metagenomic analysis among participants with cough or fever who had PCR(-) results.In total, 3174 residents in 1174 households were screened ≥1 times during the study period, among which, 669 symptomatic episodes were reported. We identified 108(16%) SARS-CoV-2, 28(4%) Flu A, 14(2%) human Parainfluenza virus (HPIV), 10(1%) Rhinovirus, and 5(1%) RSV cases. Flu, HPIV, and RSV infections peaked in Nov and Dec 2021 (summer), during which low transmission of the Delta variant occurred. Whole Genome Sequencing revealed the emergence of the Omicron BA.1 variant in Jan2022. Furthermore, Flu and RSV exhibited low transmission during the winter months. The most prevalent influenza genotype was H3N2. The secondary attack rate (SAR) among house contacts was 25% (95%CI 10-47%) for Flu and 50.0% (95%CI 38-62%) for Omicron BA.1. Flu cases presented similarly to SARS-CoV-2 clinically, while HPIV-infected participants were younger (p<0.01) and experienced more symptoms (p<0.01).Our genomic surveillance for respiratory viruses during the pandemic identified an off-season summer Flu wave of transmission. This wave followed a prolonged period of low transmission and may have been caused by relaxed respiratory hygiene measures post the Delta variant transmission decline and before the emergence of Omicron variant. Finally, the household SAR for influenza was lower than the Omicron BA.1 variant, reflecting its lower transmissibility.

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VIRAL ETIOLOGY AND EPIDEMIOLOGIC INVESTIGATION OF PATIENTS WITH SEVERE ACUTE RESPIRATORY ILLNESS IN GHANA, JANUARY 2021-MAY 2022

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Severe acute respiratory illness (SARI) is prevalent in sub-Saharan Africa (SSA), contributing to approximately 77% of hospitalizations. In Ghana, limited diagnostic tools have hindered understanding of SARI etiologies. Our study aimed to determine the etiologies among individuals with SARI in Ghana. Archived oropharyngeal and nasopharyngeal specimen (n=307) collected from 29 SARI surveillance sentinel sites across Ghana during January 2021 to May 2022 were tested at the National Influenza Center using the Fast-Tracked Diagnosis Respiratory Pathogens 21 real-time quantitative polymerase chain reaction (RT-qPCR) kit and the Illumina Respiratory Pathogen ID/AMR enrichment panel for multi-pathogen detection. These specimens had previously tested negative for influenza virus and SARS-CoV-2 using the RT-PCR. Sequencing data were analyzed using the Explify Respiratory Pathogen ID/AMR Enrichment Panel application. Chi-squared analyses were used to assess statistically significant associations ($p<0.05$) between pathogens and sex, age, and symptoms. Etiology was determined for 56% (171/307) of specimens, identifying 14 viral pathogens, including adenovirus (20%), human rhinovirus (13%), human coronavirus (8%), and respiratory syncytial virus (4%). Multiple pathogens were detected among 24% (41/171) of positive specimens. Adenovirus and rhinovirus (19%, (8/41)) co-infection was the most common. Cytomegalovirus was detected most frequently among cases aged <5 years (13.8%, $p=0.005$) whilst adenovirus was most prevalent among 5-24 age group ($p=0.046$). Epstein-Barr virus detection varied by sex ($p=0.035$). Adenovirus was detected among patients with cough (28%, $p=0.060$)) and sore throat (37%, $p=0.054$). Human rhinovirus was predominant in cases with difficulty in breathing (24%, $p=0.803$). This study demonstrates the need to expand pathogen detection methods for surveillance of SARI to better understand respiratorydisease burden and to inform policy and resource allocation for medications, vaccination, and early detection of outbreaks.

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INCIDENCE OF ACUTE RESPIRATORY ILLNESSES IN CHILDREN IN A PERIURBAN COMMUNITY OF LIMA, PERU

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Acute respiratory illness (ARI) is among the leading causes of morbidity and mortality among children each year, and most occur in low- and middle-income countries. Traditional studies of common acute respiratory infections are mainly carried out in primary healthcare centers, emergency departments, and hospitals, but those do not reflect the real burden of infection within households and communities. We conducted a prospective household-based cohort study in a peri-urban community of Lima, Peru. Eligible households included at least one child 5 to 60 months of age at enrollment, which were followed through weekly home visits to identify symptoms of ARI defined as the presence of cough and/or runny nose with fever. 119 children were enrolled and followed from October 2019 to February 2020, accruing 10576 child-days at risk. Incidence rate of ARI was 5.5 episodes child/year. Higher incidence was found in female children 6.0 episodes/child/year vs. 5.1 episodes/child/year in males. The highest incidence was found in children less than 12 months with 7.8 ARI episodes/child/year (8.3episodes/child/year in female and 7.2 episodes/child/year in male) and in children between 2 and 3 years of age (6.2 episodes/child/year). Median duration of symptoms was 6 days (IQR 3-35). The most common ARI symptoms were cough (92.5%) and runny nose (81.3%), followed by fever (38.8%), difficulty breathing (25%) and wheezing (7.5%). In 49.3% episodes of ARI, caregivers sought medical attention at an outpatient clinic and 4 (0.025%) cases were treated at an emergency room. Antibiotics were used in 46 (28.8%) cases, prescribed mainly by physicians (82.6%). Our findings demonstrate a high incidence of ARI in children less than 5 years in this peri-urban community in Lima and highlights the amount of disease that remains undetected at healthcare units and the high, mostly unjustified, use of antibiotics. Further studies are needed to evaluate the burden of ARIs at the community level, their impact on child development, and the cost to society.

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TUBERCULOSIS: MEN DIE MORE

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Tuberculosis (TB) is still one of the largest killers in low-middle income countries. The World Health Organization estimates that there are more cases in men. This is thought to be due to a combination of care-seeking, biological and behavioral factors, such as increased smoking, alcohol consumption, drug use and HIV infection. The objective of this analysis was to evaluate gender-related risk to TB mortality. We invited all patients above 15 years old who started treatment for tuberculosis from 32 community health centers in Callao, Peru to participate in the Prevent TB cohort study (http://www.isrctn.com/ISRCTN17820976). They were followed-up for 18 months post recruitment during household visits. If a participant died during this time, a verbal autopsy was performed with family members .Date of death was confirmed from multiple sources including TB treatment records or death certificates. For participants who were alive, survival analysis was censored on the day of the follow-up interview or the last day someone saw the participant. 2283 participants were recruited between 07/2016 and 11/2018 with 2028 (89%) having follow-up data available for survival analysis. Males were 1.7-times more likely than females to have TB. There were 132 deaths over 1,765,504 person-years, with males 2.6-times more likely to die compared with females in this follow-up period. Therefore, time-to-event analysis with the Cox Proportional Hazard Model demonstrated that males had approximately 1.5-times higher hazard of death compared to females (HR:1.53, 95%CI:1.04-2.24,$p<0.005$). In models adjusted for age, comorbidity, rifampicin resistance treatment, diagnostic delay and disease severity (HR:1.81, 95%CI:1.08-3.02,$p<0.005$). These findings suggest that males have an increased risk of death during TB treatment independent of comorbidities, and behavioral factors that are associated with increased death. These sex differences require more research and could be explained by anything from PK/PD, adherence and immunological differences between sex.

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INCIDENCE OF SARS-COV-2 INFECTION IN A COMMUNITY COHORT IN PONCE, PUERTO RICO

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Characterizing the incidence of SARS-CoV-2 infections is important to estimate morbidity and mortality rates, identify high-risk groups, and inform mitigation efforts. Asymptomatic and mild infections often go undetected, complicating the estimation of infection rates from surveillance reports. In 2020, we implemented a community-based cohort study in Ponce, Puerto Rico (PR) to assess local SARS-CoV-2 transmission dynamics. All participants provided weekly self-collected anterior nasal swabs (ANS); additional ANS were collected from those reporting COVID-like symptoms or contact with an infected person. ANS were tested for SARS-CoV-2 by RT-PCR to identify incident infection events. Participant demographics, preventive and health care-seeking behaviors, and acute symptom data were collected using standardized questionnaires. We used Poisson regression to estimate overall and univariate infection incidence rates. Among 1,030 participants enrolled, mean age was 35.9 (range 1-97) years, 99.6% identified as Hispanic/Latino, and 37.9% had an annual household income <$20,000. In Jun 2020-Apr 2022, we detected 262 SARS-CoV-2 infection events, of which 83 (31.7%) were asymptomatic, participants sought care for 19 (10.2%), and 1 (0.4%) was fatal. Overall incidence was 3.56 (95%CI: 3.13-3.98) infections per 1,000 person-weeks (PW). Incidence was lower among participants ≥65 years (0.94, 95%CI: 0.32-1.56 per 1,000 PW) than in all other age groups. Incidence increased dramatically beginning in Dec 2021 after the Omicron variant was introduced in PR, from 0.91 (95%CI: 0.68-1.15) to 11.87 (95%CI: 10.26-13.48) infections per 1,000 PW. There was no evidence of infection rate differences by sex, employment status, household income, or COVID-19 vaccine or infection history. The frequency of mild infections and low rate of health care seeking in our cohort suggest that routine surveillance severely underestimates regional SARS-CoV-2 burden. Analyses are underway to assess the potential role of mobility, preventive behaviors, and other time-varying factors on SARS-CoV-2 infection risk.

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ASSOCIATION OF PRE-EXISTING ANTIBODY RESPONSES AND THE RISK OF SARS-COV-2 INFECTION IN A HIGHLY EXPOSED BRAZILIAN COHORT DURING THE OMICRON BQ.1 EPIDEMIC WAVE

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Post-vaccination neutralizing antibodies were found to be a correlate of protection against symptomatic illness in clinical trials of COVID-19 vaccines. However, the association between neutralizing antibodies and subsequent infection risk remains poorly characterized for variants of concern, including Omicron BQ.1, which emerged in 2022. We conducted serial household-based serosurveys in a cohort of informal settlement residents in Salvador, Brazil, in March-August 2022 ("pre-BQ.1 period"), and in November-December 2022 after the emergence of BQ.1. We identified cases of incident PCR-confirmed SARS-CoV-2 infections during the BQ.1 period. Each case was matched by age and sampling time with one PCR-negative control. We measured BQ.1-specific serum antibody responses using a pseudo-neutralization electrochemiluminescence assay (Meso Scale Discovery) and compared cases vs. controls using linear regression adjusted for age, sex, and vaccination history. Of 511 participants who underwent PCR testing in the BQ.1 period, 95.2% had at least one prior exposure to SARS-CoV-2 infection or vaccination. Of 59 PCR-positive cases, 33 (55.9%) had symptomatic illness and 34 had serum collected in the pre-BQ.1 period. Unexpectedly, in pre-BQ.1 sera collected a median 7.4 (interquartile range [IQR] 6.8-7.7) months prior to PCR testing, median pseudo-neutralization against BQ.1 was higher among cases (71.2%, IQR 38.9-86.4%) than controls (39.9%, IQR 25.9-70.9%). In contrast, there was no statistically significant difference in median pseudo-neutralization among cases (58.7%, IQR 38.5-72.6%) and controls (51.4%, IQR 27.9-83.0%) whose sera were collected at the time of PCR testing in the BQ.1 period. The lack of association between BQ.1 antibody responses and incident infection suggests that neutralizing antibodies may no longer be a meaningful correlate of protection and raises questions about their relevance for immunogenicity bridging trials of COVID-19 vaccines. The observed association of pre-BQ.1 pseudo-neutralization with higher risk of infection may reflect a combination of high attack rates and delayed time to infection.

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BIOMARKER DISCOVERY AND ASSAY DEVELOPMENT TO DETECT ANTIBODIES TO *SCHISTOSOMA HAEMATOBIUM*

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While a number of recombinant antigens have been described for detection of *Schistosoma mansoni* and *S. japonicum* infections, antigens specific for *S. haematobium* diagnosis are limited. Antibody testing is not necessarily appropriate for the monitoring and evaluation use case described in WHO's target product profiles (TPP) for schistosomiasis but it still has potential as a screening tool in the use case for determining transmission interruption and post-verification surveillance. In addition, *S. haematobium*-specific antibody tests may be helpful to support diagnosis of female genital schistosomiasis (FGS). To this end, we have identified and qualified two antibody biomarkers, rSh_SAP1 and rSh_quadruplet, for *S. haematobium.* The sensitivity and specificity of combined antigens in a multiplex bead assay (MBA) that detects total IgG (including IgG4) were 88% and 97%, respectively. As these tests met the TPP criteria as the screening assay for interruption of transmission, we conducted validation of the MBA based on these two antigens. Using a set of defined sera from paristologically-confirmed positive individuals, negative individuals, and from people who had parasitic infections that might cross-react with *S. haematobium*, the sensitivity and specificity of the MBA were 88% and 97% for rSh_quadruplet and 88% and 92% for rSh_SAP1. Combining both antigens gave a sensitivity of 92% and a specificity of 97%. Cross-reactivity was detected mostly sera from individuals infected with *Fasciola hepatica* and *Paragonimus westermani*. Next steps will include evaluation in an independent laboratory and evaluation of these antigens in a lateral flow rapid diagnostic test. Such a test could contribute to a diagnostic algorithm for FGS by identifying a history of *S. haematobium* infection in women presenting with urogenital symptoms.

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UNDERSTANDING THE IMPACT OF *SCHISTOSOMA HAEMATOBIUM* INFECTION AMONG GAMBIAN SCHOOL-AGED CHILDREN: EPIDEMIOLOGICAL AND IMMUNOLOGICAL INSIGHTS

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Schistosomiasis, caused by blood fluke of the genus *Schistosoma*, is the second deadliest parasitic disease and is found mostly in Sub-Saharan Africa. In The Gambia, infection is predominantly caused by *S. haematobium* which causes urogenital schistosomiasis, with 10% of adolescents in 2015 found to be infected by urinary egg microscopy. To assess level of infection and associated morbidity, a cross-sectional study was performed to determine the prevalence of anaemia, haematuria and *S. haematobium* infection. First, 1650 healthy children from 29 villages in Upper River region in 2018 were screened. Next, 308 children were surveyed two months later to provide longitudinal data on infection and quantitative assessment of associated morbidity. Persistent anaemia unrelated to malaria infection and/or *S haematobium* infection were identified. Prevalence of moderate to severe anaemia was 33.7% (557/1650), while 41.5% (622/1498) had urinary haematuria and 17.3% (121/698) were positive for *S. haematobium* eggs detected by microscopy. The distribution of *S. haematobium* infection exhibited a localized pattern, within two specific villages, Nyamanari and Dingiri, with the high prevalence levels, 66.9% (81/121). Overall, the intensity of infection was low, with a median of 4 eggs/10mL urine. Urinalysis of the follow-up cohort found that the prevalence of haematuria did not change across the time points (41%). Proteinuria and leukocyturia was less evident, 11% and 4% respectively. IL-6 was detected in urine and was significantly higher in those with haematuria (p=0.01). Further work includes quantification of plasma inflammatory cytokines and diagnosis of *S. haematobium* by qPCR for more accurate levels of infection. In pilot work (n=24/308), infection was found in microscopy-negative samples using qPCR. Together, these data show high levels of anaemia, haematuria and *S. haematobium* infection in The Gambia than previously reported. Therefore, using a more sensitive diagnostic to detecting low-density infections, coupled with targeted interventions in persistent areas of infection could help lead to elimination or transmission interruption

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PREVALENCE AND CHARACTERIZATION OF HEPATIC FIBROSIS AND PORTAL HYPERTENSION AMONG INDIVIDUALS LIVING IN AN *SCHISTOSOMA JAPONICUM* ENDEMIC REGION OF THE PHILIPPINES

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The Niamey protocol was developed to characterize hepatic fibrosis due to *Schistosoma mansoni*. Similar guidelines do not exist for *S. japonicum* and little is known with respect to response to Praziquantel treatment for *S. japonicum*. As a part of an NIH funded longitudinal study designed to assess the impact of annual treatment (three years) for *S. japonicum* on hepatic fibrosis, we screened individuals from endemic villages in Leyte, The Philippines. We enrolled N = 288 subjects ages 14-60 with *S. japonicum* infection who were invited to the field laboratory where history and physical exam, serum chemistries, hepatitis B antigen assay, and ultrasound of the liver and spleen using a modified Niamey protocol were conducted. Individuals with Hepatitis B and those with ultrasound findings of cirrhosis or fatty liver due to other causes such as alcohol intake were excluded. Individuals with Image Pattern A or B were considered not to have fibrosis. Individuals with Image Pattern C-F were considered to have Periportal Fibrosis and individuals with Image Pattern G were considered to have Interseptal Fibrosis. The presence or absence of portal hypertension was assessed based on the portal vein quotient (portal vein diameter/height < 7.5). Of N=203 subjects after exclusions for hepatitis B or cirrhosis (N=10, 74 respectively) fibrosis of any type due to *S. japonicum* was found in 118 (58%) of subjects. Specifically, Periportal Fibrosis was demonstrated in 70 (33%), Interseptal Fibrosis in 85 (42%), and 37 subjects (18%) had evidence of both. Men were almost twice as likely to have any type of fibrosis and over four times as likely to have both patterns. Nine subjects (4%) had evidence of portal hypertension, a significant risk factor for bleeding. All individuals with portal hypertension were male and none had purely Interseptal Fibrosis. Subjects with any type of fibrosis were treated, enrolled, and will be treated annually and followed to determine responsiveness of types of fibrosis to treatment. Interseptal Fibrosis is uniquely seen in *S. japonicum* and we will examine its responsiveness to treatment over three years.

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FEMALE GENITAL SCHISTOSOMIASIS (FGS) KNOWLEDGE GAPS AND NEEDS IN SUB-SAHARAN AFRICA: ANALYSIS AND REVIEW OF ACTION PLANS GENERATED FROM A PEER-TO-PEER EDUCATION METHOD

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Female Genital Schistosomiasis(FGS) is a neglected gynecological manifestation of schistosomiasis, affecting girls and women in sub-Saharan Africa. Misdiagnosis is common due to lack of awareness and the similarity of symptoms to other sexually-transmitted infections leaving chronic manifestations and indicating a need to increase awareness and knowledge of FGS. This mixed-method research included an inductive thematic analysis of action plans, developed by participants attending the 2021 FGS Accelerated Scale Together (FAST) Packaged virtual workshop hosted by Bridges to Development and the Geneva Learning Foundation, aimed to identify key challenges and solutions to address FGS. This study conducted quantitative analyses of baseline and endline surveys, descriptive statistics and the McNemar test, to evaluate the peer-to-peer methodology used during the workshop. The peer-to-peer education methodology was well received by participants and was associated with an increase in participant awareness, knowledge, and confidence (p<0.001). Five predominant themes describing challenges emerged: lack of awareness, misdiagnosis, lack of knowledge, lack or inadequate preventative measures and high exposure risk. Within solutions, six key themes emerged: sensitization, knowledge and education, capacity strengthening, increasing awareness, intersectoral collaboration and implementation of preventative measures. This study presents the results of a novel virtual workshop, and confirms its success and effectiveness. This study sheds light on the multifaceted challenges and potential solutions surrounding FGS, in the eyes of those who work in the target regions, highlighting the essential participation of local professions when developing projects. The training generated a holistic approach that was highlighted by multiple participants, and it is deemed essential in tackling FGS issues in multiple sub-Saharan countries. Furthermore, the peer-to-peer virtual approach is a highly effective tool for raising awareness of FGS, with the possibility of being used with NTDs.

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PREVALENCE AND INFECTION INTENSITIES OF *SCHISTOSOMA MANSONI* IN VILLAGES DESIGNATED PERSISTENT HOTSPOTS AND NON-PERSISTENT HOTSPOTS IN WESTERN KENYA

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Efforts have lately been intensified to control schistosomiasis using preventive chemotherapy using praziquantel mass drug administration (MDA) in most countries where the disease is prevalent. Previous have reported the existence of 'persistent hotspots,' villages where schistosomiasis prevalence and infection intensities remained high despite years of preventive chemotherapy. Western Kenya is one of the regions where such persistent hotspots were reported. Many years later, following implementation of school-based deworming in western Kenya, it has not been established whether further gains have been made in reducing infection prevalence and intensities. This study sought to determine whether persistent hotspot remain following years of school-based deworming program by comparing the prevalence and infection intensity of *Schistosoma mansoni* between five randomly selected persistent hotspot and non-hotspot regions in Siaya County, Western Kenya. We carried out a cross sectional study involving 500 participants (250 from the persistent hotspots, and the other 250 from non-hotspots villages) who were recruited into the study between May and September 2023. The average prevalence in the persistent hotspot villages was significantly higher than in the non-hotspot villages, *P=0.0006*. Children <18-years were 0.99 times more at risk of infection compared to adults, OR 0.99(95% CI 0.98-1). Males also had a higher risk of infection of 0.99 times compared to females, 0R 0.99(95% CI 0.98-1).The overall prevalence in the selected ten villages was 39.2%, quite significant proportion of the sampled population despite ongoing control efforts. The most notable finding of this study is the continued existence of persistence hotspots, first described in 2017, despite continuation of mass drug administration especially in school children. This finding necessitates a rethink of the control strategies currently in use, including incorporating vector control and other sanitation and hygiene (WASH) based control measures in the persistent hotspots.

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A FRAMEWORK FOR UNDERSTANDING AND ADDRESSING BIOLOGICAL AND OPERATIONAL HOTSPOTS IN SCHISTOSOMIASIS CONTROL

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Recognition of both biological and operational hotspots is crucial for effective schistosomiasis control, as each requires distinct mitigation strategies and resource allocation. To achieve the World Health Organization's (WHO) goal of eliminating schistosomiasis as a public health problem by 2030, a greater understanding of what is driving persistent high transmission, prevalence and morbidity in endemic regions is needed. Persistent 'biological hotspots', are areas which meet specific prevalence and treatment intervention targets, but transmission persists. Establishing universal thresholds to define these hotspots and effectively allocate interventions such as biannual mass drug administration and snail control, along with regular surveillance for drug resistance, can be challenging due to the inconsistency in definitions, and region-specific complexities. Recognising that there could also be 'operational hotspots', particularity stemming from insufficient treatment coverage due to factors such as a lack of access, community compliance, along with the challenge of accurately measuring treatment coverage, is vital to understand alternative drivers of ongoing transmission. In light of these challenges, we conducted an extensive literature review to evaluate WHO's current provisional definition of a persistent hotspot. We then interviewed stakeholders in the field and, using insights from both sources, proposed modifications to the definition of a biological persistent hotspot. Using this definition and the WHOs own recommendation for routine monitoring for effective treatment coverage, we produced a definition framework that aims to guide decision-making by introducing regional flexibility to the thresholds and identifying regions that require additional investigations and support to address treatment shortfalls, thereby designating regions for targeted control initiatives. By acknowledging and addressing both biological and operational drivers of transmission, we believe that the effectiveness of schistosomiasis control efforts can be enhanced toward achieving the WHO's goal of elimination.

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THE IMPACT OF EXTREME RAINFALL EVENTS ON SCHISTOSOMIASIS TRANSMISSION IN COMMUNITIES LIVING AROUND MANOMBO SPECIAL RESERVE, MADAGASCAR

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Schistosomiasis is a parasitic disease affecting over 200 million people worldwide. Madagascar ranks among the countries with the highest prevalence, with up to 52% of the population at risk. Infection occurs through contact with contaminated freshwater bodies that contain schistosome-infected aquatic snails, and is directly linked to frequency and duration of water contact, with hygiene activities and rice paddy farming being key risk factors. Climate change, through increased global temperature and extreme precipitation, can create new habitats suitable for schistosome snails, thereby potentially shifting or expanding transmission zones in Madagascar. Importantly, climate change may also affect the risk of infection by influencing the frequency and duration of water contact with freshwater bodies. This project is determining how extreme rainfall events are affecting water-based hygiene activities and schistosomiasis infection in communities living around the Manombo Special Reserve in south-eastern Madagascar. 10 rural rainforest villages with known *Schistosoma mansoni* prevalence were enrolled in this study. Microbial water contamination and snail presence was assessed in a total of 19 freshwater bodies used by villages for water contact activities. This included rivers, ponds and rice paddy fields. Additionally, we assessed *S. mansoni* prevalence and infectivity in 40 school-aged children and high-risk adults per village using duplicate Kato-Katz. Stool sample collection was paired with household surveys about water, sanitation and hygiene (WASH) infrastructure and practices. Sampling is repeated twice, in the dry season and after extreme rainfall at the beginning of the rainy season. Data collection is ongoing, and results will be available mid-2024. This project enables an in-depth assessment of how extreme rainfall events affect WASH infrastructure and practices, freshwater quality, schistosomiasis prevalence, and snail densities across a range of water sources contacted by high-risk rainforest communities.

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A PUBLIC DATABASE CATALOGING GEOGRAPHICAL, SEQUENCE AND FUNCTIONAL VARIATION IN TRPM$_{PZQ}$, A CANDIDATE LOCUS FOR PRAZIQUANTEL RESISTANCE.

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The drug praziquantel (PZQ) is used to treat NTDs caused by parasitic flatworms such as schistosomiasis, a disease that afflicts over 200 million people. While PZQ has been used clinically for four decades, heavy reliance on a single drug poses concerns related to drug resistance. This is

compounded by the lack of knowledge about the parasite target of PZQ. A parasite target of PZQ has finally been identified - a transient receptor potential ion channel in the melastatin family known as $TRPM_{PZQ}$. $TRPM_{PZQ}$ is a key locus that underlies variation in praziquantel susceptibility in the laboratory, such that it is reasonable to infer that different $TRPM_{PZQ}$ channel variants will be associated with varied sensitivities to PZQ in the field, and potentially differential treatment outcomes. Effort to detail standing and *de novo* variation in $TRPM_{PZQ}$ and correlating this genetic diversity with the functional sensitivity of $TRPM_{PZQ}$ to PZQ, and ultimately treatment outcomes, is now a priority. Here, the functional consequences of $TRPM_{PZQ}$ sequence variants from both laboratory and field studies performed by various groups have been compiled into a publicly available database (trptracker.live). This database aggregates the functional impact of each variant in a resource that allows users to assess the impact of mutations throughout the channel sequence. Each variant has been profiled in a standardized Ca^{2+} reporter assay under identical conditions enabling cross comparison of functional effects relative to the accession sequence. For field studies, geographic information is also integrated. This portal enables rapid assessment of the PZQ sensitivity of sequenced variants, and thereby prioritization of 'variants for concern' in the context of surveillance for the emergence and/or spread of variants that could underpin PZQ resistance. Users are also able to request functional profiling of any sequence variants isolated from their own data in natural schistosome populations, expanding the scope of this community-driven database to various schistosome species that infect humans and animals.

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DETECTION OF *NEORICKETTSIA SPP*. IN SUSCEPTIBLE OR RESISTANT *FASCIOLA HEPATICA* OBTAINED FROM NATURALLY INFECTED CATTLE IN CUSCO, PERU

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The genus *Neorickettsia* comprises obligate intracellular bacteria present in digeneans and capable of causing disease in animals and humans. *Fasciola hepatica* obtained from sheep in Oregon and Uruguay have been shown to harbor Neorickettsia. The role of this endosymbiont on Fasciola's lifecycle is unknown. Our study objective was to describe the prevalence of Neorickettsia sp. in adult F. hepatica with different susceptibility patterns to triclabendazole obtained from naturally infected cattle in Cusco, Peru. A total of 409 Fasciola were collected from three slaughterhouses in Cusco city, transported to the laboratory, and incubated at 37°C with 5% CO2 for 48 hours. Fully motile Fasciola were exposed to triclabendazole at a concentration of 15ug/ml. Parasite motility as a proxy of viability was evaluated at 24 and 48 hours to determine sensitivity to triclabendazole. Parasites with motility score of zero at 24 hours were considered sensitive and parasites with a motility score of 2 or 3 after 48 hours were considered resistant. DNA was extracted from adult parasites using the E.Z.N.A.® Tissue DNA Kit following the manufacturer's instructions. *Neorickettsia sp*. DNA was detected by real-time PCR targeting the bacteria heat shock protein gene (GroEL). Sixty-one parasites were classified as sensitive and 87 as resistant. The prevalence of Neorickettsia was 27.8% in sensitive and 51.5% of resistant parasites (p= 0.004). Our results suggest that Neorickettsia infection occur more often in triclabendazole resistant parasites. Further research should confirm these results and explore the potential role of Neorickettsia in resistance to triclabendazole.

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COMMUNITY PREFERENCES FOR INTERVENTIONS TO REDUCE HUMAN TO SNAIL TRANSMISSION OF SCHISTOSOMIASIS IN MAYUGE DISTRICT UGANDA

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Over 240 million people have schistosomiasis. *Schistosoma mansoni* transmission occurs when eggs in faeces enter fresh water, hatch into miracidia, penetrate intermediate snail hosts, which releases infective cercariae. Governments have deployed praziquantel mass drug administration to control schistosomiasis. However, alternative interventions are required for communities to reach the WHO 2030 goal. Understanding community preferences for control interventions will help improve uptake and sustainable use. This study elicited community's preferences for interventions aimed at minimizing human to snail transmission. Stakeholder workshops, with school-age children, women, fisherfolks and opinion leaders, were held in three highendemicity communities in Mayuge, Uganda. The life cycle and interventions, previously suggested by rapid ethnographic appraisals, were presented. Enforcing fines for open defecation, constructing latrines at the lake, market, within a five minute walk from homes and maintaining latrines to higher standard were discussed and prioritized by popularity, affordability and preferred attributes. Facilitators for the use of the top two were discussed. Latrines by the lake and market were the most preferred interventions, followed by open defecation fines. Latrines with many stanzas, working hand washing facilities, cleaning materials and easily accessed were the most reported preferences. Forming open defecation committees, Having bylaws and sensitizing community members on dangers of open defecation. Facilitators included hand washing facilities, well maintained, having a caretaker, and open defecation fines. Stakeholders emphasized community member sensitization as facilitators. Findings indicate preferences of communities who live around infected water bodies that are popular, affordable and sustainable for interventions that reduce human to snail transmission. These would improve on routine usage and coupled with enforcing open defecation would contain excreta from reaching water bodies reducing disease transmission.

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UNRAVELLING THE TRUE IMPACT OF SCHISTOSOMIASIS: REDEFINING THE WHO ELIMINATION AS A PUBLIC HEALTH PROBLEM TARGET

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Schistosomiasis remains a global health challenge, affecting millions worldwide. Current strategies for morbidity control and targets for elimination as a public health problem (EPHP) are based on the intensity of infection, the latter focusing on having <1% heavy-intensity infections. However, evidence suggests that associations between intensity and morbidity are not linear, and as the distribution of schistosomiasis morbidity moves towards more subtle rather than severe disease, correlations between intensity and morbidity become even more complex. Additionally, conventional diagnostic methods, relying on egg counts in urine or faeces, are inadequate in detecting low-intensity infections or predicting long-term morbidity. The delayed onset of symptoms further complicates early diagnosis and intervention. In this context, does the concept of EPHP and

the emphasis on egg counts have true meaning to those affected by the disease? We performed a comprehensive review to highlight the impact of schistosomiasis, extending beyond the established physical health consequences, as well as the pitfalls in current research to address the complexity of schistosomiasis and its far-reaching impacts. We provide a broader perspective to inform more effective public health interventions and policy frameworks and how to monitor them. We discuss how incorporating novel biomarkers and assessing the broader and "true" impact of schistosomiasis on overall quality of life, including physical, psychosocial, downstream economic and societal aspects, and spillover opportunity costs, can offer promising avenues for deeper insights into the lived experiences of those grappling with the disease. There is a need for a holistic approach to schistosomiasis control, one that embraces advanced diagnostics, and expands morbidity metrics. Only by addressing these challenges head-on can we ensure that interventions are not only effective but also equitable and responsive to the needs of individuals and communities, improving global health outcomes.

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MAPPING AND VALIDATION OF MICROSATELLITE MARKERS FOR *SCHISTOSOMA HAEMATOBIUM*: INSIGHTS FROM POOLED SAMPLES IN SENEGAL AND GABON

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Understanding the population genetics of *Schistosoma haematobium* transmission within and between communities is crucial for identifying transmission agents, monitoring resistance and reinfections, and evaluating mass treatment effectiveness. Microsatellite markers have proven effective in estimating these measures. While 10 markers are sufficient, 15-20 markers are ideal for *S. mansoni*. Therefore, we aimed to create and validate a catalog of published microsatellite markers for *S. haematobium*. A literature review compiled published *S. haematobium* tri- and tetramer microsatellite markers, which were then mapped in silico to the karyotyped Shae.V2 *S. haematobium* reference genome using Geneious software. Marker characteristics, including chromosomal location, orientation, repeat region presence, uniqueness, and overlap, were recorded. Selected markers were validated using both a lab strain and pooled field samples from Senegal and Gabon, with fragment analysis employed to observe allele presence and proportions.Results: Of the 41 published markers, 10 are on the sex chromosome, rendering them unsuitable for some population genetic analyses, 7 have primer sites on different chromosomes, 3 enclose a complex repeat region which leads to more difficult interpretation than for simple repeats, 3 do not contain a repeat region, and 2 overlap with another 2 so we can only use one for each overlap. There are 16 published microsatellite markers suitable for population genetic analyses. Fragment analysis revealed 87 alleles across these markers in a laboratory strain. The presence and proportions of alleles were compared between a lab strain and 125 samples from human infections from Senegal and Gabon. Not all published microsatellite markers are useful for population genetic analyses of *S. haematobium*. Pooled samples demonstrate efficacy in estimating diversity and differentiation measures for *S. haematobium* infrapopulations, paralleling findings from previous studies on *S. mansoni* communities in Brazil. In silico analyses may change with subsequent versions of the genomic sequence.

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EFFECT OF *SCHISTOSOMA MANSONI* INFECTION ON GUT MICROBIOTA IN PRE-SCHOOL AGED CHILDREN IN ALBERTINE REGION, UGANDA.

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Schistosomiasis is associated with changes in gut microbiota, a key player in egg transit as evidenced from experimental mouse models. Microbial diversity is widely considered a measure of gut health. We present comparison of microbial communities between *S. mansoni* infected (*Sm+)* and non-infected Pre-school aged children (PSAC) using 16S-amplicon sequencing. We further offer a clinical perspective on the observed effects of infection on gut microbiota community structure and function. PSAC aged 12–47 months were recruited from Albertine region of Western Uganda. *S.mansoni* infected samples were from the Praziquantel in Pre-schoolers (PIP) dose finding trial. Non-infected controls were recruited from the same region. Stool microbial DNA was extracted using QIAamp® Fast DNA Stool Mini Kit. A V4-16S-rRNA-amplicon library was generated by PCR amplification and sequenced using the Illumina MiSeq v3 Reagent kit. The data were analysed/visualised using box plots, Principal Coordinates Analysis, UniFrac and other functional parameters. A total of 114 participants were recruited with equal numbers between the groups. Median age was 30.0 months (IQR 27.0 – 34.4) and 42.4% were female. (Sm+) was associated with higher species relative abundance, increased alpha diversity – Shannon Index (p-value<0.001) and Simpson Index (p-value=0.002); increased beta diversity – Bray Curtis distances (p-value=0.001). In the Sm+ group, Oscillospirales, *Prevotella* and *Oscillospiraceae* were expanded while *Bacilli, Enterobacteriaceae, Lactobacillales*, Lachnospirales and *Lachnospiraceae* were reduced. PiCrust2 analysis inferred that pyruvate synthesis, starch metabolism and amino acid synthesis were downregulated. We report increased abundance and diversity of microbial communities in *Sm+* PSAC. While these alterations aid schistosome egg passage, the reduction in pyruvate, amino acids and starch metabolism are likely to have adverse effects on nutrition and cognition, both of which are clinical entities associated with schistosomiasis. Research exploring further clinical perspectives is required.

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CHARACTERIZATION AND FUNCTIONAL ANALYSIS OF THE MICROBIOTA OF THE INTERMEDIATE HOSTS OF SCHISTOSOMES

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Aquatic snails act as the important intermediate hosts of schistosome helminths. Snail haemolymph has been shown by others to have a diverse microbiome, but the impact of a helminth infection has not yet been reported. Since the host microbiome has the potential to influence the transmission of the parasites we sought to investigate this area of host-parasite-bacteria interactions. Here, we characterised the bacterial species and abundance comprising the whole snail microbiota using 16S rRNA sequencing. Naïve, "infection failed" and patent snails were examined for *Biomphalaria glabrata* and *Schistosoma mansoni* parasites. The results of our study show that there are significant differences in beta diversity metrics based on infection status and highlighted key genera with linear discriminant analysis. Additionally, we carried out predicted functional analysis on these reads using PICRUSt2 to highlight key metabolic pathways between infected and uninfected snails. Based on these results

we further explored the *B. glabrata* microbiome using metagenomics. Snail homogenates containing microorganisms were added to microbiological growth media and gDNA extracted for shotgun sequencing. Our results present a new view on the unique interplay between the aquatic snail host, the schistosome infection and the bacteria present. From this information we a better understanding of mutualism between parasites and bacteria, as well as better understanding of the biology of the schistosome lifecycle during the aquatic transmissible stages.

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DNA METHYLATION PROFILES IN UROTHELIAL BLADDER CANCER TISSUES AND CHILDREN WITH SCHISTOSOMIASIS FROM EGGUA, OGUN STATE NIGERIA

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Squamous cell carcinoma, the most frequent kind of bladder cancer in regions where schistosomiasis is endemic, has been connected to chronic schistosomiasis. In this study, we set out to evaluate early promoter DNA methylation in a few genes linked to bladder cancer associated with schistosomiasis. In the Eggua Community of Ogun State, 159 school-age children provided urine samples, which were then analysed by microscopy to check for Schistosoma haematobium eggs. A subset of 34 (21.1%) urine samples positive for *S. haematobium*, was age and sex-matched with negative urine samples. These samples, together with 16 formalin-fixed paraffin-embedded bladder cancer tissues from University College Hospital Ibadan, were all processed using DNA isolation and bisulphite DNA conversion techniques. The methylation status of APC, RARβ2, and other target genes was assessed using quantitative methylation-specific PCR. Schistosomiasis positive samples had higher levels of methylation of the genes RARβ2 (67.7%), RASSF1A (38.2%), and TIMP3 (52.9%) compared to negative urine samples and bladder cancer tissues. In comparison to the matched controls, the positive urine samples had promoter DNA methylation that was 1.4, 13.3, 3.4, and 3.8 times greater in *APC, RARβ2, RASSF1A, and TIMP3*, respectively. Although there were no significant associations, the odds of promoter methylation were expected to increase with age group for *APC* (OR: 1.615) and *TIMP3* (OR: 2.000); sex for *TIMP3* (OR: 2.644); and haematuria for *RARβ2* (OR: 1.094), *RASSF1A* (OR: 1.143), and *TIMP3* (OR: 1.842). In patients with schistosomiasis, gene promoter DNA methylation was observed in tumour suppressor genes. Thus, children with active schistosomiasis may experience promoter DNA methylation. This might serve as an early non-invasive biomarker to detect and hint at the risk of developing schistosomiasis-associated bladder cancer later in life.

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DEEP HUMORAL PROFILING COUPLED WITH MACHINE LEARNING REVEALS NOVEL DIAGNOSTIC AND MORBIDITY BIOMARKERS FOR SCHISTOSOMIASIS PATHOPHYSIOLOGY

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Schistosomiasis continues to cause substantial morbidity in endemic regions. Current diagnostic methods relying on parasite egg detection or existing antibody (Ab) tests do not provide a way to detect disease-associated morbidity. Here we use a multiplexed 'Ab-omics' platform to obtain a comprehensive array of anti-helminth humoral profiles (isotypes, FcR-binding, and glycosylation). We apply machine learning to this high-dimensional data to reveal unique Ab signatures predictive of infection and morbidity. Serum from subjects (n=60, from Kenya), with and without abdominal ultrasound-detectable morbidity, previously screened for parasite eggs (Kato-Katz), were characterized with the Ab-omics workflow with multiple *S. mansoni* antigens (SEA, Sm25, Sm29, MEG, CD63, Calumenin) and other helminth and non-helminth antigens. Antigen-coated barcoded beads were incubated with serum and probed. Overall, a complex interplay with increases in both activating (IgG1) and inhibitory subclasses (IgG4) and pro-inflammatory (FcR2A, FcR3A) and anti-inflammatory (FcR2B, galactosylation) changes in antigen-specific Abs were seen in Egg+ vs Egg- sera. With a total of 144 measured features (12 Ab Fc probes x 12 antigens) from each patient, application of a LASSO-SVM machine learning model, revealed a minimal Ab signature capable of differentiating Egg+ from Egg- individuals accurately (AuC>0.9). This included both antigen-specific Ab titer (SEA-IgG) and Fc receptor binding (Sm29-FcR1, SEA-FcR2b). Within the Egg+ subset, interestingly reduced IgG1 but increased IgG4 was seen in those with morbidity. While neither Ab titer nor egg counts were predictive of ultrasound morbidity, the machine learning model revealed a distinct Ab signature, including IgG1 Abs against Sm29, and Fc receptor binding (Calumenin-FcR1, Sm25-FcR3b), that was able to distinguish those with and without morbidity (AuC>0.8). Our findings suggest that a purely Ab-based biomarker can achieve accurate diagnosis of both schistosome infection and associated morbidity in endemic areas.

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THE ROLE OF INTESTINAL MORBIDITY IN THE PATHOGENESIS OF ANEMIA AMONG YOUNG CHILDREN FROM LAKE ALBERT, UGANDA WITH *SCHISTOSOMA MANSONI* INFECTION

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There is a significant global burden of disease due to anemia among individuals living in low- and middle-income countries. Schistosomiasis has been shown to cause both iron deficiency anemia (IDA) and non-iron anemia (NIDA), the latter largely due to anemia of inflammation. Though the presence of worms and eggs in the vasculature and tissues are thought to drive inflammation, it is possible that disruptions in the gut wall as eggs pass from the sterile bloodstream to the intestines also contribute, specifically, through microbial translocation (MT) as microbial products enter the blood stream culminating in inflammation. In this study, 345 Ugandan children aged 12-48 months infected with egg patent Schistosoma *mansoni* were recruited from villages along Lake Albert, Uganda. Infection intensity was determined by Kato Katz. WHO age adjusted cutoffs for hemoglobin (< 11 g/dL) were used to determine presence of anemia. Among anemic children, serum ferritin levels were used to classify children as having IDA (≤ 30 ng/mL) or NIDA (> 30 ng/mL). Biomarkers capturing gut wall integrity/MT [occult blood loss and serum endotoxin core antibody (EndoCAb)], epithelial damage [serum intestinal fatty acid binding protein (I-FABP)], gut inflammation (fecal calprotectin), and epithelial permeability [fecal alpha-1 antitrypsin (AAT)] were assessed. We used multivariable regression models to assess the relationship between markers of intestinal morbidity and anemia type. Higher schistosomiasis intensity was associated with increased risk of both IDA (OR 1.36, 95% CI 1.12-1.65, p=0.002) and NIDA (OR 1.23, 95% CI 1.03-1.46, p=0.02) compared to no anemia after adjusting for confounders. Calprotectin and AAT were associated with increased risk of IDA (OR 1.36, 95% CI 1.02-1.81, p = 0.03; OR 1.25, 95% CI 0.99-1.58, p = 0.06, respectively). Further, both AAT and calprotectin were associated with occult blood loss, suggesting intestinal morbidity culminates in IDA due to occult blood loss in the stool.

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SCHISTOSOMIASIS JAPONICUM INFECTION IN THE PHILIPPINES: LOW PREVALENCE AMONG CHILDREN AGED 1-4 YEARS AND CORRELATION BETWEEN HELMINTH BURDEN AND INTESTINE INFLAMMATION

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Schistosomiasis remains a public health problem in endemic areas in the Philippines. Infection with *Schistosoma japonicum* in children is associated with poor nutritional status. Preventive chemotherapy, through annual mass drug administration (MDA) of praziquantel has been conducted in endemic provinces among 5-65 years old. There is limited data on clinical trials on praziquantel for children under 5 years old. This age window coincides with the "praziquantel treatment gap," which highlights the fact that this age group remains excluded from preventive chemotherapy campaigns, which represent the primary approach to reducing infections in endemic regions globally. We screened 1081 participants in 64 barangays. 975 participants submitted three stool samples for Kato-Katz and 17 (1.74%) turned positive for *S. japonicum* which was eventually recruited for treatment and follow up. Mean age was 2.29 years and 70% (12) were males. Co-infection with *Ascaris lumbricoides* was found in five participants and three participants had *Trichuris trichiura*. Stool calprotectin test was used to check for inflammation in the gastrointestinal tract, elevated calprotectin concentration (> 80 ug/g) was at 64% (11). All 17 participants tested negative for fecal occult blood test. Elevated white blood cell count (WBC), in the absence of other concomitant infection was found in 64% (11) of the participants. One participant with schistosomiasis, ascaris and trichuris coinfection had a hemoglobin of 9 g/dL. Our study has several limitations including the sample size, light intensity of infection, limited inflammatory markers used among others. Despite the considerable size of our study population and light intensity of infection we observed an elevated calprotectin and WBC in our study participants. Follow up of participants is being done to determine whether treatment of schistosomiasis and STH infection would result in significant changes in the markers and to monitor for possible reinfection. Future work to investigate schistosomiasis burden and treatment in this age group would significantly decrease the morbidity and end organ complications.

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SCHISTOSOMA MANSONI INFECTION IN THE SNAIL *BIOMPHALARIA GLABRATA*, IS ASSOCIATED WITH EXPRESSION PERTURBATION OF CARBONIC ANHYDRASE, THE HIV TRANS-ACTIVATOR OF TRANSCRIPTION, AND TELOMERASE

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Telomerase is a ribonucleoprotein complex that maintains telomeres at the proximal ends of chromosomes, adding repeats to the 3' chromosome end. Human telomerase (hTERT) regulation is tightly linked to the cell cycle and cell differentiation states governing both malignancy and senescence. The HIV Trans-Activator of Transcription (HIV-TAT) is used by HIV to upregulate viral transcription, thus increasing viral transmission between cells. TAT proteins also alter cell membrane selective permeability by rearranging phospholipid bonds; these altered cells have ultimately shown resistance to apoptosis and necrosis. Carbonic anhydrases (CA's) govern intracellular conversions of carbon dioxide into bicarbonate ions and protons. CA's combine with proton transporters to move ions across the cell membrane to maintain homeostatic intracellular pH. In cancer cells, CA's favor proton-expelling activity, creating an acidic extracellular environment which promotes cancer cell growth and tumor proliferation. Cancer development resembles parasitic disease as it depends on the host's biochemical and molecular pathways to progress. The snail/schistosome relationship provides a model to examine the regulation of cancer-associated genes, such as the gastropod homologs of hTERT, CA, and TAT. To test this hypothesis in relation to the development of *Schistosoma mansoni* in *Biomphalaria glabrata*, we identified *B. glabrata's* hTERT, CA, and TAT homologs and studied their expression by qPCR. A temporal-dependent regulation of CA, TAT, and snail TERT during the progression of *S. mansoni* infection was observed; these transcripts were upregulated in *B. glabrata* 30 minutes post-infection. Treating susceptible snails with anti-telomerase drugs BPPA and BIBR before infection blocked parasite cercariae shedding in the drug-treated snails, and treating susceptible snails with sodium salicylate before infection resulted in CA downregulation and prevented cercariae shedding. These findings indicate that as in malignancy, regulation of TERT, CA, and TAT may be critical for the intra-molluscan stage of development in the *B. glabrata* snail host.

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TROGOCYTOSIS: A POTENT MECHANISM FOR HOST RESISTANCE TO SCHISTOSOMIASIS

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Host specificity is the outcome of long-term coevolution between pathogens and their hosts, and remains an area of paramount importance extensively studied within the field of disease ecology, yet many mechanisms are still enigmatic. *Schistosoma japonicum* exhibits a typical host specificity, being susceptible to humans and most mammals (including mice), while *Microtus fortis* exhibits natural anti-schistosome characteristics. Thus, comparison of schistosome infection in *M. fortis* with the infection in laboratory mice provides a unique perspective for exploring and understanding host specificity. In this study, we found that a large number of immune cells adhered to the surface of schistosomes in *M. fortis*, a phenomenon that was not observed in mice. By isolating immune cells attached to the parasite surface for single-cell RNA-sequencing, most of these cells were identified as macrophages. We further confirmed that the *M. fortis* macrophages kill schistosomes through a novel pathway known as "trogocytosis". This is the first report of host immune cells using "trogocytosis" to kill multicellular pathogens. Furthermore, we demonstrated that the adherence of *M. fortis* macrophages to the surface of the schistosomes and their subsequent trogocytosis are mediated by complement C3 and complement receptor 3 (CR3). We also clarified that the activation of the Ca^{2+}/NFAT signaling is a key regulator enabling macrophages to perform "trogocytosis". These findings not only elucidate a novel anti-schistosome mechanism in *M. fortis* but also provide a better understanding of host-parasite interactions, host specificity and the potential generation of novel strategies for schistosomiasis control.

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THE INTERACTION OF HOP, STRESS PROTEINS, AND PIWI IN THE MECHANISM OF CANALIZATION UNDERSCORES THE SUSCEPTIBILITY OF *BIOMPHALARIA GLABRATA* TO *SCHISTOSOMA MANSONI* INFECTION

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Schistosoma mansoni is a parasitic flatworm that is the causative agent for the chronic debilitating disease schistosomiasis. *Biomphalaria glabrata*, is the obligatory intermediate host of this parasite, enabling the larval forms to develop into infectious cercariae. With praziquantel being the single drug for schistosomiasis, which is only effective in killing adult parasites but not any larval stages. There is an impetus towards developing new remedies against schistosomiasis. To develop new intervention tools to eradicate schistosomiasis, emphasis has been placed on interrupting the development of the parasite in the snail. Thus far, results have shown that the early induction of stress, manifested by the induction of heat shock proteins (HSPs), such as Hsp70 and Hsp90, is a prerequisite step in juvenile

snail susceptibility to parasite infection. To determine the involvement of HSPs in the snail-schistosome interaction, we hypothesized that stress inhibitor drugs, such as curcumin and PU-H71, affecting Hsp70 and Hsp90, respectively, would affect the outcome of infection in susceptible snails. Results show that treatment of susceptible snails with these drugs inhibited parasite infection (no cercariae shedding) after 6-weeks post-exposure in drug-treated snails. To determine the effect of these drugs in inhibiting *S. mansoni* infection in the snail host, we examined the regulation of the specific transcripts encoding Hsp70, Hsp90, HOP, and PIWI in drug-treated versus non-treated infected snails. In addition, we examined whether the mechanism of canalization, involving the expression of HOP concurrent with the expression of the stress encoding transcripts underscores *B. glabrata* susceptibility to *S. mansoni* infection. By using gene silencing studies with siRNA corresponding to HOP, results showed that suppressing the expression of HOP prevented schistosome infection in the snail host. This data provides evidence that the interaction of HOP with Hsp70, Hsp90, and PIWI maintains cell homeostasis by a mechanism known as canalization in the snail-schistosome relationship.

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COMMUNITY AND INDIVIDUAL PREFERENCES FOR A NEW WATER INFRASTRUCTURE FOR NON-DRINKING ACTIVITIES IN A SCHISTOSOMIASIS ENDEMIC AREA

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Schistosomiasis is a water-borne parasitic disease affecting 240 million people worldwide. Schistosomes sexually reproduce in humans releasing eggs through urine/faeces which infect freshwater snails, where they reproduce asexually releasing hundreds of cercariae/day. These cercariae burrow directly into humans on contact with contaminated water. Mass drug administration has been the WHO recommended strategy for nearly 20 years, and whilst successful in some areas, there are hotspots across Africa. Additional non-pharmaceutical interventions are needed to meet the WHO goal of eliminating schistosomiasis as a public health problem by 2030 such as improved access to safe water, sanitation and hygiene (WaSH). Non-governmental organisations (NGOs) play a vital role in implementing WaSH infrastructure in low-income countries, however 30-50% of WaSH projects implemented cease to be used after 2 – 5 years. To increase access, both uptake *and* sustainability of WaSH infrastructure needs to be considered. Qualitative research can provide valuable insights into community needs and help co-design solutions that effectively address these needs. In February 2023, data were collected from community members in Bugoto, a high-endemicity community in Uganda, through in-depth interviews (IDIs) (n=21) and focus group discussions (FGDs) (n=4). Thematic analysis using NVIVO14 software was employed to code the data into themes, followed by iterative characterization to analyse selected themes. Insights gained from this research shed light on non-drinking water usage patterns, as well as facilitators and barriers to accessing various water sources within the community. Furthermore, preferences for future water infrastructure for non-drinking purposes were identified resulting in five major themes. These findings, combined with observational data gathered during the researcher's time in Bugoto, will inform the design of future interventions tailored to the community's preferences and requirements.

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ASSOCIATIONS BETWEEN INDICATORS OF WATER, SANITATION AND HYGIENE (WASH) AND MALARIA RISK: A STUDY OF URBAN SETTLEMENTS IN NIGERIA

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While global efforts have made strides in malaria control, Nigeria's rapid urban growth, along with other challenges of urbanization, often outpaces infrastructure development. This leads to inadequate access to clean water, sanitation facilities, and proper hygiene practices, thereby increasing the risk of infectious diseases like malaria. Consequently, there is a pressing need for further investigation into the relationship between Water, Sanitation, and Hygiene (WASH) practices and malaria infection in urban settlements. A cross-sectional survey conducted in Ibadan metropolis during the 2023 wet season investigated the impact of WASH practices on malaria across formal, informal, and slum settlements. Water and sanitation variables were categorized into improved (e.g., piped water sources, flush toilets) and unimproved (e.g., rainwater, pit latrines without slabs). Hygiene practices were derived using Principal Component Analysis (PCA) based on environmental factors, identifying ineffective hygiene practices below the median PCA. Malaria presence was assessed using rapid diagnostic tests, adjusting for age, gender, and insecticide-treated net (ITN) presence through multiple linear regression. Of 7123 individuals tested, weighted malaria rates were 3.45%, 3.96%, and 12.16% in formal, informal, and slum areas, respectively. Poor WASH practices were more prevalent in slums (87%) than formal (63%) and informal (79%) settlements. Across all areas, unimproved sanitation and poor hygiene correlated with higher malaria risk (unimproved sanitation facilities: aOR 1.74, 95% CI 1.30–2.32, $P < 0.0002$; ineffective hygiene: aOR 1.41, 95% CI 1.12–1.78, $P < 0.004$). Due to the correlation between WASH practices and malaria risk observed in this study, suggested interventions to boost urban WASH infrastructure include upgrading water sources, enhancing sanitation facilities, and promoting hygiene. Strategies may include building or renovating sanitation facilities, installing piped water systems, and distributing water purification tablets or hygiene kits, thereby reducing malaria and enhancing public health.

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ASSOCIATIONS BETWEEN MICRONUTRIENT STATUS, HORMONES, AND IMMUNE STATUS DURING PREGNANCY AND CHILD GROWTH IN RURAL BANGLADESH

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Poor growth in early childhood is associated with increased mortality, impaired cognitive development, and reduced adult economic productivity, which may result in higher risks of social immobility and intergenerational poverty. This observational study used data collected from the WASH Benefits trial in rural Bangladesh to examine associations between maternal hormones (CRP, AGP, cytokine-sum-score), immune status (plasma cortisol, estriol), and micronutrient status (Vitamin D, ferritin, sTfR, RBP) during the first and second trimesters of pregnancy and subsequent measures of child growth. Length-for-age z-score (LAZ) weight-for-length z-score (WLZ), and insulin-like growth factor 1 (IGF-1) at 3, 14, and 28 months were measured as the primary outcomes. All outcomes were adjusted for confounding variables, and the p-values were adjusted using the Benjamini-Hochberg procedure. We used generalized additive models, adjusted for covariates, and reported the mean difference in outcomes between the 25th and 75th percentile of the exposure distribution. In this substudy (n=575), maternal prenatal α1-acid glycoprotein (AGP), the cytokine sum score, retinol binding protein (RBP), and estriol were associated with child growth. AGP was inversely associated with WLZ at age 14 months. The cytokine sum score was inversely associated with WLZ at 28 months. RBP was positively associated with WLZ at 3 months and 14 months. Estriol was positively associated with LAZ and IGF-1 at 14 months. Identifying early interventions aimed at optimizing the *in-utero* milieu may be a helpful strategy for promotion of healthy growth trajectories throughout childhood.

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WEATHER AND SEASON PREDICTORS OF INFANT DIARRHEAL ILLNESS AND HOUSEHOLD STORED WATER CONTAMINATION IN CLIMATE-VULNERABLE, URBAN, COASTAL MOZAMBIQUE

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Improvements in water, sanitation, and hygiene (WASH) have the potential to reduce the global burden of diarrhea, a leading cause of mortality for under-5 children. However, extreme weather events associated with climate change may compromise the effectiveness of WASH infrastructure to reduce the risk of diarrhea. We quantified associations between weather conditions, drinking water quality, and infant diarrhea in a climate-vulnerable low-income urban setting. We leveraged the data from a cluster-matched cohort study in Beira, Mozambique, that followed 642 mother-child dyads from pregnancy through 12 months old. We collected information on demographics and health using household surveys, tested for bacterial contamination in household stored water, and obtained weather data from a land surface station. We used generalized linear mixed-effects models to evaluate associations between (1) weather (i.e. season [rainy vs. dry], heavy rainfall events [presence vs. absence of 95th percentile rain event], ambient temperature [continuous (°C)], and flooding [presence vs. absence of flooding around household (reported)]) and stored water quality, (2) weather and infant diarrhea, and (3) stored water quality and infant diarrhea. We found that heavy rainfall (aOR: 1.66; 95% CI: [1.09, 2.51]), temperature (β: 1.40 [1.27,1.55]), and season (aOR: 1.95 [1.58,2.40]) were all associated with higher odds of stored water contamination. Rainy season was associated with a 32% higher period prevalence of infant diarrhea (aOR: 1.32 [1.01,1.73]), and there was a 10% increase in infant diarrhea per 1 °C of ambient temperature. We did not find an association between stored water quality and infant diarrhea. Our findings suggest associations of season and extreme weather on stored water quality and infant diarrhea, highlighting the importance of integrating climate resiliency into WASH strategies for reducing the burden of diarrhea, particularly in low-income urban settings.

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PROCESS EVALUATION FOR THE DELIVERY OF A WATER, SANITATION AND HYGIENE MOBILE HEALTH PROGRAM IN THE DEMOCRATIC REPUBLIC OF THE CONGO: RANDOMIZED CONTROLLED TRIAL OF THE PREVENTIVE INTERVENTION FOR CHOLERA FOR 7 DAYS (PICHA7) PROGRAM

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In the Democratic Republic of the Congo (DRC), there over 85 million diarrhea episodes annually. Effective and scalable water, sanitation, and hygiene (WASH) interventions are needed to reduce diarrheal diseases. Mobile health (mHealth) reminders of public health information has been shown to reduce disease morbidity and increase health-protective behaviors. Given the high household mobile phone coverage in DRC (>80%), WASH mHealth programs present a promising approach to improve WASH behaviors. The objective of the Preventive-Intervention-for-Cholera-for-7-days (PICHA7) study was to develop evidence-based WASH interventions to reduce severe diarrheal diseases in DRC using a combination of mHealth and in-person visits. The PICHA7 mHealth program delivered weekly voice, text, and interactive voice response (IVR) quiz messages to diarrhea patient households promoting handwashing with soap, water treatment, and safe water storage over a 12-month period. The randomized controlled trial (RCT) of the PICHA7 program was in urban eastern DRC from November 2021 to November 2023. The objective of this study was to assess the implementation of the PICHA7 mHealth program in delivering mHealth messages during this RCT. During the PICHA7 RCT, 1196 participants received weekly text, voice and IVR quiz messages from the PICHA7 mHealth program over the 12-month program. Outcome indicators included unique text, voice, and IVR messages received (fidelity) and % of unique messages fully listened to (dose). Unique text messages were received by 84% of program households, and 85% of unique voice and 77% of unique IVR messages answered were fully listened by at least one household member. Less than 2% of mobile messages failed. These findings show high fidelity and dose of mobile messages delivered for the PICHA7 mHealth program. This demonstrates the feasibility of delivering the PICHA7 mHealth program in eastern DRC and provides important insights for delivering WASH mHealth programing in low- and middle-income countries globally.

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SYSTEMATIC REVIEW OF THE ASSOCIATION BETWEEN COLIFORM BACTERIA IN DRINKING WATER AND DIARRHEA

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In this systematic review, we challenge whether *Escherichia coli* (E. coli) and fecal coliforms in water predict disease outcomes. Our objective was to review existing observational studies and assess the impact of water quality on various health indicators, including diarrhea, nutritional status, and gastrointestinal diseases in low- and middle-income countries. We searched using PRISMA guidelines on PubMed and web of science to identify the relevant articles using search criteria that identified studies that included water quality, health outcomes, and coliforms. We included peer-reviewed observational studies in low and middle-income countries that explored the relationship between fecal coliforms and/or E. coli in water and health outcomes. 18 studies were used for data extraction. Furthermore,

we included the relevant articles from a previous systematic review. Based on our inclusion criteria, an additional 11 studies were included from Gruber et al., totaling 29 studies included in our systematic review. The final search was performed on June 22nd, 2023. Of the thirty-one studies, only six had significant results (20.7% of all), one studied fecal coliforms, and five studied E.coli. Even within the studies with significant results, some did not control for confounding, others only sampled water at the source in the public domain and not in the domestic or personal domain, the time between sampling and diarrhea cases was weeks (up to 12), and seasonality was not considered. These results undermine the association between E.coli and fecal coliforms as proxies for health outcomes related to water quality in observational studies. Based on our systematic review of available literature, despite tradition, there is limited evidence to support using E.coli and fecal coliforms as proxy measures for human health outcomes. Based on this systematic review, future research should focus on the effects of water quantity, animal proximity, food, and water storage practices to establish a more concrete link to human health outcomes.

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UNIVERSITY STUDENT AWARENESS OF INTESTINAL PARASITES AND PREVENTIVE BEHAVIOR IN EASTERN SAUDI ARABIA

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Good awareness and preventive behaviors among populations mitigate the prevalence of intestinal parasitic infection (IPI). A cross-sectional study was conducted from January to May 2023 to assess and compare the awareness and preventive behaviors towards IPIs among 1,829 students from health (562) and non-health (1,267) colleges, at Imam Abdulrahman bin Faisal University. Data on student characteristics were collected through questionnaires. Nearly half (48.9%) of the students delineated good awareness about IPIs, students from health faculty had higher awareness than non-health faculty (P<0.001). Female students were more aware of intestinal parasites than males (P<0.001). There was no significant association between student academic year and parent's education level, on student awareness of IPIs and preventive behavior. The majority of the students possessed poor intestinal parasite preventive behavior. Interestingly, students from non-health faculty had better intestinal parasite preventive behavior than students from health faculty (P<0.05), and male students had better prevention behavior than female students (P<0.05). Strategies and curricula must be developed to reinforce preventive behavior and promote awareness of IPIs in university students.

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INFLUENCE OF MATERNAL AND CHILD FUT2 SECRETOR STATUS ON GROWTH AND ON THE EFFICACY OF WATER, SANITATION, HANDWASHING, AND NUTRITION INTERVENTIONS ON ENVIRONMENTAL ENTERIC DYSFUNCTION IN RURAL BANGLADESH

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The fucosyltransferase-2 (FUT2) gene indicates blood group secretor status, which can affect risk of infection, possibly affecting child growth. We investigated whether maternal and child secretor status are risk factors for poor child growth and whether they are effect modifiers of interventions on child environmental enteric dysfunction. In the WASH Benefits trial in rural Bangladesh, 720 clusters of 5551 pregnant women were randomized to 7 arms. We assessed 4 arms: control; combined water, sanitation, and handwashing intervention (WSH); nutrition intervention (N); and combined N+WSH. Across 1499 children, 68.2% were secretors (S), 21.5% non-secretors (NS), and 10.3% inconclusive; across 1379 mothers, 64.8% were S, 22.3% NS, and 12.9% inconclusive. Measurements were taken at ages 3, 14, and 28 months, analyzed using generalized linear models adjusted for baseline confounders. Child NS status was associated with 0.10 SD lower length-for-age Z score (-0.15, -0.05), 15% higher risk of stunting (1.06, 1.24), and 25% higher risk of severe stunting (1.02, 1.53). NS status was associated with 0.06 SD lower weight-for-age Z score (WAZ) (-0.11, -0.01) and 0.09 SD lower head circumference Z score (-0.15, -0.04). By measurement round, maternal NS status was associated with 0.13 SD higher WAZ at 3 months (0.05, 0.20). Child and maternal NS status were both associated with 0.10 log ng/ml lower child myeloperoxidase [(-0.14, -0.05), (-0.15, -0.06), respectively]. Maternal S status was a significant modifier of the effect of WSH on child alpha-1 antitrypsin at 14 months (p=0.03) and the effects of WSH and N on child myeloperoxidase at 28 months (p=0.01, p=0.03, respectively). Child S status was a significant effect modifier of WSH on myeloperoxidase at 14 months (p=0.02). Overall, we report mixed associations: maternal NS status was associated with lower child gut permeability and inflammation and child NS was associated with lower gut inflammation, but child S had improved growth outcomes. FUT2 secretor status was not a significant effect modifier of interventions on most outcomes, but future studies using targeted genomics may find new associations.

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USE OF SOLAR DISINFECTION WITH ALUMINUM TO IMPROVE WATER QUALITY IN RURAL AREAS OF THE NORTHERN ANDES OF PERU

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The Calo River basin, situated in the Amazon region within the montane forests of the Andes in Northeastern Peru, serves as a crucial hub for livestock activities. Extensive cattle ranching constitutes the primary economic activity in this region, with cattle having unrestricted access to water sources for drinking. However, this unregulated leads to significant environmental and health issues, impacting environmental sustainability and public health. The main objective of this study was to assess the efficacy of employing solar water disinfection (SODIS) with commercial aluminum to enhance water quality sustainably while evaluating its suitability for use by livestock and the general population. The most important parameters for water quality were established and variations of these

parameters were analyzed based on the type of SODIS and season. Simultaneously, the study compared these parameters against national and international standards for water quality targeting animal and human consumption. It was determined that parameters such as fecal coliforms, Escherichia coli, turbidity, ammonium, iron, calcium, lead, and arsenic are essential for the study. By applying Principal Component Analysis (PCA), it was demonstrated that all models of the SODIS system incorporating photocatalysis are viable options for treating water intended for animal consumption which was particularly evident during the dry season, spanning from June to November. Conversely, regarding water for human consumption, although the levels of contaminants were reduced, certain parameters such as fecal coliforms, E. coli, lead, and arsenic remained above regulatory limits. Therefore, it is recommended to employ SODIS with commercial aluminum as a complement to other treatment systems, such as multiple filtration systems. Finally, the implemented systems have proven to be effective in producing water suitable for animal consumption after undergoing one month of treatment.

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SEVEN YEARS OF EXPOSURE TO A HIGHLY FECAL CONTAMINATED ENVIRONMENT: A STUDY IN 24 INFORMAL SETTLEMENTS IN THE ASIA-PACIFIC REGION

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People living in urban informal settlements of the Global South are at high risk of contractingdiarrhoeal disease, which causes 500,000 deaths among children every year. Globally, a billion peoplelive in informal settlements, where they are underserved by critical infrastructure including water andsanitation services – giving rise to environmental contamination. Determining the scale of faecalcontamination in water sources and soil that residents interact with is crucial for understandingimpacts on their health and wellbeing. Since 2018, the Revitalising Informal Settlements and theirEnvironment (RISE) program has collaborated with 24 informal settlements in Fiji and Indonesia toassess the impacts of a nature-based intervention for managing wastewater on human exposure tofaecal contamination. The intervention, a treatment train consisting of pressure tanks and constructedwetlands, aims to reduce environmental faecal contamination in these communities. Approximately1200 water samples and 1100 soil samples have been collected longitudinally between 2018 and 2024,prior to completion of the intervention. We found that more than 90% of recreational water samplesshowed *E. coli* levels to be above good quality inland water guidelines, indicating persistent exposureto human and/or animal faecal waste over the 7-year pre-intervention period. Well samples, which areused for washing, bathing, or drinking, failed to meet WHO drinking water guidelines, also implyingpotential exposure to faecal pathogens. Soil samples collected from the local environment also showed*E. coli* contamination, reaching 10^4 MPN/g (dry weight). Our study provides novel insights into the scaleof contamination in a wide variety of water sources and soil, expanding our understanding of humanexposure to faecal contamination in informal settlements in Asia-Pacific.

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MATERNAL ESTRIOL DURING EARLY GESTATION IS ASSOCIATED WITH CHILD DEVELOPMENT IN RURAL BANGLADESH

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Maternal factors during pregnancy may affect child development during the postnatal period. This study investigated the potential associations between maternal hormones, immune status, micronutrient status, and child development. This was an observational substudy nested in a randomized controlled trial that took place in rural areas in Bangladesh (n=516). We examined maternal cortisol, estriol, micronutrient status, C-reactive protein (CRP), alpha-1-acid glycoprotein (AGP), and 13 cytokines during the first and second trimesters of pregnancy. Child development outcomes were assessed using the WHO gross motor milestones module at age 1 year, the MacArthur-Bates Communicative Development Inventories, and the Extended Ages and Stages Questionnaire. For the data analysis, we constructed generalized additive models and reported the mean difference in the outcome between the 25th and 75th percentile of the exposure after adjusting for covariates. Maternal estriol during pregnancy was positively associated with the sum score of WHO gross motor milestones at age 14 months (an adjusted difference of 0.22 more motor milestones attained in the 75th percentile compared to the 25th [95% confidence interval 0.07, 0.38]). This result remained significant after the Benjamini-Hochberg procedure was used to determine the false discovery rate (FDR correction) ($p = 0.04$). There were no significant associations between maternal cortisol, CRP, AGP, interferon gamma (IFN-γ) as a measure of the inflammatory process, cytokine sum score, vitamin D (25-hydroxy-D [25(OH)D]), ferritin, soluble transferrin receptor (sTfR), retinol binding protein (RBP), and child development at ages 14 and 28 months. Maternal estriol levels during pregnancy may play an important role in a child reaching their motor milestones during the first year of life.

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MONITORING ANTIBIOTIC RESISTANCE GENES ACROSS NEW ORLEANS RIVER AND LAKE WATERS

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The World Health Organization's list of priority pathogens highlights *Enterobacteriaceae* resistant to carbapenems and 3rd generation cephalosporins as a critical threat to human health. These bacteria cause severe disease and systemic infection, posing significant danger to care facilities, particularly when first-line antibiotics prove ineffective. *E. coli* and *Klebsiella*, specifically, are gut commensals that can be found in highly contaminated surface waters and have high potential for developing resistance. The Mississippi River receives organic waste from sources such as agriculture and human excretion, making it a favorable environment for the development and exchange of antibiotic resistance genes (ARGs). This study investigates the water microbiome of two shoreline sites on the Mississippi River and a site on the more brackish Lake Ponchartrain, all of which see a high flux of visitors year-round. In this study, abundance and composition of resistant bacteria are evaluated by coliform count estimates and cultivation of resistant *E. coli* and *Klebsiella.* Additionally, we evaluate the presence/absence of ARGs responsible for 3rd generation cephalosporin and carbapenem resistance. Fecal contamination levels are measured using qPCR of markers for both human and ruminant indicative *Bacteroidales* and *Lachnospiraceae.* Microbiome diversity is assessed by 16S rRNA gene sequencing. We hypothesize that there is a quantifiable difference in counts of antibiotic resistant bacteria and ARGs across the three sites. Over a one-year time scale, the highest levels and diversity, over the year, are expected in the river at Jackson Square, a high-density urban area. Preliminary data show similar counts of resistant bacteria at the two river sites, yet the lake exhibits higher counts. Of importance, all sites show much lower levels of fecal contamination indicators and resistant bacteria than urban sites in Brazil, for example. This study establishes a baseline for antibiotic resistance in New Orleans waters that will inform future monitoring efforts.

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DETECTION OF *SALMONELLA* TYPHI AND *BLA*$_{CTX-M}$ GENES IN DRINKING WATER, WASTEWATER, AND ENVIRONMENTAL BIOFILMS IN SINDH PROVINCE, PAKISTAN

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Typhoid fever poses a significant public health risk, particularly in low- and middle-income countries where access to clean water and improved sanitation may be limited. In Pakistan, this risk is especially serious given the emergence of an extensively drug-resistant (XDR) *Salmonella* Typhi strain, a strain attributed to *S*. Typhi acquisition of the *bla*$_{CTX-M-15}$ gene. This now-dominant XDR *S.* Typhi strain, non-XDR *S.* Typhi strains, and *bla*$_{CTX-M}$ genes are readily disseminated via drinking water and wastewater in Pakistan and may also be present in biofilms associated with these environmental sources. This study investigates the presence of *S*. Typhi and *bla*$_{CTX-M}$ genes within these environmental compartments. Drinking water (n=35) or wastewater samples (n=35) and samples of their associated biofilms were collected from Karachi and Hyderabad, Pakistan. Samples were tested by PCR for *S*. Typhi and *bla*$_{CTX-M}$ group 1 genes as a proxy for *bla*$_{CTX-M-15}$. Heterotrophic plate counts (HPC) were conducted to assess sample microbial load. *S*. Typhi was detected by PCR in one bulk wastewater sample and one drinking water biofilm. *Bla*$_{CTX-M}$ group 1 genes were detected in all sample types and were detected more frequently in bulk wastewater (n=13/35) than in drinking water (n=2/35) and more frequently overall in biofilm samples (n=22/70) versus bulk water (n=15/70). Detection of *bla*$_{CTX-M}$ in biofilm was not significantly associated with detection in the associated bulk water sample. This study marks the first detection of *S*. Typhi in drinking water biofilms and the first report of *bla*$_{CTX-M}$ genes in environmental biofilms in Pakistan. Environmental biofilms, particularly in drinking water systems, may serve as reservoirs for human exposure to *S*. Typhi and drug resistance genes. This study underscores the importance of expanding surveillance strategies to include biofilm sampling, providing valuable insights into pathogen dissemination in water systems, and informing targeted public health interventions to prevent waterborne diseases.

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THE INTERPLAY AMONG GLUCOSYLCERAMIDE TRANSFERASE AND ENCYSTATION-SPECIFIC PROTEINS IS IMPORTANT FOR DRIVING THE PROCESS OF CYST FORMATION BY AN ANCIENT PROTOZOAN, *GIARDIA LAMBLIA*

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Giardia lamblia is an intestinal protozoan and the primary cause of waterborne illness known as "giardiasis." *Giardia* cysts, transmit the infection via contaminated water, contain a protective fibrous cyst wall composed of unique N-acetylgalactosamine (GalNAc) polymer and giardial cyst wall proteins (gCWPs). We have demonstrated that encystation stimulation induced the expression of giardial glucosylceramide transferase (gGlcT1) enzyme, while giardial long chain fatty acyl elongase (gFAELO) is expressed in trophozoites and downregulated during encystation. The current study examines how gGlcT1 interacts with the changes in the production of gCWPs and drives the encystation and cyst production process. We are also interested in exploring if gFAELO counteracts the function of gGlcT1 and the possible dynamic interactions between these enzymes, which are critical for continuing the encystation-excystation cycle of this waterborne pathogen. In a novel approach, we assessed gGlcT1 expression during encystation using enzymatic and immunoblot analysis. We also generated gGlcT1 overexpressed, knockdown, and mutant cell lines of *Giardia* to elucidate the role of full-length and truncated gGlcT1 on encystation hall marks. Furthermore, we investigated the possibility of gFAELO affecting gCWP production by overexpressing and coexpressing gFAELO and gGlcT1. We found that the level of CWP expression changed in various gGlcT1 clones, suggesting a possible link between gGlcT1 and CWPs during encystation. Furthermore, changes in expression levels of gGlcT1 alter the morphology of the cyst wall, implicating the importance of gGlcT1 and CWPs interplay for cyst formation and maintaining the cyst morphologies. Overexpression and coexpression of gFAELO changed the expression pattern of gGlcT1, lowered the production of gCWP and reduced cyst-wall thicknesses—indicating the formation of unstable and osmotically sensitive cysts that facilitate the excystation of *Giardia*. The interplay among gGlcT1, CWPs, and gFAELO is critical for triggering the encystation process but is also likely to facilitate the excystation process.

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HIGH BURDEN OF ENTERIC PATHOGEN INFECTION IN MOTHER-CHILD PAIRS AND WASH INDICATORS IN RURAL AND PERI-URBAN COMMUNITIES OF BOLIVIA

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Enteric infections in developing countries are frequent among children who are exposed to poor environmental conditions from an early age. The pathogens associated with acute gastroenteritis (AG) are transmitted by the fecal-oral route and through contaminated food and water, particularly in areas lacking access to WASH services. The objective of this study was to analyze the presence of enteric pathogens and their association with WASH indicators in mother-child pairs from 12 rural and peri-urban communities in the La Paz River Basin. 376 stool samples collected from mothers and children under 5 years of age, were evaluated for 20 enteric pathogens by real-time PCR including viruses (rotavirus, norovirus GI/II, astrovirus, sapovirus, and adenovirus), bacteria (*Salmonella*, *Shigella*, ETEC (estA/eltB) and EPEC (eae/bfpA), *Clostridium difficile* (tcdA/tcdB), *Helicobacter pylori*, and *Campylobacter*), protozoa (*Cryptosporidium parvum*, *Giardia lamblia*, and *Entamoeba histolytica*), and helminths (*Ascaris lumbricoides*, *Necator americanus*, *Strongyloides stercoralis*, *Ancylostoma duodenale*, and *Trichuris trichiura*). 85% of the analyzed population was infected with at least one pathogen. The most frequently found pathogens were *H. pylori* (34%), adenovirus (29%), EPEC (27%), *Giardia* (26%), and *Shigella* (22%). Differences were found between peri-urban and rural communities in relation to WASH indicators, drinking water treatment, and pathogen carriage, highlighting the presence of risk factors associated with hygiene practices and sanitation conditions. Analysis of the distribution of enteropathogens revealed that children carry a higher burden of viral pathogens and protozoa than their mothers. The same pattern was observed in co-infections with ≥ 3 pathogens. In conclusion, these data indicate that the study population carried a high burden of enteric pathogens, considering its asymptomatic status. This suggests a wide circulation of pathogens, and different sources of contamination. These findings, represent one of the first studies of enteric pathogens in peri-urban/rural communities in Bolivia.

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"FLORENCE"- A SMARTPHONE COPILOT BASED ON LARGE AI MULTIMODAL MODELS: TESTS IN CÔTE D'IVORE IN PATIENTS WITH SUSPECTED SKIN NEGLECTED TROPICAL DISEASES

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Large Multimodal Models (LMMs) present an innovative approach in healthcare leveraging the integration of heterogeneous data types to improve and optimize patient diagnosis and management. This approach shows particular promise for diseases in which combining data is crucial for accurate diagnosis, or when expert personnel are scarce, and the differential diagnosis is complex. Neglected Tropical Diseases (NTDs), particularly skin NTDs such as Buruli ulcer, leprosy, yaws or scabies, represent an optimal scenario in which to apply this methodology, given the need for an early diagnosis, the complex differential diagnosis and the scarcity of dermatologists in rural areas. We developed and tested two assistants for the diagnosis, management and follow-up of patients with suspected skin NTDs in Côte d'Ivoire: i) "Florence," an expert in Skin NTDs; and ii) "Florence Pro," an augmented version of Florence equipped with a guide from World Health Organization on skin NTDs tailored for front-line health workers and the ePilly Trop book on tropical infectious diseases. The configuration of these two assistants has adhered to the CO-STAR framework augmented with one-shot learning. Afterward, these were deployed into a mobile App, MultiSpot, facilitating the combination of clinical data and images of skin lesions. This system was tested at the Divo Regional Hospital in Côte d'Ivoire, where clinicians evaluated its effectiveness in diagnosing simulated cases of patients with skin conditions. Following testing, a performance survey was conducted, measuring system usability and accuracy metrics, reaching promising results. Preliminary findings underscore the potential of this tool in diagnosing and managing patients with suspected skin NTDs, being particularly useful for health workers and individuals with limited expertise in dermatology. Subsequent steps entail implementing a user journey in the assistants, and conducting this study on a larger scale, encompassing a broader spectrum of cases and diverse personnel.

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DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH CHROMOBLASTOMYCOSIS AND EUMYCETOMA IN EIGHT MEDICAL CENTERS, UNITED STATES

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Chromoblastomycosis and eumycetoma, mycoses acquired via traumatic inoculation, are Neglected Tropical Diseases causing substantial disability and stigma. US epidemiologic and clinical data on these diseases are lacking. Monitoring local acquisition and causative organisms for these mycoses is needed given potential climate change- and migration-related shifts in geographic distribution. We reviewed medical records of cases diagnosed 1/1/03-8/1/23 at 8 US medical centers. We identified 48 chromoblastomycosis and 9 eumycetoma cases as of 4/5/24. For chromoblastomycosis, most patients were male (n=37), non-Hispanic (n=41), White (n=33); average age was 62 years. Most (n=36) were immunocompromised; 29 received organ transplantation, and 21 had immunosuppressive therapy. Twenty-eight had no lifetime international travel. Nine recalled traumatic inoculation; 8 had US acquisition (3 in AL, 2 in TN; 1 each in FL, NC, and HI). Sixteen had culture data: 6 *Exophiala* spp; 3 *Cladosporium* spp; 3 *Fonsecea spp*; 1 each *Wangiella* spp, *Phialophora verrucosa*, *Bipolaris* spp, *Rhizopus* spp. Common presentations and symptoms were nodules (n=24), raised and crusted lesions (n=11), and pain (n=11). Most infections were on the upper limbs (n=33) and of mild severity (n=39). Most were treated with itraconazole (n=18); 33 had surgical lesion excision. For eumycetoma, most patients were men (n=7), non-Hispanic (n=9), White (n=4); average age was 57 years. Only 2 were immunocompromised. Three recalled traumatic inoculation location (2 in AL, USA; 1 in Vietnam). Six had culture data: 1 each *Fusarium* spp, *Medicopsis romeroi*, *Scedosporium boydii*, *Trematospheria grisea*, *Exophiala jeanselmei*, *Acremonium* spp. Seven had pain and 8 had lesions on lower limbs. Five received voriconazole treatment, and 5 had local surgical excision. Study limitations were difficulty distinguishing chromoblastomycosis and cutaneous phaeohyphomycosis due to limited histopathology data and causative organism identification gaps. Clinicians should be aware of locally-acquired and travel-associated cases. Continued surveillance could increase disease recognition.

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TALAROMYCOSIS IN THE UNITED STATES: AN ANALYSIS OF COMMERCIAL HEALTH INSURANCE CLAIMS AND MEDICAID DATABASES, 2016 TO 2022

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Talaromycosis (formerly penicilliosis), an emerging severe fungal disease caused by the environmental pathogen *Talaromyces marneffei* (formerly *Penicillium marneffei*), is endemic in tropical and sub-tropical parts of Southeast Asia, southern China, and northeastern India. Talaromycosis mainly affects immunocompromised people, particularly those with advanced HIV disease. In the US, data on talaromycosis frequency and patient features are lacking. We leveraged the 2016-2022 Merative™ MarketScan® Commercial/Medicare and Multi-state Medicaid databases, which contain health insurance claims data for >70 million people combined, to identify talaromycosis based on ICD-10-CM code B48.4, excluding rule-out diagnoses. We selected patients with continuous insurance enrollment within -90-30 days of diagnosis and examined demographic characteristics, underlying conditions, and treatment. We identified 99 patients (commercial/Medicare insurance: 77, Medicaid: 22). Median age was 56 years (interquartile range [IQR] 43-65); 66% were female. Among commercial/Medicare insurance patients, 46% were from the South, followed by 25% Midwest, 21% West, and 7% Northeast. Total, 34% were hospitalized (median 8 days, IQR 4-14). Over half (56%) had a documented immunosuppressive condition (18% cancer, 17% primary immune deficiency, 6% immune-mediated inflammatory disease, 6% transplantation, and 3% HIV) and/or immunosuppressive medication use (32%, primarily prednisone). Other co-diagnoses included chronic obstructive pulmonary disease (52%), pneumonia (42%), asthma (37%), diabetes (23%), aspergillosis (19%) and COVID-19 (17%). Outpatient antifungal prescriptions included amphotericin B (19%), itraconazole (14%), and voriconazole (11%). Limitations are possible case misclassification and lack of data on travel, exposure characteristics, laboratory test results, inpatient medications, and mortality. This is the first large-scale description of US talaromycosis cases and underscores the need for US healthcare providers to remain vigilant for the possibility of travel-associated talaromycosis.

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IMPORTED LEISHMANIASIS IN THE UNITED KINGDOM: CASE DATA AND OUTCOMES FROM A NATIONAL MULTIDISCIPLINARY TEAM MEETING

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Leishmaniasis, caused by the parasitic protozoan *Leishmania*, is a neglected tropical disease which is rare in the UK. Expert clinical guidance is vital for optimal case management, and the national UK Leishmaniasis Multi-Disciplinary Team (UKLMDT) meeting offers a monthly virtual forum to which clinicians across the UK refer cases. Experienced specialists from dermatology, ENT, infectious diseases, tropical medicine, parasitology, and pharmacy advise on diagnosis, treatment, and procuring medications. We describe the caseload and outcomes from the UKLMDT's first two and a half years. Data for patients discussed between November 2021 and April 2024 were extracted from the University College London Hospitals electronic patient record, and referring teams contacted for information on patient outcomes. Data analysed included patient age, location of referring hospital, number of discussions per patient, clinical manifestations, immune status, number of relapses, time since last relapse, causative species of *Leishmania*, and diagnostic results. Over this time, 65 patients were discussed, referred from throughout the UK, as well as four international referrals. Clinical phenotypes included cutaneous (34/65), mucosal (7/65), visceral (22/65), and post-kala-azar dermal leishmaniasis (1/65). The median number of discussions per patient was one (range 1-8); additional discussions were common for relapse, lack of response to treatment, pregnancy, and children (12% of cases). The commonest causative species were *L. donovani* complex (n=26), *L. Viannia* subgenus (n=17), and *L. mexicana* complex (n=4). Seven patients were determined not to have leishmaniasis. Examples of advice given in complex cases, and treatment undergone and clinical outcomes of patients at >6 months post-treatment will be discussed. The UKLMDT is a model for decentralised care of a rare infection, enabling clinicians to access expert advice provide improved, evidence-based care locally. Future considerations include how best to share data and outcomes with international colleagues, with a view to improving diagnosis and case management of leishmaniasis.

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CUTANEOUS LEISHMANIASIS IN NORTHERN SYRIA: A ONE YEAR DESCRIPTIVE ANALYSIS OF EPIDEMIOLOGICAL AND CLINICAL DATA

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Leishmaniasis remains a serious public health issue in northern Syria. Exacerbated by over a decade of conflict and displacement, cutaneous leishmaniasis (CL) in Syria is a major cause of discrimination, social isolation and economic loss. The MENTOR Initiative has been supporting local static health facilities and mobile clinics to deliver adequate treatment for CL. In this work, we describe key epidemiological characteristics and clinical manifestation of CL in northern Syria.In 2023, a total of 38,077 new CL cases were diagnosed across 11 districts in Northwest Syria (NWS) and 8 districts in Northeast Syria (NES). Areas with the highest number of reported cases were Harim (20.6%), Afrin (12.2%) and Jebel Saman (11.1%) districts in NWS. The CL cases were reported in 6,360 (16.7%) children under 5, 18,485 (48.5%) children (5-17 years), and 13,232 (34.8%) adults. Of these, 18,328 (48.1%) were females. Internally displaced persons (IDPs) accounted for 48.9% of the detected cases, 50.7% of cases were detected among host populations, while the remaining 0.4% were refugees. Most patients presented with lesions on the face (42.6%), upper limb (38.7%), and lower limb (23.7%). The diameter of the lesions ranged between 10 - 160 mm, with an average of 16 mm and a median of 10 mm. Most commonly, lesions were in the shape of nodules (82.6%), followed by papules (13%). Other lesions were in the form of ulcers (2.4%) and plaques (1.9%). The number of lesions detected per patient ranged between 1 - 75, with an average of 1.7. The majority (38.4%) of new cases were diagnosed between January and March. On average, patients presented to health facilities 67 days after noticing the lesion. From the 31,586 cured patients, 31,578 (99.97%) received five or more rounds of treatment with Glucantime and/or Pentostam before being discharged. This study showcases essential epidemiological features of CL cases attending to health facilities/seeking care in Northern Syria. The findings reinforce the need to continue to provide essential medical assistance to affected populations in Syria as CL continues to be a major cause of disability and social discrimination.

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PEERING INTO THE CRYSTAL BALL - PREDICTING OUTCOMES IN VISCERAL LEISHMANIASIS

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Visceral leishmaniasis (VL) is a neglected tropical disease prevalent in populations affected by poverty, war and famine. In resource limited settings, effective risk stratification is crucial for equitable care, including judicious allocation of hospital beds, medicines, and specific interventions e.g. blood transfusions. We present our work on the application of individual participant data (IPD) from the Infectious Diseases Data Observatory (IDDO) VL data repository, to improve clinical decision making through prediction model research. Specifically, we present evidence gaps highlighted in a novel systematic review of VL prognostic models, and how IPD can be harnessed to predict relapse, supporting the ongoing South Asian Elimination Programme (SAEP). Adhering to best practice guidelines, we reviewed all studies that developed or validated models predicting outcomes in VL patients. Bibliographic databases were searched from database inception to March 2023 with no language restriction. Screening, data extraction and risk of bias assessments were performed in duplicate. Eight studies, published 2003 - 2021, were identified describing 12 models (9 in Brazil, 3 in East Africa). All models predicted mortality (10 models predicting in-hospital mortality, 2 registry-reported mortality). Risk of bias was high for all models, due to small sample sizes or poor reporting of model performance. Importantly, no models predicted treatment failure or relapse, or were developed in South Asia, despite representing the highest global VL case burden prior to 2010. In the context of the ongoing SAEP, and the lack of a non-human disease reservoir, prompt diagnosis and treatment of patients with relapse is needed to limit further transmission. Since 2018, through close collaboration with VL investigators across the world, we have built a repository of over 9,300 prospectively collected IPD from 36 clinical trials, with the majority of patients from South Asia with robust 6-month relapse outcomes. At ASTMH 2024 we look forward to sharing our preliminary relapse model, it's relevance in the elimination programme, and the clinical implications.

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EPIDEMIOLOGY, HEALTH-SEEKING BEHAVIORS AND TRADITIONAL PRACTICES RELATED TO SNAKEBITES IN RURAL AND TRIBAL COMMUNITIES IN SOUTHERN INDIA

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Nearly 60,000 people die of snakebites in India annually, accounting for more than half of all global snakebite deaths in 2019. With limited access to healthcare, there is a constant reliance on traditional healers in communities, especially remote tribal areas, due to easier access and high trust. This study describes the epidemiology and health-seeking behaviors of snakebite victims in a rural and tribal block in Tamil Nadu in southern India. During the survey in Timiri (rural block) and Jawadhu hills (inhabited predominantly by tribal groups within a reserve forest), 322 of 151,293 individuals reported a snakebite in the preceding year. When these individuals were followed up with a detailed questionnaire, snakebite incidence was confirmed to be 174/100,000 (64/286) persons in Jawadhu Hills and 194/100,000 (222/286) in Timiri. The proportion of cases belonging to households in the lowest wealth index quintile was higher in Jawadhu Hills (55%) than Timiri (7%). Only 59% (168/286) received first-aid within an hour, mostly with tourniquet application (76%), followed by ingestion of herbal concoctions (23%) more in Jawadhu Hills (90%,45/64) compared to Timiri (69%,82/222). Overall, 80% of all snakebite victims first visited a public hospital or private clinic; however, only 25% in Jawadhu Hills (16/64) first visited a hospital compared to Timiri (88%,195/222). In Jawadhu Hills, 11% initially stayed home after the incident, compared to Timiri (1%). Traditional healers were the first point of contact in 17% (49/286) of snakebites, of which 64% (41/64) were in Jawadhu Hills, and primarily accessed on foot or by motorcycle. The mortality rate was 2.7/100,000 population in the Jawadhu Hills and 4.4/100,000 in Timiri. Our study highlights healthcare access challenges for snakebite envenomation in rural and tribal communities. Key challenges identified include inadequate first aid, reliance on traditional healers, and limited emergency transport. Addressing these requires a multifaceted approach, combining community awareness, collaboration with traditional healers, and infrastructure improvements for timely healthcare access.

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SEASONAL TRANSITION OF *ANOPHELES STEPHENSI* AND *AEDES AEGYPTI* LARVAL HABITAT SUPERPRODUCTIVITY IN KEBRIDEHAR, ETHIOPIA

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The invasion and spread of *Anopheles stephensi*, an Asian native mosquito species, across Africa, poses a significant threat to malaria control and elimination because of its adaptability to urban areas and efficiency in transmitting both *Plasmodium falciparum* and *Plasmodium vivax*. Field observations indicate that *An. stephensi* and *Aedes aegypti* overlap in their larval habitat use of artificial water storage containers. We document the seasonal shift in *An. stephensi* and *Ae. aegypti* in Kebridehar, Ethiopia. Mosquito larvae were sampled for four consecutive months in Nov, Dec 2020 and Jan, Feb 2021. A total of 90 water storage containers identified as potential larval habitats were sampled; 75% were ground level cisterns, followed by tires (13%) and ground level barrels (7%). A total of 13,635 *An. stephensi*, 1,168 *Ae. aegypti* and 757 *Culex* spp. were collected by standard dipping. Habitat positivity for *An. stephensi* increased from 61% (55/90) in November to 82% (63/77) in February, and *Ae. aegypti* habitat positivity decreased from 47% in November to 21% in February. Larval productivity of each container for *An. stephensi* was highly heterogeneous, with a mean number of larvae per 20 dips of 41 (or 2.1 per dip) and a range of 0-700 per 20 dips (or 0-35 per dip). Conversely, *Ae. aegypti* larval productivity was an order of magnitude lower and had a much narrower range (4.3, 0-70 per 20 dips, or 0.22, 0-3.5 per dip). Such heterogeneity was characterized by a negative binomial distribution with parameter $k<0.5$, which indicates strong aggregation. Further, a fit to a Pareto function identified that up to 77% of all larvae originated from only 23% of the larval sites. The 23% of sites, here defined as "superproductive" habitats, increased as the dry season progressed. This study shows that both *An. stephensi* larval productivity is strongly aggregated, leading to opportunities for impactful larval source management, and that *Ae. aegypti* coexists in the same larval sites as *An. stephensi*.

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A FOCUSED CASE-RESPONSE APPROACH TO MALARIA VECTOR SURVEILLANCE IN AREAS OF UNSTABLE TRANSMISSION

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Current mainstay approaches to routine malaria vector surveillance are based longitudinal monitoring on a cohort of fixed, designated households representing a wider area (average population of 200,000 residents). In regions of unstable seasonal transmission, this routine surveillance approach is hampered by several factors, such as but not only the following: (i) transmission occurring in foci that are prone to unpredictable shifts of locale; (ii) eruption of transmission in non-traditional malaria zones amid a backdrop of climate change; (iii) repeated sampling readily depletes the designated households of vector abundance, rendering them no longer representative of the wider area. Thus, upon successive surveys, designated households may reach a point when they capture little or no vectors while malaria transmission is raging in the wider surveillance area. In the present study, routine monthly entomological surveillance based on fixed longitudinal households was compared with a focused case-response approach based on non-fixed households from the village with prevailing highest number of cases for the week in a given health centre catchment. Both routine standard and focused case-response (FRC) approaches were conducted simultaneously every month in 24 health centre catchments of Mutasa district from 2022 - 2023, using regular prokopack aspiration, CDC light trap and larval vector collections. A total of 1,912 mosquitoes were caught through the standard longitudinal approach while the FCR approach yielded 7,149. The FCR approach exhibited 2X higher odds of catching sporozoite-positive vector mosquitoes than the standard approach (OR [95% CI]: 2.1 [1.72 - 2.49], P lt 0.001, N = 9,061). The FCR approach promptly detected non-traditional and outbreak malaria vectors, unlike the standard approach delimited to fixed households. Community fatigue to surveillance activities was encountered with the standard but not the FCR approach. The focused case-response approach can be an effective complementary entomological surveillance approach in regions of unstable transmission or those zeroing towards malaria elimination.

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DOES IVERMECTIN IMPAIR ANOPHELES ATTRACTIVENESS TOWARD TREATED HOSTS UNDER FIELDS AND LABORATORY CONDITIONS?

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Ivermectin administered to hosts as a systemic insecticide is viewed as a complementary tool against malaria vectors. However, whether its metabolization would modify hosts' attractiveness to Anopheles has never been addressed, despite ethical and operational concerns. Hence, the objective of this study was to evaluate, in the fields and the laboratory, if major malarial mosquitoes are more or less attracted to ivermectin-treated vs control hosts. A two-arms design was used: 4 cattle received no treatment (controls) and 4 were treated with a long-acting ivermectin formulation (1mg/kg) from the BEPO® technology (2-3 months efficacy, IMPACT project). Cattle exposures were performed at t=2 days, 1, 2, 3, and 4 months post-treatments, under nets in the fields of Bama, Burkina Faso, and using a dual-choice olfactometer in the laboratory. In the fields, trapped wild mosquitoes were counted and identified. A random subsample of 100 alive, engorged mosquitoes was followed for survival. In the laboratory, colony female *An. coluzzii* were released into the olfactometer and activated females counted according to their choice for treated or control cattle. In the fields, the formulation's efficacy was up to 4 months on wild *An. coluzzii* of all insecticide resistance status. A total of 181,696 mosquitoes was collected for which the cattle treatments did not influence their attractiveness (χ_2^2=0.8791; P=0.3484). For Anopheles spp., treated bovines were more attractant than controls at t=4 months (Z= 0.584; P =0.001). *An. coluzzii* tended to be more trapped around treated than control cattle for all instances but this was not significant. In the laboratory, dual choice-tests on *An. coluzzii* colony showed similar attractiveness whatever cattle treatments (Z=0.215 ; P=0.83). We showed an insecticidal effect for up to 3-4 months on major wild malaria vector, meeting the WHO target product profile for endectocide-based malaria control. Dual-choice experiments with wild mosquitoes may help concluding on potential attractiveness impairment by ivermectin treatments, from which disentangling parts of the princeps molecule and the vehicle will also be needed.

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COMPARING ANOPHELES BEHAVIOR WITH INTERCEPTOR® G2'S DUAL VS SINGLE ACTIVE INGREDIENTS: 3D VIDEO TRACKING ANALYSIS

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All WHO prequalified insecticide-treated bed nets contain pyrethroids. However, the rise of insecticide resistance in mosquitoes to these pyrethroids presents an imminent threat to the success of malaria vector control. A new net, Interceptor® G2 (BASF), has come to the market that combines alpha-cypermethrin, a pyrethroid, with chlorfenapyr, a pro-insecticide that is bio-activated through the oxidative metabolism within the mosquitoes' mitochondria. Interceptor® G2 has demonstrated increased efficacy against pyrethroid-resistant mosquitoes in large-scale epidemiological field trials. This investigation attempts to clarify how a net with combinations of both active ingredients influence mosquito behaviours from exposures. Implementing the use of flight tunnels, we assessed the influences of a net with both active ingredients of a commercial Interceptor® G2 netting and solo dipped netting with each discrete active ingredient. In the tunnel, mosquitoes had to negotiate an insecticide-treated net with nine 1 cm large holes to reach an artificial host. We recorded the flight paths using a 3D video tracking system and monitored the time to death post-exposure using a set of infrared time-lapse cameras. Data suggest that susceptible mosquitoes are killed mainly by alpha-cypermethrin exposures, while pyrethroid-resistant mosquitoes are primarily intoxicated by the chlorfenapyr with delayed mortality. We will present an in-depth analysis of the flight trajectories and their relationship with mortality, blood feeding and insecticide conversion rates.

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VECTORCAM - A NOVEL AI-POWERED DIGITAL TOOL FOR AUTOMATED MORPHOLOGICAL IDENTIFICATION OF MOSQUITO SPECIES, SEX, AND ABDOMINAL STATUS BY VILLAGE HEALTH TEAMS IN UGANDA: A RANDOMIZED CONTROLLED TRIAL

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The shortage of entomological expertise in malaria control programs poses a significant challenge for effective vector interventions. VectorCam, an innovative, cost-effective tool, utilizes deep learning to rapidly identify mosquito species, empowering local health workers. Our ongoing randomized controlled trial in Uganda assesses VectorCam's performance over 12 months, focusing on the accuracy, timeliness, and completeness of surveillance reports by village health teams (VHTs). VHTs were recruited in two districts in Uganda. All VHTs were trained to collect mosquitoes using standard methods, and randomly selected study participants (N = 24) used VectorCam for on-site mosquito identification and data reporting, whereas the control arm assisted in the collection and sent specimens to district vector control officers (VCOs) for morphological identification under microscopy. Molecular analysis confirmed mosquito species, while sex and abdomen status were determined by microscopy to benchmark accuracy. Built-in timestamps in the software measured identification speed, and both arms were reported to DHIS2 for completeness evaluation. Currently, VectorCam reports an average of 93±2% identification accuracy across all current classes for species, 95±2% for sex, and 78%±4% for abdomen status identification. Furthermore, the VHTs analyze mosquitoes with a median time of 16.52 ± 0.21 seconds per mosquito. Real-time dashboards and comprehensive surveillance reports are also generated. Intermediate analysis from the RCT shows better performance on all metrics (accuracy, timeliness, and completeness) as compared to the control arm. VectorCam offers the possibility of enabling task sharing of vector surveillance with VHTs and concurrently generating surveillance reports automatically, thereby helping countries mitigate a crucial expertise and resource constraint in scaling up vector surveillance programs.

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GENOMIC EVALUATION REVEALS A STRONG POPULATION STRUCTURE OF *ANOPHELES FUNESTUS* COLLECTED IN COAST AND LAKE MALARIA ENDEMIC REGION IN KENYA

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Efforts to reduce malaria impact have been successful through implementation of insecticide-based interventions but rising resistance and mosquito adaptations threaten these gains. Understanding the molecular, ecological, and evolutionary factors behind these changes is crucial for prolonging insecticide effectiveness and developing new vector control strategies. We used whole genome sequenced data of 105 *Anopheles funestus* mosquitoes from genome surveillance MalariaGEN vector observatory project. The samples were collected from Kisumu, Migori and Bungoma counties in Lake malaria endemic region and Kwale county in the Coast malaria endemic regions in Kenya. To investigate their geographical population structure, we used principal component analysis, neighbour-joining tree and fixation index. To understand the demographic history, we computed the genetic diversity summary statistics for mosquito cohorts grouped by geographical region. Selection pressure was analyzed by scanning the whole genome for signal of recent selection using H12 statistics. We found population structure between Lake and Coastal Kenya populations of *An. funestus* based on genetic diversity statistics. *Anopheles funestus* from the Lake region are separated by high differentiation from the Costal population with a mean F_{ST} 0.117. The genetic divergence was low among *An. funestus* from Lake region (F_{ST} < 0.0005) but higher between the Coastal County and the Lake region counties (F_{ST} ~ 0.128-0.138). Additionally, *An. funestus* from Lake region share selection signal at the *CYP6rp1* on the 2RL chromosome and *CYP9k1* at the X chromosome, while Coast (Kilifi) samples had a selection signal near the Esterase and *GSTe1* region on the 2RL chromosome and around the *NADH-cyp* region on the X chromosome. Our findings indicate that *An. funestus* from the Coast are highly differentiated from the population at the Lake region. Due to the regional population diversity of *An. funestus*, targeted approach of intervention should be considered for effective intervention against malaria. Reiterating the need for incorporating genomics in routine vector surveillance in Kenya.

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EFFECT OF ECOLOGICAL ZONES AND CLIMATIC CONDITIONS ON MOSQUITO DIVERSITY IN GHANA: A LONGITUDINAL STUDY FROM 2017 - 2022

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Globally, mosquito diversity has been observed to decline due to land use and environmental conditions. However, this decline has not affected all species or geographical locations equally. In Africa, there is an estimated total of 677 mosquito species representing 16 genera. A majority of species and mosquito-borne pathogens are predominantly in West and Central Africa. To determine the influence of ecological zones and weather conditions on changes in mosquito diversity, mosquito surveillance data from three distinct settings in Ghana (Deciduous Forest, Forest-Transition zone, and Guinea Savannah) were analyzed and compared. From 2017 to 2022, mosquitoes were collected using the Centers for Disease Control and Prevention (CDC) light traps with either incandescent or ultra-violet light sources and Biogents Sentinel (BG) traps. Climate data was obtained from the National Aeronautics and Space Administration (NASA) Prediction of Worldwide Energy Resource (POWER) program. A total of 98,127 mosquitoes were morphologically identified as 54 species belonging to 8 genera: *Culex*, *Aedes*, *Anopheles*, *Mansonia*, *Coquillettidia*, *Culiseta*, *Eretmapodites* and *Toxorhynchites* all of which are of medical importance except *Toxorhynchites*. The species diversity was significantly affected by changes in the ecozones (p<0.01). In summary, the species richness in Deciduous Forest (Generalized Linear Mixed Model, GLMM=0.52, p<0.01) and Guinea Savannah (GLMM=0.40, p<0.01) was higher than the Forest-Transition zone. The Deciduous Forest zone (GLMM=-0.05, p<0.01) recorded the lowest species evenness. Additionally, species diversity was significantly higher with the CDC incandescent light traps (p<0.05) than BG traps. Understanding how the various ecological zones affect species diversity could be useful in disease surveillance and public health interventions for controlling mosquito-borne diseases and predicting "hot spots". Further studies investigating the influence ecozones have on mosquito species diversity and their potential implications for disease transmission is needed to inform vector control and prevention strategies.

8302

USING A VARIANT-SPECIFIC, ELECTROCHEMILUMINESCENCE MULTIPLEX SERONEUTRALIZATION ASSAY TO DELINEATE TRANSMISSION DYNAMICS OF SARS-COV-2 AS THE PANDEMIC TRANSITIONED TO ENDEMICITY

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Understanding the transition of the COVID-19 pandemic to endemicity and implementing surveillance has become increasingly difficult as infections more often are asymptomatic and home-based testing is not routinely reported to health authorities. Estimates from serological surveys may be less prone to under-reporting bias than symptom-based virologic surveillance, but their use has been limited as most populations now have pre-existing antibodies from infection or vaccination.
We conducted serial serological surveys of a community-based cohort in Salvador, Brazil to identify SARS-CoV-2 infections throughout the pandemic. We obtained vaccination history and sera in July-October 2021 and March-September 2022, before and after the peak of BA.1 transmission in Brazil. We identified infections based on increases in variant-specific pseudo-neutralization antibody responses with the Meso Scale Discovery V-Plex assay. To validate our serology-based method, we performed active screening for PCR-confirmed infection by identifying symptomatic individuals during household visits. Of 733 participants who underwent serial testing, 84.0% had detectable anti-SARS-CoV-2 IgG as measured by ELISA before the BA.1 wave. In contrast, median BA.1-specific pseudo-neutralization was low (7.1%, interquartile range [IQR] 3.3-14.9%) and increased to 39.0% (IQR 19.1-80.1%) after the wave. A 5% increase in BA.1-specific neutralization was 81.3% (95% confidence interval 66.9-90.6%) sensitive in identifying individuals with a PCR-confirmed infection. Among those who did not receive a vaccine dose between surveys, 92.0% had increased BA.1-specific neutralization indicative of infection. By measuring variant-specific pseudo-neutralization responses, we found high SARS-CoV-2 incidence during the Omicron BA.1 wave in a population with high pre-existing immunity. We are using this approach to estimate incidence during subsequent waves of Omicron sub-variants, identify immunological factors that drove transmission to endemicity, and inform future surveillance that minimizes bias from limited access to testing and underreporting.

8303

RETHINKING DENGUE PROTECTIVE IMMUNITY: MULTIPLE REPEAT SYMPTOMATIC INFECTIONS IN A SINGLE TRANSMISSION SEASON

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Dengue continues to be a major public health threat, with increasing disease burden worldwide. Dengue virus is comprised of 4 serotypes (DENV1-4); primary (1°) infection with one serotype confers lifetime immunity to disease with that serotype and transient immunity towards the other serotypes, typically protecting against infection for at least 6 months to 2 years. In 2022, all 4 DENV serotypes co-circulated in Nicaragua after post-pandemic introduction of new lineages. Leveraging 2 cohort studies in Managua (A2CARES Arbovirus Cohort Study, n=~2,000; Pediatric Dengue Cohort Study, n=~4,000), we evaluated heterotypic repeat symptomatic DENV infections in 2022. All enrolled participants presenting with suspected dengue or undifferentiated febrile syndrome were tested for dengue via real-time RT-PCR and serological tests. DENV-positive samples were serotyped via multiplex real-time RT-PCR. Unexpectedly, we observed 10 patients with repeated symptomatic DENV infections within a single transmission season. We recorded 2nd symptomatic infections as soon as 31 days post-1° infection (mean=94 days, range 31-158). We documented 7 repeat cases of DENV1 followed by DENV4 (6) or DENV3 (1) and 3 2nd infections after an initial DENV-4 case (2 DENV1 and 1 DENV3). All 1st infections were 1°, with 3 classified as Dengue with Warning Signs (DwWS) and 7 as Dengue without Warning Signs (DwoWS). Six 2nd infections were DwoWS and 4 were DwWS. Interestingly, the patient with 2 symptomatic infections 31 days apart presented with DwWS in both episodes. We are currently evaluating the immune profile of each infection series after the first and 2nd infections using a multiplex Luminex-based platform with multiple antigens from DENV1-4 and the related Zika flavivirus as well as focus reduction neutralization tests to DENV1-4 to investigate potential immunological explanations for these clinical/epidemiological observations. Our results demonstrate the need to re-evaluate the protective immunity of DENV after a first infection. These data can help inform public health policy regarding disease transmission risk during epidemics with multiple serotypes.

8304

INAPPARENT PRIMARY DENGUE VIRUS INFECTIONS REVEAL HIDDEN SEROTYPE-SPECIFIC EPIDEMIOLOGICAL PATTERNS AND SPECTRUM OF INFECTION OUTCOME: A COHORT STUDY IN NICARAGUA

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Dengue is the most prevalent mosquito-borne viral disease and a major public health problem worldwide. Most primary infections with the 4 dengue virus serotypes (DENV1-4) are inapparent; nevertheless, prior research has primarily focused on symptomatic infections, limiting understanding of the epidemiological burden and spectrum of disease of each DENV serotype. Our study addresses this bottleneck by providing a new method and a detailed examination of primary (1°) inapparent infections. Here we present (1) the evaluation of a multiplex DENV1-4 envelope domain III multiplex microsphere-based assay (EDIII-MMBA) to serotype 1° symptomatic and inapparent infections and (2) its application leveraging 17 years of prospective sample collection from the Nicaraguan Pediatric Dengue Cohort Study. The EDIII-MMBA demonstrated excellent diagnostic accuracy of symptomatic and inapparent 1° DENV infections when evaluated against gold-standard serotyping methods. After evaluation of the method, we analyzed 46% (N=574) of total inapparent primary DENV infections with the EDIII-MMBA. Remaining infections were inferred using stochastic imputation, taking year and neighborhood of infection into account. Significant within- and between-year variation in serotype distribution between symptomatic and inapparent infections and circulation of serotypes undetected in symptomatic cases were observed in multiple years. We show that a significant majority of 1° infections remained inapparent: 77% for DENV1, 80% for DENV2, and 64% for DENV3. DENV3 exhibited the highest likelihood of symptomatic and severe 1° infections (Pooled OR compared to DENV1 = 2.24, 95% CI 1.33-3.77, and 5.46, 1.50-19.89, respectively), whereas DENV2 had similar likelihood to DENV1 in both analyses. In conclusion, our study indicates that case surveillance skews the perceived epidemiological footprint of DENV and reveals a more complex and intricate pattern of serotype distribution in inapparent infections. Further, the significant differences in infection outcomes by serotype emphasize the importance of serotype-informed public health strategies.

8305

UNVEILING THE DYNAMICS OF DENGUE VIRUS TRANSMISSION ACROSS A GRADIENT OF URBANICITY IN THREE COUNTRIES: INSIGHTS FROM PARALLEL LONGITUDINAL COHORT STUDIES IN ECUADOR, NICARAGUA, AND SRI LANKA

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In recent years, dengue has expanded into rural areas worldwide, challenging its traditional conception as an urban disease. The Asian-American Centers for Arbovirus Research and Enhanced Surveillance (A2CARES) of the NIH Centers for Research in Emerging Infectious Diseases (CREID) Network aims to understand dengue virus (DENV) transmission dynamics and seroprevalence in parallel longitudinal cohort studies across a gradient of urbanicity, encompassing forest edge/remote and urban areas in Ecuador and peri-urban and urban areas in Nicaragua and Sri Lanka. Central to A2CARES is technology transfer and harmonization of DENV serological assays across sites. Here, we implemented the same in-house DENV Capture IgG ELISA across sites and transferred a DENV Inhibition ELISA (iELISA) established in Nicaragua to all partners. Each A2CARES cohort includes ~2,000 participants aged ~2-80 years and yearly serosurveys in inter-epidemic periods in addition to case surveillance. Seroprevalence analysis revealed that forest edge and remote areas in Esmeraldas, Ecuador, have seroprevalence rates (79-92%), as high as urban areas in Managua, Nicaragua (88%), and even Colombo, Sri Lanka (96%), where the population sampled was substantially older and has higher densities. By age 21, nearly all individuals in all three sites had been exposed to DENV, regardless of their rurality/urbanicity status. The average age of infection for Ecuador, Nicaragua and Sri Lanka was 20, 29 and 45 years old, respectively. Analysis of primary and secondary DENV infections using the iELISA revealed that the forest edge/remote area of Ecuador had

the highest number of primary infections (48%) when compared to urban and peri-urban areas in Nicaragua (32%) and Sri Lanka (33%), suggesting more recent introduction of DENV. This study highlights the value of comparative analysis using integrated methods and cohort studies across continents, as well as the need for continued research to understand the evolving dynamics of DENV transmission in different settings. Together, our results fundamentally challenge the concept of dengue as an urban disease.

8306

RESPIRATORY SYNCYTIAL VIRUS (RSV) EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF HOSPITALIZED CHILDREN < 2 YEARS OF AGE DURING THE SARS-COV-2 PANDEMIC (OCTOBER 2020-JANUARY 2023) AT KENEMA GOVERNMENT HOSPITAL, SIERRA LEONE

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Respiratory Syncytial Virus (RSV) is a leading cause of acute lower respiratory tract infections in children under five years of age, resulting in significant morbidity and mortality worldwide. This study aimed to investigate the prevalence and clinical features of RSV disease in hospitalized infants in Sierra Leone. A prospective study was conducted on children under 2-years of age who were hospitalized at Kenema Government Hospital between October 1, 2020, and January 31, 2023. A total of 912 children participated in the study, with 147 (16.1%) testing positive for RSV. Of these, 106 (72.1%) were attributed to RSV-A, and 41 (27.9%) to RSV-B. The distribution of RSV exhibited distinct seasonal patterns, with fluctuations in transmission rates corresponding to climatic and environmental factors. During the rainy seasons of both 2021 and 2022 (May to November), we observed a surge in RSV cases, particularly those attributed to RSV-A. Conversely, RSV activity during the dry season (December to April) was relatively lower. In multivariable In logistic regression, detection of RSV-B was significantly associated with a higher severity score and increased likelihood of requiring oxygen therapy or referral to the ICU. younger age was significantly associated with a higher likelihood of requiring oxygen therapy, referral to the ICU, and higher severity scores. These findings highlight the importance of early detection and prompt treatment in young children infected with RSV, as they are at a higher risk of developing severe illness. In conclusion, our study provides valuable insights into the epidemiology and clinical characteristics of RSV in hospitalized children under 2 years of age in Sierra Leone. RSV-A was found to be associated with more severe respiratory illness compared to RSV-B, and both types of RSV showed a seasonal pattern, with a peak during the rainy season. These findings highlight the need for continuous surveillance and monitoring of RSV infections, especially during the peak and transitional seasons, to inform public health interventions and reduce the burden of RSV on children's health.

8307

EPIDEMIOLOGICAL CHARACTERISTICS AND HOSPITAL OUTCOMES OF HOSPITALIZED LASSA FEVER CASES DURING THE 2022-2023 OUTBREAK IN LIBERIA

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Lassa fever is an endemic and immediately notifiable disease in Liberia, and one laboratory confirmed case constitutes an outbreak. We described the epidemiological characteristics and hospital outcome of Lassa fever cases hospitalized during the 2022-2023 outbreak in Liberia.We conducted a retrospective cohort study using routine Lassa fever surveillance data from the 2022-2023 outbreak in Liberia. Descriptive statistics were used to summarize the data and log binomial regression to assess the association between epidemiological characteristics and mortality. A total of 439 suspected Lassa fever cases were reported. The median age was 22 (interquartile range: 10-33) years and 233 (53%) were women. The median number of days between symptom onset and admission was 4 (IQR 2-7). Of the 439 cases, 416 (95%) were tested for Lassa fever and 138 were confirmed with 33% positivity rate. The majority, 290 (69%), of confirmed cases were <30 years, 78 (57%) were females, and 81 (59%) were reported during the dry season (October – March). Contact with rodents, 94 (89%), was the commonest mode of exposure. Fever, 128 (93%), malaise, 121 (88%), headache, 114 (83%) and myalgia, 114 (83%) were the most common clinical characteristics. There were 83 (19%) deaths among hospitalized suspected Lassa fever cases - 42 deaths (15%) among 278 individuals who tested negative and 41 among confirmed cases with 30% case fatality rate (CFR). The highest CFR was recorded among those aged 40-49 years, 8 (67%) and those aged≥50, 5 (63%). There was no significant association between epidemiological characteristics and Lassa fever mortality.The outbreak highlighted a high disease burden of Lassa fever with young adults disproportionately infected, and substantial mortality, even among those who tested negative for the virus. This underscores the urgent need for preventive measures like vaccines and health education campaigns.

8308

INCIDENCE OF LASSA FEVER DISEASE AND LASSA VIRUS INFECTION IN FIVE WEST AFRICAN COUNTRIES: A PROSPECTIVE, MULTI-SITE, COHORT STUDY (THE *ENABLE* LASSA RESEARCH PROGRAM)

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Lassa fever (LF), a haemorrhagic illness caused by the Lassa fever virus (LASV), is endemic in West Africa causing an estimated 100 000 to 300 000 cases and 5 000 fatalities every year. LF is a WHO priority pathogen for vaccine development due to its pandemic potential. However, vaccine trial design requires accurate prevalence and incidence data, challenging due to asymptomatic infections and varied clinical presentations. The Enable Lassa program aims to estimate LASV infection and LF disease incidences in five West African countries. We conducted a prospective cohort study in communities known to be LF hotspots in Benin, Guinea, Liberia, Nigeria (three sites) and Sierra Leone from 2021 to 2023, with a 24-month follow-up. Household surveys collected demographic and LF risk factors, while blood samples determined LASV IgG serostatus. Febrile cases were tested biweekly with LASV RT-PCR for LF disease, and a subset of participants provided blood samples every six months for IgG serostatus assessment. We enrolled 23,193 participants overall. Baseline seroprevalence was low (<15%) in Benin and one Nigerian site, intermediate (15%-30%) in Guinea and Sierra Leone, and high (>30%) in Liberia and the other two Nigerian sites. Adjusted seroprevalence increased with age (p<0.001). Overall, 39 confirmed LF cases were detected over 2 years: 2 in Benin, 14 in Liberia and 23 in Nigeria, corresponding to an incidence rate of respectively 0.23 (95% CI: 0.03 - 0.81), 1.45 (95% CI: 0.79 - 2.44) and 1.90 (95% CI: 1.20 - 2.85) per 1000 person-years. Serology testing will be completed for ASTMH conference but preliminary results suggest that LASV infection is much more common than LF disease. This is the first epidemiological study

to measure the incidence of LF disease and LASV infection in West Africa. Our results suggest that pre-exposure to LASV may temporarily reduce the risk of LF disease. Finally, we found evidence that children may be at greater risk of LF disease than adults due to lower pre-exposure. Our results are currently being used to inform the design of future vaccine efficacy trials.

8309

THE COMPOUND EFFECTS OF CLIMATIC EXTREMES ON DENGUE RISK IN THE CARIBBEAN: A PREDICTION MODEL FRAMEWORK USING LONG- AND SHORT-LAG INTERACTIONS

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Weather and climate extremes have detrimental health impacts through increased risk of injury, displacement, adverse mental health, food insecurity, respiratory illness and infectious disease. Small islands in the Caribbean are highly vulnerable to increasingly frequent and intense events, which can exacerbate outbreaks of arboviral diseases such as dengue. Disease risk drivers are often complex, delayed and interacting. To date, few operational forecasting tools that consider the compound effects of climatic extremes using long-lag and short-lag interactions have been created. Here, we developed a modelling framework to predict the probability of a climate-sensitive disease outbreak 3 months ahead in a small island setting, focusing on dengue in Barbados. Using confirmed cases from 1999 to 2022, we tested combinations of interacting long- and short-lag meteorological predictors within a Bayesian hierarchical mixed model, controlling for seasonal and interannual variation. We found that a three-way interaction between 3-month averaged mean temperature (lagged 3 to 5 months), 6-month standardised precipitation index (SPI-6) (lagged 5 months) and SPI-6 (lagged 1 month) best predicted dengue risk in Barbados. This is consistent with previous research showing elevated outbreak risk following long-lag dry and short-lag wet conditions using distributed lag nonlinear models. However, our methodology explicitly accounts for the interacting effects of temperature, drought and excessive wetness on dengue outbreaks in Barbados. We used this model to create a dengue prediction framework that estimates the probability of exceeding a predefined epidemic threshold 3 months in advance. These probabilities translate to outbreak risk levels that link to national guidance on public health interventions set by the Barbados Ministry of Health & Wellness. This scheme was adopted for the recently launched climate-integrated dengue early warning system in Barbados to produce monthly forecasts. The framework was also deployed to forecast dengue risk over the Caribbean during the International Cricket Council Men's Twenty20 World Cup 2024.

8310

MASSIVE GLOBAL IMPACTS OF CLIMATE CHANGE ON DENGUE TRANSMISSION

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Climate change is having pervasive impacts on health, but its impacts on infectious disease transmission are often difficult to quantify, predict, and attribute in the face of multiple concurrent changes. Thermal biology predicts that warming temperatures have a nonlinear effect on mosquito-borne disease transmission, and despite empirical and theoretical support from laboratory studies, evidence of nonlinear effects of warming on disease transmission in the field remains rare. Here, we compiled a global dataset on monthly, sub-country dengue incidence from 21 countries over an average of 11 years and performed a population-weighted Poisson fixed effects panel regression to identify the causal effects of temperature warming on dengue. Supporting predictions from thermal biology, we found that dengue incidence peaked at 28ºC and that warming had the largest effect at 15-20ºC, where temperature is most limiting to transmission. Using a counterfactual historical climate scenario, we found that anthropogenic warming that has already occurred is responsible for 19% of the existing dengue burden, and this ranges up to 30-40% of the burden in some cooler locations in Latin America. After accounting for underreporting, we estimate that climate change is already responsible for over 45 million cases per year. By midcentury under a high emissions scenario (SSP3-7.0), we expect dengue burden to increase by 61% on average and to more than double in some cooler regions, where over 257 million people live. By contrast, mitigating carbon emissions (SSP1-2.6) reduces this increase in dengue by 18%, indicating a substantial public health benefit of slowing climate change. This work paves the way for climate change attribution of infectious diseases and provides some of the first rigorous evidence that warming-driven increases in dengue are already underway.

8311

MAPPING THE GLOBAL ENVIRONMENTAL SUITABILITY FOR SCRUB TYPHUS

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Scrub typhus (ST) is a neglected vector-borne infectious disease that causes epidemics in many parts of the Asia-Pacific region. The absence of specific symptoms and lack of awareness lead to underdiagnosis and chronic underreporting. It has seroprevalence of 23.11% among febrile patients and a median mortality of 5.00%. The disease's vectors, larval mites (chiggers), are widespread, exposing vast populations to risk. Recent outbreaks in non-endemic areas underscored significant knowledge gaps regarding the true extent and distribution. Here, we undertook an exhaustive assembly of known human ST occurrence records worldwide and combined it with environmental covariates using an ensemble modelling framework to map the probability of occurrence at 5 × 5-km globally. This dataset compiled 10,586 unique human occurrence locations across 27 countries/regions from 2000 to 2020, along with 28 climatic, geographic, and socio-economic covariates. We employed an ensemble machine learning approach to capture possible nonlinear effects and complex interactions. This approach involved stacking of three sub-models (generalized additive models, boosted regression trees and random forest). The fivefold cross-validation was utilized to improve performance and avoid overfitting. Our findings reveal that ST suitability is highest in moderate to tropical climates, notably extending beyond the classic "tsutsugamushi triangle" into large sections of South America, Central Africa, and Southeast Asia. Based on a suitability probability threshold >0.5, Brazil, Australia, America, India, the Democratic Republic of the Congo, Mexico, Sudan, Indonesia, Argentina, and China were identified as the most at-risk countries, with most never having reported a case, expect Australia, India,

Indonesia, and China. This data assembly and modelled occurrence risk surface provide novel insights into the public health impact of ST, and we foresee this serving as a catalyst for broader discussions regarding the potential global impact of this disease, improve public awareness, drug and vector control methods, and leading to further burden assessment.

8312

HETEROGENOUS SPATIO-TEMPORAL DISTRIBUTION OF COVID-19 PANDEMIC PROGRESSION IN PERU

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Socioeconomic and demographic factors play a key role in spreading infectious diseases, exhibiting specific geographical and temporal dynamics that contribute to understanding the emergence of a pandemic. Peru, characterized by socioeconomic and health policy divisions, experienced significant impacts during the COVID-19 crisis. Despite government efforts, the pandemic's effects were not uniform across the country. The main objective of this study was to explore epidemiological data to identify clusters that help explain the spatiotemporal heterogeneity in the pandemic's dispersion in Peru. We analyzed Peruvian Ministry of Health data, including COVID-19 cases, deaths, hospitalizations, and vaccine doses. Using agglomerative hierarchical analysis, we identified an optimal number of clusters that best represent the dynamics of Peruvian provinces during the pandemic. Finally, we characterize the clusters using socioeconomic variables. The 196 Peruvian provinces were classified into five clusters, explaining the epidemiological behavior of the pandemic. Significant differences were identified among the clusters, highlighting marked geographic variability. Clusters located in the Peruvian central highland experienced milder pandemic effects, marked by lower economic activity and population density. This likely influenced lower virus spread. More urbanized provinces that have larger populations in main cities with higher economic resources experienced more cases and deaths in their clusters, facing more severe consequences during the pandemic. We also analyzed hospitalization and vaccine dose indicators. This research enables us to categorize and characterize Peruvian provinces using diverse epidemiological indicators and socioeconomic features, revealing trends that could drive a better distribution of resources in low and middle-income countries. Therefore, this scope highlights the potential to integrate this data for a better approach to epidemiological studies and implement adequate strategies for preventing and controlling other infectious diseases developed under similar conditions.

8313

ASSESSING THE IMPACT OF CLIMATE CHANGE ON VECTOR BEHAVIOR AND VECTOR CONTROL STRATEGIES

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Vector-borne diseases constitute about 17% of global infectious diseases, significantly impacting health and economic progress. With climate change and increased global mobility, these diseases increasingly threaten human and animal health, as well as food security. Vectorial capacity, defined as the total number of potentially infectious bites that would eventually arise from all the mosquitoes biting a single host on a single day, quantifies the potential of vector populations to transmit pathogens. Existing models of vectorial capacity vary, typically focusing on singular phenomena such as climatic factors or vector control measures. However, the interplay between these elements remains underexplored. We developed an integrated model of vectorial capacity that synthesises elements from previous models while introducing novel considerations of vector behaviours, including the impact of climate on vector control strategies and the effects of multiple feeding behaviours within a single gonotrophic cycle. Utilising historical climate data this model can then be used to observe historic changes in vectorial capacity and identify effective vector control strategies. Our findings indicate that regions previously free from or only sporadically affected by vector-borne diseases have experienced an increase in vectorial capacity over the past fifty years. This trend suggests a likely increase in the frequency of disease outbreaks in these areas. Effective disease control programs will require enhanced coverage and adherence to mitigate the effects of climate change on disease burden. Our analysis further demonstrates that vector control is particularly effective against vectors that exhibit multiple feeding behaviour per gonotrophic cycle. The increasing vectorial capacity driven by climate change poses significant economic and public health challenges globally. Moreover, our results highlight the increased efficacy of vector control measures against vectors with multiple-feeding behaviours, which could inform the development of more effective disease mitigation strategies.

8314

PRESSURE-TESTING AND PROTOTYPING AI TOOLS FOR ENHANCED QUALITATIVE DATA ANALYSIS IN GLOBAL HEALTH: A CASE STUDY ON DRC VACCINATION SURVEYS

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The Democratic Republic of the Congo is currently facing multiple disease outbreaks driven by low rates of childhood vaccination. Understanding the barriers to immunization services is key to effectively adapting the immunization program. Detailed information on reasons for non-vaccination exists in free-text responses to survey questions but analysis of such data is resource-intensive and often infeasible. This study evaluates the use of large language models (LLMs) to analyze qualitative responses from caregivers, surveyed nationally in three rounds during 2020-2023. The surveys revealed a vaccination rate of 40% and considered 29 categories of reasons for non-vaccination. Approximately 8,000 responses selected 'other' and entered free text, requiring deeper analysis. We employed multiple methodological approaches, ex., combining natural language processing (NLP) techniques with the generative capabilities of GPT-4, to categorize responses and identify novel, emergent themes. The AI-assisted computational workflow can be executed quickly and with an ~85% accuracy rate benchmarked against a human intelligence (HI) evaluation of 1000 responses. The AI assistant successfully classified responses into both existing categories and identified insightful new categories such as "Number of children present does not warrant opening a new vaccination vial". We also identified and quantified the limitations of this approach with regards to choice of LLM, model parameters, and prompt engineering designs. The integration of LLMs like GPT-4 with NLP methodologies presents a promising avenue for analyzing vast amounts of unstructured qualitative data in global health. It facilitates the discovery of nuanced factors influencing vaccination rates, which traditional survey data analysis might overlook. This study demonstrates the potential of AI in streamlining data analysis in global health research and underscores the opportunity for building new data collection instruments that incorporate LLMs to generate more granular insights. The adaptability of AI tools suggests broad applicability across diverse studies.

8315

AN AI ASSISTANT TO SUPPORT DISEASE MODEL BUILDING, SIMULATION, AND ANALYSIS: ACCELERATING MODELING RESEARCH AND DEVELOPMENT IN RESOURCE-CONSTRAINED SETTINGS

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Dynamic disease modeling is an essential tool in understanding and predicting disease patterns, aiding in the planning and implementation of health interventions. However, the complexities involved in building and running these models, including the need for specialized training and software, can be prohibitive, especially in resource-constrained settings. We propose an AI-based modeling assistant, leveraging OpenAI's latest

models and API features, including file retrieval, code analytics, and custom functions. The assistant is designed to leverage existing disease model simulation engines and enable users to either build model and configuration files from natural language prompts or import a document that includes an explicit model description. For this proof-of-concept, we leverage existing and open-source disease simulation engines like the Compartmental Modeling Software (CMS). Our AI assistant facilitates the entire process from characterization to execution and analysis of disease models. It correctly interprets model specifications, produces a syntactically correct model files, runs simulations using a dockerized CMS, and analyzes results with the aid of Code Analytics for plotting and downstream analysis. The AI assistant incorporates expert knowledge and established best practices, offering customized support for users at various skill levels, from those merely model-curious to seasoned disease modelers. We also identify the current limitations of the assistant, i.e., when the assistant begins to hallucinate with the specification of complex system setup. By democratizing access to disease modeling and augmenting existing capacity-building activities such as training and workshops, this AI assistant represents a significant step toward enhancing global disease modeling capabilities. It empowers researchers in resource-limited settings with the ability to rapidly and independently iterate on building models for their own use-cases. This is a novel approach in disease modeling research, with potential broad-reaching implications for global health.

8316

THE MOST FORETOLD HUMAN RABIES CASE IN LATIN AMERICA VIEWED UNDER THE ONE HEALTH APPROACH

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In 2014, a rabid dog was detected in Arequipa, Peru, signaling the first reintroduction of the virus to an area previously declared rabies-free in Latin America. Since then, a combination of reactive ring vaccination, city-wide mass vaccination campaign, community-based and spatially targeted surveillance activities, and education campaigns have been conducted. However, the number of detected rabid dogs has remained constant for years, culminating in the first detected human rabies case reported in October 2023, in Arequipa. We aimed to integrate epidemiological, socio-ecological, and policy data to understand the conditions leading to this human rabies case and potential future cases, threatening the goal of zero dog-mediated human cases by 2030. We conducted multi-year surveys combined with qualitative studies to understand barriers to dog vaccination; visited the 'grout' of the city (e.g., water channels, periphery) to characterize the ecology of free-roaming dogs; and evaluated surveillance efforts, dog rabies incidence, and socio-economic status (SES) to estimate social and spatial inequities associated with rabies. We discovered feral dogs living in caves around the city. We found behavioral, logistical, and geographical barriers that prevent owners from vaccinating their dogs, but also revealed organizational, economic, and operational barriers that impede the optimization of mass vaccination campaigns. We found a strong negative association between SES, rabies incidence, and surveillance efforts, evidencing deep social and spatial inequities associated with rabies. Dog-mediated human rabies remains being neglected globally, potentially due to its elimination from high-income countries. We report for the first time that for dog rabies inequities are also present within very fine spatial scales. Challenges to reaching herd immunity exist both in communities and implementing organizations. The presence of cave-dwelling dogs poses new One Health challenges. Our data show that the persistence of conditions that led to the 2023 human case threatens the prospects of eliminating dog-mediated human rabies by 2030.

8317

ONE HEALTH SURVEILLANCE APPROACH ILLUMINATES SILENT SLEEPING SICKNESS TRANSMISSION HOTSPOTS IN HAMLETS OF OYO STATE, NIGERIA

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Approximately 55 million individuals in sub-Saharan Africa face the peril of contracting sleeping sickness (SS). Its occurrence is driven by an epidemiologic triad comprising *Trypanosoma brucei gambiense*, tsetse flies, humans, animals, and a propitious environment. Despite advancements in diagnostics, the actual status of SS in Nigeria remains elusive. In our quest for clarity, we embraced a holistic approach: one health surveillance comprising human and animal population surveys, entomological and ecological assessments to illuminate SS transmission hotspots and risk factors in sparsely-populated remote rural hamlets. To do this, we collected blood samples from 72 consenting humans and 145 animals. Furthermore, tsetse flies were captured using odor-baited traps, and species diversity and spatial distribution were assessed. Captured tsetse flies, human and animal blood samples were screened for *T. b. gambiense* infection, and sources of tsetse bloodmeal were identified using colorimetric Loop-mediated amplification respectively. Captured tsetse flies were *Glossina palpalis palpalis* with 16.90% *T. b. gambiense* infection rate. Humans were preferred bloodmeal source (41.67%, p= 0.010). Alaho has the highest tsetse fly density of 10.33 flies/trap/day, highest human-tsetse fly contact and transmission risk index of 80787.31. Anthropogenic activities and ecological conditions were found to impact tsetse fly density ($p < 0.0001$). The prevalence of *T. b. gambiense* among humans and domestic animals was 40.28% and 40.69% respectively. Illiteracy (p= 0.01) and defecation in forests (p= 0.0004) were major determinants of SS occurrence. We identified thirteen SS transmission hotspots. Correlation exist between humans, animals and tsetse fly infection ($p < 0.0001$) depicting one health implication. Silent transmission of SS is ongoing warranting intensified sensitization and surveillance. Animals serve as reservoir hosts aiding persistence of SS in the hamlets. An urgent one health and WASH-guided strategic control approaches are imperative to prevent SS epidemic in the hamlets and devastating resurgence in Nigeria.

8318

MORPHOLOGICAL AND MOLECULAR IDENTIFICATION OF *B. MALAYI* AND OTHER FILARIAL SPECIES IN ANIMALS FROM BELITUNG, INDONESIA: IMPLICATIONS FOR LYMPHATIC FILARIASIS ELIMINATION

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In Indonesia, *Brugia malayi* is the most common filarial parasite causing lymphatic filariasis (LF) in humans. Belitung District was considered free of LF in 2017 after 5 rounds of mass drug administration (MDA) and 3 transmission assessment surveys (TAS). However, surveys in 2021 and 2022 revealed microfilaria (Mf) rates exceeding 1% in some villages. This study investigates the presence of *B. malayi* and other filarial species in potential animal reservoirs comparing microscopy and real-time PCR targeting filarial, *B. malayi*, *Brugia pahangi* and *Dirofilaria immitis* DNA. Blood samples were collected from 495 animals in villages with and without human LF infections. PCR showed a higher detection rate (94%) compared to microscopy (78%) for identifying any filarial infection in blood. It also showed a higher detection rate in identifying different filarial species. Using PCR *B. malayi* was detected in 7.1% (35/495) of all the samples.

Infection rate in cats was 4.1% (12/291), 2.4% (1/41) in dogs, and 13.5% (22/163) in macaques. *B. pahangi* DNA was only found in 5.1% (17/332) of dog and cat samples while *D. immitis* DNA was exclusively detected in 39% (16/41) of the dog samples. Using microscopy an unknown *Dirofilaria* species was found in 20.3% (33/163) of the macaque samples that could not be speciated and has not been characterized molecularly previously. Morphologically, a co-infection in one dog with *B. malayi* and *D. immitis* was observed, but PCR only detected *B. pahangi* and *D. immitis* DNA. By microscopy identified as a single infection, PCR detected dual co-infections in one cat (*B. malayi*/*B. pahangi*) and one dog (*B. pahangi*/*D. immitis*) and a triple co-infection in one dog. The highest mean *B. malayi* Mf density was found in macaques (712 Mf/mL, N=22), which was even higher compared to the mean Mf density in humans (583 Mf/mL, N=42) living in the same area. This study highlights the need for molecular methods to accurately identify Mf, particularly due to multiple filarial species found in animals. In order to eliminate LF in humans enhanced surveillance and intervention may be required in areas with animal reservoirs, especially in those with macaques.

8319

PAN-CANADIAN RESPONSE TO HIGHLY PATHOGENIC AVIAN INFLUENZA (HPAI) A(H5N1): BENEFITS AND CHALLENGES OF A ONE HEALTH APPROACH

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Human and animal health are interdependent and linked to the ecosystems where they coexist. Wild birds, especially waterfowl, are considered natural reservoirs for avian influenza A viruses, such as the currently circulating highly pathogenic avian influenza (HPAI) A(H5N1). This virus was introduced into Canada in Autumn 2021 through wild bird migration and quickly spilled-over into domestic poultry by December 2021. Infections in other species that eat wild birds or are exposed to common contaminated environments such as cats, red foxes, skunks, raccoons, and marine mammals have been reported during the current outbreak. Increased infections in birds and non-human mammals, and the prolonged duration of the epizootic provides more opportunity for replication and mutation of the virus. To date, while human infections with the current strain of A(H5N1) have been rare, the virus has the potential to cause serious disease in people. Concerns regarding A(H5N1) are wide-ranging, and include: animal health and wellbeing; business and employment; food systems, safety and security, including traditional foods of Indigenous and Inuit Peoples; value chain impacts and international trade; wildlife susceptibility in endangered and at-risk species; and, mental health and wellbeing of individuals in many sectors. A One Health approach, involving a network of partners and stakeholders has been taken in Canada through a range of activities, including: development of surveillance plans in wild birds; on-farm response and control; multisectoral research to explore the link between domestic and wild birds; prioritization exercises to inform surveillance and research; development of risk communications and guidance for key audiences, including the public; sharing of intelligence through cross-sector multidisciplinary Working Groups; and, international reporting and collaboration. This presentation will describe a range of benefits and challenges associated with taking a One Health approach for the prevention, response and control of HPAI A(H5N1) in the Canadian context.

8320

A ONE HEALTH APPROACH IN DETECTION OF INFECTIOUS DISEASES IN NORTHERN GHANA

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Interactions between a pathogen, host, environment, and habitat disruption can provide opportunities for new or emerging disease spillover events. A collaborative One Health approach is needed to develop appropriate plans for response and control of some of these diseases. We investigated infectious etiologies of febrile illnesses among adults presenting at the War Memorial Hospital in Northern Ghana from May 2022 to June 2023. Those who presented with thermal dysregulation of ≤ 35.5°C or ≥ 38°C with unknown disease origin were enrolled. Confirmed zoonotic febrile cases triggered targeted entomological surveillance activities and enrollees were invited to participate in quantitative household surveys and purposive focal group discussions to investigate animal-rearing practices and socio-behavioral risk factors. In addition, weather monitoring stations were installed at three local senior high schools and data were collected daily as part of the students' science education. Malaria was detected in 50 (50%) of the enrolled febrile patients using the BioFire Global Fever Panel, with a notable increase during the rainy season. Of 2,369 mosquitoes collected using CDC light traps, 1,817 comprised Anopheles (76.7%), followed by Culex (20.7%) and Aedes (2.6%). Plasmodium falciparum infections were confirmed in 15/1185 (1.26%) of Anopheles tested - with positives identified only as An. gambiae s.s. and An. arabiensis by species-diagnostic PCR. Using the BioFire Respiratory Panel, the following viral infections were also detected: Hepatitis C virus (n=6), Influenza virus (n=4), Enterovirus (n=3), Human Immunodeficiency Virus (HIV) (3), Respiratory Syncytial Viruses (RSV) (n=3), Human Metapneumovirus (n=1), Parainfluenza virus (n=1) and SARS-COV-2 (n=3). Based on social surveillance interviews, close-contact animal housing withing within homesteads and uninspected meat consumption were found to constitute potential risks for pathogen transmission. This study illustrates the need for further multidisciplinary approaches that consider social and environmental factors to mitigate human and animal health threats in Ghana.

8321

THE ONE HEALTH INITIATIVE FOR ZOONOTIC DISEASE RESPONSE IN EASTERN UGANDA. OPPORTUNITIES AND AREAS FOR IMPROVEMENT

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The One Health initiative focuses on linkages of human, animal, and environmental health and is pivotal for global health security. Collaborative efforts in One Health are imperative to effectively address emerging health threats. We conducted an evaluation of the One Health initiative in the districts of Eastern Uganda, January to March 2024, targeting the pillars of zoonotic outbreak response including coordination, case management, surveillance, vaccination, and risk communication. Three outbreaks, anthrax in Bukedea and Kapchorwa, and rabies in Katakwi, occurred in 3 (11%) of 27 districts. Response meetings involving multisectoral teams and partners were conducted regularly, but without the inclusion of One Health plans and committees. Human alerts consistently followed animal alerts, yet Public Health authorities were only notified after alerts from humans. Animal samples were collected only after disease manifestation in humans for anthrax, while no samples were obtained for rabies. The absence of a regional animal laboratory led to improvised sample collection from animals. There were no surveillance dashboards for real-time updates of animal or human surveillance data. Efforts in capacity building focused on surveillance, sample collection, and infection prevention and control, with collaborative support in only Katakwi. Rabies vaccination for animals and humans occurred in Katakwi, whereas there was a shortage of anthrax vaccines. Community engagement lacked coordination across sectors and standardized sensitization activities. Poor refuse disposal practices were observed in Katakwi, while Bukedea and Kapchorwa experienced unregulated cattle movement and meat sale without intervention from the environmental health team. While some aspects of the One Health initiative, including multi-sectoral teams and sample transport, are in place, critical gaps remain, including lack of a regional animal laboratory and the need for improved disease notification systems. Urgent actions are needed to assist districts in One Health planning, and the establishment and operationalization of One Health committees.

8322

A ONE HEALTH APPROACH TO PREVENTION, DETECTION, AND RESPONSE TO CRIMEAN-CONGO HEMORRHAGIC FEVER IN THE KURDISTAN REGION OF IRAQ

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In 2022, Iraq experienced the largest outbreak of Crimean-Congo hemorrhagic fever (CCHF) in over 40 years, recording 379 human cases and 74 deaths. The stark increase in reported cases, primarily from governorates across the southeast, was attributed to interruptions in vector control and prevention activities during the COVID-19 pandemic. In an effort to prevent additional surges in cases and deaths, the Federal Government of Iraq (GIOI) and the Kurdistan Regional Government (KRG) designed multisectoral, One Health (OH) initiatives for CCHF prevention, detection, and response. In coordination with the GOI, KRG's Ministries of Health (MOH) and Agriculture (MOA) conceived joint activities for implementation in the Soran and Khabat Districts of the Erbil governorate to pilot their targeted interventions. Beginning in spring 2024, awareness campaigns, data collection, and acaricide spraying were applied to households with previously confirmed CCHF cases. Surveys captured information on residential demographics, owned animals, as well as vector presence and concentration. Tick samples were collected by field teams from animals, outdoor shelters, and the surrounding property and transported to the Central Veterinary Laboratory for identification and testing. Acaricide spray was then applied to residences, animals, and any outdoor facilities; follow-up investigations and tick sampling were also performed post-acaricide spray. Finally, educational risk campaigns were conducted to support household and community awareness. KRG's OH approach has also been adopted by the GOI to better integrate multisectoral strategies for tickborne disease threats across the country. This integrated response to CCHF in Iraq is an on-going, evolving collaboration on One Health; however, it highlights the importance of comprehensive surveillance, field research, and evidence-based strategies for tickborne diseases. Actively engaging in multisectoral collaboration has proven effective in aligning priorities, consolidating resources, and implementing disease prevention and control initiatives.

8323

FIRST PILOT RELEASE OF X-RAY STERILIZED MALE *AEDES AEGYPTI* TO CONTROL INVASIVE MOSQUITOES IN SOUTHERN CALIFORNIA: STRATEGY, LESSONS LEARNT AND THE WAY FORWARD

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The urban-adapted, daytime-biting *Aedes aegypti* is the primary mosquito vector of dengue and has the potential to transmit several other arboviruses, including Zika, chikungunya, and yellow fever. In California, *Ae aegypti* has spread in over 300 cities within 22 central and southern counties in less than a decade. Due to its cryptic breeding habitats, control efforts have been extremely challenging. Sterile Insect technique (SIT) has brought novel opportunities to strengthen mosquito control programs. The West Valley Mosquito and Vector Control District in southern California has embarked on SIT as part of the integrated vector management to control invasive *Aedes* mosquitoes. Our approach utilizes SIT in targeted *Aedes* hotspots instead of large-scale mass releases. This work aims to assess the impact of targeted X-ray sterilized male mosquito releases on local population dynamics of invasive *Aedes* mosquitoes. In our pilot program, we released X-ray sterilized male *Ae. aegypti* mosquitoes at three locations in southern California. First, a site was selected based on counts from weekly surveillance data using BG Sentinel traps. Baseline (prior to release) and follow-up cluster mosquito trapping was conducted within 100 and 200 yards from each site. A 100-times the number of female *Ae. aegypti* from BG Sentinel traps were released at each site. Follow-up cluster mosquito trapping was conducted at nine sites around each release site for four consecutive weeks. The results indicated a reduction of *Ae. aegypti* population as high as 71% four weeks after release. Preseason sterile mosquito releases are currently underway. Lessons learnt from this pilot program help to optimize SIT as an additional tool in our invasive mosquito control program.

8324

CHANGING PARASITE SPECIES DYNAMICS AND SPECIES-SPECIFIC ASSOCIATIONS OBSERVED BETWEEN *ANOPHELES* AND *PLASMODIUM* GENERA IN SOUTHWEST BURKINA FASO

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The prevalence of malaria parasite species in some parts of Africa is rapidly changing. Relatedly, the natural vector competence and vectorial capacity of African anophelines for human *Plasmodium* species has only been well described for *P. falciparum* and is unclear in the context of mixed and non-falciparum infections. Over the course of the two RIMDAMAL clinical trials (2015 and 2019-2020) testing ivermectin for malaria control in the same region of Burkina Faso, we sampled participants' blood and their households for *Anopheles* spp. mosquitoes and tested these samples for *Plasmodium* species. *Plasmodium* prevalence in participants' samples was high in both trials (>50%). However, *P. falciparum* mono-infections predominated in the 1st trial but infections with mixed and non-falciparum species compromised 11-27% of infections in the 2nd trial with notable changes in species detected in participants over time. Furthermore, while *An. gambiae* s.l. was main vector captured in both trials, *An. funestus* mosquitoes were unexpectedly prevalent in the first season of the 2nd trial. Notably, *An. funestus* had a significantly higher overall sporozoite rate (15.3%; 38/249) over the intervention period than *An. gambiae* s.l. (4.8 %; 122/2528) ($P < 0.0001$) in the 2nd trial. We further found that the *Plasmodium* species detected in abdominal and head+thorax tissues of these two vector species significantly differed; *P. falciparum* sporozoites were more prevalent in *An. gambiae* s.l. ($P < 0.0001$), while *P. ovale* sporozoites were more prevalent in *An. funestus* ($P < 0.0001$). Our field-derived mosquito data suggest differential vector competence or vectorial capacity for *P. falciparum* and *P. ovale* at the field site in two of the most common African *Anopheles* species. Further work is underway to determine the mechanisms underlying these potential differences, as well as how these findings could impact the existing control measures and their resulting efficacy.

8325

EVALUATION OF HUMAN EXPOSURE TO MALARIA VECTORS USING AN IMMUNO-EPIDEMIOLOGICAL BIOMARKER (*ANOPHELES*-GSG6-P1 SALIVARY PEPTIDES) IN FOUR RURAL AREAS IN CAMEROON

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In some areas of Africa, malaria still poses a threat to the health of urban dwellers. Vector control remains the main strategy to combat this disease. Due to significant limitations in methods currently used to assess human exposure to Anopheles bites, novel indicators assessing human antibody responses to Anopheles salivary peptides (gSG6-P1) represent a promising biomarker tool that could determine human-*Anopheles* contact and malaria risk. This study assessed sociodemographic factors influencing human exposure to *Anopheles* bites in rural cities of Cameroon. The study was conducted in Njombe (NJ), Kekem (KE), Belabo (MB) and Ouami (OU). Information on villages, gender, age, presence of vegetation around the house, bed net use was recorded using a questionnaire, human blood was collected to determine the level of IgG against *Anopheles* gSG6-P1 salivary peptide, using ELISA method. IgG levels to gSG6-P1 varied significantly bites by village. Specifically, IgG levels to gSG6-P1 were significantly higher in Njombé compared to Belabo and Ouami (all $p=0.01$). Age groups, gender, and owning a bed net did not seem to influence the exposure to *Anopheles* in the study area (all $p>0.05$). However, bed net use, condition and presence of vegetation around the house significantly influenced the exposure to *Anopheles*. Study participants who declared using their bed nets had significantly lower IgG responses to the *Anopheles* gSG6-P1 ($p<0.0076$), thus lower exposure to malaria vector bites, than those who declared not using their bed nets. Expectedly, participants who declared using bed nets with holes or reported vegetation around their houses had significantly higher levels towards *Anopheles* (median= 0.269 and 0.269, respectively) compared to those who didn't (all $p<0.05$). Antibody responses towards *Anopheles* gSG6-P1 salivary peptides vary with the village of residence, bed net use and condition and the presence of vegetation around the house. This immunological tool could be relevant to help malaria control programs to evaluate vector control strategies on human-vector contact at national and even international scale.

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ASSESSING INSECTICIDE TREATED NETS PERFORMANCE WITH BIOMARKER OF *ANOPHELES GAMBIAE* S.L GSG6-P1 SALIVARY PEPTIDE ANTIGEN: A LONGITUDINAL STUDY IN MALI

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The Anopheles gSG6-P1 salivary peptide antigen enables the detection of individual and population-wide human exposure levels to Anopheles bites. This represents a novel evaluation tool for assessing insecticide-treated net (ITN) effectiveness for malaria control traditionally performed using entomological and parasitological indicators. This study investigates the correlations among Anopheles biting rate, ITN hole index (HI), and malaria *Plasmodium falciparum* prevalence, alongside the novel use of the Anopheles gSG6-P1 salivary peptide antigen as an indicator of ITN performance. A durability monitoring of ITN was conducted over three years in Kénieba and Kita, western Mali, with a cohort of 549 ITNs (Yorkool and PermaNet 2.0) and 311 children under five. Assessments of ITN physical integrity and *Anopheles* biting rates were conducted annually. Malaria *P. falciparum* prevalence and the immunoglobin G (IgG) response to the gSG6-P1 antigen were assessed alongside net use. An association between ITN physical condition and malaria transmission indicators was observed. *An. gambiae* sl biting rate remained low, under 3 bites/person/night. After three years of usage, when 78% PermaNet 2.0 remained in serviceable condition, malaria prevalence (43%) and the IgG responses to gSG6-P1 (dDO 0.16) were low, and when 50% for Yorkool remaining in serviceable condition, malaria prevalence (65%) and the IgG responses to gSG6-P1 was (dDO 0.35). Higher hole indices of ITN were associated with increased malaria prevalence and elevated IgG anti-gSG6-P1 levels, indicating greater exposure to mosquito bites. The biomarker gSG6-P1 antigen of *An. gambiae* sl was used for the first time in Mali to determine ITN performance, and the results were consistent with physical integrity and parasitological indicators. This biomarker when added to existing traditional indicators may provide a comprehensive view of ITN effectiveness and help in decision-making by the National Malaria Control Program.

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CHARACTERIZATION OF LARVAL HABITATS TO ASSESS THE FEASIBILITY OF LARVAL SOURCE MANAGEMENT AS A SUPPLEMENTARY INTERVENTION IN A HIGH MALARIA TRANSMISSION AREA IN NIGERIA AND A LOW MALARIA TRANSMISSION AREA OF ZAMBIA - OPERATIONALIZING THE WORLD HEALTH ORGANIZATION'S THE FEW, THE FIXED. AND THE FINDABLE

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Malaria remains a major public health concern in Africa, and larval source management (LSM) is (re)emerging as a tool for some National Malaria Programs to supplement contemporary vector control efforts for reducing the burden. In 2022-2023 the U.S. President's Malaria Initiative (PMI) VectorLink project, utilized geospatial tools to assess and map all potential *An. gambiae* s.l. or *An. funestus* s.l. larval habitats in a high-burden rice irrigation farm area of Nigeria - Argungu, Bunza, and Kalgo Local Government Areas in Kebbi State, and in a low-burden area of Zambia- Katete and Chipata districts in Eastern Province. Each habitat was characterized by habitat type, presence of larvae, water longevity in the habitat, size, and other factors. The number of larval habitats enumerated and assessed ranged between 2088-3218 from two surveys in Nigeria and 775-1338 from four surveys in Zambia. In Nigeria, 98.7% of the habitats were permanent or semi-permanent, while in Zambia this number was 90.1%. *Anopheles* larvae were present in the habitats at each survey round in both countries; the highest habitat positivity in Nigeria ranged from 79-87% in August 2022 and 22-74% in Zambia in May 2023. In Kebbi, the main larval habitats were small to large rice basin irrigation farms averaging about 7.5 hectares; in Zambia, habitats were small to medium-sized such as ditches associated with gardens measuring 14-23m in habitat perimeter. More than 90% of the habitats in both countries were accessible. These larval habitats comply with the WHO's "fixed" and "findable" guidance for larviciding. In Zambia, we conducted field simulations to derive an operational definition for "few" habitats. One person doing weekly larviciding in a 10km^2 settlement could cover a 2km^2 area per day each with a total habitat perimeter of 1800m per km^2. We determined that habitats are "few" when there is less than 1800m of habitat perimeter per km^2 of a settlement. All sites in Zambia met this criterion for "few" habitats. An LSM pilot study may demonstrate impact in the high transmission area in Nigeria and possible added acceleration towards elimination in the low transmission area in Zambia.

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MODELS TO INFORM THE DESIGN OF FIELD TRIALS OF NOVEL GENE DRIVE INTERVENTIONS TO SUPPRESS MALARIA VECTOR POPULATIONS

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Gene drive technologies are a promising means of malaria vector control with the potential to cause widespread and sustained vector population suppression. Here we consider gene drives that have been engineered in *Anopheles* vector species to target female fertility, suppressing the vector population as the gene drive spreads. Large cage experiments have shown that these gene drives can crash mosquito populations within a year, yet their performance in wild populations remains untested. In preparation for the first field trials, we developed a data-driven mathematical model to estimate the impacts of gene drive releases on vector abundance, malaria prevalence and clinical cases in children. The model parameterisation is specific to candidate release sites in Burkina Faso, considering local vector ecology and species composition, malaria transmission intensity and the historical coverage of vector control and human treatment interventions. We simulated cluster randomised control trials designed to detect gene drive impacts over a range of trial designs, accounting for noise in measurements of mosquito abundance and malaria prevalence and incidence. Trials aiming to detect vector suppression have greater statistical power when gene drives target both *An. coluzzii* and *An. gambiae* rather than targeting *An. coluzzii* only. Regardless of the target vector species, trials have greater power using either malaria prevalence or incidence as the primary endpoint, rather than vector population suppression. We estimated the size of a trial required for 90% power to detect a reduction in malaria prevalence of at least 30%, and determined how this depends on fitness costs incurred by the gene drive on mosquitoes and the spread of the gene drive from release into control clusters. Our results can inform the development of field trial protocols for these novel interventions.

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DEVELOPMENT OF SIT FOR *AEDES ALBOPICTUS* CONTROL IN CHINA: A PRELIMINARY FIELD STUDY

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Aedes albopictus is the primary vector of dengue fever in mainland China. Vector control is essential for dengue prevention. Due to resistance from overuse of insecticides, there is a critical need for alternative control strategies like *Wolbachia*-based IIT or radiation-based SIT. Previously our team has successfully eliminated *Ae. albopictus* on two isolated islands in Guangzhou using IIT/SIT. Testing these techniques in urban centers is crucial to validate their effectiveness and support area-wide use of technique like SIT for controlling mosquito populations and mosquito-borne diseases. A *Wolbachia*-free *Ae. albopictus* GT strain was developed and its rearing efficiency was optimized under laboratory conditions before its transfer to a mass rearing facility. Standard mass rearing procedures have been established for GT strain with two important indicators: the induced sterility and female contamination rate being >99.0% and <0.1%, respectively. A field trial study performed in Guangzhou, China by releasing irradiated GT males indicated that SIT is effective in reducing the population and the biting rate of *Ae. albopictus* in urban area, where there was a reduction of the population by 40% and of the biting rate by 75%. Expansion of the releases in a larger area is needed in order to assess the cost-effectiveness of SIT for mosquito population control.

8330

A CLINICAL SCORE TO SCREEN CHILDREN IN NEED FOR CHRONIC FASCIOLIASIS TESTING IN CUSCO - PERU

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Fasciola is a trematode hyperendemic in Peru presenting with few and unspecific symptoms particularly among children in the community. Tools to identify children in need for screening are urgently needed. The aim of this study was to determine the sensitivity and specificity of a clinical score to identify children that will benefit from screening for chronic fascioliasis. This is a secondary data analysis of a study evaluating fascioliasis among children 3-16 years in Cusco. We included data collected using a demographic, symptoms, and signs questionnaire and laboratory results from stool microscopy, Fasciola ELISA, transaminases, and complete blood counts. Chronic fascioliasis was defined as having *F. hepatica* eggs in the stool. No infection was defined as not having *Fasciola* or other parasite eggs in the stool and having negative serology. ROC curves and logistic regression were used to determine the sensitivity and specificity of symptoms and laboratory combinations to identify chronic fascioliasis. The analysis included 909 children of which 162 had chronic fascioliasis and 747 had no infection. Half were female and the mean age was 9.6 years (±3.6). Comparing symptoms in children with chronic fascioliasis and no infection, right upper quadrant pain ($p \leq 0.001$), fatigue ($p \leq 0.001$), anorexia ($p=0.006$), vomiting ($p=0.009$), and diarrhea ($p=0.040$) were more common in the former. Similarly, the hematocrit ($p=0.038$), hemoglobin ($p=0.008$), leucocytes ($p=0.043$), and eosinophils ($p \leq 0.001$) levels were different between the groups. Combining right upper quadrant pain, fatigue, and eosinophilia identified children with chronic fascioliasis with 85% sensitivity and 92% specificity. A clinical score applied in the community can identify children that would benefit from stool microscopy testing for fascioliasis. This could simplify screening and allow a better use of triclabendazole.

8331

DIAGNOSTIC ACCURACY OF COLPOSCOPY FOR FEMALE GENITAL SCHISTOSOMIASIS SCREENING AT PRIMARY LEVEL OF CARE

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Diagnosis of neglected tropical diseases poses a major challenge due to the lack of tools that are adapted to endemic contexts. Among others, Female Genital Schistosomiasis (FGS), caused by persistent infection with *Schistosoma haematobium*, is an excellent example. Left untreated, it can lead to complex gynecological syndromes with consequences such as pelvic pain or infertility. The standard screening for FGS is colposcopy, a complex clinical examination that often cannot be performed in resource-limited contexts due to lack of expertise or insufficiently equipped infrastructures. This study aims to investigate the accuracy of colposcopy to detect FGS by trained midwives at the primary level of care. The study was implemented in the rural region of Boeny, Madagascar, where a prevalence of FGS above 60% is reported. Colposcopy images were collected by trained midwives and re-evaluated by two gynecologists through a blinded reconciliation process. Reference diagnosis was defined as agreement of both gynecologists on the FGS diagnosis; images with a conflicting interpretation were excluded from the analysis. Statistical analysis using R included descriptive statistics, measures of diagnostic accuracy and binary Poisson regression with robust standard errors. Among 660 women enrolled, 631 colposcopy images were collected. A final diagnosis from a gynecologist was available in 598 cases. Preliminary results show sensitivity of 95.9 % (95%CI 93.3-97.5) and specificity of 30.0 % (95%CI 23.7-37.1). Multivariate regression shows a positive influence on diagnostic agreement of increasing colposcopy routine in comparison to the start of the study. One study centre presents a negative influence on the agreement of diagnosis. This study shows the potential of implementing colposcopy at primary level of care as a screening tool for FGS due to the high sensitivity. Implementation could bridge the gap in access to health care in rural regions and holds potential to integrate other colposcopy-based screenings such as for cervical cancer into the service.

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TRANSCRIPTOMICS OF THE AFRICAN FRESHWATER SNAIL VECTOR *BIOMPHALARIA SUDANICA S.L.* REVEALS CANDIDATE LOCI FOR SCHISTOSOME RESISTANCE

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Biomphalaria sudanica s.l. is a major freshwater snail vector for *Schistosoma mansoni*, the causative agent for intestinal schistosomiasis, in the hyperendemic Lake Victoria basin. The disease afflicts millions of people dependent on this water source, and methods to control snail populations to curb schistosome transmission are impractical to implement. Methods to curtail transmission of the disease could be developed from the snails' naturally occurring genetic resistance, which in some cases can thwart schistosome infection. We have previously identified potential pathogen recognition receptors/effector genes within the *B. sudanica* genome. We hypothesized that genes relevant to parasite resistance will show differential expression following exposure to *S. mansoni*, allowing for more precise identification of key genetic pathways. Here, we compared the differential transcriptomic profiles of 100 *B. sudanica* snails 8, 24 and 72 hours post-exposure to either *S. mansoni* with which they are compatible or incompatible to, or sham exposed (control). Significant differential expression of transcripts was assessed (EdgeR) using pairwise comparisons (control vs. exposed groups at each timepoint). 1,472 of 23,598 genes showed differential expression at one or multiple time points. Eight hours after exposure, snails exposed to the compatible parasite showed no differentially expressed genes to sham exposed snails, whereas snails exposed to the incompatible parasite had both up- (n=41) and downregulated genes (n=175). The highest upregulated genes in both exposed snail groups 8 and 24 hours after exposure were candidate immune genes that had been shortlisted as pathogen recognition receptors prior to this study due to signs of balancing selection in the *B. sudanica* genome. Therefore, these data directly support their involvement in the *B. sudanica* immune response to *S. mansoni* and future experimental work will test their functional role in the resistance pathways of this African snail vector.

8333

AUTOMATED DIAGNOSIS OF *SCHISTOSOMA HAEMATOBIUM* WITH ARTIFICIAL INTELLIGENCE ON HANDHELD DIGITAL MICROSCOPES IN RURAL CÔTE D'IVOIRE

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Schistosomiasis continues to plague over 200 million people globally and disproportionately impacts children in Africa. The World Health Organization has called for novel tools to help monitor schistosomiasis control and elimination programs, and portable digital microscopy with artificial intelligence (AI)-supported diagnostics are a promising tool for these schistosomiasis public health initiatives. We used the computer vision model YOLOv8 to train AI object detection models for the purpose of detecting Schistosoma haematobium eggs in digital images of urine samples. These models were trained with images acquired from an earlier version of the mobile microscope during field studies conducted in Côte d'Ivoire between 2020-2022 We then used the latest generation of our mobile microscopy platform (the "NTDscope") to acquire images of urine samples processed from patients in the Azague region of Côte d'Ivoire, in January of 2024, as part of broader schistosomiasis screening and treatment programs. The digital images were acquired in both brightfield and darkfield contrasts. 75 samples were evaluated on Day 1 and again on Day 2, with an equal distribution of high-intensity and low intensity infection, and non-infected samples. Given the slight changes in optics and illumination on the new NTDscope hardware, we used the images acquired on the first day of the field study to re-train and recalibrate our AI models before the second day in the field. Preliminary sensitivity and specificity of AI models compared to conventional light microscopy was 48-95% and 16-88%, respectively on day 1, and 83-97% and 48-87%, respectively, on Day 2 following AI recalibration. These data suggest that handheld digital microscopy with automated parasite identification may be a helpful tool for schistosomiasis control initiatives.

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CHARACTERIZATION AND PROCESS DEVELOPMENT OF A *SCHISTOSOMA HAEMATOBIUM* SERINE PROTEASE INHIBITOR (SHSERPIN-P46): A NEXT GENERATION VACCINE FOR UROGENITAL SCHISTOSOMIASIS

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Urogenital schistosomiasis, caused by *Schistosoma haematobium*, currently affects millions of people in Sub-Saharan Africa. *S. haematobium* eggs trapped in urogenital tissues result in intense inflammation and eosinophilia leading to bladder wall thickening and development of masses and pseudopolyps. Urogenital schistosomiasis is also associated with hydronephrosis, active-stage lesions, cervical scarring, decreased fertility and bladder squamous cell carcinoma. In addition, people infected with *S. haematobium* have significantly higher risks of sexually transmitted infections such as HIV. Furthermore, transmission of a more virulent hybrid strain of *S. haematobium* / *S. bovis* is now being reported in Europe, a region previously considered schistosomiasis free. Hence, an urgent need to develop an effective vaccine for long term protection. Serine protease inhibitors (serpins) are key factors used by many pathogens to evade their host immune responses, and serpin-based vaccines have shown promising results in many parasite systems. In this study, we developed and characterized a candidate vaccine based on a secretory serpin from *S. haematobium* (Shserpin-p46). Transcriptional profiling and proteomics demonstrated that Shserpin-p46 is expressed in the intra-mammalian life cycle stages and localized to the parasite tegument. Recombinant Shserpin-p46 inhibited neutrophil elastase in a dose-dependent manner and was strongly recognized by putative resistant individuals and experimentally-infected rat (naturally-resistant hosts) sera when compared to chronically-infected mouse counterparts, indicating that rShserpin-p46 is not only highly immunogenic, but critically involved in disease resistance. A pilot study evaluating the efficacy of a Shserpin-p46 antigen formulated in proprietary TLR4-agonist-based adjuvants, EmT4™ and LiT4Q™ in hamster model of urogenital schistosomiasis is now underway. An effective schistosomiasis vaccine would play a major role in the overall reduction of disease morbidity thereby improving quality of life for people living in endemic regions.

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MULTIPLE ROUNDS OF PRAZIQUANTEL TREATMENTS OF *SCHISTOSOMA MANSONI* HOSTS (MICE AND HUMANS) GRADUALLY RENDER THEM LESS SUSCEPTIBLE TO REINFECTION

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Beyond transient control of the infection, additional benefits of mass drug administration (MDA) of praziquantel in endemic communities have been suggested in communities but yet to be unequivocally demonstrated. Recent studies conducted by our group revealed, in a complementary manner, the benefits of repeated administration of praziquantel. First, using *Schistosoma mansoni* infected mice, repeated infection-treatment cycles led to reduced host susceptibility to reinfection burden, but not to the onset of associated liver fibrosis. This result highlighted the development of an enhanced humoral response in mice following praziquantel treatment leading to resistance to reinfection. Resistant mice displayed higher baseline levels of serum IL-4 and IgE. Secondly, in children from communities endemic for *S. mansoni* in rural Cameroon, that have received different numbers of praziquantel MDA rounds, we similarly observed a reduced reinfection rate and burden, but not that of liver fibrosis onsets, after multiple rounds of praziquantel MDA. This was also associated with higher baseline levels of plasma IgE and IL-4 in children and robustly persisted even after correcting for all possible identifiable confounders such as age, gender, numbers of daily contacts with infested waters, body mass index, length of residence in the endemic area (AOR of the predictor variable numbers of praziquantel rounds in affecting the odds of having heavy reinfection= 0.16; p=0.03) . Taken together, our data reveal that treatment of *S. mansoni*-infected hosts with praziquantel might rewire the immune system to a conformation less permissive to subsequent reinfection under sustained infection pressure, opening up discussions on how this might affect infection prevalence, intensities, associated morbidity and transmission at community levels.

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EMPOWER: ENRICHMENT METAGENOMIC PROFILING FOR WOMEN'S REPRODUCTIVE HEALTH

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Schistosomiasis is a chronic parasitic disease, affecting the health of more than 200 million people, with devastating clinical and socio-economic impact. Female genital schistosomiasis (FGS) is a long-term, debilitating consequence of urogenital *Schistosoma haematobium* infection - estimated to affect up to 56 million girls and women in sub-Saharan Africa. FGS is

associated with significant maternal complications such as sub/infertility, ectopic pregnancy, intrauterine growth restriction and preterm labour, likely increased risk of human papillomavirus (HPV)/cervical cancer and susceptibility to sexually transmitted infections (STIs; including HIV). STIs are another ongoing global health burden, with over one million infections acquired every day worldwide. FGS is frequently misdiagnosed as an STI (symptoms often mimic) - leading to inappropriate antibiotic treatment, furthering antimicrobial resistance, while causing social harms and stigma. In settings where adequate laboratory service is lacking, the coexistence of FGS/STIs poses a significant diagnostic challenge for healthcare providers managing patients with urogenital complaints. Since its advent, Next Generation Sequencing (NGS) has been prohibitively expensive for routine diagnostic/epidemiological use in low- and middle-income countries. We have developed in-country (Zambia), cost-effective enrichment NGS protocols together with computational pipelines, for organism detection, drug resistance and vaginal microbiome analysis. We have designed a targeted metagenomic multi-pathogen sequencing panel (~45, 000 x120 base pair oligonucleotide bait-capture probes), comprising all common STI related viruses, bacteria, and parasites (including S. haematobium). Multi-pathogen and drug resistance analysis will be shown utilizing cervicovaginal swabs from different communities in Zambia. The utilization of this novel technology will EMPOWER vulnerable girls and women, within longer-term public health strategies, to engage with effective rapid diagnostics and treatment, while minimizing stigma and disruption to daily life.

8337

SEROPREVALENCE AGAINST MULTIPLE VIRUSES AT HUMAN ANIMAL INTERFACE IN BUKAVU, DEMOCRATIC REPUBLIC OF CONGO

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The Democratic Republic of Congo has a long history of emerging zoonotic infections, such as Ebola and Monkeypox. This study aims to determine the prevalence of serological markers of zoonotic infectious diseases in Bukavu, South Kivu. A cross-sectional study was conducted from April to May, 2023, among humans and domestic animals in Bukavu. Pregnant women, blood donors, and individuals in contact with animals were included. After obtaining their consent, participants completed a questionnaire and provided a blood sample on filter paper. Consent was also obtained to collect blood samples from animals. Samples were stored at -20°C. Detection of antibodies against antigens for Ebolavirus (NP, GP, VP40), SARS-CoV-2 (SP, NP), Arboviruses (ONNV_E2, USUV_NS1, DENV2_NS1, DENV3_NS1, DENV4_NS1, CHKV_E2, ZIKV_NS1, WNV_NS1, WNV_DIII), and Mpox was conducted using previously developed multiplex serology with the Luminex® technique for humans. Adaptation of the assay for domestic samples is in development. Out of 1427 human participants, 1407 provided a blood sample, of which 1181 samples were analyzed. Among them, 62.3% were females and 37.7% males, with a median age of 24 years. The majority (89.9%) were either blood donors or pregnant women, while 10.1% were at-risk workers. The seroprevalence of Ebola virus, considering positivity for at least two Ebola antigens, was 0.2%. No positive cases were detected among individuals in contact with animals. For SARS-CoV-2, the seropositivity was 32.4%. Among arboviruses, the seropositivity for ONNV was 4.2% in the at-risk group and 0.8% in the general population (p=0.0009). The prevalence of WNV was 1.2%. Among farmers and slaughterhouse workers, Mpox seroprevalence was 5% versus 1.8% in the general population (p=0.021). 507 animals were sampled and analysis is ongoing. These preliminary results demonstrate that SARS-CoV-2, ONNV, WNV, and Mpox viruses are the most prevalent in the human population in Bukavu. Expanding research to include animals is crucial for a better understanding of zoonotic infections for more effective prevention strategies, and mitigating future outbreaks

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EXPOSURE TO MAYARO VIRUS IN THE IN THE PERUVIAN AMAZON

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Iquitos is the largest urban center (~400K people) in the Peruvian Amazon, an epidemiological island only accessible by boat or air, with a range of nearby communities along three major rivers and a 90-km road. The area has a well-documented history of dengue outbreaks, and low numbers of infections with other arboviruses, including Mayaro virus (MAYV), are detected in residents, with occasional small outbreaks. To assess MAYV circulation in and around Iquitos, we leveraged samples from a 2016-2018 community-based cohort study for *Aedes*-borne viruses (ABV) and a 2022-2024 study conducting concurrent sampling of wildlife, mosquitoes, and humans along a gradient of ecological disturbance. In the first study, we tested sera from 1,575 children in highly urbanized areas in Iquitos. In the second, we tested sera from 416 community participants (ages 3 - 88) in two Amazon River islands with established secondary forest, one peri-urban community with disturbed forest, and homes of Iquitos residents with frequent contact with non-human primates. The ABV cohort was screened by nLUC showed seroprevalence of <1% for MAYV neutralizing (NT) antibody. For the second study, sera were screened by PRNT. A total of 104 of 416 (25%) of participants screened positive for MAYV neutralizing antibody. Endpoint titers ranged from 640 to 5120. Seropositivity was higher in adults (34%) compared to children less than 18 years of age (12%), and highest in the peri-urban area (31%) followed by the more forested sites (21% and 26%) and finally Iquitos City (9%). Household clustering of seropositive people as young as three years of age was observed. Viruses detected in concurrent mosquito and bat collections demonstrate circulation of additional arboviruses. The city has a large human population living near forest ABV cycles, with significant spillover risk. Our large community pediatric cohort suggest no or limited transmission within the city, but evidence of recent infection in at least one island site. One health research programs are required to better understand local transmission cycles and the risk of adaptation to urban disease cycles.

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RISK FACTORS FOR ACUTE Q FEVER IN KILIMANJARO, TANZANIA: A PROSPECTIVE OBSERVATIONAL FEBRILE ILLNESS SURVEILLANCE STUDY

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Acute Q fever, caused by *Coxiella burnetii*, is a common cause of febrile illness among patients admitted to hospital in northern Tanzania. We sought to identify risk factors for acute Q fever in a prospective febrile illness cohort. We screened for fever among adults and children presenting to two referral hospitals in Moshi, Kilimanjaro, 2012-14. Medical and pediatric ward inpatients were eligible if they had fever >=38 ° C or report of fever within the previous 72 hours; outpatients were eligible if they had fever >=38 ° C. After consent, a standardized clinical history was obtained, including a risk factor questionnaire on animal exposures, animal husbandry activities, and outdoor activities within 30 days of enrollment. Venous blood was collected at enrollment and at a follow-up visit 4-6 weeks post-enrollment and serum tested for immunofluorescent IgG antibody (IFA) to *C. burnetii* Phase II antigen. Acute Q fever was defined as a participant with >=4-fold increase in reciprocal antibody titer between acute and convalescent serology. Non-cases were defined as participants with paired IFA results that did not meet the case definition. Participant household or village global positioning system (GPS) coordinates were obtained. Environmental co-variates linked to participant GPS coordinates were extracted from open data sources. A multivariable logistic regression model was fitted to identify risk factors. Acute Q fever was identified in 64 (8.3%) of the 773 febrile participants included in this analysis. Median (range) age was 12.5 (0.25-61) years, with 18 (28.1%) cases in children <2 years; 31 (48.4%) cases were female. Cattle density (OR 1.12 [95% CI 1.01-1.24], p=0.031), maximum mean temperature (average of monthly means for the 3 months prior to enrollment, ° C) (OR 0.88 [95% CI 0.80-0.98], p=0.014), and age <2 years (ORs 3.10 to 3.45 compared to other age quintiles, p=0.004 to 0.067) were independently associated with acute Q fever. Our findings suggest next steps to understand Q fever epidemiology should focus on identifying risk factor behaviors and exposures in young children and on the role of climate and livestock exposures.

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BAT HUNTING PRACTICES AND HEALTH RISKS: INSIGHTS FROM A BANGLADESHI BAT-HUNTING COMMUNITY

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Bats are natural reservoirs of many emerging infectious diseases that cause significant human morbidity and mortality. Hunting and bat bushmeat can cause serious zoonotic diseases such as a Nipah-like henipavirus in humans. However, bat-hunting is a common practice in Bangladesh. This research aimed to explore bat-hunting practices including socioeconomic factors, cultural beliefs, and related health risks in a bat-hunting community in Bangladesh. The study was conducted in a bat-hunting community in the central part of Bangladesh from May 2017 to April 2018. A qualitative ethnographic approach was employed which included observations of bat-hunting events, and in-depth interviews with 4 bat-hunters, and 20 individuals involved in bat meat processing and selling. Collected data was analyzed using a thematic analysis approach. The bat hunters were involved in hunting when there was no work to earn in winter. They stated that hunting bats is an alternative source of income and lower-cost animal protein compared to domestic animal meats that they could not avail for the higher price. They faced several health risks including falls from trees, bat bites, and scratches during hunting. While no laboratory-confirmed cases of Nipah virus were found among them, one individual exhibited symptoms of Nipah-like encephalitis and died before testing, leading to beliefs in supernatural causes among the community people. They believed that bats don't transmit infections, rather they used bat meat and body parts for treating several illnesses like asthma, heart disease, and sexual vigor. We observed that bat processing was placed at their homestead where family members including children were exposed to bat blood and raw meat and domestic animals like dogs and cats eat the offal of bats. The study findings highlight the statements of livelihood, cultural beliefs, and health risks associated with bat hunting and consumption. The study underscores the urgent need for a culture-sensitive intervention with educational outreach programs aimed at augmenting awareness and economic outcomes of these hunters to reduce the health risks of zoonotic diseases.

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MICROBIOMES AND RESISTOMES IN HOUSEHOLD ENVIRONMENTS WITH DOMESTIC ANIMAL COHABITATION: A STUDY IN RURAL BANGLADESH

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In low- and middle-income countries, frequent cohabitation of domestic animals in rural households leads to household contamination with animal feces. Young children frequently touch and ingest soil and animal feces within household environments. These exposures increase their risk of enteric pathogen and antimicrobial resistant infections. Our objective was to understand whether cow cohabitation in homes with soil floors in rural Bangladesh contributed to pathogen and antimicrobial resistance genes (ARGs) in soil floors. We randomly sampled 10 households with soil floors and cows that resided inside the home in rural Chauhali sub-district, Sirajganj District, Bangladesh and concurrently collected cow dung and household soil floor samples. We extracted DNA, performed shotgun metagenomic sequencing, and used the Chan Zuckerberg Infectious Disease bioinformatics pipeline to detect pathogens and ARGs. We detected 5 pathogens in soil, 14 pathogens in cow dung, and 23 in both soil and cow dung. Pathogens that were present in at least 3 of 10 households in both soil and cow dung were *Acinetobacter baumannii*, *Agrobacterium tumefaciens*, *Bacillus cereus*, *Clostridium botulinum*, *Escherichia coli*, *Elizabethkingia anopheles*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella enterica*, and *Stenotrophomonas maltophilia*. 100% of household floors and cow dung samples contained ARGs against various classes of antibiotics including sulfonamides, rifamycin, aminoglycosides, macrolides, lincosamides, and tetracycline. Paired floor and cow dung samples from the same households shared ARGs against aminoglycosides, cephamycin, lincosomides, macrolides, rifamycin, streptogramin, and tetracycline. Our findings suggest that the cohabitation of animals in homes with soil floors is associated with shared pathogens and ARGs between cow dung and floors, presenting a risk of exposure for household members. Future research is needed to establish whether these exposures are linked to increased enteric infections and antimicrobial resistant infections.

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ASSESSING ANIMAL FECAL CONTAMINATION IN FLOORS AND HAND SAMPLES FROM HOUSEHOLDS IN NORTHWESTERN COASTAL ECUADOR

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Interaction between humans and animals is commonplace in low- and middle-income countries, with animals often sharing living spaces with families. Factors such as hand-to-mouth contact, interaction with contaminated surfaces, and caregivers' hygiene could contribute to infants' exposure to animal feces. To assess animal fecal contamination in household settings, we collected floor swabs and infant and caregiver hand rinses in 141 households from nine communities in coastal Ecuador. We measured four microbial source tracking (MST) markers to assess animal fecal contamination from avian (GFD), canine (DG37), swine (Pig2Bac), and ruminant (Rum2Bac) sources. We found that 43% of floors, 31% of infant hands, and 23% of caregiver hands tested positive for at least one MST marker. Mean $\log_{10}$ concentrations were 1.21, 1.82, and 1.24 gene copies (gc)/cm^2 for floor, infant hands, and caregiver hands, respectively. We used generalized estimating equations with robust standard errors to determine the association between sample type and MST marker prevalence (modified Poisson) and loads (Gaussian). Caregiver and infant hands were 48% (95%CI: 0.37,0.73) and 28% (95%CI: 0.56, 0.94) less likely to test positive for any MST marker compared to floor samples. Specifically, caregiver hands were 69% (95%CI: 0.15, 0.64) less likely to test positive for the avian MST marker and 59% (95%CI: 0.24, 0.70) less likely to test positive for the MST canine marker; no difference was found for other markers. Though floors were more likely to have contamination, we found higher MST loads on infant and caregiver hands. On average, infant hands had 0.6 $\log_{10}$ MST gc/cm^2 (95%CI: 3.80, 4.35), and caregiver hands had 0.03 $\log_{10}$ gc/cm^2 more than floors(95%CI: 1.01, 1,16). Our findings indicate that floors and hands are contaminated with animal feces, with higher concentrations of MST markers detected on infant hands. Both sample types could serve as reservoirs and pathways for contaminant transmission. Understanding the dynamics of animal fecal contamination within households is essential to inform targeted interventions to reduce health risks associated with animals.

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DISCOVERY OF NEW SPECIES OF WILD MAMMALS AS POTENTIAL RESERVOIRS IN AMAZONIA OF *COXIELLA BURNETII*, THE AGENT OF Q FEVER

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Q fever is a ubiquitous bacterial zoonosis due to *Coxiella burnetii* with a worldwide distribution. In most parts of the world, transmission to humans occurs via infected livestock. In French Guiana, a French territory located in Amazonia, the incidence of human Q fever is the highest in the world, but the animal reservoir remains a mystery. The aim of this study was to investigate the reservoir of *C. burnetii* in wild Amazonian mammals. From Feb 2021 to Jan 2023, various mammalian feces, tissues and anal and vaginal swabs were collected from bat captures, roadkill mammal corpses, zoo and animal care centers, feline and forest herbivore droppings collected by the French Biodiversity Office and tissues from collections of the Institut Pasteur in French Guiana. Specific detection of the *C. burnetii* IS_{1111} target was carried out by real-time PCR on extracted DNAs. Over the study period, 2014 samples were analyzed by qPCR (swabs N=218, droppings N=498, urine N=15 and tissues N =1283) from 16 different orders. Thirty-four samples from 29 individuals of 7 different orders and 16 different species were positive for *C burnetii*: 1 artiodactyla (1 *Dicotyles tajacu*), 2 carnivoras (1 *Panthera onca*, 1 *Potos flavus*), 2 chiropteras (1 *Carollia perspicillata,* 1 *Molossus molossus*), 5 marsupialia (4 *Didelphis marsupialis,* 1 *Philander opossum*), 1 xenarthra (*Choloepus didactylus*), 6 primates (1 *Sapajus apella*, 3 *Saimiri sciureus*, 2 *Alouatta macconnelli*), 12 rodents (7 *Rattus rattus*, 1 *Rattus norvegicus*, 1 *Makalata didelphoides*, 1 *Proechimys guyannensis* , 2 Mus musculus). For all samples, bacterial loads were low. Organs were more strongly positive than feces.This study reveals a remarkable diversity of wild mammal species carrying *C. burnetii* in Amazonia, suggesting a complex ecosystem in which *C. burnetii* could spread and maintain itself. Further research into the interactions between wild species and human populations is required to better understand and control the spread of this zoonosis in Amazonia.

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TRANSPOSON MUTAGENESIS OF *PLASMODIUM KNOWLESI* REVEALS DETERMINANTS OF ANTIMALARIAL SUSCEPTIBILITY

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Forward genetic approaches have been applied to identify essential gene function in two *Plasmodium* species. However, the lack of essentiality data for parasites in the *P. vivax* clade limits the ability to prioritize targets for vaccines and therapeutics for this important group of malaria parasites, especially for large clade-specific gene families. Moreover, zoonotic cases of malaria are increasing in prevalence in Southeast Asia caused by infection with *P. knowlesi* and *P. cynomolgi*, which are closely related to *P. vivax* and serve as powerful models since *P. vivax* cannot be cultured *in vitro*. Here we conduct a transposon mutagenesis screen in *P. knowlesi*, to provide the most complete determination of gene essentiality for blood-stages of any *Plasmodium* spp., informing drug and vaccine development. Our screen has reached near site-level saturation providing the resolution to identify non-essential domains within essential genes. Analysis of the data revealed considerable conservation of the druggable genome within *Plasmodium* spp., as well as divergences in pathways related to the TCA cycle and metabolism. We investigated the utility of transposon mutagenesis in *P. knowlesi* to identify genes that modulate sensitivity to antimalarial drugs in unbiased genome-wide perturbation screens. Selection with the ganaplacide analog, GNF179, enriched 1000-fold for mutants containing insertions in an acetyl-CoA transporter 1 gene, whose deletion confers GNF179-resistance in *P. falciparum*. Artemisinin selection revealed known modulators of susceptibility, including knowpain 3 and hemoglobin digestion, as well as new candidates in known pathways, such as FBXO7 involved in protein ubiquitination, and new genes such as PATPL1, disruption of which leads to increased susceptibility to dihydroartemisinin. The *P. knowlesi* essentiality data and piggyBac transposon system will serve as valuable resources to the community for identifying novel *Plasmodium* biology.

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IMPROVING CESTOCIDES THROUGH TARGET-BASED DESIGN

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The anthelmintic drug praziquantel (PZQ) has been used for decades to treat parasitic flatworm infections of clinical and veterinary importance.

Recent identification of $TRPM_{PZQ}$, the parasite target of PZQ, has enabled target-based design opportunities to develop novel anthelmintic chemotypes. Two tantalizing approaches towards this goal are exploitation of (i) binding pocket variation between parasite $TRPM_{PZQ}$ orthologs to target specific diseases, and (ii) metabolically stable PZQ derivatives to prolong target exposure. The latter is challenging for trematode $TRPM_{PZQ}$, as metabolically stable derivatives resulting from cyclohexyl ring modifications typically lose potency at $TRPM_{PZQ}$ owing to the stringent binding pocket architecture. Here, we capitalized on both these strategies to develop potent, metabolically stable ligands targeting cestode $TRPM_{PZQ}$. First, an amino acid difference from trematode $TRPM_{PZQ}$ makes the cyclophyllidean cestode $TRPM_{PZQ}$ binding pocket more sterically accommodating. This allows incorporation of modifications that show greater metabolically stability than PZQ. Second, cestodes possess a histidine residue at a critical position in the binding pocket that can be exploited to enhance ligand potency. Additionally, *in silico* experiments guided the design of new molecules that are potent agonists of pseudophyllidean $TRPM_{PZQ}$, a characteristic lacking in PZQ. This was accomplished through the rational design of molecules that interact with this histidine residue. Pursuing both these target-based design opportunities led to the identification of PZQ derivatives that showed improved potency at cestode $TRPM_{PZQ}$ and stability *in vitro*. Based on these improvements, testing these analogs against various cestode *ex vivo* and *in vivo* models has merit. Ultimately, these studies demonstrate the power of target-based design in improving treatments for cestode infections.

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DISCOVERY AND OPTIMIZATION OF ANTHELMINTIC CANDIDATES FOR SOIL TRANSMITTED HELMINTHS

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Soil-transmitted helminths (STH) are among the most common neglected tropical diseases (NTDs), affecting about 1.5 billion people, with children and pregnant women in endemic countries being the most vulnerable. To control STH, Mass Drug Administration (MDA) campaigns are conducted to target preschool and school-aged children using two benzimidazole drugs, albendazole and mebendazole. However, the efficacy of these drugs is not optimal, and new drugs with new modes of action are urgently needed to overcome recalcitrant parasites and inevitable resistance. To find new anthelmintics, we built a novel screening pipeline based on human parasitic nematodes. We screened over 30,000 small molecules covering various compound libraries using human hookworms. We identified novel compounds with broad-spectrum anthelmintic activity against whipworms and hookworms. We further evaluated these compounds using cheminformatics, data mining, and *in vitro* characterization to determine their potency, safety, and speed of action against adult parasites. Based on these criteria, we prioritized over twenty compounds for *in vivo* studies in hamsters infected with the zoonotic hookworm parasite, *Ancylostoma ceylanicum.* We identified multiple lead compounds with significant *in vivo* activity against nematode parasites. Our top candidates, including ones with completely novel anthelmintic scaffolds, were equally potent against the sensitive and resistant isolates of two important veterinary parasites resistant to multiple classes of currently deployed anthelmintics. We then screened analogs of the top anthelmintic candidates to understand the structure-activity relationship and to establish the SAR model for at least four leads. We analyzed cell permeability and intestinal solubility of *in vitro* potent analogs with varying *in vivo* activities to understand the discrepancy between the two. We will present our ongoing studies on these newly emerged anthelmintic candidates, including lead optimization using medicinal chemistry approaches, target deconvolution using click chemistry and pulldown techniques, and mode of action studies.

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INVESTIGATING THE MECHANISM OF ACTION FOR THE AMOEBICIDAL AGENT NITROXOLINE AGAINST *BALAMUTHIA MANDRILLARIS*

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Balamuthia mandrillaris is a free-living amoeba that causes granulomatous amebic encephalitis, a condition with a mortality rate of 90%. This disease is currently treated with a six-drug regimen of limited efficacy and frequent toxicities. Our lab previously discovered that a quinolone antibiotic, nitroxoline, is a potent *in vitro* inhibitor of *B. mandrillaris.* Nitroxoline has since been used successfully to treat a human patient. In this project, we sought to understand the mechanisms of action of nitroxoline, create a high-quality annotated reference genome for *B. mandrillaris,* and analyze the transcriptional response to nitroxoline as compared to other cellular stressors. We demonstrated that nitroxoline's amoebicidal activity can be rescued by supplementing with iron and copper divalent cations, consistent with nitroxoline's known ability to chelate metals. We next interrogated the mechanism of amoebicidal activity with electron microscopy. *B. mandrillaris* is thought to respond to stressors by encystment. Scanning electron microscopy revealed that nitroxoline acts by undermining the structural integrity of *Balamuthia* cysts and interfering with the encystment process. To interrogate this phenomenon further, we next created a high-quality annotated reference genome by generating extensive Pacbio Hifi reads, Illumina, and HiC datasets. This new genome surpasses its predecessors in completeness, sequence continuity, and telomere-to-telomere coverage for most chromosomes. Finally, building on this resource, we conducted a transcriptomic study that revealed the amoeba's dynamic and distinct responses to nitroxoline, as compared to other triggers of encystment such as galactose and hypoxia. Our findings argue against a common encystment transcriptomic program and highlight nitroxoline's effect on metal-requiring pathways. These insights not only highlight nitroxoline's potential as a transformative therapeutic agent for this rare, but deadly pathogen, but also significantly advance our molecular understanding of *Balamuthia* itself.

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GLUCOSE IN - LACTATE OUT: GLUCOSE AND LACTATE TRANSPORT IN *SCHISTOSOMA MANSONI*

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Only praziquantel is available for treating schistosomiasis, a disease affecting more than 200 million people. Treatment of hundreds of millions of people with praziquantel alone is not sustainable, and new drugs for schistosomiasis treatment are needed. Schistosome worms in the mammalian host use aerobic fermentation of glucose to generate ATP with concomitant production of lactate. Both glucose and lactate are cell impermeable and require specific transport proteins for cell uptake and secretion. Previous studies have found that RNAi suppression of facilitative glucose transporters (GLUTs) resulted in *Schistosoma mansoni* worms with decreased viability.(PMID: 17040830). We present results that inhibitors targeting human GLUTs have LD_{50} < 10 micromolar against *S. mansoni* worms. Because GLUTs are found primarily on the worm surface, we hypothesize that additional glucose transporters must be present on internal worm cells. We have found that two genes encoding proteins with high homology to human sodium-coupled glucose transporters (SGLTs) are present in the *S. mansoni* genome and that both have wide tissue

expression. We present results that compounds clinically used for diabetes treatment by inhibiting human SGLTs are active against *S. mansoni* worms with low micromolar LD_{50}. Excretion of lactate at the schistosome surface has been shown to involve aquaporins.(PMID: 20454673) Excretion of lactate by internal cells has not been characterized. We hypothesize that uncharacterized lactate transporters must be present on internal worm cells. We have identified two genes in the *S. mansoni* genome encoding proteins with homology to human monocarboxylate transporters (MCTs). Both genes have wide tissue expression. We present results that inhibitors targeting human MCTs block lactate excretion from worms and have LD_{50} < 10 micromolar. Identification and validation of schistosome glucose and lactate transporters will provide a solid basis for future studies for target-based drug development for new schistosomiasis drugs.

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INDIVIDUAL-LEVEL EFFICACY OF ALBENDAZOLE AND FIXED-DOSE FORMULATION OF IVERMECTIN/ALB (FDC) AGAINST *TRICHURIS TRICHIURA* AND HOOKWORMS IN ETHIOPIA, KENYA AND MOZAMBIQUE. PER PROTOCOL ANALYSIS OF THE ALIVE CLINICAL TRIAL

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Albendazole (ALB) shows low to moderate efficacy against *Trichuris trichiura (Tt)* and hookworm (Hk) infections. We conducted a per-protocol analysis at individual level of the ALIVE clinical trial, aimed at evaluating a fixed-dose formulation of ivermectin/ALB (FDC) in single doses, and ALB in participants infected with *Tt* (n=369) and Hk (n=226) in Ethiopia, Kenya and Mozambique. We used a mixed model fitted in a Bayesian framework to calculate the percentage of participants with therapeutic failure, defined as those not cured and with an individual egg reduction rate (ERRi) insignificantly different from zero. We evaluated the impact of age, sex, body composition, study site, ivermectin dose, and co-infection with another soil-transmitted helminth (STH) on efficacy. Posterior means and 95% credible intervals (95% CI) of the ERRi were calculated for each participant and covariate. In *Tt*-infected participants, 53.6% (ALB) and 5.7% (FDC) of participants had therapeutic failure. In the ALB arm, an average participant co-infected with *A. lumbricoides* exhibited a superior response (ERRi: 65.0 (95% CI: 30.7,83.8)), compared to an average participant with single infection (ERRi: -49.0 (95% CI: -143.5,0.9), p=0.032). In the FDC arm, an average participant co-infected with *S. stercoralis* displayed a poorer response (ERRi: -25.0 (95% CI: -355.2,77.2)) than an average participant with single infection (ERRi: 95.5 (95% CI: -92.4,97.4), p=0.011), and an average participant from Mozambique exhibited a better response (ERRi: 99.1 (95% CI: 97.0,99.9)) compared to an average participant from Kenya (ERRi: 88.7 (95% CI: 75.1,94.1), p=0.017). Among Hk-infected participants, 14.7% (ALB) and 9.7% (FDC) had therapeutic failure. In the FDC arm, an average participant co-infected with *S. stercoralis* exhibited a poorer response (ERRi: 59.6 (95% CI: 0.1.85.2)) compared to an average participant with single infection (ERRi: 95.7 (95% CI: 91.5.97), p=0.012). Our findings suggest significant improvements in efficacy with FDC compared to ALB in *Tt* infections. Moreover, co-infections may influence treatment responses, warranting further investigation.

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A MULTI-COUNTRY COMMUNITY EVALUATION OF THE LONG-TERM PERFORMANCE OF PERMANET 3.0, A LONG-LASTING PYRETHROID-PBO NET

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Pyrethroid-PBO nets have received a WHO recommendation for deployment in place of pyrethroid-only nets where malaria vectors are resistant to pyrethroids. The recommendation is conditional, due to uncertainty around the long-term performance of PBO in pyrethroid-PBO nets. Three-year, multi-country community studies are useful in evaluating long-term performance. This study evaluated PermaNet 3.0, a pyrethroid-PBO net formulated with 25g/kg of PBO and 4g/kg of deltamethrin on the roof. The long-term community studies were conducted in Ghana, India, and Kenya, following the 2013 WHO guidelines. The physical and chemical components were evaluated at 12, 24, and 36 months. Bioefficacy was tested using a pyrethroid susceptible *Anopheles gambiae s.s.* Kisumu laboratory strain. With the development of standard operating procedures for testing with pyrethroid-resistant strains, additional samples of PermaNet 3.0 were collected from Uganda, Tanzania, and Malawi at 3 years of use. The bioefficacy of these additional samples was tested using two well-characterized pyrethroid-resistant laboratory strains of *An. gambiae s.s.*. PermaNet 2.0 was used as a pyrethroid-only positive control for all assessments. PermaNet 3.0 had optimal bioefficacy. The loss of deltamethrin was more gradual than the loss of PBO. PBO had a rapid 38-58% loss in year 1, followed by a more gradual loss in years 2 (20-40% loss) and 3 (19-25% loss). PermaNet 3.0 retained 5-10g/kg of PBO at the 3-year end-of-use period. In the additional samples (Uganda, Tanzania, and Malawi), the PBO content was between 3-10g/kg, comparable with the community studies. Against pyrethroid-resistant mosquitoes, four times higher mortality was observed with 3-year used PermaNet 3.0 relative to the pyrethroid-only net. Fabric integrity and attrition levels were similar for PermaNet 3.0 between all sites. PermaNet 3.0 is a durable pyrethroid-PBO LLIN, that protects against pyrethroid-resistant malaria vectors through three years of use.

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RANDOM CONTROLLED TRIALS AND BEYOND - RESULTS FROM THE FIRST MULTI- COUNTRY STUDY OF THE EFFECTIVENESS OF SPATIAL REPELLENTS TO CONTROL VECTOR BORNE DISEASES AMONGST FORCED DISPLACED POPULATIONS IN CONFLICT AFFECTED AREAS OF N. SYRIA, YEMEN AND N. NIGERIA, 2019 - 2024

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Over 80% of the world's population is affected by one or more vector borne diseases resulting in over 1 million deaths each year. Indeed, 17% of all infectious disease results from pathogens biologically transmitted to humans by blood-feeding sandflies, mosquitoes and others that vector pathogens such as Leishmaniasis, malaria, dengue, their feeding time preferences often correlate with common human behaviour patterns, creating a defined time and context when humans are vulnerable to attack and infection. Frequency and intensity of armed conflicts and extreme weather events have multiplied since the 1960s, disproportionately affecting some regions and displacing 110 million people by 2023. Changes to

the context in which disease vectors, pathogens and humans exist. Extreme events often generate hazardous environmental conditions in which arthropod vectors thrive, human vulnerability increases, and the effectiveness of core vector tools such as ITNs and indoor residual spraying (IRS), are most limited, and death rates rise sharply. The MENTOR Initiative, between 2019 to 2024 conducted a multi-county evaluation of spatial repellent devices (SRD) for control of different vectors and diseases amongst 64,000 displaced people living in temporary shelter camps in N. Syria, Yemen and N. Nigeria. The study findings demonstrate high acceptance and retention (73-98%) for SRD and show the tools ability to exert effective disease control. *Phlebotomine* sandfly density reduced by >74%, incidence of cutaneous leishmaniases was halved (0.52 times lower, 95% CI = 0.37-0.73, p<000); blood fed *aedes* mosquitoes which vector flaviruses were reduced by 89.6% (t test=13.5, p<0.000), and *anopheles* mosquitoes and incidence of malaria reduced. SRD are light weight, low cost, easy to transport, deploy, and use with minimal instruction. Their ability to achieve control both indoors and also in peri-domestic spaces make these tools a vital addition to the expanded vector control toolbox now urgently required. Innovate new tools fit for purpose and approved for use by WHO are vital, but currently missing due to regulatory bottlenecks.

8352

HOUSE MODIFICATIONS USING INSECTICIDE TREATED SCREENING OF EAVE AND WINDOW AS VECTOR CONTROL TOOL: EVIDENCE FROM A SEMI-FIELD SYSTEM IN TANZANIA AND SIMULATED EPIDEMIOLOGICAL IMPACT

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Simple house modification tools that target eaves and windows have the potential to reduce human exposure to mosquito bites in the home. This study assessed the performance of Insecticide Treated Screening (ITS) comprising Eave Nets and Window Screens (ITENs & ITWS), incorporated with deltamethrin and piperonyl-butoxide (PBO) in Tanzania. A randomised Latin square (4 X 4) was conducted in four experimental huts built in a semi-field system (SFS). Four treatment arms were evaluated: 1) new ITS; 2) 12-months naturally-aged ITS; 3) estimated 12 months field-used Olyset® Plus ITNs (Standard-of-Care in Tanzania), and; 4) no treatment for 32 nights using a minimum of 30 mosquitoes per strain per night (a total of 120 per hut). Four laboratory-reared strains were used: transmitters of malaria (*Anopheles arabiensis* and *An. funestus*) and dengue infection (*Aedes aegypti*) and those known for nuisance biting (*Culex quinquefasciatus*). Recaptured mosquitoes were assessed for mortality at 72 hours (M72), blood feeding and hut entry endpoints. A simulation exercise with a modified mechanistic model tracking *Plasmodium falciparum* malaria was used to illustrate the potential epidemiological impact from these products. New ITS induced higher M72 than field-used ITNs against all mosquito species tested [OR: 2.25 (95%CI: 1.65-3.06), p<0.0001], while M72 was similar between aged ITS and field-used ITNs [OR: 0.80 (95%CI: 0.59-1.08), p=0.141]. Both new, and aged ITS reduced more mosquito blood feeding and hut entry than field-used ITNs for all mosquito species tested (p<0.0001). Transmission model estimates indicate epidemiological impacts of ITS may supersede those of ITNs at the population level. The model results indicate that the potency of these impacts depends on assumed intervention percentage cover, durability and mosquito bionomics. ITS is an efficacious tool for controlling vectors transmitting malaria, and dengue, and those known for nuisance biting in a semi-field setting. Given the intervention's simplicity, it should be considered as an additional (or stand-alone) tool.

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ENTOMOLOGICAL EFFECTS OF ATTRACTIVE TARGETED SUGAR BAIT STATION DEPLOYMENT IN WESTERN ZAMBIA: VECTOR SURVEILLANCE FINDINGS FROM A TWO-ARM CLUSTER RANDOMIZED PHASE III TRIAL

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Attractive targeted sugar bait (ATSB) stations are a novel tool with potential to complement current approaches to malaria vector control. To assess the public health value of ATSB stations in the context of high coverage with standard malaria vector control, a two-arm cluster-randomized controlled trial was conducted in Western Province, Zambia. The broader trial was designed to measure the effect of Sarabi v1.2 ATSB® station (Westham Ltd., Hod-Hasharon, Israel) deployment on malaria case incidence and infection prevalence over two seven-month deployments. To provide key entomological context for overall interpretation of trial findings, monthly vector surveillance was conducted in 10 intervention and 10 control clusters. Human landing capture (HLC) and ultraviolet light trap (LT) collections were used to monitor *Anopheles funestus* parity, abundance, biting rates, sporozoite prevalence, and entomological inoculation rates (EIR). Over the course of the study, 11,229 female *An. funestus* specimens were collected from control clusters and 9,108 from intervention clusters. The primary entomological outcome was the proportion of *An. funestus* that were non-parous, and a subset of 3,131 specimens collected during HLC were successfully assessed for parity via ovarian dissection. There was no difference in non-parous proportion (NPP) across the study arms: mean NNP was 23.0% (95%CI 18.2% - 28.7%) in the control and 21.2% (95%CI 18.8% - 23.9%) in the intervention, an OR = 1.05 (95%CI 0.82 - 1.34; p = 0.688). A non-significant 35% reduction in LT abundance (RR = 0.65 [95%CI 0.30 - 1.40, p = 0.267]) was associated with ATSB deployment, consistent with the observed epidemiological impact of ATSB reported previously. Human landing rates were highly variable, but model results indicate a similar non-significant trend, with a RR = 0.68 (95%CI 0.22 - 2.00; p = 0.479). There was no observed effect on sporozoite positivity or EIR. Similar trials in Kenya and Mali conclude in 2024 and will provide additional evidence of ATSB efficacy in other settings, but additional research is needed to understand how to maximize the impact of ATSB approaches in Zambia.

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FIELD TRIAL RESULTS OF A VOLATILE PYRETHROID SPATIAL REPELLENT USING A TRANSFLUTHRIN ACTIVE INGREDIENT AS A CONTROL INTERVENTION FOR OUTDOOR-BITING *ANOPHELES* MOSQUITOES

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Presently, the most common malaria control tools - i.e. long lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) are limited

to targeting indoor biting and resting behaviors of *Anopheles* mosquito species. Few interventions are targeted towards malaria control in areas where transmission is driven or persists due to outdoor biting behaviors. A volatile pyrethroid-based spatial repellent (VPSR) using a transfluthrin active ingredient was designed to address this gap in protection. A collection of one semi-field and three field trials were conducted in communities vulnerable to outdoor biting in Zambia and Indonesia, assessing the protection provided by the VPSR in outdoor spaces where biting is known to occur. The product provided significant protection to users during semi-field trials by reducing observed host-seeking activity by roughly 40% per night and increasing mortality among exposed mosquitoes, with evidence that this effect was under-estimated due to the all-night containment inherent to the semi-field study design. Host-seeking was significantly reduced in structures protected by the VPSR device across the remaining three field trials, with significant nightly reductions of around 70% and similar rates of hourly protection. These results are reported along insights gained from additional field measurements as they relate to product efficacy over the duration of the field trials.

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FINAL YEAR RESULTS FROM A FOUR-ARM CLUSTER-RANDOMIZED TRIAL IN TANZANIA COMPARING THE EFFECTIVENESS OF THREE TYPES OF LONG-LASTING INSECTICIDAL NETS (LLINS) - PYRIPROXYFEN-PYRETHROID, CHLORFENAPYR-PYRETHROID, AND PIPERONYL BUTOXIDE-PYRETHROID - VERSUS A PYRETHROID-ONLY LLIN, AGAINST MALARIA

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New classes of LLINs containing two active ingredients (a.i.) have been recently recommended by WHO in areas where malaria vectors are resistant to pyrethroid. This policy was based on evidence generated by the first two years of our recently published trial in Tanzania. In this paper, we report the final third-year trial findings which are required to assess the lifespan of the new classes of LLIN in the community and the replacement intervals required. A third year of follow-up of a four-arm cluster-randomized controlled trial of dual-a.i. LLINs which was conducted between January 2021 and February 2022 in Tanzania. Restricted randomisation was used to assign 84 clusters to the four LLIN groups (1:1:1:1) to receive either standard pyrethroid (PY)-LLINs (reference), chlorfenapyr-PY LLINs, pyriproxyfen-PY LLINs or piperonyl butoxide (PBO)-PY LLINs. Households received one LLIN for every two people. The field team, laboratory staff, analysis team and study participants were blinded to the allocation. The primary 24 months' endpoint was reported previously; here we present malaria infection prevalence in children 6 months to 15 years old at 36-months post LLIN distribution. Analysis was according to intention-to-treat (ITT). The trial was registered with ClinicalTrials.gov (NCT03554616) and is now completed.Overall usage of study nets was 22% at 36 months' post distribution. In the chlorfenapyr-PY LLIN arm, there was strong evidence of a reduction of malaria prevalence compared to the standard LLIN arm at 36 months (OR 0·57 [95%CI 0·38-0·86] p=0·0069). There was only weak evidence of a difference in malaria prevalence at 36 months in groups receiving pyriproxyfen-PY LLINs and PBO-PY LLINs compared to the standard LLIN.

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A CLUSTER-RANDOMIZED CONTROLLED PHASE III EVALUATION OF 3D WINDOW DOUBLE SCREEN (3D-WDS) IN REDUCING MALARIA TRANSMISSION WHEN COMBINED WITH PYRETHROID-TREATED LONG-LASTING INSECTICIDAL NETS IN NORTHEASTERN TANZANIA

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The emergence of insecticide resistance in malaria vectors has prompted the need to develop alternative vector control methods that do not depend on insecticides. The 3D-Screen is an innovative window screen composed of 3D conical structures assembled onto a screen mesh. When installed as a double screen setup in window openings, creating the 3D-Window Double Screen (3D-WDS), its unidirectional design permits mosquitoes to enter from outside and leave from inside the house through the 3D-WDS, effectively trapping them between the double screens. Prior laboratory and experimental hut studies have demonstrated the remarkable efficacy of 3D-WDS in capturing host-seeking mosquitoes. This trial aimed at the elucidation of the epidemiological and entomological impact of implementing 3D-Screens in community settings. A two-armed, cluster randomized controlled trial was undertaken to assess whether houses equipped with both 3D-WDST, and long-lasting insecticidal nets (LLINs) provide superior protection against malaria compared to LLINs alone. In Muheza, Tanzania, fourteen hamlets with similar epidemiological and entomological profiles were randomly assigned to either the treatment or control arm. Seven hamlets received both 3D-WDST and LLINs (the treatment arm), while the remaining seven received only LLINs (the control arm). Epidemiological (malaria and anaemia prevalence in children) and entomological (indoor mosquito densities and the entomological inoculation rate) surveys were conducted at 10-week intervals over a 52-week period of follow-up. The trial findings demonstrated a significant decrease in the entomological inoculation rate of malaria mosquitoes sampled from households with 3D-WDST compared to those without. Additionally, malaria prevalence was significantly reduced in both study arms. Therefore, the 3D-Screen shows promise in reducing malaria transmission and providing a non-insecticidal alternative for mosquito control.

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ARTIFICIAL INTELLIGENCE LEVERAGING A VISION FOUNDATION MODEL FOR RECOGNITION OF MULTIPLE BLOOD PARASITES IN MICROSCOPY IMAGES

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Blood parasites that cause malaria, filariasis, and Chagas disease remain global health threats. Swift and precise parasite identification is crucial for treatment and epidemiological control. Although microscopy is the main diagnostic tool, its slow process and reliance on skilled experts hinder its effectiveness, especially in areas with less common parasites or resource-limited. In this context, AI for microscopy image analysis can provide a

more rapid and accurate diagnostic. We propose a data-efficient AI-based methodology to disease diagnosis focusing on the blood sample rather than the disease, enabling the identification of multiple parasites. In order to reduce the need for extensive annotated databases to train our method, we first use a self supervised learning (SSL) algorithm, which leverages large unannotated datasets to learn meaningful representations of blood parasites without the need for labels, usually scarce in parasitology. As a result, we came up with a foundation model based on a total of more than 100K microscope images (10x, 40x and 100x magnification, from 4 sites) acquired from thin blood smears of 332 patients. From this database, more than 89K images were used for SSL pretraining. In a subsequent step, the remaining 15K images were labeled (11 parasite species, including 5 filariae, 5 *Plasmodium* species and *T. cruzi*) by experts and used for finetuning with an 80%-20% patient level split. We used a transformer based model, ViT, with DINO as the SSL strategy.Results show that we achieve 95% accuracy (F1 Score) across the 11 parasite species. If just 10% of labeled data is used for finetuning (an average of approx 100 labels per class), we still achieve a high accuracy of 90% across all 11 species-comparable to the performance obtained with all data without using SSL. This shows that further species can be included with a very limited number of labels.Our work presents a generalized AI framework to classify multiple blood parasite species within a single model aligning with the real-world need, and has the potential to be integrated into smartphones facilitating real-time diagnosis and monitoring.

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EVALUATING THE ACCURACY OF CLINICAL MALARIA DIAGNOSES USING TAQMAN® ARRAY CARD MOLECULAR DETECTION IN NIGERIA

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In Nigeria, a high malaria endemic region, routine clinical diagnoses frequently attribute acute febrile illnesses (AFIs) to malaria, which may mask the presence of other pathogens. This study assesses the accuracy of these clinical diagnoses compared to molecular detection using the TaqMan® Array Card (TAC) as part of the larger SAFIAN Study, aiming to uncover misdiagnoses and identify undiagnosed pathogens. Participants clinically diagnosed with malaria at two surveillance sites in Nigeria were tested with TAC PCR analysis to detect a broad panel of pathogens. Participant samples from 181 patients with acute febrile illness (AFI), clinically diagnosed with malaria and treated accordingly, were analyzed using TAC PCR to identify *Plasmodium spp.* as well as 24 other pathogens. The study compared clinical diagnoses, hospital laboratory tests (including microscopy or rapid diagnostic tests), and molecular testing results. Of the 181 cases diagnosed clinically with malaria, only 64 (35.4%) were confirmed by PCR for *Plasmodium spp.*, indicating a significant gap in clinical diagnostic accuracy. Additionally, molecular testing identified alternative pathogens in 38 cases (21%). Of these, 17 were viral while 21 were bacterial; including 8 cases (4.4%) of viral hemorrhagic fevers (VHF), 9 cases (5.0%) of other viral infections, and 21 cases (11.6%) of bacterial infections. Notably, 47 patients (26%) had a molecular detection of *Plasmodium spp.* only, suggesting over-treatment based on clinical suspicion alone. There is a marked discrepancy between clinical diagnoses of malaria and molecular confirmation with PCR in this sample of AFI patients in Nigeria. A substantial proportion of patients received malaria treatment despite the absence of *Plasmodium spp.* detection by molecular testing. This misdiagnosis risks masking other significant infections, highlighting the need for improved diagnostic strategies, such as the broader implementation of molecular diagnostics in routine clinical practice to enhance disease surveillance and patient management in malaria-endemic areas, and reduce the overdiagnosis of malaria.

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SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS 1 (STREM-1) TO RISK-STRATIFY PEDIATRIC AND ADULT PATIENTS WITH FEBRILE ILLNESS IN SOUTHERN MOZAMBIQUE

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Fever is a leading reason for seeking healthcare globally. Early in the course of illness, it is challenging to identify the subset of patients at risk of severe and fatal infections. However, many life-threatening infections share common pathophysiological pathways. We hypothesized that quantifying plasma biomarkers of immune and endothelial activation at presentation may help identify patients at high risk of adverse outcomes. This study was conducted in the Mozambican cohort of the Febrile Illness Evaluation in a Broad Range of Endemicities (FIEBRE) study. From December 2018 to February 2021, children ≥2 months and adults who presented with fever to two Mozambican hospitals were prospectively enrolled. Levels of Angpt-2, CHI3L1, CRP, IL-6, IL-8, PCT, sFlt-1, sTNFR1, sTREM-1, and suPAR at presentation were retrospectively determined in plasma using Luminex and ELISA. Standard clinical and laboratory parameters were assessed at presentation, and clinical outcomes were evaluated up to ≥28 days later. A total of 1,955 participants were enrolled and had biomarkers measured. Of these, 1,040 were managed as outpatients and 915 were admitted to hospital, with 531 and 509 being children aged <15 years, respectively. 93 deaths occurred in the following 28 days. All biomarkers were elevated in inpatients compared to outpatients and were associated with 28-day mortality (all $p<0.001$). sTREM-1 was the top-performing biomarker for predicting 28-day mortality with an AUROC of 0.82 (95% CI: 0.78-0.86), superior to that of PCT, CRP and lactate. Its prognostic accuracy was consistent across age and sex, but reduced in HIV-positive patients. sTREM-1 added value to clinical severity scores for 28-day mortality. Among inpatients discharged alive, sTREM-1 correlated with length of hospital stay. Among outpatients, sTREM-1 was associated with seeking further care or subsequent admission after being sent home. These findings confirm sTREM-1 as a promising biomarker for risk-stratification of all-age febrile illnesses in resource-constrained settings.

8360

COULD WE USE CONVENTIONAL MALARIA RDT TO IDENTIFY SEVERE MALARIA IN TRAVELERS?

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Mortality due to malaria remains unacceptably high, even in non-endemic settings, where WHO criteria for severe malaria (SM) are inaccurate. Therefore, identification of easy to detect biomarkers to discriminate malaria patients at risk of developing SM is key to improve the management of malaria in endemic and non-endemic countries. We performed an observational cross-sectional study of international travellers with fever returning from an international trip. Patients were classified as SM or uncomplicated malaria (UM) based on WHO criteria, except for parasitemia (threshold of 2% parasite density was used according to European and Spanish guidelines). HRP2 and pLDH concentrations were measured in

whole blood samples, extracted at the initial diagnostic workup, through Luminex. Samples were also tested with a dual lateral flow assay (LFA) allowing to detect HRP2 and pLDH (05FK60, Abbott, Chicago, IL, USA). Pictures of the LFA strips were used to quantify the signal of each strip line. We included a total of 121 travelers with febrile illnesses: 75 travelers with malaria (50 with SM and 25 with UM) and 46 travelers with non-malarial fevers. As expected, HRP2 and pLDH resulted undetectable in travellers with non-malarial fevers. In travellers with malaria, the median concentration of HRP2 and pLDH were 8537.4ng/ml and 219.8ng/ml, respectively, and resulted significantly higher in patients with SM ($p<0.001$). HRP2 showed 78% sensitivity and 84% specificity to predict severe malaria (AUC-ROC 0.86), and pLDH showed 80% sensitivity and 88% specificity (AUC-ROC 0.88). Quantification of pLDH signal in LFA also showed a good diagnostic performance to identify SM cases (83% sensitivity, 68% specificity and 0.84 AUC-ROC). In conclusion, besides being good diagnostic tools for the diagnosis of malaria, parasite biomarkers such as HRP2 and pLDH can be useful tools to predict patients at risk of developing severe malaria. Quantification of pLDH signal in rapid diagnostic tests could be a rapid and reliable tool to identify SM in returning travellers.

8361

ADMISSION POINT-OF-CARE TESTING FOR THE CLINICAL CARE OF CHILDREN WITH CEREBRAL MALARIA

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Cerebral malaria (CM) continues to be a driver of child mortality and morbidity in endemic regions. Point of care testing (PoCT) is a cost-effective alternative to laboratory-based testing in the clinical care of critically ill children, including those with CM. The lower cost and easy scalability of PoCT may be useful in acute patient management in resource-limited settings (RLS) but little is known about the clinical utility of PoCT in the recognition or management of organ dysfunction in pediatric CM. We evaluated the clinical utility of PoCT in the care of 193 Malawian children with CM hospitalized between March 2019 and May 2023 who had both PoCT and laboratory-based testing. We determined the frequency of abnormal PoCT values of creatinine, lactate, glucose, and electrolytes on hospital admission, and evaluated how often these values resulted in changes in clinical management. We determined if there were associations between abnormal PoCT results and patient outcomes. Overall, 53.6% of all PoCT results were abnormal. Clinical interventions followed 15.1% of abnormal results and were most likely to occur with abnormal results of potassium (32.1%), lactate (22.0%), creatinine (16.3%), or glucose (9.8%). The most frequent interventions were blood transfusions (in response to high lactate or anemia), administration of furosemide (after elevated creatinine or potassium results), administration of fluid boluses (in response to high lactate, low bicarbonate, and low sodium levels), administration of intravenous glucose in those with hypoglycemia, and the initiation of epinephrine infusions after abnormal lactate results with concurrent clinical findings of shock. Children with hyperlactatemia or hypocalcemia had higher mortality rates. PoCT result values largely correlated well with laboratory-based testing results. High rates of abnormal PoCT testing results combined with lower intervention rates suggest the need for further research to develop evidence based diagnostic and treatment algorithms incorporating PoCT testing.

8362

FLUID BOLUS RESUSCITATION INCREASES MORTALITY IN MALAWIAN CHILDREN WITH CEREBRAL MALARIA

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The Fluid Expansion As Supportive Therapy (FEAST) trial conducted in 2011 found that fluid bolus resuscitation in African children with signs of hypovolemia increased mortality risk, including in patients with malaria. However, no specific subgroup analysis was performed in the FEAST study for children meeting the diagnostic criteria for cerebral malaria on admission. We evaluated the association between fluid bolus resuscitation and mortality in Malawian children with CM using a retrospective review of 1674 children admitted to Queen Elizabeth Central Hospital in Blantyre from 2000 to 2018. Informed by the findings of the FEAST trial, we hypothesized children with CM would have increased risk of mortality with fluid bolus resuscitation. Twenty-two patients with missing systolic blood pressure (SBP) measurements, three patients missing data for sex, and five patients with hypotension were excluded from the analysis. Using covariate balancing propensity score weighting, participants who received fluid bolus resuscitation were matched to participants who did not receive the intervention. Our final population included 252 children who received fluid bolus resuscitation and 252 matched children with similar propensity scores who did not. We found that fluid bolus resuscitation in children with CM increased mortality (OR 1.92; 95% CI: 1.36-2.71). Patients with a SBP over 100 mmHg on admission who received bolus fluids had an even higher risk of mortality (OR 3.15; 95% CI: 1.81-5.48). For children with CM and a SBP less than or equal to 100mmHg, there was no statistically significant impact of fluid bolus resuscitation on outcome (OR 1.44; 95% CI: 0.91-2.26). We additionally found that children with CM had decreased survival with hypoglycemia (OR 1.86; 95% CI: 1.05-3.29), deep breathing (OR 1.85; 95% CI: 1.25-2.72), and a lower Blantyre Coma Score on admission (for BCS=1, OR 0.48; 95% CI: 0.29-0.77; for BCS=2, OR 0.36; 95% CI: 0.22-0.60, both compared to BCS=0). Our results support the findings of the 2011 FEAST trial for Malawian children with cerebral malaria and indicate fluid bolus resuscitation has the potential to cause harm in this group.

8363

DEREGULATED IL-10 EXPRESSING T CELLS IN CHILDREN WITH ACUTE *PLASMODIUM FALCIPARUM* MALARIA: IMPLICATIONS FOR ETIOLOGY OF BURKITT LYMPHOMA

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Plasmodium falciparum malaria and EBV co-infections in children living in malaria-endemic areas are associated with EBV-linked cancer, endemic Burkitt lymphoma (eBL). EBV infection in most African children occurs before the age of 1 year, yet eBL does not occur until later in childhood. It is postulated that repeated episodes of malaria suppress immunity to EBV, creating a permissive environment for eBL pathogenesis. However, the mechanisms responsible for the suppressed immunity to EBV are not fully understood. Previous studies have characterized the immunological alterations that pathologically link malaria exposure and EBV co-infections to eBL tumorigenesis, but the malaria-driven mechanisms still remain obscure.

To precisely understand how a single episode of acute clinical *P. falciparum* malaria perturbs EBV T cell immunity, we intensely characterized T cell activation, co-inhibitory receptor expression, and cytokine secretion profiles in children with acute clinical *P. falciparum* malaria following antigenic stimulation with EBV and CMV peptides. We observed upregulated levels of CD69 and OX40 in both CD4+ and CD8+ T cell subsets in children with acute *P. falciparum* infection, on the contrary, CD25 and CD137 levels were highly elevated in community controls. Interestingly both children with acute clinical *P. falciparum* malaria and community controls were responsive to stimulations by EBV and CMV-specific peptides. Further, analysis of cytokine profiles revealed polarization of IL-10 responses compared to IFN-γ in acute cases than in community controls. Lastly, we did see differential expression patterns of LAG-3 and PD-1 in both acute cases and controls. Interpreted together, our data imply active T cell activation during acute malaria with shifts towards immunoregulatory cytokine production. Also, we report a more global malaria-induced immune suppression rather than EBV-specific.

8364

LONG-TERM DURABILITY AND PUBLIC HEALTH IMPACT OF WMEL WOLBACHIA DEPLOYMENTS FOR AEDES-BORNE DISEASE CONTROL IN NITERÓI, BRAZIL

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Introducing *Wolbachia* (*w*Mel strain) into *Aedes aegypti* mosquitoes reduces their capacity to transmit dengue and other viruses. Field trials in multiple countries have shown reductions in dengue incidence following releases of *w*Mel-infected *Ae. aegypti*. In Brazil, *w*Mel-*Ae. aegypti* have been deployed in 5 cities with a combined population of >3 million since 2015, and previous studies have shown significantly lower dengue, chikungunya and Zika incidence in *Wolbachia*-treated areas of Niterói and Rio de Janeiro than untreated areas, 1-2 years post-release. We present the long-term entomological and public health outcomes of city-wide *Wolbachia* coverage in Niterói, a city of 500,000 people where *Wolbachia* releases were completed in three-quarters of the city in Dec 2019 and expanded to cover the remainder by June 2023. Despite initial variability in *Wolbachia* establishment after the 2019 releases, last monitoring in late 2023 indicated *w*Mel was stably established at >90% prevalence throughout these areas, demonstrating area wide coverage and long-term stability in the *Ae. aegypti* population 4 years post-release (6y in the earliest release areas). Ovitrap monitoring indicates *w*Mel is also well-established in the more recently treated 25% of the city. In the four years 2020-23 since *Wolbachia* was deployed across the majority of Niterói, there was a sustained absence of dengue outbreaks in the city. A total of 305 dengue cases were notified in Niterói in 2020-23: a median of 65 cases per year, or 13 cases per 100,000 people [annual range 6 - 30 /100,000]. By comparison, during ten years (2007-16) prior to *Wolbachia* releases, a median of 4140 dengue cases were reported each year [range 366 - 11619] corresponding to 854 per 100,000 people [75 - 2396/100,000]. Using interrupted time series analysis to account for temporal trends and phased *Wolbachia* deployment, dengue incidence in Niterói was estimated to be 95.5% lower (95% CI: 89.8 to 98.0%) following *Wolbachia* releases, compared to pre-intervention. Preliminary evidence indicates this protective effect has continued into early 2024, during which Brazil is experiencing record high dengue incidence.

8365

INTERACTIONS BETWEEN TEMPERATURE, VIRUS STRAIN, AND DOSE INFLUENCE EXTRINSIC INCUBATION PERIOD AND COMPETENCE OF *CULEX PIPIENS* FOR WEST NILE VIRUS

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West Nile virus (WNV) is a mosquito-borne flavivirus considered to be the most prevalent arthropod-borne virus in the United States. It is maintained in an enzootic cycle between *Culex* species mosquitoes and avian hosts, with human infection resulting from spillover from this cycle. Vector competence (VC) and extrinsic incubation period (EIP) of WNV is influenced by intrinsic factors including mosquito and virus genetics, as well as extrinsic factors including temperature. Previous studies have generally demonstrated that increases in temperature are associated with increased VC and shortened EIP, yet strain-specific variation of these relationships has not been adequately assessed. Further, quantification of EIP has historically relied on estimations based on subpopulation data from individual timepoints. We assessed infection and dissemination rates of WNV in *Culex pipiens* at 20^{0}C, 24^{0}C, 28^{0}C using 4 historic WN02 genotype strains and 4 contemporary NY10 genotype strains. Our results support previous findings of increased average transmission efficiency of NY10 strains, particularly at higher temperatures, but further demonstrate significant variability resulting from distinct interactions between temperature and strain. We additionally demonstrated that EIP can be effectively tracked with individually housed mosquitoes by daily molecular testing for WNV RNA in sucrose pads. Using this methodology, we quantified temperature specific EIP at 15^{0}C, 20^{0}C, 25^{0}C and 30^{0}C following infection of *Cx. pipiens* with representative WNV02 and WNV NY10 strains. We measured differences in temperature-dependent competence and EIP between strains and found that the relationship between temperature and EIP was dose dependent. Together, these data can help inform more accurate predictive models of WNV transmission with changing temperatures.

8366

PATHOGENESIS AND TRANSMISSION OF SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS IN EXPERIMENTALLY INFECTED ANIMALS

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Severe fever with thrombocytopenia syndrome virus (SFTSV; order *Bunyavirales*, family *Phenuiviridae*, genus *Banyangvirus*) is a newly recognized arbovirus of significant human health concern. Since its discovery in 2009, there have been over 15,000 cases across Eastern Asia, with case fatalities primarily in people over the age of 50. With this evolving threat, significant gaps exist regarding the pathogenesis, serological surveillance, and transmission dynamics of SFTSV. To address these gaps, we explored the pathogenesis and serology of SFTSV in juvenile cats, as they are natural hosts for the virus and present with similar symptoms to humans. Our data demonstrate that all the directly infected cats demonstrated liver pathologies and seroconverted, and 4/8 of directly infected cats became viremic, panleukopenic, and febrile, but ultimately recovered. Serum from these cats was then used to establish serological diagnostic criteria similar to what has been previously reported for dengue virus. We demonstrated a >4-fold difference in $PRNT_{90}$ values for SFTSV and Heartland virus, an endemic bandavirus within the United States. These results provide a framework for wildlife surveillance of SFTSV to monitor its potential emergence in the United States. During our initial pathogenesis studies, we observed that one of our uninfected "contact" cats contracted SFTSV and ultimately succumbed to the disease. This is

notable, as this infection occurred without a vector. These findings align with previous reports of nosocomial infections in human and animal patients and the occupational infections of veterinarians and health care staff after encountering SFTSV-positive patients. To identify these non-canonical routes of infection, we performed intramuscular, ocular, intranasal, and oral infections using several animal models. We demonstrated that non-canonical routes of inoculation can result in infection and severe disease. These studies provide the necessary foundations for surveillance and preparedness for the United States to respond to the possible emergence of SFTSV.

8367

HIGH MOUSE PATHOGENESIS ASSOCIATED WITH A NEW YORK POWASSAN VIRUS LINEAGE II ISOLATE

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Powassan virus is an emerging tick-borne flavivirus that can cause severe neurologic disease in humans including encephalitis and meningitis. There are two genetically and ecologically distinct lineages of Powassan virus (POWV). A recent phylodynamic study of POWV lineage II in North America showed geographical structuring of Northeastern and Midwestern clades. The extent that this phylogeographic structure is associated with various phenotypes is unclear. Therefore, we sought to determine whether geographically and genetically defined isolates of POWV lineage II differ in mouse pathogenesis. C57BL/6 mice were inoculated with POWV isolates originating from various regions such as New York, Massachusetts, and Wisconsin. Two New York isolates, NY19 #12 and NY19 #32, caused mice to present early, severe neurological symptoms compared to other isolates in this study. 100% of mice succumbed to infection within seven days of inoculation. In contrast, an isolate from Nantucket, MA (NFS9601) produced only 20% mortality. We further characterized the pathogenesis of NY19 #12 and NY19 #32 by serially sacrificing infected mice over ten days. Viral loads were characterized in serum, spleen, and brain tissues using qRTPCR. Mice infected by higher pathogenesis strains had viral RNA in the serum and brain two and three days earlier than those infected with a standard POWV strain (DTV-SPO). This suggests that significant variation in pathogenic phenotype occurs within lineage II POWV. Specifically, strains that produce 100% mortality rapidly produce viremia and neuroinvade sooner than strains that produce less mortality. NY19 #12 and NY19 #32 share three amino acid mutations in the envelope, NS1, and NS5 proteins compared to other strains in our study. To further understand the observed high pathogenic phenotype in mice, we are currently engineering these mutations into an infectious clone to define viral genetic correlates and mechanisms of POWV pathogenesis and neuroinvasion.

8368

COLLABORATIVE CROSS MICE AS A NEW MODEL FOR IDENTIFYING IMMUNE CORRELATES OF PROTECTION FROM NEUROINVASIVE ST. LOUIS ENCEPHALITIS VIRUS DISEASE

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St. Louis encephalitis virus (SLEV) is a re-emerging mosquito-borne flavivirus endemic to the United States that causes a spectrum of outcomes in humans, ranging from febrile illness to potentially fatal neuroinvasive disease. There is no specific treatment for SLEV disease, and correlates of protection against neurologic disease are unknown. Existing SLEV mouse models are limited as they rely on hyper-virulent mouse brain passaged strains or intracranial administration; both techniques restrict assessment of how peripheral infection leads to neuroinvasion. To circumvent these limitations, Collaborative Cross (CC) mice were subcutaneously administered low mammalian cell passaged SLEV. CC mice are a novel model intended to recapitulate human-like population genetic diversity. CC mice, including the CC71 genotype, have been used to study the disease spectrum and neuroinvasion for other flaviviruses, including Powassan, Zika, and West Nile (WNV) viruses, where WNV is neuroinvasive in CC71. We hypothesized that CC71 mice are susceptible to SLEV infection and neuroinvasion. We inoculated CC71 with 4 strains of SLEV representing California lineages. All strains produced infection, evidenced by viremias that peaked 3 days post inoculation (dpi). Infectious virus and viral RNA were detected in multiple tissues including the brain of all mice from 8 dpi. All mice also lost weight and showed signs of neurologic disease, achieving euthanasia criteria (loss of 20% of starting weight) by 9 dpi. Gene expression data showed interferon regulatory factor 3 is not induced in the brain during SLEV infection, likely causing reduced downstream expression of antiviral factors These data show high susceptibility of CC71 to SLEV neuroinvasive disease. Together with ongoing work using additional CC genotypes that produce less severe disease, this model will be used to characterize the SLEV disease spectrum and to identify immune correlates of protection. Continued development of this model represents a novel tool to recapitulate human SLEV outcomes that will allow studies on pathogenesis, virus-host interactions, and evaluation of countermeasures.

8369

FEASIBILITY OF TRACKING NIPAH VIRUS-INDUCED BRAIN CHANGES AND LESION DETECTION USING 0.05T MRI AND RADIOMICS

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High-consequence pathogens, such as Ebola, Lassa, and Nipah viruses (NiV), are associated with acute or long-term neurological manifestations that can be visualized using MRI (Capone and Scheller, Neurol Clin. 2014). However, high-field (HF) MRI scanners (3T or higher) are challenging to deploy in geographic areas where disease outbreaks naturally occur or in their immediate proximity for long-term monitoring of human survivors. This inaccessibility is due to the cost, power, weight (~ 6 tons), local expertise, and siting requirements of high-field MR systems that impede longitudinal imaging in large populations, especially those in low-resource settings (Geethanath and Vaughan, J Magn. Reson. Imaging, 2019). Portable, very low-field (VLF) MRI systems may represent the only viable strategy to characterize and monitor neurological manifestations of infectious diseases in humans, *in vivo*, non-invasively, and in low-resource settings in a scalable manner. In this work, we determined the 3T radiomic features of lesions found in NiV-exposed non-human primates that showed differences between survivors and deceased patients. We developed a low-field simulator that converted high-field MR images to lower signal-to-noise ratio (SNR) images corresponding to 0.05T and performed textural analysis. The specifications matched a portable scanner in the laboratory weighing 280 kg. Subsequently, we manually detected all 3T lesions in the simulated 0.05T images. The textural variance feature at 0.05T matched better with the 3T data than lesion areas due to the sensitivity to local MR signal intensity changes. We determined that a resolution of 1.5 x 1.5 x 2 mm^3 at 0.05T is required to detect all lesions identified at 3T MRI. We prospectively acquired an in vivo human brain image at this resolution. In conclusion, we have demonstrated the potential of structural neuroimaging with a portable scanner concerning image resolution, SNR, and image analysis. Current work involves prospective neuroimaging of NiV-exposed NHPs at 0.05T in a paired manner with 3T and performing radiomics to identify and interpret classification features.

8370

HENDRA VIRUS GENOTYPE 2 LACKS SEVERE PATHOGENIC HALLMARKS OF PROTOTYPE HENDRA VIRUS INFECTION IN AFRICAN GREEN MONKEYS

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Hendra virus (HeV) emerged nearly 30 years ago and causes severe, often fatal disease in humans and livestock. Until recently, all known human and equine cases of HeV disease were attributed to isolates belonging to the prototype HeV genotype. A novel genotype of HeV, HeV-g2 was identified and retrospectively revealed to be the causative agent responsible for several fatal equine encephalitis cases with previously unknown etiology. All human cases of HeV disease have resulted from direct contact with severely ill, HeV-infected horses. Given the global public health risk of HeV, documented lethality of HeV-g2 in horses, and presently unknown pathogenicity of HeV-g2 in primate species, we performed studies to assess the pathogenicity of HeV-g2 in African green monkeys. Five adult AGMs were experimentally infected with HeV-g2 via a combined intranasal and intratracheal route, at a dose known to be uniformly lethal in AGMs infected with prototype HeV. Four of the five AGMs survived until study endpoint and developed subclinical or mild signs of disease. All four surviving subjects seroconverted and serum antibodies cross-neutralized HeV-g2, HeV-prototype, and Nipah virus (NiV) *in vitro*. Infectious virus was not identified by plaque assay in plasma or tissues of infected AGMs, however viral genomes were detected by qRT-PCR throughout the study. Gross lesions observed at necropsy were mild to moderate compared to the severe pathologic lesions produced by fatal prototype HeV infection in the AGM species. Gross lesions were restricted to prominent lymphoid tissues, particularly lymphadenomegaly of mandibular and mesenteric lymph nodes. Histologic findings included multifocal pulmonary lesions including interstitial pneumonia, vasculitis, and thickening of alveolar septa. Neurological lesions included perivascular cuffing and gliosis in the temporal lobe and brain stem. Viral antigen was not detected by IHC in any subjects. Findings from this study suggest that HeV-g2 is less pathogenic than prototype Hendra virus isolates in a nonhuman primate species known to be highly susceptible to lethal henipaviral disease.

8371

EVALUATION OF *IN SILICO SHIGELLA* SEROTYPING TOOLS USING A GLOBAL *SHIGELLA* COLLECTION

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Shigella is a major public health problem and a common cause of diarrhoea globally. Accurate identification of *Shigella* serotypes is crucial for understanding its epidemiology and designing vaccination strategies which is complicated by a phenomenon known as serotype switching, where mobile genetic elements that are horizontally exchanged among *Shigella* can generate new serotypes within a given genomic background. Standardised serotyping scheme classifies *Shigella* strains into four serogroups and over 50 serotypes based on biochemical tests and O-antigen structures. Apart from the laborious, time-consuming, and expertise-requiring standardised serotyping method, several *in silico* serotyping tools for predicting *Shigella* serotypes from whole-genome sequencing data have been developed, such as Shigatyper and ShigaPass. In this work, we conducted phylogenomic analyses of the serotypes of 1074 *S. flexneri* and *sonnei* isolates from South Asia and sub-Saharan Africa collected during the Global Enteric Multicentre Study (GEMS) using ShigaPass and Shigatyper. The results showed that the ShigaPass and Shigatyper serotype predictions were 87.5% and 84% concordant (respectively) with laboratory serotype data**.** Importantly, we found 36/109 of *S. flexneri* serotype 3a were predicted to be *S. flexneri* serotype 5b by ShigaPass, and that this switch occurred on multiple occasions over the course of evolution, suggesting a higher 5b prevalence and greater frequency of serotype switching than previously understood. We also found 22 out of the 24 isolates predicted to be none-*Shigella* by ShigaPass were *Shigella* by Shigatyper. The findings highlighted the error-prone nature of the standardised serotyping method due to the high similarity between *Shigella* and Enteroinvasive *Escherichia coli* (EIEC) and cross-reactivity between serotyping antisera, and potential inconsistencies in laboratory testing. The findings also demonstrated the value of using multiple *in silico Shigella* serotyping tools to ensure a more accurate prediction.

8372

IDENTIFYING OPTIMAL ENDPOINT DEFINITIONS TO MINIMIZE OUTCOME MISCLASSIFICATION IN UPCOMING SHIGELLA VACCINE TRIALS

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Shigella vaccine candidates are approaching phase III trials, but primary trial endpoints have not been evaluated. Enteropathogens frequently cause subclinical infections and can be detected during diarrhea caused by another pathogen. Therefore, when there are co-infections with Shigella during diarrhea, etiologic attribution may be biased. If a Shigella vaccine has high vaccine efficacy (VE) against moderate-to-severe diarrhea but little to no VE against infection, Shigella diarrhea cases prevented by the vaccine would likely become subclinical infections. An endpoint defined as Shigella detected at any quantity would misclassify diarrhea with subclinical Shigella as cases, thereby biasing VE estimates towards the null. In this analysis, we use a simulation to identify Shigella vaccine trial endpoints that minimize misclassification of true Shigella-attributable diarrhea episodes and therefore bias in the observed VE. We simulate a birth cohort and randomly assign vaccination to half of children. Using a time-to-event model, we assign etiology-specific mild and moderate-to-severe diarrhea episode event times among the unvaccinated children to mimic empirical age- and etiology-specific incidence rates observed in the multisite Malnutrition and Enteric Disease (MAL-ED) birth cohort study. We then use an assumed VE to similarly simulate diarrhea among vaccinated children. We evaluate the performance (e.g., sensitivity and specificity) of various endpoint definitions compared to simulated true vaccine-preventable Shigella diarrhea with the goal of minimizing misclassification of outcomes. Evaluated endpoint definitions include: Shigella detected at any quantity, Shigella detected above a certain quantity cutoff, Shigella detected with restrictions on other pathogen detections, Shigella detected and presence of certain clinical syndromes (e.g., dysentery). We generate a ranking of endpoints and estimate the magnitude and direction of the bias in the observed VE. Lastly, we perform power calculations to determine the sample size needed for a trial to observe the simulated VE when using selected endpoints.

8373

MULTIPLEX PCR DETECTION OF ENTERIC PATHOGENS IN A COMMUNITY-BASED BIRTH COHORT IN ECUADOR: COMPARISON OF XTAG-GPP AND TAQMAN ARRAY CARD ASSAYS

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Enteric pathogens are a leading cause of morbidity and mortality among children. Multiplex, nucleic acid-based assays to detect enteric pathogens are an emerging tool for surveillance and epidemiologic studies due to their high throughput and ability to detect co-infections. Little is known about comparability of multiplex assays in detection of pathogens in community-based, pediatric stool samples. We compared results from Luminex xTAG Gastrointestinal Pathogen Panel (GPP) and a custom TaqMan Array Card (TAC) based on an overlapping panel of 13 viral, bacterial, and protozoan enteric pathogen targets in a community-based birth cohort in Ecuador. We selected a stratified random sample of 156 stool samples that were positive for at least one pathogen by the TAC assay, stratified by age (6, 12, 18 months) and four levels of a rural-urban gradient. Prevalence measured by GPP or TAC ranged from 1% (*Entamoeba histolytica*) to 38% (LT-producing enterotoxigenic *Escherichia coli,* [LT-ETEC]). Agreement between assays was high, ranging from 87% (*Campylobacter*) to 98% (Norovirus GI). There was some evidence of systematic differences for three pathogens: rotavirus (1% by GPP, 8% by TAC, McNemar's P=0.001), *Campylobacter* (20% by GPP, 29% by TAC, P=0.002), and ST-ETEC (5% by GPP, 15% by TAC, P<0.001), likely due to differences in assay gene targets. Assays were not significantly different for other targets studied (Norovirus GI and GII, Adenovirus 40/41, STEC toxins 1 and 2, *Shigella*, LT-ETEC, *E. histolytica*, *Cryptosporidium, Giardia*), and both assays led to similar pathogen rank based on prevalence. GPP and TAC assays showed high levels of agreement in a community-based sample of stool specimens from children aged 6 to 18 months in Ecuador across a rural-urban gradient with a high infection burden. Consistency between assays in most prevalence estimates suggests studies using the different platforms should yield broadly comparable results.

8374

OPTIMAL AZITHROMYCIN TREATMENT RULES FOR CHILDREN WITH WATERY DIARRHEA IN THE ANTIBIOTICS FOR CHILDREN WITH SEVERE DIARRHEA (ABCD) TRIAL

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WHO diarrhea treatment guidelines that only recommend antibiotics for dysentery likely miss many episodes responsive to therapy. In a randomized trial of azithromycin for acute watery diarrhea, treatment benefit was observed among diarrheal episodes attributed to bacteria. There was residual benefit among episodes in which bacteria were detected at lower, non-attributable quantities suggesting that etiology may not fully capture who benefits from antibiotics. In the Antibiotics for Children with Severe Diarrhea trial, we used machine learning to estimate and compare optimal treatment rules for the decision to treat watery diarrhea with azithromycin. We used all available characteristics for the gold standard rule and 7 various subsets of clinical, diagnostic, and/or sociodemographic characteristics to discern the most informative variables for the treatment rule. We estimated the azithromycin effect on day 3 diarrhea and day 90 hospitalization or death via an augmented inverse probability of treatment weighted estimator in the subset of children assigned treatment under each rule. For day 3 diarrhea, the gold standard rule recommended to treat 33% of children who were predicted to benefit from antibiotics. Among the treated, 82% had ≥1 bacterial pathogen, and the risk of day 3 diarrhea was 7.3% less (95% CI: -11.5%, -3.2%) when receiving azithromycin compared to if they were not treated. For day 90 hospitalization or death, the gold standard treated 35% of children, of whom 71% had ≥1 bacterial pathogen. Among the treated, the day 90 hospitalization or death risk was 2.1% less (95% CI: -3.8%, -0.4%) than if they were untreated. For day 3 diarrhea, rules with pathogen quantities (RD: -9.2%, (95% CI: -13.4%, -5.0%)) performed similarly to the gold standard. Rules with malnutrition indicators and sociodemographics approximated the gold standard rule best (RD: -2.8%, (95% CI: -4.3%, -1.0%)) for day 90 hospitalization or death. Pathogen diagnostics are most informative for treatment decisions to improve proximal outcomes such as diarrhea duration, but targeting children based on host characteristics may suffice to prevent severe outcomes.

8375

ENTERIC PATHOGEN DETECTION AMONG CHILDREN DISCHARGED FROM OUTPATIENT TREATMENT FOR SEVERE ACUTE MALNUTRITION AND ASSOCIATIONS WITH SUBSEQUENT RELAPSE IN SOUTH SUDAN

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Severe acute malnutrition (SAM) affects millions of children each year, putting them at increased risk of death and disease. Many children relapse to acute malnutrition (AM) or SAM following community-based management of acute malnutrition (CMAM) programmes. Enteric infection is hypothesized to be a risk factor for relapse. We collected rectal swabs from children recently recovered from uncomplicated SAM in South Sudan and tested them for a suite of enteric pathogens using a TaqMan Array Card. We estimated enteric pathogen prevalence and examined associations between pathogen detection and risk of relapse to AM and SAM within three and six months of recovery. One or more enteric pathogen was detected in 82% of children (389/476). Bacterial and protozoan pathogens were the most frequently detected pathogen types, with each detected in 57% of children, followed by enteric viruses (10%) and helminths (4.4%). Detection of one or more enteric pathogen, protozoan pathogen, or viral pathogen was not associated with relapse to AM or SAM at either time point. Detection ≥1 helminth was associated with increased risk of relapse to SAM, and ≥1 bacterial pathogen was associated with decreased risk of relapse to AM. Both enterotoxigenic *E. coli* and enteroaggregative *E. coli* were associated with decreased risk of relapse to SAM and/or AM at three- or six-months post-recovery. *Shigella* was the only individual pathogen associated with increased risk of relapse to AM and SAM. In this setting, most children suffering from SAM were exposed to enteric pathogens during treatment. However, we found no consistent relationship between pathogen detection at treatment discharge and risk of relapse to AM or SAM within three or six months of recovery. Despite this, limiting pathogen exposures during this vulnerable period remains important given the high risk of serious

adverse health effects. These results highlight the lack of access to safe water, sanitation, and hygiene and reinforce the potential importance of anthelmintics as part of CMAM.

8376

HIGH LEVELS OF GUT *BIFIDOBACTERIUM* ASSOCIATED WITH INTESTINAL INFLAMMATION AND FECAL METABOLITES IN CHILDREN IN RURAL BANGLADESH

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Childhood stunting has been associated with impaired development of the gut microbiota. However, the immune and metabolic consequences of microbiota immaturity have yet to be explored. Here, we studied 1726 rural Bangladeshi children sampled longitudinally at 3, 14, and 28 months of age and enrolled in the WASH Benefits randomized controlled trial evaluating the efficacy of water, sanitation, handwashing (WASH), and nutritional interventions. Across all ages after adjusting for covariates, the relative abundance of a single infancy-associated *Bifidobacterium* 16S rRNA gene amplicon sequence variant (ASV) was positively associated with intestinal permeability (fecal alpha-1-antitrypsin, Spearman's rho 0.13-0.22, $P<10^{-6}$) and T cell-mediated inflammation (fecal neopterin, Spearman's rho 0.24-0.26, $P<10^{-12}$), but not with inflammation from innate pathways (fecal myeloperoxidase, Spearman's rho -0.029-0.048). Metagenomic sequencing revealed that 14-month old children with high levels of the infancy-associated *Bifidobacterium* ASV harbored a diversity of species (*B. longum, B. breve, B. catenulatum,* and *B. pseudocatenulatum*) that were more abundant than in children with age-appropriate levels of *Bifidobacterium* (all $P<0.01$). To determine the metabolic effects of retaining high levels of infancy-associated *Bifidobacterium* at 14 months of age, we performed untargeted metabolomics on stool from 192 children: 96 pairs comprised of one child with high (>85th percentile) and one child with median *Bifidobacterium* relative abundance and matched on demographic variables, study arm from the trial, breastfeeding frequency, and length-for-age z-score. Tryptophan metabolites and pathways related to long-chain fatty acid metabolism and oxidative stress were elevated in children with high levels of *Bifidobacterium* for age. Our data suggest that gut microbiota immaturity affects the immune system and metabolic capabilities of the host and microbiota. Next steps include strain-level evaluation of *Bifidobacterium* genomes from this cohort to identify differential capabilities in carbohydrate and fatty acid utilization.

8377

NEONATAL ACQUISITION OF ESBL-PRODUCING ENTEROBACTERALES IN MADAGASCAR AND CAMBODIA

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Bacterial infections are responsible for 23% of neonatal deaths in low- and middle-income countries (LMICs), with *Enterobacterales* being the primary cause. Of particular concern are extended-spectrum beta-lactamase-producing *Enterobacterales* (ESBL-PE), which are resistant to most first-line antibiotics. Neonatal colonization with ESBL-PE, acquired either vertically from the mother during delivery or horizontally from the environment, increases the risk of subsequent sepsis development. Maternal colonization rates with ESBL-PE are high in LMICs, suggesting a pivotal role in the transmission to the newborn. However, molecular data supporting this hypothesis are limited. This study aims to quantify rates of vertical and horizontal transmission of ESBL-PE in two LMICs and to identify associated risk factors. This work is based on data from the BIRDY study, a community cohort conducted in Cambodia and Madagascar in 2016-2022. Stool samples from mothers at delivery and from newborns < 72h were cultured on a selective ESBL medium. Each colony underwent whole-genome sequencing for characterization and comparison using phylogenetic inference techniques. Multivariate logistic regression was performed to identify risk factors associated with ESBL-PE horizontal transmission. The cohort included 496 mothers, 131 in Cambodia and 365 in Madagascar, who gave birth to 498 newborns. The prevalence of ESBL-PE colonization was 78% in mothers and 53% in newborns in Cambodia, compared to 41% and 32% in Madagascar. Preliminary findings showed 13% vertical transmission in Cambodia and 11% in Madagascar, with 87% and 89% horizontal transmission, respectively. Horizontal ESBL-PE acquisition was associated with C-section (adjusted odds ratio 3.15 [1.7-6.0]), neonatal resuscitation (2.05 [1.2-3.7]), and hospital birth (1.91 [1.1-3.4]). Vertical transmission of ESBL-PE appears to account for a small proportion of neonatal colonization cases. Medical procedures may be important risk factors for horizontal transmission. Further investigation is required to elucidate transmission routes and develop preventive strategies.

8378

EFFICACY AND SAFETY OF THERMOTHERAPY IN COMBINATION WITH MILTEFOSINE IN COMPARISON TO MILTEFOSINE MONOTHERAPY FOR THE TREATMENT OF CUTANEOUS LEISHMANIASIS IN THE AMERICAS: A PHASE III, OPEN LABEL, MULTICENTER, RANDOMIZED TRIAL

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Oral miltefosine and injectable meglumine antimoniate continue to be the first-choice drugs for treatment of cutaneous leishmaniasis in the Americas, despite their toxicity, difficult administration, and cost. In the search for therapeutic alternatives, combining two interventions has emerged as a potential approach to reduce the toxicities of standard drugs and to increase their efficacy as compared to monotherapy. Here we report the results of a randomized, open label, multi-center, non-inferiority study conducted in Brazil, Bolivia, Panama, and Peru; aiming to assess efficacy and safety of combining thermotherapy (one application, 50^{0}C for 30 seconds) plus 3-weeks MF (2.5 mg/kg/day) with miltefosine monotherapy (2.5 mg/kg/day for 28 days orally) for uncomplicated CL cases. Primary endpoint was measured by the percentage of patients with initial clinical cure at day 90, defined as 100% re-epithelialization of lesions. The last patient follow-up visit took place in February 2024. Data analysis is ongoing with final results expected by July 2024. In total, 128 subjects were randomly assigned to either study arm (64 per arm) One patient in the combination arm withdrew consent before receiving any study intervention.

Preliminary results show positive efficacy at D90 in both study arms. Three serious adverse events were reported in the study, none related to study interventions. All adverse events reported in both study arms were similar to those previously reported for these interventions: nausea, vomiting, and diarrhea associated with miltefosine, and signs of first- and second-degree burns at the site of the thermotherapy application. Further statistical analysis will be performed and presented to assess efficacy and non-inferiority and to determine the frequency and severity of adverse events per treatment arm. Preliminary results show comparable efficacy in both

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FIRST-IN-HUMAN, RANDOMIZED, DOUBLE BLIND CLINICAL TRIAL OF LXE408 FOR KINETOPLASTID DISEASES

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Existing therapies for kinetoplastid diseases are far from ideal due to toxicities, treatment length, and variable efficacy. LXE408 is a novel proteasome inhibitor with potent in vitro and in vivo activity against *Trypanosoma cruzi and* Leishmania. This study aimed to evaluate the safety and tolerability of LXE408 in humans. This open label, first in human, phase 1 clinical trial of healthy adult fasted participants included single ascending dose (SAD, 10, 30, 100, 300 and 600 mg) and multiple ascending dose (MAD, 10, 50, 150, 300 and 600 mg daily for 10 days) cohorts. Eight subjects were recruited per cohort and randomized to LXE408 or placebo in a 3 to 1 ratio. A cohort to assess glomerular filtration rate (GFR) received 300 mg of LXE408 or placebo for 10 days plus iohexol solution (intravenously at Day -1, 5 and 10). Among the 88 participants, no serious or severe adverse events (AEs) occurred. All AEs were Common Terminology Criteria for Adverse Events (CTCAE) Grade 1,2. In the SAD cohort, the most common AEs in participants on LXE408 were headache (16.7%) and nausea (10%), in the MAD cohort, 30% of those on LXE408 and 20% on placebo reported headache. Three participants discontinued the study due to AEs (constipation, headache, and nausea). One participant (LXE408 600mg MAD) experienced a grade 2 AE of asymptomatic bilirubin increase with a transient ALT increase, and one (LXE608 50mg MAD) experienced a grade 2 AE of asymptomatic lipase increase. Transient increases of ALT, amylase or lipase occurred in the SAD and MAD cohorts, but these were not considered clinically meaningful and not reported as AEs. Serum creatinine increases (grade 1 to 2) were observed, Cystatin C remained normal among those who had it measured, and the mGFR cohort data showed no significant GFR decrease. This suggests creatinine increase is not indicative of renal toxicity but rather results from altered physiology due to inhibition of renal transporters. LXE408 was safe and well tolerated. Clinical studies are planned or ongoing to assess efficacy in patients with visceral leishmaniasis, cutaneous leishmaniasis, and Chagas disease.

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TOPICAL APPLICATION OF AC2-26, AN ANNEXIN A1 PEPTIDOMIMETIC, REDUCES LESIONS AND IMPROVES IMMUNE RESPONSES IN A MURINE MODEL OF *LEISHMANIA AMAZONENSIS* INFECTION

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Cutaneous leishmaniasis is a parasitic neglected tropical disease that causes slow-healing lesions that can lead to long-lasting scars. Social and self-stigma have been known to influence the quality of life and well-being of patients, urging the search for more efficient therapies that could limit lesion development. Annexin A1 (AnxA1) is a glucocorticoid-inducible protein known for its anti-inflammatory and pro-resolving properties. AnxA1 actions can be mimicked by the administration of its N-terminal domain with 26 amino acids termed Ac2-26 peptide. Recent studies have demonstrated a therapeutic potential for Ac2-26 in infectious diseases, including cutaneous leishmaniasis. We have shown that the lack of endogenous AnxA1 is associated with susceptibility during *Leishmania amazonensis* infection. Moreover, treatment of *L. amazonensis*-infected AnxA1 KO mice with Ac2-26 increases the production of anti-inflammatory cytokines and improves pathogen clearance. Therefore, we aimed to further explore the protective effects of Ac2-26 in cutaneous leishmaniasis. Systemic treatment of WT mice with Ac2-26, by i.p injection, increases the numbers of activated T cells, improving the clearance of the parasite. To evaluate whether local treatment with Ac2-26 could potentiate these effects, we developed a topical formulation and administered it to WT mice. Mice treated topically presented diminished lesions, parasite burden and IFN-γ production when compared with i.p. treated mice. Interestingly, we found lower numbers of Th2 cells and $CD4^+$ $Arginase1^+$ T cells and increased Tregs in topically-treated mice compared to i.p.-treated mice. These results could signify that local treatment of *L. amazonensis* lesions with Ac2-26, rather than systemic administration, is a more efficient way to balance the effector responses with the regulatory responses, preventing parasite replication while controlling the damage caused by the exacerbated inflammation. Our findings suggest topical treatment with Ac2-26 may be an effective treatment approach to localized cutaneous lesions, helping reduce the social impact of the disease in patients.

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SEVERE ANAEMIA AND HAEMOGLOBIN TRAJECTORY FOLLOWING TREATMENT OF VISCERAL LEISHMANIASIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS USING THE INFECTIOUS DISEASES DATA OBSERVATORY DATA PLATFORM

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In patients with visceral leishmaniasis (VL), the normalisation of haemoglobin (Hb) following treatment remains poorly understood. An individual patient data meta-analysis (IPD-MA) was undertaken to explore the Hb evolution using 29 studies (1994-2018; 7,358 patients). Anaemia and severe anaemia (SA) were classified using the WHO definitions. Risk factors of baseline SA and Hb changes during treatment and follow-up were modelled with hierarchical mixed effects regression. Of the 7,358 patients included, 4,339 (59.0%) were from the Indian subcontinent (ISC), 2,896 (39.4%) were from East Africa (EA), and 123 (1.7%) were from Greece. 447 (6.1%) patients were of <5y old, 2,904 (39.5%) were 5-15y, 4,007 (54.5%) were aged >15y. Treatment received included: miltefosine (n=1,675, 22.8%), pentavalent antimony (n=1,740, 23.6%), amphotericin B deoxycholate (n=2,068, 28.1%), liposomal amphotericin B (L-AmB) (n=338, 4.6%), paromomycin (n=712, 9.7%), a combination of these drugs (n=417, 5.7%) or other (n=408, 5.5%). At presentation, 97.8% of patients were anaemic and 47.6% had SA. In a multivariable analysis (including age, sex, and region), factors associated with increased SA risk at baseline were: age <=15y, female sex, and patients from EA (compared to the ISC). Following treatment, 21,080 follow-up Hb measurements were available from 6,585 patients. The mean Hb (unadjusted for site clustering) was 8.2 g/dL (standard deviation (SD)=2.46; n=7,358 measurements) on day 0 and 9.9 g/dL (SD=1.72, n=5,782) on day 30. The mean Hb reached 11 g/dL at around 2 months post-treatment. In multivariable analysis (including age, sex, region and drugs), male sex was associated with a higher Hb during follow-up, whereas there were no differences between region or drug. In summary, approximately half of all trial patients were severely anaemic at baseline; the true population prevalence is likely to be much higher. The marked increase of Hb during the 1st month of treatment (almost 2 g/dL) likely serves as an important surrogate of overall treatment response. Further work continues to elucidate the relationship between poor Hb response and clinical outcome.

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EFFICACY OF SHORT-COURSE TREATMENT FOR PREVENTION OF CONGENITAL TRANSMISSION OF CHAGAS DISEASE: A RETROSPECTIVE COHORT STUDY

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In regions with controlled vector transmission of *Trypanosoma cruzi*, congenital transmission is the most frequent route of infection. Treatment with benznidazole (BZ) or nifurtimox (NF) for 60 days in girls and women of childbearing age showed to be effective in preventing mother to child transmission of this disease. Reports on short-course treatment (30 days) are scarce. Offspring of women with Chagas disease who received short course treatment (30 days) with BZ or NF, attended between 2003 and 2022, were evaluated. *T. cruzi* Parasitemia (microhaematocrit and/or PCR) was performed in infants younger than 8 months of age, and serology (ELISA and IHA) at 8 months to rule out congenital infection. A total of 27 women receiving 30 days of treatment and their children were included in this study. NF was prescribed in 17/27 (63%) women, and BZ in 10/27 (37%). The mean duration of treatment was 29.2 days. None of the women experienced serious adverse events during treatment, and no laboratory abnormalities were observed. A total of 40 infants born to these 27 treated women were included. All newborns were full term, with appropriate weight for their gestational age. No perinatal infectious diseases or complications were observed. Several studies have shown that treatment of infected girls and women of childbearing age for 60 days is an effective practice to prevent transplacental transmission of *T. cruzi*. Our study demonstrated that short-duration treatment (30 days) is effective and beneficial in preventing transplacental transmission of Chagas disease.

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IMPACT OF ASCARIDOLE ON METABOLIC BIOENERGETICS IN LEISHMANIASIS

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Leishmania parasites, causative of Leishmaniasis, rely on a single 'mitochondrion' as their 'powerhouse' and have a compromised antioxidant defence system. Consequently, therapeutic strategies include triggering oxidative burst via mitochondrial dysfunction and subversion of host metabolic bioenergetics, but such information remains poorly defined in case of *Leishmania* infection. Thus, this study aimed to delineate the impact of an endoperoxide ascaridole on the metabolic bioenergetics of *Leishmania* parasites. The impact of ascaridole on cellular redox status, generation of mitochondrial superoxide, mitochondrial membrane potential (MMP), annexin V positivity and cell cycle arrest was evaluated by flow cytometry while extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) evaluated by XF Analyzer. In *Leishmania* infected macrophages, expression of metabolic bioenergetics regulatory pathway AMPK-SIRT1-mTOR axis were assessed by ddPCR (droplet digital PCR) and immunoblotting. In *Leishmania donovani* parasites, ascaridole demonstrated strong anti-promastigote and anti-amastigote activities, IC_{50} being 2.6 and 2 μM respectively. At the respective IC_{50}-IC_{90} doses, ascaridole enhanced the generation of reactive oxygen species and caused depletion of thiols in promastigotes; however, mitochondrial superoxide remained unchanged. It failed to impact on mitochondrial respiration rather inhibited the glycolytic functions, along with diminished levels of ATP and MMP, and exhibited higher annexin V positivity, which ultimately translated into a cell cycle arrest at sub G_0/G_1 phase. Ascaridole substantially downregulated the enhanced expression of AMPK-SIRT1-mTOR axis and glycolysis regulatory enzymes in *Leishmania* infected macrophages as compared to uninfected macrophages, whereas markers of mitochondrial respiration stayed unaltered. To summarize, ascaridole selectively targeted the glycolytic bioenergetics and AMPK-SIRT1-mTOR axis suggesting that screening for compounds that mediate metabolic reprogramming could augment the limited armamentarium of anti-leishmanials.

8384

INVOLVING PATIENTS IN DRUG DEVELOPMENT FOR NEGLECTED TROPICAL DISEASES (NTDS): A QUALITATIVE STUDY EXPLORING AND INCORPORATING PREFERENCES OF PATIENTS WITH CUTANEOUS LEISHMANIASIS INTO TARGET PRODUCT PROFILE DEVELOPMENT

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Target Product Profiles (TPPs) are instrumental to help optimise the design and development of therapeutics, vaccines, and diagnostics. These products, in order to achieve the intended impact, should be aligned with users' preferences and needs. However, patients are rarely involved

as key stakeholders in building a TPP. Our study focuses on cutaneous leishmaniasis (CL), a parasitic NTD. At present, there is no treatment which is effective, safe and easy to administer. Thirty-three CL patients from Brazil, Colombia, and Austria, infected with New-World Leishmania species, were recruited using a maximum variation approach along geographic, sociodemographic and clinical criteria. Semi-structured in-depth interviews were conducted in the respective patient's mother tongue. Transcripts, translated into English, were analysed using a framework approach. We matched disease experiences, preferences, and expectations of CL patients to a TPP developed by DNDi (Drugs for Neglected Diseases initiative) for CL treatment. Patients' preferences regarding treatments ranged from specific efficacy and safety endpoints to direct and significant indirect costs. Respondents expressed views about trade-offs between efficacy and experienced discomfort/adverse events caused by treatment. Reasons for non-compliance, such as adverse events or geographical and availability barriers, were discussed. Considerations related to accessibility and affordability were relevant from the patients' perspective. NTDs affect disadvantaged populations, often with little access to health systems. Engaging patients in designing adapted therapies could significantly contribute to the suitability of an intervention to a specific context and to compliance, by tailoring the product to the end-users' needs. This exploratory study identified preferences in a broad international patient spectrum. It provides methodological guidance on how patients can be meaningfully involved as stakeholders in the construction of a TPP of therapeutics for NTDs. CL is used as an exemplar, but the approach can be adapted for other NTDs.

8385

DEVELOPMENT OF NOVEL HOOKWORM MRNA VACCINE CANDIDATES BY ALTERING THE INTRACELLULAR TRAFFICKING OF *NECATOR AMERICANUS* GST-1 ANTIGEN

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RNA platforms offer rapid adaptability for modifying and optimizing vaccine antigens. By adding and editing signal sequences within mRNAs, antigens can be translated more efficiently and guided to diverse locations in recipient cells. Here, we present the production of three versions of an mRNA vaccine encoding *Necator americanus* (*Na*) GST-1 protein, a previously identified hookworm antigen. The mRNA candidates, differing only in their signal sequences, code for either wild-type *Na*-GST-1 (wt), secretory *Na*-GST-1 (SS), or plasma membrane(PM)-anchored *Na*-GST-1 proteins. Translation efficiency of the mRNA candidates was tested *in-vitro* via transfection of DC 2.4 cells and quantified by immunostaining and flow cytometry. The localization of *Na*-GST-1 (intracellular, secreted, or membrane-bound) was determined by immunocytochemistry and Western blot. Forty BALB/C mice were divided into five groups and immunized intramuscularly twice. In addition to the three mRNA groups, mice were also vaccinated with either placebo LNPs or recombinant *Na*-GST-1 protein expressed in *Pichia pastoris*. ELISA analysis of the mouse sera showed higher titers of antigen-specific IgG in groups vaccinated with mRNAs than with recombinant *Na*-GST-1. While all groups induced similar levels of IgG1, IgG2a was only elicited in the mRNA groups. Furthermore, an increase in cytokine production and memory T cells using certain mRNA vaccine candidates was also observed after stimulation of splenocytes with recombinant *Na*-GST-1. Significant differences in immune response were also seen among the mRNA vaccines, reflecting the exposition of *Na*-GST-1 as an antigen. Finally, all vaccinated mice generated neutralizing antibodies capable of inhibiting the glutathione-transferase activity of *Na*-GST-1 *in-vitro*. Combined, our data illustrates the potential of the mRNA platform for better tailoring the immune response. While ongoing challenge studies in a mouse model infected with *Nippostrongylus brasiliensis* will further elucidate efficacy, we found that when using optimized signal sequences, Na-GST-1 mRNA vaccines can induce a strong immune response in mice.

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CONTROL OF HOOKWORMS USING *BACILLUS THURINGIENSIS* CRY PROTEINS AND VACCINES

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Human hookworms—*Necator americanus, Ancylostoma duodenale, and Ancylostoma ceylanicum*—are intestinal parasites that siphon blood and afflict approximately 500 million people globally. These parasites are primary contributors to iron-deficiency anemia in the developing world. Alarmingly, nearly 90 million children suffer chronic infections, experiencing stunted growth and delayed cognitive and intellectual development. Additionally, millions of pregnant women are affected, which results in adverse birth outcomes. Historically, infections by soil-transmitted helminths (STHs) have been managed with small-molecule anthelmintic drugs. However, prolonged usage of these drugs has frequently led to the development of drug resistance. In response to these challenges, our objective is to develop a new therapeutic intervention and a vaccine to combat hookworm infections. To achieve this, we have pursued two innovative approaches. Firstly, we have utilized *Bacillus thuringiensis* crystal (Cry) proteins, the world's most extensively deployed biological insecticides, which are non-toxic to vertebrates. Our research has demonstrated that Cry proteins, especially Cry5Ba, are highly effective against a wide array of both free-living and parasitic nematodes that affect plants, animals, and humans. Secondly, we have employed transcriptomics, proteomics, and immunoinformatics to screen the *Ancylostoma ceylanicum* genome for potential pan-hookworm vaccine candidates and developed vaccines with excretory/secretory (ES) products from *Ancylostoma ceylanicum*. We are excited to discuss several promising new Cry proteins—CryH18, CryH1, and CryH13—as well as novel validated antigens identified through omic approaches and ES products as potential vaccine candidates against hookworm infections.

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OPISTHORCHIS VIVERRINI ANTI-CANCER VACCINE TARGETING THE LIVER FLUKE HOST-PARASITE INTERFACE

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Infection with the food-borne liver fluke *Opisthorchis viverrini* is the principal risk factor for bile duct liver cancer (cholangiocarcinoma, CCA) in SE-Asia, and a vaccine is needed to reduce future infections and the many thousands of annual deaths. We explored the role of the parasite growth factor *Ov*-GRN-1 in malignancy using a novel model of liver fluke infection induced hamster CCA. We produced CRISPR/Cas9 gene knockout flukes (*ΔOv-grn-1)* and confirmed depletion of transcripts and protein. *ΔOv-grn-1* parasites colonized the hamster biliary tract and developed into adult flukes, but less hepatobiliary tract disease and high-grade CCA manifested during chronic infection with *ΔOv-grn-1* flukes compared to control flukes. The reduced liver disease was marked by less local and global fibrosis, reduced cholangiocyte proliferation, and fewer *p53* tumor suppressor gene mutations. This clinically-relevant phenotype of reduced pathology and malignancy confirmed a role for this secreted virulence factor and supports pursuit of *Ov*-GRN-1 as an anti-pathogenesis vaccine candidate. But flukes are difficult foes, and an effective vaccine will need to target a number

of key parasitism pathways to be sufficiently efficacious. To this end we are targeting *Ov*-TSP-2 alongside *Ov*-GRN-1 in a multivalent approach. *Ov*-TSP-2 is abundant on the surface of *O. viverrini* secreted extracellular vesicles (EVs), and antibodies raised to recombinant *Ov*-TSP-2 interrupt host-parasite communication by blocking the uptake of fluke EVs by host cholangiocytes. Moreover, *Ov-tsp-2* gene knockout is lethal for flukes *in vivo*. We are currently exploring the efficacy of *Ov*-GRN-1, *Ov*-TSP-2, and other nutrient acquisition antigen combinations as both protein and mRNA vaccines in the hamster model of fluke infection and CCA. We believe that targeting fluke-host communication in combination with nutrient acquisition pathways will ultimately combat this liver fluke infection associated malignancy in the form of a novel anti-fluke/anti-cancer vaccine, a public health development with the potential to benefit millions of impoverished residents of endemic regions.

8388

A LIVE-ATTENUATED *LEISHMANIA* VACCINE SHAPES THE CELLULAR RESPONSE IN THE BONE MARROW

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Leishmaniasis is a neglected tropical disease for which no vaccine is available. We developed a live-attenuated *Leishmania major* lacking the *Centrin* gene (*LmCen*$^{-/-}$) as vaccine, which showed safety and immunogenicity in pre-clinical studies. Immunization with *LmCen*$^{-/-}$ induced protection against homologous and heterologous challenge infections in murine models; protection mediated by IFN-γ secreting T effector cells. Studies in leishmanization (virulent *L. major*; *Lm*WT) models showed that persistent infection is necessary for maintaining protective immunity, in addition to central and skin resident memory T cells. Similar studies with live attenuated vaccine strains regarding persistence and durability of protection have not been undertaken. Here, we evaluated the presence of latent parasites in cells from the bone marrow (BM) that could define the immune landscape. We used dual-scRNAseq to identify cells harboring parasites within the BM 28 days post-infection. We identified that about 1% cells from mice infected with virulent *LmWT* or vaccinated with *LmCen*$^{-/-}$ harbored leishmania transcripts suggesting parasitization. We investigated the effect of parasitized cells on the immune landscape in the BM. Using scRNAseq, identification of different cell populations within the BM after intradermal inoculation of both parasites showed that *LmCen*$^{-/-}$ infection led to differential expansion of neutrophil and megakaryocyte populations, compared to *Lm*WT infection. Validation via flow cytometry confirmed that vaccination with *LmCen*$^{-/-}$ leads to the expansion of myeloid progenitors of megakaryocytes (MPPII), while this change was not observed in *Lm*WT infection. In conclusion, vaccination with a live-attenuated *LmCen*$^{-/-}$ vaccine elicits neutrophils and megakaryocyte expansion in the BM, which could be responsible for strong protection against leishmaniasis. Further studies will determine the mechanisms by which the persistent presence of latent parasites within the bone marrow induce protection.

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SEROLOGICAL, CELLULAR, AND BLOOD TRANSCRIPTOMIC RESPONSES TO A RECOMBINANT ONCHOCERCIASIS VACCINE IN CATTLE NATURALLY EXPOSED TO *ONCHOCERCA OCHENGI*

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Human onchocerciasis is a neglected tropical disease affecting 21 million people in sub-Saharan Africa caused by the filarial nematode *Onchocerca volvulus*. Disease elimination via mass administration of the microfilaricidal drug ivermectin has achieved marked but qualified success, indicating a need for additional tools. Here, we use the bovine *O. ochengi* natural infection system to assess the efficacy and immunogenicity of a recombinant onchocerciasis vaccine. Immunologically naïve calves were recruited for a trial of a recombinant fusion protein (Fus1) composed of antigen candidates *Ov*-103 and *Ov*-RAL-2 and formulated in Montanide ISA 201 VG (n = 15). The control group received adjuvant only (n =1 5); primary and booster immunisations were administered at an interval of four weeks in both groups. Four weeks post-immunisation, animals were transferred to a site of natural *O. ochengi* transmission for 24 months, receiving a further booster immunisation 6 months after turnout. All animals were sampled routinely to measure serum and peripheral blood leucocyte (PBL) responses, as well as parasite load (nodules and microfilaridermia). Immunological investigations to determine T- and B-cell responses included antigen-specific serum antibody ELISAs and peripheral blood leucocyte cultures with subsequent analyses via flow cytometry and transcriptomics. All immunised calves showed strong antigen-specific serum IgG isotype responses to immunisation, which progressively waned over the subsequent exposure period. Network analysis of RNA-Seq data from PBLs indicated differential expression of a number of pathways relating to immune function in immunised calves, including upregulation of interleukin-10, negative regulation of macrophage function, complement activation, and induction of nitric oxide synthase. However, flow cytometry demonstrated no evidence of memory T-cell responses and vaccination was not significantly associated with reductions in either adult or microfilarial worm burdens. These results underline the challenges of inducing strong immune memory when vaccinating against helminth infections.

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A PHASE I/II STUDY OF THE SAFETY, IMMUNOGENICITY, AND EFFICACY OF *SM*-TSP-2/ALHYDROGEL WITH OR WITHOUT AP 10-701 FOR INTESTINAL SCHISTOSOMIASIS IN HEALTHY UGANDAN ADULTS

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Tetraspanins (TSPs) are membrane spanning proteins on the schistosome's outer syncytial surface that function in tegument formation and host-parasite interface and are targets of vaccine development. Studies in schistosomiasis endemic areas showed that putatively resistant individuals express antibodies against these antigens, leading to selection of the TSP-2 antigen as a lead candidate targeting disease caused by *Schistosoma mansoni*. Recombinant *Sm*-TSP-2 expressed in *Pichia pastoris* was purified by a series of chromatography steps and adsorbed to Alhydrogel (Al: aluminum hydroxide adjuvant). Two Phase I trials conducted in the USA and Brazil of *Sm*-TSP-2/Al with or without AP 10-701, a synthetic Toll-like receptor-4 agonist, showed the vaccine to be safe, well tolerated and induced anti-*Sm*-TSP-2 IgG antibodies. A Phase I/II study is being conducted in healthy Ugandan adults aged 18-45 years. Ninety subjects were enrolled in 3 groups of 30 in the Phase I stage, a randomized, double-blind, dose escalation trial with progression to the next dose determined by review of predefined criteria, done 7 days after all subjects in the active cohort received the first vaccination. Two formulations of *Sm*-TSP-2 were tested: one using Al only, and one using Al plus AP 10-701, with Hepatitis B vaccine (HBV) as a comparator (12 subjects per study vaccine group

and 6 subjects in the HBV group), each at 3 different antigen doses: 10, 30 and 100mcg. Vaccinations were administered by intramuscular injection in the deltoid at 0, 2, and 4 months. Common adverse events (AEs) included mild to moderate injection site pain and tenderness, headache, malaise, fatigue, and dizziness. Solicited AEs were well tolerated and short-lived. No significant differences were observed in AEs between dose groups. There were no vaccine-related serious AEs. The highest IgG antibody response, as determined by ELISA, was detected among participants who received 100mcg *Sm*-TSP-2/Al with AP 10-701, which was thus chosen as the optimal dose for the Phase II stage of the study that is currently underway. Addition of AP 10-701 to *Sm*-TSP-2/Al improved IgG responses but did not compromise safety.

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THE ANTI-CIRCUMSPOROZOITE ANTIBODY RESPONSE OF CHILDREN TO SEASONAL VACCINATION WITH THE RTS,S/AS01$_E$ MALARIA VACCINE OVER FIVE YEARS OF FOLLOW-UP (4 BOOSTER DOSES)

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Combining seasonal vaccination with RTS,S/AS01$_E$ vaccine with seasonal malaria chemoprevention (SMC) has reduced the incidence of uncomplicated and severe malaria compared to either intervention given alone, at 3 and 5 years of follow-up. This study reports the anti-CSP antibody response and potential correlates of protection during the 5 years. Sera from randomly selected subset of children (N=1634) collected before 1 month and after 3 priming doses and 4 annual booster doses were tested for *P. falciparum* anti-CSP (NANP repeat) antibodies using GSK enzyme-linked immunosorbent assay (ELISA) protocol. A subset of these samples was also tested using the Oxford MSD multiplex ELISA protocol (NANP repeat), to explore correlation between the two ELISA protocols. The rise in titers were compared using geometric mean ratios. In addition, the association between post vaccination antibody titer and incidence of malaria. The 3 priming doses induced strong anti-CSP antibody response (Geometric mean titer 368.9 IU/mL), subsequent annual, pre-malaria transmission season booster doses also induced a strong antibody response but a lower than the primary vaccination series (geometric mean titer of the fourth booster was 128.5IU/mL) and previous boosters. The rise after the first booster was higher than subsequent boosters. Children whose antibody response was in the upper and middle terciles post vaccination had lower incidences of malaria during the following year than children in the lowest tercile (hazard ratio, 0.53; 95% CI, 0.39-0.72 and 0.75 95%CI, 0.56 to 0.99, for upper and middle terciles, respectively). The two ELISA protocols were strongly correlated (Pearson's correlation coefficient, r = 0.92; 95%CI, 0.91-0.93). Seasonal vaccination with RTS,S/AS01$_E$ induced strong booster antibody response that was lower after the subsequent boosters than the first booster. The diminished antibody response was not associated with diminished protection/efficacy. Measurements of anti-CSP antibody titers from the two ELISA protocols were strongly correlated.

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EFFECTS OF HUMIDITY AND TEMPERATURE VARIATIONS ON *ANOPHELES* GENETIC TARGET CANDIDATES FOR MALARIA CONTROL

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The malaria mosquito innate immune system is the first line of defense against pathogens and a major regulator of vector competence and malaria transmission. Mosquitoes are influenced by environmental factors that shape their physiology and behaviour. However, the extent to which climatic factors affect the malaria vector immunity with repercussions to malaria transmission remains mostly unexplored. A limited number of studies has investigated temperature and mosquito immunity interactions. However, the role of humidity on *Anopheles* immune responses has been largely ignored. In this study, we aim at understanding how climate change will affect mosquito immune responses to *Plasmodium* infection with consequences for malaria transmission. The experimental approach we employ challenges standard methods used in vector studies that rely on static humidity/temperature parameters; instead, we incorporate ecological realism (i.e. variable humidity/temperature) into research by mimicking current and potential future climatic scenarios in nature. Using RNA-seq transcriptomic analysis and qRT-PCR, we discovered *Anopheles* genes with immunity and/or *Plasmodium* infection modulating functions that are differentially expressed in mosquitoes exposed to current climate or future climate according to climate change predictions. In addition, we observed that humidity and temperature variations selectively affect the fitness of *An. stephensi* mosquitoes at different developmental stages, impacting vector competence. Using CRISPR/Cas9-mediated gene knockout, or knockin, of *Plasmodium* host/restriction factors (that facilitate/block *Plasmodium* replication in the mosquito, respectively) as in previous studies (Simões *et al.* 2017, 2022), the novel genetic targets identified here can be exploited for the engineering of fit-for-purpose transgenic vectors for malaria transmission reduction in climate change-affected regions.

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TNF SIGNALING ACTIVATES CELLULAR IMMUNITY TO PROMOTE MALARIA PARASITE KILLING IN *ANOPHELES GAMBIAE*

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Tumor Necrosis Factor-α (TNF-α) is a proinflammatory cytokine and a master regulator of immune cell function in vertebrates. While previous studies have implicated TNF signaling in invertebrate immunity, the roles of TNF in mosquito innate immunity and vector competence have yet to be explored. Herein, we confirm the identification of a conserved TNF-α pathway in *Anopheles gambiae* consisting of the TNF-α ligand, Eiger, and its cognate receptors Wengen (Wgn) and Grindelwald (Grnd). Through gene expression analysis, RNAi, and *in vivo* injection of recombinant TNF-α, we provide direct evidence for the requirement of TNF signaling in regulating mosquito immune cell function by promoting granulocyte midgut attachment, increased granulocyte abundance, and oenocytoid rupture. Moreover, our data demonstrate that TNF signaling is an integral component of anti-*Plasmodium* immunity that limits malaria parasite survival. Together, our data support the existence of a highly conserved TNF signaling pathway in mosquitoes that mediates cellular immunity and influences *Plasmodium* infection outcomes, offering potential new approaches to interfere with malaria transmission by targeting the mosquito host.

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PIXEL INTENSITY OF WING PHOTOS USED TO PREDICT AGE OF *ANOPHELES GAMBIAE* SENSU LATO CAUGHT DURING THE RIMDAMAL II CLINICAL TRIAL

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Mosquito age-grading is pivotal for understanding population structures, evaluating mosquito control efforts, and allows for estimates of pathogen transmission risk from the mosquito population. While traditional age-grading techniques can be burdensome and inexact, recent age-grading methods can require costly supplies or machines, and the destruction of samples for precise results. We previously developed a simple, low-cost, nondestructive, and high throughput method to quantitatively age-grade mosquitoes by computing the pixel intensity (PI) of wing photos, evaluating wing scale loss over time. Here the technique is refined by measuring mean rather that the total PI per wing image. Additionally, we developed and applied an age model to wild *Anopheles gambiae* s.l. captured during the RIMDAMAL II cluster-randomized clinical trial, evaluating the use of ivermectin for malaria control. Wing photos from newly eclosed lab-reared *An. gambiae* had a PI of 128.45 (128.35-128.62), while mosquitoes ≥ 10 days had a PI of 129.00 (128.65-129.45). Comparatively, wing photos from wild mosquitoes had a PI range of 127.85-133.08. Binned PI from wild mosquitoes exhibited a distribution reflective of traditional age-grading methods, with >80% of the population having a PI in the 3 lowest bins and <20% of mosquitoes distributed among 14 bins of the highest ranges (128.74-133.38). The distributions of mosquitoes placed in PI bins across the trial largely reflected the expected effect of ivermectin in the treatment arm. Finally, a symmetrical sigmoidal variable slope was the best fit model for lab mosquitoes of known ages, which we used to interpolate unknown ages from the field. With this model, 30% (578/1920 samples) of wild *An. gambiae* could be interpolated. These had an estimated median age of 4.96 (0.8-14.93) days and the interpolated age structures reflected the effect of the mosquito control interventions across the years of the trial. Overall, these data demonstrate how the use of wing photo PI can rapidly generate expected age distributions of wild mosquito populations and assist in evaluating the efficacy of mosquito control interventions.

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EXPLOITING MOSQUITO SALIVARY PROTEINS TO DEVELOP VECTOR-TARGETED VACCINES FOR MALARIA AND ARBOVIRUSES

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Despite on-going control efforts, mosquito-borne diseases account for over 700,000 deaths annually. Two genera of mosquitoes are responsible for the majority of disease transmission; *Anopheles* species carry the parasites that cause malaria and *Aedes* species are vectors for viruses such as dengue, Zika, and Chikungunya. Factors within mosquito saliva interact with the host immune response to facilitate faster feeding and immune evasion, which is also beneficial to pathogen survival. For example, the *Anopheles* salivary protein, TRIO, influences the local inflammatory response in favor of *Plasmodium* motility and infection. Similarly, the *Aedes* salivary peptide, sialokinin (SK), increases blood vessel permeability, causing a rapid influx of virus-permissive cells. Targeting salivary proteins offers the potential for developing universal, vector-targeted vaccines, which would be especially valuable in endemic areas, providing broad protection against many diseases as they emerge. Our lab specializes in using virus-like particles (VLPs) as versatile vaccine platforms. The multivalent display of antigens on VLPs is particularly effective at eliciting high-titer and long-lasting antibody responses. This project focuses on using VLPs to develop 1) a malaria vector/pathogen combination vaccine targeting *Anopheles* TRIO and *P. falciparum* circumsporozoite protein (CSP), and 2) a pan-viral vaccine targeting *Aedes* SK. Both TRIO- and SK-VLPs resulted in high antibody titers that have not dropped up to 18 months post-immunization, essentially the lifespan of a mouse. TRIO-VLPs elicited equally high titers in interstitial fluid, a critical site for initial infection. After malaria challenge, mice vaccinated with TRIO-VLPs alone were significantly protected from infection, and the combination with CSP-VLPs further increased protection. Importantly, no cross-reactivity or sensitivity to the salivary peptides was seen in immunized mice. These preliminary data demonstrate the potential for designing interventions that target important disease vectors, as well as the promise of vector/pathogen combination vaccines.

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PLASMODIUM FALCIPARUM INFECTION IN THE HUMAN HOST AND THE VECTOR INFLUENCE NATURAL ANOPHELINE BITING BEHAVIOR AND PARASITE TRANSMISSION

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Understanding mosquito biting bias in a natural setting can help target interventions to efficiently interrupt transmission. In a 15-month longitudinal cohort study in a high transmission setting in western Kenya, we investigated human and mosquito factors associated with differential mosquito biting by matching human DNA in single- and multi-source *Anopheles* bloodmeals to the individuals they bit using short tandem repeat (STR) genotyping. We employed risk factor analyses and econometric models of probabilistic choice to assess mosquito biting behavior with respect to both human-to-mosquito transmission and mosquito-to-human transmission. Among the 1064 mosquitoes with bloodmeals that were STR typed, 777 (73%) bit a human, and 662 (85%) matched to at least one community member. Biting patterns were highly heterogeneous; 20% (118/588) of community members received 88% (631/720) of observed bites, and *Plasmodium falciparum*-infected school-age boys accounted for 50% of bites potentially leading to onward transmission to mosquitoes. *P. falciparum* sporozoites were detected in 22% (146/662) of matched mosquitoes. Using discrete choice models to explore mosquito biting preferences, infectious mosquitoes were nearly 3x more likely to bite cohort members harboring *P. falciparum* parasites compared to noninfectious mosquitoes (relative risk ratio 2.76, 95% CI 1.65-4.61). Further, this preference to feed on infected people was enhanced by the presence of higher sporozoite loads in the mosquito head-thorax. This is the first observation in a natural setting that *P. falciparum* sporozoites modify mosquito biting preferences to favor feeding on infected people. Thus, persistent *P. falciparum* transmission in this setting was characterized by disproportionate onward transmission from school-age boys and by the preference of infected mosquitoes to feed upon infected people.

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LANDSCAPES OF INFECTION: REDEFINING THERMAL SUITABILITY OF URBAN MALARIA TRANSMISSION BY THE INVASIVE MOSQUITO SPECIES *ANOPHELES STEPHENSI* IN THE CONTEXT OF RELATIVE HUMIDITY

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Vector-borne diseases cause significant financial and human loss, with billions of dollars spent on control. Arthropod vectors experience a complex suite of environmental factors that affect fitness, population growth, and species interactions across multiple spatial and temporal scales. Temperature and water availability are two of the most important abiotic variables influencing their distributions and abundances. While extensive research on temperature exists, the influence of humidity on vector and pathogen parameters affecting disease dynamics are less understood. Humidity is often underemphasized, and when considered, is often treated as independent of temperature even though desiccation likely contributes to declines in trait performance at warmer temperatures. In this study, we explore how variation in relative humidity affects the thermal performance of mosquito life history traits that are relevant for transmission (probability of larval survival, mosquito development rate, adult longevity and fecundity, and daily biting rate) in the Asian malaria vector (*Anopheles stephensi*) and human malaria (*Plasmodium falciparum*) system. We find relative humidity to significantly alter the predicted Tmin, Tmax, thermal breadth, and qualitative shape of the temperature-trait relationship in distinct and sometimes surprising ways depending on the trait being considered. These results demonstrate that if we do not account for temporal and spatial variation in relative humidity, mechanistic models used to forecast interannual and spatial variation in malaria risk will fail to accurately predict malaria incidence. This also has ramifications for making future projections with temperature-dependent models of disease risk with ongoing climate and land use change. As *Anopheles stephensi* is currently invading urban centers of Africa and poses a significant threat to ongoing malaria elimination efforts, accurately predicting its current and future distribution, abundance, and transmission potential is crucial.

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ANGIOGENESIS AND CHRONIC EXPOSURE TO *ANOPHELES* SALIVARY PROTEINS

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Exposure to mosquito saliva can have prolonged effects on human physiology, impacting mosquito-borne diseases like malaria. Mosquito salivary proteins, acting as anticoagulants or immunomodulators, facilitate blood uptake by mosquitoes and may influence angiogenesis. However, the impact of exposure to mosquito salivary proteins on factors important in angiogenesis has not yet been described. In this study, we investigated the effects of *Anopheles quadrimaculatus* salivary gland proteins on endothelial cells. Human Umbilical Vein Endothelial Cells (HUVECs) were treated with salivary gland protein fractions from 100 pooled *An. quadrimaculatus* salivary gland pairs and cell proliferation was measured by MTT test. Based on the MTT test, we selected three fractions displaying significant differences ($p<0.05$) compared to untreated cells to further evaluate their effect on expression of angiogenesis associated factors. First, we used an ELISA-based test and observed that cells treated with fraction C2 presented higher TNFα and PDGFBB levels by 1.7-fold and 1.8-fold, respectively. We also observed that the fraction E6 upregulated IGF-1 by 1.7-fold, while fraction F9 enhanced FGFb and EDF by 1.6-fold and 2.1-fold, respectively. Further analysis via qPCR revealed that fraction F9 also induced an increase in TYMP (3.5-fold), VEGFB (2.3-fold), VEGFC (2.2-fold), ANGPTL2 (3.2-fold), NRP1 (3.2-fold), NRP2 (2.6-fold), and EDG1 (2.3-fold) while a 2-fold decrease was observed in CSF3 when compared to the level in untreated cells. Protein fractions were sent for sequencing. These findings highlight the role of mosquito saliva in angiogenesis, offering insights into potential therapeutic avenues for future research.

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USING ANCESTRAL SEQUENCE RECONSTRUCTION FOR GENERATION OF BROAD-SPECTRUM VACCINE PLATFORMS AGAINST TICK-BORNE FLAVIVIRUSES

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Tick-borne flaviviruses (TBFs) pose a significant health threat and there is a significant need to develop more efficient countermeasures. However, most vaccines developed target a specific viral species, requiring new vaccines be developed against each pathogen. The development of vaccines that provide broad protection against a range of related viruses has the potential of reducing disease burden against known and unknown TBFs. Towards this need, we used ancestral sequence reconstruction (ASR) to design antigens of extinct ancestral viruses that might generate antibodies capable of neutralizing a broad array of related modern-day viruses. Among the flaviviruses, envelope (E) is immunodominant and antibodies targeting particular regions are strongly neutralizing. The flavivirus NS1 protein is also a determinant of pathogenesis and is highly immunogenic. Using alignments of extant human-pathogenic TBFs, we reconstructed ancestral E and NS1 sequences that possess high sequence and structural identity to several modern-day pathogens of concern. Ancestral antigens were then inserted into infectious clones (ICs) to generate chimeric vaccine candidates. Three different vaccine platforms were used, including yellow fever virus 17D, a double subgenomic Sindbis virus, and a deer tick virus IC that had been attenuated by mutagenesis of conserved residues present in other established attenuated vaccine platforms. We observed that while the yellow fever and deer tick virus ICs had reduced viral replication and antigen presentation, Sindbis virus ICs had similar viral kinetics and antigen expression, supporting further investigation in vivo. We predict that immune responses generated against ancestral antigens will provide a reasonable level of protection against multiple modern day TBFs. The results of this study contributes to the development of a much-needed vaccine that could be used in TBF-endemic areas.

8400

PRECLINICAL DEVELOPMENT OF AN ORALLY AVAILABLE NS4B INHIBITOR FOR YELLOW FEVER

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In a high-throughput-screening, we identified a small-molecule hit compound BDAA that specifically inhibits yellow fever virus (YFV) replication through direct targeting YFV nonstructural protein 4B (NS4B). A preclinical lead BSBI-67003 has been nominated from a hit-to-lead optimization campaign with >200 analogs, which has nanomolar EC_{50} and a selectivity index of ~10,000 against the YFV vaccine strain, as well as clinical isolates, in 7 cell lines. BSBI-67003 has a favorable pharmacokinetic profile in mice with 96% oral availability with a plasma concentration maintained above EC_{90} 24 hours post a single oral dosing at 10 mg/kg. In a 5-day repeated dosing experiment in mice, the maximum tolerated dose was determined to be >100 mg/kg BID. *In vivo* efficacy was evaluated in a YFV lethal infection model in immune competent hamsters and the minimum efficacy dose was determined to be 1 mg/kg BID. Treatment initiated as late as 4 days post infection (peak of viremia) led to 100% protection of lethal infection and significant improvement in disease markers such as body weight, liver function and viremia. A significant reduction in viremia was observed as early as 6 hours post treatment indicating a rapid acting mechanism. Regarding the mode-of-action, we demonstrated that BDAA binds NS4B and disrupts the integrity of viral replication organelles (ROs) in YFV infected cells. Such action promptly inhibits nascent YFV RNA synthesis within 30 minutes of treatment. Furthermore, the treatment also causes viral replication intermediates leaking from RO leading to activation of three major cytoplasmic double-stranded RNA sensors and a broad spectrum antiviral inflammatory response within 90 minutes of treatment. Apart from the optimal druggable properties, such unprecedented multi-mode of action should contribute to the rapid-acting and potent inhibition of viral replication *in vivo*, a feature that is essential for acute hemorrhagic fever therapy with short treatment window. A chemical process has been developed for scaleup synthesis and preclinical pharmacology/toxicology studies to prepare for IND and first-in-class Phase I clinical trials.

8401

B CELL RESPONSES TO A ZIKA PURIFIED INACTIVATED VACCINE ARE SHAPED BY PREVIOUS IMMUNIZATION WITH JAPANESE ENCEPHALITIS AND YELLOW FEVER VACCINES

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Flaviviruses cause widespread morbidity and mortality despite efforts towards vaccination. There are gaps in our understanding of how B cell responses are shaped in humans following sequential infections or immunizations with flaviviruses such as Zika (ZIKV), dengue (DENV), Japanese encephalitis (JEV), and Yellow fever (YFV). We evaluated antibody responses in a phase I clinical study representing 3 groups: (group a) flavivirus-naïve individuals vaccinated with a Zika purified inactivated whole virus vaccine (ZPIV), (group b) JEV (IXIARO®) followed by ZPIV, and (group c) YFV (YF-VAX®) followed by ZPIV. We found that ZIKV-neutralizing antibodies were diminished in participants primed with either JEV or YFV vaccination compared to flavivirus-naïve participants after two ZPIV vaccinations. To determine the cause of the diminished ZIKV neutralization, we characterized the longitudinal flavivirus-specific B cells. In flavivirus-naïve participants, the frequency of ZIKV-reactive B cells significantly increased following ZPIV vaccination ($p<0.05$), and these ZIKV-reactive B cells associated with the level of binding antibodies to Zika virions ($p<0.01$). Vaccination with JEV or YFV yielded high frequencies of B cells cross-reactive to ZIKV and DENV prior to ZPIV vaccination. Following two ZPIV vaccinations, the frequency of crossreactive B cells was significantly higher in JEV-vaccinated participants compared to B cells in flavivirus-naïve ZPIV vaccinees ($p<0.001$). Cross-reactive B cells had wanned by 6 months following the 2nd ZPIV vaccination and then were boosted to a higher frequency following a 3rd ZPIV vaccination ($p<0.05$). The third ZPIV vaccination coincided with the appearance of ZIKV neutralization in the YF-VAX® primed vaccinees. These studies demonstrate the elicitation of cross-reactive B cells following flavivirus vaccination, and provide insights into the memory recall B cell response upon subsequent flavivirus exposure. Characterizing these cross-reactive B cell populations and specificities is a critical step towards eliciting cross-protective responses following flavivirus vaccination.

8402

DEVELOPMENT OF A CONTROLLED ZIKA HUMAN INFECTION MODEL (CHIM)

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Zika virus (ZIKV) is a mosquito-borne flavivirus that was first isolated from the blood of a sentinel rhesus macaque in the Zika forest of Uganda in 1947. A large outbreak occurred in Latin America in 2015-16 resulting in the identification of congenital Zika syndrome (CZS) cases. Despite the development of numerous candidate vaccines for Zika, Phase 3 clinical trials have not been successfully performed due to the rapid resolution of the outbreak and the sporadic report of Zika cases. A ZIKV CHIM could play a critical role in the licensure pathway of potential Zika vaccines and therapeutics as a tool to down-select candidates and provide proof-of-concept for effectiveness. Two different ZIKV human isolates were obtained and expanded under cGMP (ZIKV-SJRP/2016-184 and ZIKV-Nicaragua/2016). Normal, healthy men and non-pregnant and non-lactating women ages 18 - 40 who were DENV and ZIKV-naïve were recruited from the Baltimore area. Twenty-eight women and 28 men were enrolled. Volunteers were block randomized to receive either ZIKV or placebo (5:2) in 4 cohorts of 14 volunteers. Volunteers were admitted to an inpatient unit and administered 100 PFU of ZIKV (or placebo) subcutaneously. Blood, cervico-vaginal secretions (CVS), semen, urine and saliva were collected and assayed for ZIKV. *Aedes albopictus* mosquitoes were fed on 7 volunteers from cohort 3 (ZIKV-SJRP, men) and 7 volunteers from cohort 4 (ZIKV-Nica, men) on days of peak viremia (days 5, 6, and 7 post-infection). Infectious ZIKV was recovered from serum in all volunteers who received ZIKV. ZIKV was recovered by culture and quantitative RT-PCR from multiple specimen types. Ninety - 100% of infected volunteers within each cohort developed a characteristic ZIKV rash. The clinical presentation and viral kinetics for both ZIKV-Nicaragua/2016 and ZIKV-SJRP/2016-184 in men and women will be presented. Both ZIKV strains were poorly transmissible to mosquitoes via feeding with only 1.8 - 2.4% of mosquitoes having ZIKV-Nica or ZIKV-SJRP detectable in the head (salivary glands), respectively.

8403

IMOJEV LIVE, ATTENUATED CHIMERIC VACCINE AGAINST JAPANESE ENCEPHALITIS: AN UPDATE AFTER 25 YEARS IN USE

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Japanese encephalitis (JE) is a mosquito-borne Flavivirus disease and a leading cause of encephalitis in Asia where ~5 billion live in 24 endemic countries. JE is characterized by high lethality and neurological sequelae in 30-50% of survivors. As for other zoonotic flaviviruses (e.g. West Nile, and Zika), there is a risk that JEV will invade the US. JE vaccines have been widely deployed in Asia, including inactivated vaccines; a live attenuated vaccine (SA-14-14-2); and a recombinant live vector vaccine (ChimeriVax-JE marketed under the trade name IMOJEV) . IMOJEV was engineered by replacing the prM-E genes of yellow fever 17D vaccine virus with the corresponding genes of the JEV SA14-14-2 virus, which contain 10 attenuating mutations that contribute to loss of neurotropism. Compared to YF-Vax®, IMOJEV was less neurovirulent in mice and non-human primates. Monkeys given a single SC dose rapidly developed high titers of neutralizing antibody and were protected against lethal IC JEV challenge. A total of 18 clinical trials in over 15,000 subjects, including 9,000 infants 9-24 months) showed the vaccine to be safe and highly immunogenic after a single SC inoculation of 4-5 logs. In adults , neutralizing antibodies are elicited rapidly, with 99% of subjects seroprotected by 30 days, with GMTs greater than 1000. The vaccine induced a durable response with 87% seroprotected 5 years after vaccination. There is no interference by anti-vector (yellow fever) immunity. First approved for persons 9 months of age or greater in Australia in 2010, and subsequently in 13 other countries in Asia, IMOJEV has enjoyed an excellent safety record, with over 11 million doses sold. IMOJEV's product profile, single-dose administration, rapid onset and durable protection, age limits, precautions and contraindications (pregnancy, breastfeeding, immune deficiency) are similar to the highly successful YF 17D vaccine from which it was derived, but with a better safety record. IMOJEV manufacturing in Vero cells is exceptionally robust and could meet unexpected demands resulting from an introduction of JEV into Europe or the Americas.

8404

SIMULTANEOUS INHIBITION OF DENGUE VIRUS INFECTION AND NS1-MEDIATED ENDOTHELIAL HYPERPERMEABILITY WITH A NATURAL STEROIDAL SAPOGENIN

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The four dengue virus serotypes (DENV1-4) cause the most prevalent mosquito-borne viral disease in humans. While most cases are mild or asymptomatic, some progress to severe disease characterized by endothelial barrier dysfunction that is mediated by vasoactive cytokines and by the DENV non-structural protein 1 (NS1). Despite the urgent need for therapeutics, there is currently no specific antiviral treatment for dengue. However, spirostane-type compounds isolated from plant extracts exhibit antiviral effects against DENV and ZIKV in vitro. Based on structural similarities, we found in the Drug Bank database the spirostane compound smilagenin (SMI), a natural product, previously studied for its role in modulating inflammatory processes due its steroidal structure. We evaluated the antiviral effect of SMI in vitro by measuring the reduction of focus forming units (FFU) in the supernatants of Vero cells treated with SMI before and after DENV2 infection. We observed a significant reduction of 47% and 44% FFU/mL when cells were treated with SMI before and after DENV2 infection, respectively. Additionally, we investigated the ability of SMI to inhibit DENV NS1-induced endothelial hyperpermeability in Human Pulmonary Microvascular Endothelial Cells (HPMEC) using a trans-endothelial electrical resistance (TEER) assay, and we observed that SMI completely inhibited DENV NS1-induced hyperpermeability. We also evaluated the in vivo therapeutic efficacy of SMI in C57BL/6 mice deficient for the interferon α/β receptor infected with a lethal dose of DENV2 (strain D220) that were treated with 2mg/kg of SMI daily for 5 days starting on the day of infection. Treatment with SMI significantly reduced morbidity in mice compared to the vehicle control group, resulting in 100% survival. Our study demonstrates that SMI is a promising therapeutic for dengue, exhibiting potent antiviral effect in vitro and in vivo and protecting against NS1-induced endothelial barrier dysfunction. Further research is needed to elucidate the antiviral mechanisms of SMI and its impact on NS1-induced vascular leakage in vivo.

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ANTIBODY RESPONSE PROFILE ELICITED BY A LIVE-ATTENUATED TETRAVALENT DENGUE VACCINE IN CHILDREN AND ADOLESCENTS FROM ENDEMIC AREAS

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Immunoglobulin (Ig) M, IgG1, and IgA have been implicated in protective responses against dengue virus (DENV) by promoting neutralization, clearance, and destruction of infected cells and virus by innate immune effector cells and/or the complement system (CS). TAK-003, a live-attenuated tetravalent dengue vaccine, was efficacious in preventing dengue disease and hospitalization in the phase 3 DEN-301 (NCT02747927) trial. Anti-DENV neutralizing antibodies (NAb) were quantified as part of immunogenicity endpoints of the trial. In exploratory assessments, we also investigated antibody isotype and subclasses (IgM, IgG1, and IgA), as well as complement-fixing antibody (CFA) effector function elicited by TAK-003 in randomly selected baseline (BL) seronegative (SN; n=48) and seropositive (SP; n=48) children/adolescents (4-16 years old). Antibody responses were assessed in samples collected before (day 1) and after (days 120, 270, and 450) two doses of TAK-003, administered subcutaneously 3 months apart, using Luminex-based multiplex assays. TAK-003 stimulated a multi-pronged humoral response profile in both groups. IgG1 and CFA were among the predominant responses, detected in 80-100% of the study participants. Both IgG1 and CFA targeted mostly all four DENV serotypes, often with comparable concentrations. The impact of TAK-003 on IgA and IgM responses was observed mainly in BL SN participants, with IgA detected at higher rates over time, targeting >3 DENV serotypes. Correlation analysis indicated the presence of heterogeneous relationships between function (NAb or CFA) and binding (IgG1, IgA, and IgM) antibody features, underscoring a cooperative and complex role for vaccine-driven virus neutralization and CS activation. In summary, this is the first report on a dengue vaccine-driven IgM, IgG1, IgA, and CFA response where study participants presented diverse humoral responses targeting multiple DENV serotypes for at least 1-year post-vaccination, confirming broader and long-lasting TAK-003-mediated immunity coverage, potentially allowing a sustained efficacy against infection and severe disease.

8406

COMBINING WEARABLE GPS LOGGERS WITH ENVIRONMENTAL AND SNAIL DATA TO UNCOVER FINE-SCALE *SCHISTOSOMA MANSONI* TRANSMISSION DYNAMICS IN UGANDA

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The complex and locally specific environmental interactions between humans and intermediate snail hosts give rise to highly focal schistosome

transmission patterns. To approximate these complex interactions, empirical studies have typically used proxy measures such as self-reported water contact for exposure and snail abundance or infectivity for environmental risk to predict infection outcomes. Yet, it has been difficult to empirically capture and validate which proxy variables are relevant for infection. Here, we demonstrate how granular human water contact data from wearable GPS loggers, combined with site-level snail data and remote sensing indicators, can be used to identify relevant drivers of *Schistosoma mansoni* infection at fine spatial scales. To achieve this, we draw upon a subsample of 450 participants from the SchistoTrack Cohort in Eastern and Western Uganda. All participants wore wearable GPS loggers for ten days. Using geolocated data on 144 water sites mapped by the field study team as well as remote sensing data on waterbodies, we derive water contact measures from GPS data and construct site-level and individual-level water contact networks (i.e., bipartite networks connecting all sites that are visited by the same individuals). We then use simple metrics such as degree centrality to identify key sites and individuals within these water site networks. By repeating the network construction, but instead of considering all water sites using only water sites with snails, sites with infected snails, and sites with observed faecal contamination, we describe how the topology of water contact networks that incorporate environmental risk differs from networks without consideration of environmental risk. Using the individual-level water contact networks, we apply network regression techniques to predict either infection status or one-year reinfection as the outcome. Our results identify key drivers of local infection patterns and clarify the relevance of human behavioral versus environmental drivers for explaining transmission hotspots.

8407

ACCEPTABILITY AND FEASIBILITY OF A ONE-STOP HOME-BASED GENITAL SELF-SAMPLING FOR FEMALE GENITAL SCHISTOSOMIASIS, HUMAN PAPILLOMA VIRUS AND TRICHOMONAS AND HIV SELF-TESTING: BASELINE DATA FROM A LONGITUDINAL COHORT STUDY IN ZAMBIA

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Female genital schistosomiasis (FGS) is a gynecological complication of *Schistosoma haematobium* infection affecting millions of women in sub-Saharan Africa. FGS is associated with sexual dysfunction, reproductive tract morbidity and increase prevalence of HIV and cervical precancer lesions. Diagnosis is poor, but studies have shown acceptability of genital self-sampling, for STI, FGS and HPV. We aim to determine the acceptability and feasibility of a multi-pathogen genital self-sampling method in a large cohort in Zambia. The Zipime Weka Schista study is a longitudinal cohort (2021- 2025) integrating home-based genital self-sampling for *S. haematobium* and HPV and self-testing for HIV and *Trichomonas vaginalis* (Tv) in three communities in Zambia. Sexually active women aged 15-50 years were randomly selected by community health workers. During a home visit two cervicovaginal self-swabs and a urine sample were obtained and HIV and Tv self-test were provided. Information was collected on the acceptability and feasibility of the methods for multi-pathogen genital self-sampling. From January 2022 to March 2023, 2,531 (93.7%) were enrolled. A total of 2,389 (94.3%) had self-swabs for Tv and 1,404 (55.4%) self-tested for HIV. High acceptability was found for the home self-administered procedures (2,208/2531; 87.2%). Women preferred to be seen at home than in clinic. Some reasons stated were convenience (n=1585 (71.8%)); more privacy at home (n=1215 (55.0%)); inconvenience of going to the clinic (n=264 (12.0%)); lack of transport to go to the clinic (n=208 (9.4%)); unavailability due to work commitments (n=118 (5.3%)) and lack of childcare options, (n=69 (3.1%)). A home-based multi-pathogen self-sampling and testing approach is highly acceptable and feasible in three communities in Zambia and has a high potential to increase access to diagnosis of HIV and other genital infections in women of childbearing age. This strategy shows promise as an evidence-based novel approach which could be scaled up both in Zambia and other similar contextual settings.

8408

SCHISTOSOMA MANSONI AND *HELICOBACTER PYLORI* CO-INFECTIONS AMONG SCHOOL-AGED POPULATIONS: A STUDY IN NIGERIAN COMMUNITIES

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Helicobacter pylori is strongly associated with stomach ulcers, and gastric cancer. There are established evidence of altered pathology among persons co-infected with *Schistosoma mansoni*, a water borne trematode infection that also colonizes the intestine. For the correct clinical management of *H. pylori* disease, obtaining thorough information on the other concurrent infections is essential. Information regarding the prevalence of co-infections and associated risk factors among coinfected persons are lacking but emerging in Nigeria. This study therefore reports the epidemiological findings from school-aged population across five study communities around Kainji lake in Nigeria using the PCR technique. Of the 299 participants, an overall prevalence of 19.7% was recorded for *H. pylori*, and 34.4% for *S. mansoni*, while co-infection of both was *7.0%.* Infections were significantly different across the study communities for *S. mansoni* ($p<0.05$) when compared to *H. pylori* ($p > 0.38$). There were however no significant association between infection and gender ($p > 0.05$), with the following odd of infection for *S. mansoni* (OR=0.69 (95% CI: 0.42, 1.12)), *H. pylori* (OR=1.33 (95% CI: 0.75, 2.36)), and combination of both infection (OR=1.31 (95% CI: 0.83, 2.09)). By age category, children below 14years were twice likely to be exposed to the combination of both infections; age 12-14 years ((OR=1.9 (95% CI: 1.06, 3.44)), and age 9-11 years ((OR=1.96 (95% CI: 1.11, 3.48)). But they were also less likely to be exposed to *S. mansoni*; age 12-14 years ((OR=0.52 (95% CI: 0.27, 0.97)), and age 9-11 years ((OR=0.43 (95% CI: 0.23, 0.79)). These findings highlight about 7% of the studied population are co-infected with both pathogens, and majority were only with *S. mansoni* infection. Complementary interventions alongside treatment campaigns for *S. mansoni*, may be necessary to address *H. pylori* co-morbidity.

8409

MAIN RESULTS FROM A PHASE II RANDOMISED PLACEBO-CONTROLLED TRIAL OF PRAZIQUANTEL IN PRESCHOOL CHILDREN WITH INTESTINAL SCHISTOSOMIASIS

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Praziquantel (PZQ) is an effective drug against the parasitic disease schistosomiasis, delivered annually through control programs. However, the optimal dose for parasitic cure in preschool age children is not known. We conducted a Phase II randomized placebo-controlled trial in Uganda, testing PZQ at single standard (40 mg/kg) versus repeated standard dosing (80 mg/kg delivered as two doses of 40 mg/kg three hours apart) at baseline and same or placebo at six months, in children 12-47 months infected with the parasite *Schistosoma mansoni.* Co-primary outcomes were parasitological cure and egg reduction rate at 4 weeks. Secondary outcomes included antigenic cure at 4 weeks, adverse

events, toxicity 12 h post-treatment, morbidity and nutritional outcomes, biomarkers of inflammation and enteropathy at 6 and 12 months and PZQ pharmacokinetic/dynamic parameters. A total of 354 children (median age 36 months, 49% female) were randomised (1:1:1:1). For the primary outcomes, cure rates were 90% and 67% in the 80 mg/kg and 40 mg/kg groups, respectively (absolute difference 23%, 95% CI: 14-31%, p<0.001). Egg reduction rates were higher in the 80 mg/kg versus 40 mg/kg/ group (absolute difference 2% (1-3%), p<0.001) and 22% (5-59%, p<0.001) respectively). There were no differences in adverse events or toxicity comparing the two doses. At 12 months, no difference was found in anemia or nutritional status by PZQ dose arm. A repeated 40 mg/kg dose 3 hours apart is safe and significantly more effective in achieving parasitic cure than the current proposed single 40 mg/kg dose and can be recommended for young children living in *S.mansoni* endemic areas.

8410

THE USE OF WATER EDNA IN SNAIL IDENTIFICATION FOR THE UNDERSTANDING OF *FASCIOLA* ENVIRONMENTAL BURDEN AND SNAIL DIVERSITY IN THE HIGHLANDS OF PERU

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Fascioliasis is a snail borne infection of the *Lymnaeidae* family. The impact of the interplays between snail species on *Fasciola* transmission has not been studied. We aimed to evaluate the seasonal variations of snail abundance and species diversity in highly endemic regions of Peru and their association with the burden of *Fasciola* in the environment using eDNA analysis of water sources. We developed a real time single and multiplex PCR tests targeting mitochondrial and nucleic genes to differentiate snails to the genus and species levels. We focused on genera level identification of aquatic snails known to occur in Peru (*Lymnaea, Biomphalaria*, and *Physa*). Species level identification and phylogenetic analysis were performed for snails of the *Lymnaeidae* family. We tested water and extracted eDNA from water samples collected every 3 months during 12 months. The association of snail abundance and diversity with the variations in quantitative *Fasciola* eDNA in environmental waters will be evaluated accounting for spatial and temporal distributions. The relationship between snail abundance and diversity with livestock fascioliasis incidence will be explored. Statistical analysis will be done for clustering by province and community subdivisions and adjusting for water quality and weather conditions throughout the year. We collected 558 water samples corresponding to 304 households, 15.6% (n=87) had snails, and of those 12.6% (n=11) tested positive for *Fasciola*. Our results determined a good reliability of eDNA for identification of snail genera and *Lymnea* subspecies as compared to PCR as the gold standard. This innovative approach will increase our understanding of snail host factors associated with infection. We hope to validate these findings in a larger sample for its ultimate use as a surveillance tool in areas of increased transmission for environmentally sound snail control.

8411

INFLAMMATION-ADJUSTED VITAMIN A DEFICIENCY IS ASSOCIATED WITH HEAVY *SCHISTOSOMA MANSONI* INFECTION INTENSITY AMONG PRESCHOOL-AGED CHILDREN IN UGANDA

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Vitamin A deficiency impairs immune function against parasitic pathogens. In rodents, dietary-induced vitamin A deficiency causes higher schistosome burden, higher mortality, and a reduced immune response compared to animals who are vitamin A replete. This cross-sectional analysis examines pre-treatment relationships between inflammation-adjusted vitamin A status, *S. mansoni* burden, and a panel of immunologic markers among preschool-aged children (PSAC) enrolled to the praziquantel in preschoolers (PIP) trial. PSAC age 12-47 months with *S. mansoni* infection, diagnosed by Kato Katz eggs per gram of stool (EPG), were enrolled from the Lake Albert region in Uganda. The Thurnham Correction Factor inflammation-adjustment method was applied to measures of retinol-binding protein (RBP). Vitamin A deficiency was defined as adjusted RBP ≤0.7 µmol/L. Multivariate polytomous logistic regression and linear regression were applied for outcomes of categorical infection burden and continuous immunologic markers, respectively. A bivariate threshold of p<0.1 was used to select covariates and considered age, sex, socio-economic status, and coinfections of hookworm, malaria, and HIV for inclusion in models. In 339 PSAC, 36.0% were vitamin A deficient and the distribution of *S. mansoni* burden was 56.6% light (1-99 EPG), 24.2% moderate (100-399 EPG), and 19.2% heavy (≥400 EPG). Vitamin A deficiency was associated with a higher odds of heavy *S. mansoni* intensity compared to light intensity after adjusting for age (OR 1.96, 95% CI 1.07-3.56, p=0.03). We did not find significant associations between vitamin A deficiency and any of the measured immunologic markers in fully adjusted regression models. The associations between vitamin A status and infection burden agree with findings reported from animal studies, representing an important translational advance for our understanding of vitamin A metabolism. Future research is needed to determine if nutritional interventions improving vitamin A status in combination with preventive chemotherapy for schistosomiasis reduces morbidity for PSAC living in endemic areas.

8412

ASSOCIATION OF *SCHISTOSOMA HAEMATOBIUM* INFECTION WITH PREGNANCY IN TANZANIA

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Forty million girls and women in Africa suffer from female genital schistosomiasis (FGS) caused mainly by *Schistosoma haematobium* (*Sh)*. Parasitic worms that reside in urogenital venules lay eggs that migrate through mucosal tissue, causing bleeding, pain, genital discharge, and possible infertility. Associations of active *Sh* infection with confirmed pregnancy have not been investigated.

Women of reproductive age living in a community in northwest Tanzania highly endemic for *Sh* infection were screened for enrollment into a cohort study beginning in May 2021. All participants had serum schistosome circulating anodic antigen (CAA) and urine pregnancy tested. A CAA value ≥30 pg/mL was considered positive. The non-pregnant women were enrolled and had up to six follow-up visits over the ensuing 12 months, with CAA and pregnancy tested at every visit. Participants received praziquantel if the CAA value was positive. Through March 6th, 2024, 585 participants have been screened. Of those screened, 260 (44.4%) were CAA positive

at baseline and 78 (13.3%) were either pregnant at baseline or became pregnant during follow-up. Younger age, being married, and a negative CAA were all positively associated with pregnancy. The odds of pregnancy for a woman who was CAA positive, after controlling for age and marital status, was 0.54 (95% confidence interval: [0.32-0.90]; P = 0.018). In 206 enrolled women who attended at least one follow-up visit 50 (24.2%) became pregnant. The odds of becoming pregnant among those who were CAA positive during at least one follow-up visit, after controlling for age, marriage, reported infertility, and abnormal discharge was 0.82 ([0.39-1.74]; P = 0.60). This study demonstrates that women with *Sh* infection were approximately half as likely to be or become pregnant as those without *Sh* infection. For women in the cohort for whom additional data were available, a lower risk of pregnancy in those with *Sh* infection appeared to persist when controlling for sociodemographic and clinical factors. Efforts to determine reasons underlying lower fertility in *Sh* infection, and whether it is reversible after treatment, are urgently needed.

8413

PREPARING FOR VACCINE ADVERSE EVENTS OF SPECIAL INTEREST-X (AESI-X): A STANDARDIZED APPROACH APPLIED TO NOVEL VACCINES

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The Coalition for Epidemic Preparedness Innovations (CEPI) aims to make novel vaccines available within 100 days of a pandemic. To ensure preparedness for novel "adverse events of special interest-X" ("AESI-X") associated with these new vaccines, the Brighton Collaboration (BC) SPEAC Project creates tools to facilitate standardized safety assessments, including case definitions (CD). Real-time harmonization of CD created during the emergence of AESI-X can be challenging, as seen in the response to AESIs associated with COVID-19 vaccines. The ensuing heterogeneity among CDs results in lack of comparability across vaccine safety surveillance systems. SPEAC is facilitating a consensus AESI-X CD Preparedness Plan among key vaccine safety stakeholders to develop standardized CDs for AESI-X early in the response. We identified three categories of AESI-X: 1) Known-known (a recognized syndrome associated with a vaccine); 2) Known-unknown (a recognized syndrome not known to be associated with a vaccine); 3) Unknown-unknown (a novel or variant syndrome not previously associated with a vaccine). We created a checklist for CD preparation and introduced this concept in an initial meeting with a small group of vaccine safety stakeholders in regulatory agencies and health authorities in February 2024. We then convened stakeholders in several meetings to draft the AESI-X CD Preparedness Plan, consisting of the following steps: 1) Signal detection and confirmation; 2) CD Working Group formation; 3) Rapid reviews of draft CD; 4) Implementation of AESI-X CD in surveillance and studies; 5) Revise and update CD during the response; 6) Assess lessons learned from the response; 7) Update the AESI-X CD Preparedness Plan as needed. A key part of the plan is routine outreach to countries introducing new vaccines offering the availability of BC CD assistance should they encounter an AESI-X. Developing this consensus process ahead of the next AESI-X will facilitate the implementation and assessment of novel vaccines for priority pathogens and other targets, by anticipating and responding to AESI-X associated with these vaccines using harmonized CDs.

8414

ENHANCING ACCESS TO HIGHLY MULTIPLEXED DIAGNOSTICS IN LMICS: LEVERAGING OXFORD NANOPORE SEQUENCING FOR DETECTION OF RESPIRATORY VIRUSES AND EMERGING PATHOGENS

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Rapid diagnostic tests and conventional molecular testing are crucial for efficiently diagnosing diseases like dengue and SARS-CoV-2. However, these tests are often pathogen-specific and have limited ability to be multiplex. Sequencing can be used to detect and characterize a wide range of pathogens, but the availability of sequencing capabilities are often limited in low- and middle-income countries (LMICs) due to costs and/or a lack of trained personnel. The purpose of this study was to demonstrate the ability to deploy a hybrid-capture sequencing approach, adapted to Oxford Nanopore sequencing technology (ONT), for enhancing the detection of viral respiratory pathogens from a community health clinic in Johor Bahru, Malaysia. We screened 167 patients for acute respiratory infection by collecting nasopharyngeal swabs during 2023, from March to June, the hottest months, and from November to December, the seasonal flu period. In 63% of the patient samples, we detected viral sequences using the Twist Comprehensive Viral Research Panel which were confirmed with pathogen specific qRT-PCR assays. We identified viruses including SARS-CoV-2, rhinovirus, respiratory syncytial virus (RSV), influenza A/B virus (FluA/B), and an unexpected Dengue virus. By using our approach, we were able to characterize the detected viruses, revealing the predominance of JN.1 and XBB.1.9.1 (as of December 2023), which are likely linked to commutes between Singapore and Malaysia. Through international collaborations prioritizing locally-driven, capacity-building-focused development, our study enhances effective skills transfer, amplifies research impact, and aids in promptly containing emerging pathogens in South East Asia, a hotspot for outbreaks. Our hybrid-capture based ONT sequencing method provides timely epidemiological and clinical sequence data for surveillance of emerging viral pathogens in LMICs, offering added insights beyond molecular testing.

8415

INTEGRATED SEROLOGICAL SURVEILLANCE FOR INFECTIOUS DISEASES IN ZAMBEZIA PROVINCE, MOZAMBIQUE USING MULTIPLEX BEAD ASSAYS

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Multiplex immunoassays allow simultaneous measurement of antibodies to multiple antigens, potentially saving time and resources, and providing data on neglected diseases that have limited funding. They also open opportunities to examine cross-pathogen vulnerabilities in populations. We incorporated a multiplexed serosurvey for vaccine preventable diseases (VPDs), malaria, neglected tropical diseases (NTDs), and enteric pathogens as part of a Countrywide Mortality Surveillance for Action (COMSA) in Zambezia Province, Mozambique. From December 2020 to March 2021,

30 clusters in Zambezia were visited, during which dried blood spots were collected from individuals aged between 6 months to 49 years. Specimens were tested for IgG antibodies to 35 antigens from 18 pathogens using a multiplex bead assay. Weighted seroprevalence estimates by age and cluster and seroprevalence curves by age were produced. The odds of seropositivity by cluster were compared using Bayesian logistic random effects models and individual level associations were identified using multiple logistic regression. Seroprevalence ranged widely across antigens by age, sex and area of residence. Low seroprevalence (67%) to measles highlights the need for increased immunization. High seroprevalence to *Plasmodium falciparum* long-term antigen ama-1 increased from 79% in children under 5 years of age to 92% in adults demonstrating very high transmission. Rural clusters had higher odds of seropositivity for most NTDs, *Plasmodium falciparum*, and enteric pathogens but lower odds of seropositivity to SARS-CoV-2 and VPDs compared to urban clusters. At the individual level, seropositivity to an antigen was strongly associated with seropositivity to other antigens in the same disease category (enteric, malaria, NTDs and VPDs). Heterogeneities in seroprevalence identified across pathogens, age, sex, and space can inform subnational risk assessments. Understanding the co-endemicity of diseases allows for integrated strategies to target interventions to the most vulnerable communities.

8416

A SEPSIS SYNOPSIS: HETEROGENEITY OF SEPSIS PRESENTATIONS ACROSS THE ACESO NETWORK

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Although most deaths due to sepsis occur in low-and-middle income countries, data regarding affected populations, pathogens, management, and outcomes remain sparse in these regions. The Austere Environments Consortium for Enhanced Sepsis Outcomes (ACESO) was established to improve outcomes of sepsis in low-resource settings through advancing knowledge and developing novel diagnostics and interventions. The ACESO prospective observational sepsis study has operated sites in Takeo Province, Cambodia, Kumasi, Ghana, Fort Portal, Uganda, Antananarivo, Madagascar, and Bong County, Liberia, with planned enrollment in Iquitos, Peru. Consenting participants with suspected infection and meeting at least two SIRS criteria are followed longitudinally, with subjective and objective data collected at standardized timepoints. Here, we report descriptive statistics of key epidemiologic features of the three largest sites within the cohort. A total of 1,974 participants have been enrolled from Cambodia (N=728, since May 2014), Ghana (N=623, since July 2016), and Uganda (N=623 since October 2017). The majority were male (1,035/1,974, 52%) and had a median age of 48 (IQR 28). HIV prevalence based on prior known history ranged from 6/728 (1%) in Cambodia to 171/623 (27%) in Uganda. Across all sites, pneumonia was reported most frequently as the likely source of sepsis (n=534), followed by genito-urinary (n=165) and intra-abdominal sources (n=137). The most frequently identified pathogenic organisms isolated from baseline blood cultures varied widely across sites, from *Burkholderia pseudomallei* (n=42) in Cambodia, *Staphylococcus aureus* in Ghana (n=25), and *Streptococci* spp. in Uganda (n=10); *Salmonella* spp. were isolated across all sites (n=42). Malaria rapid diagnostic positivity ranged from 3% in Cambodia to 21% in Uganda. Inpatient mortality was 15/728 (2%) in Cambodia, 23/623 (4%) in Uganda, and 160/623 (26%) in Ghana. This analysis emphasizes the heterogeneity of sepsis presentations across low-resource settings, underscoring the critical need to include individuals living in these settings within the field of sepsis research.

8417

SEPSIS-RELATED DEATHS AMONG CHILDREN BELOW FIVE YEARS OF AGE ENROLLED IN THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) NETWORK PROGRAM IN SUB-SAHARAN AFRICA AND SOUTH ASIA BETWEEN 2017 - 2022

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Despite treatment advances, sepsis remains the third leading cause of death (COD) in under-5s globally. Understanding the pathogen-specific causes of sepsis has proven challenging in developing countries, where sepsis-related deaths are often diagnosed clinically or are missing from official statistics when they occur in the community. Child Health and Mortality Prevention Surveillance (CHAMPS) is a multi-country surveillance program that systematically identifies causes of under-5 mortality from defined catchment areas in seven countries in sub-Saharan Africa and South Asia. Here, we analyzed the contribution of sepsis-related deaths and pathogen-specific causes of sepsis in children <5 years enrolled in the CHAMPS Network. CODs were determined by a panel of experts using data from post-mortem investigations conducted using minimally invasive tissue specimen testing, clinical records, and verbal autopsy. Between July 2017 to January 2024, a total of 3834 children <5 years had their COD determined. Nearly a third of cases 1391(36%) had sepsis in the causal chain leading to death. Sepsis was the most common COD among late neonates (71%) and early infants (46%), with Ethiopia (60%) and South Africa (50%) having a higher proportion of sepsis-attributed deaths. *Klebsiella pneumoniae* was the predominant cause of sepsis across all age groups. In neonates, *K. pneumoniae* (48%), *Acinetobacter baumanni* (34%) and *Escherichia coli* (14%) were the most common causes, whereas, in infants and children >1 year, *K. pneumoniae* (43%), *E. coli* (17%) and *Streptococcus pneumoniae* (18%) were the most common pathogens causing sepsis. Neonatal preterm birth complications and perinatal birth asphyxia were predominant underlying conditions in neonates while malnutrition, HIV infections, and respiratory tract infections were the most common underlying conditions in late infants and children >I year. Sepsis contributed to high mortality among CHAMPS cases in LMICs, with *K. pneumoniae* predominant cause across different age groups. This highlights the need to review empirical management guidelines for the prevention and management of sepsis cases.

8418

RICKETTSIOSIS AND SCRUB TYPHUS AMONG HOSPITALIZED PATIENTS WITH ACUTE FEBRILE ILLNESS IN RURAL NORTHEASTERN AND NORTH BORDER PROVINCES OF THAILAND, 2017-2020

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Rickettsial disease (RD) and scrub typhus (ST) are acute febrile illnesses (AFI) caused by vector-borne pathogens, *Rickettsia* species and *Orientia tsutsugamushi*, respectively. RD and ST data from 2003-2018 suggest geographic and demographic differences in Thailand. We tested RD and ST among AFI patients in the northern province of Tak, bordering Myanmar, and the northeastern province of Nakhon Phanom (NP), bordering Laos. We enrolled patients aged 2 to 80 years with documented fever ≥38.0°C or reported fever lasting ≤7 days upon admission, who were admitted to 12 hospitals in Tak and NP Provinces during April 2017-May 2020. We collected data on demographics, clinical manifestations, and proxy exposures to vectors. Blood specimens were tested for pan-Rickettsia spp. and *O. tsutsugamushi* by real-time PCR. To estimate prevalence, we weighted the sample to adjust for incomplete testing. We calculated risk ratios and 95% confidence intervals for potential risk factors for RD and ST. Of the 11,275 patients enrolled, 4,470 (39.6%) were tested for RD and ST pathogens. Prevalence estimates of RD were 1.2% (95%CI: 0.5-1.8) in Tak and 1.9% (95%CI: 1.3-2.5) in NP; for ST, they were 2.6% (95%CI: 1.6-3.5) in Tak and 0.06% (95%CI: 0.001-0.1) in NP. Of 149 patients PCR-positive for either RD (94) or ST (55), 56% were female. In addition to fever, common manifestations of RD and ST were fatigue (88.4%), headache (85.3%) and chills (75.3%). Patients who visited a forest within the past month had 9.3 times the risk of being ST PCR-positive (95%CI 4.4-19.6), and those with stray animal contact within the past month had 2.3 times the risk of being RD PCR-positive (95%CI 1.1-4.5), than those who did not. Patients presenting with AFI and reporting proxy vector exposures within the past month should be evaluated for vector-borne illnesses. Although the percentage of AFI attributable to RD or ST is relatively low, ST was more prevalent in Tak province. The provincial differences in prevalence could inform regional vector-borne disease control and prevention efforts.

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MICROSTRATIFICATION OF VISCERAL LEISHMANIASIS ENDEMIC AREAS TO IDENTIFY HOTSPOTS AND DISEASE SHIFTING PATTERNS IN NEPAL

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Micro-stratification, dividing large areas into smaller, homogeneous units, is crucial for understanding and addressing visceral leishmaniasis (VL) risk. In Nepal, where VL poses a significant health challenge, micro-stratification has been limited. This study pioneers micro-stratifying VL risk in Nepal, aiming to comprehend its prevalence and distribution across administrative levels. The objectives were to assess VL risk across administrative levels, provide insights into VL prevalence, and generate detailed risk maps. Data from the Epidemiology and Disease Control Division served as the primary source, analyzed for ward-wise VL burden, vector presence, migration history, and housing characteristics. Questionnaires and checklists aided data collection, with all 77 districts stratified based on VL risk. Entomological surveys conducted by academic and research institutions supplemented vector distribution status in the country. Among Nepal's 6743 wards, initially VL cases were uniformly distributed from east to west; however, high-risk wards progressively clustered in specific districts over time. After 2018 a noticeable shift of high-risk wards occurred towards the western regions, predominantly affecting Karnali and Sudur Paschim provinces. Provincial analyses showed diverse trends: Koshi province reported 27 high-risk wards in 2022, compared with Bagmati province's mere 6 high-risk wards. Moreover, Madhesh province observed a decline in high-risk wards, while Lumbini province emerged as a focal area for VL. Sudurpaschim province exhibited a consistent upward path in high-risk wards since 2017. To mitigate the impact of VL, targeted interventions are essential. Strengthening healthcare facilities in high and moderate-risk areas is vital to ensuring prompt diagnosis and effective case management. Implementation of active surveillance measures is essential for timely detection and response to any surge in VL cases. Intensifying indoor residual spraying campaigns in VL risk areas, coupled with targeted health education initiatives, holds the potential to enhance VL awareness and control.

8420

BANGLADESHI CHILDREN HAVE IMMUNITY TO CRYPTOSPORIDIA-ASSOCIATED DIARRHEA BUT NOT TO INFECTION

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Cryptosporidium is one of the top causes of diarrhea in Bangladeshi infants. The current paradigm is that humoral immunity is not important in the development of a protective anti-Cryptosporidium immune response. However, in previous work we have found that antibody responses to the *Cryptosporidium* antigens Cp23 and Cp17 in Bangladeshi infants were associated with a decrease in both the parasite burden and the probability of diarrheal disease in subsequent infections. We have followed the frequency of Cryptosporidium infections in a cohort of Bangladeshi infants living in a community, where exposure to this parasite is common. In line with previous observations, the frequency of diarrheal cryptosporidiosis significantly declined in the repeat infections (Chi-square test for trend; $p < 0.0001$) occurred in the older children. The frequency of diarrheal disease was highest in children living in this community between 1.5 and 2 years of age when there were 0.12 diarrheal episodes per child and thereafter it occurred less frequently falling to 0.01 episodes per child between 3.5-4 years [1278-1461 days]. Sub-clinical disease did not decline in frequency over the same time period (2-4 years of life) and remained at 0.33 ± 0.05 episodes per child in each 6 months (183 days) of life. Seroprevalence of the anti-Cp17 and anti-Cp23 antibodies was common in ≥1 year-olds but a general decline in the levels of anti-Cp17 and Cp23 *Cryptosporidium* antibodies occurred in older children (1-4 years). The impact of this was however offset by an increase in anti-CP17 and anti-Cp23 antibody avidity. Our results are consistent with the development of an adaptive immune response associated with protection from cryptosporidial diarrhea.

8421

MECHANISM OF INTESTINAL BARRIER REPAIR IN GIARDIASIS

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Giardiasis is a common diarrheal disease caused by the protozoan parasite *Giardia duodenalis*. Acute symptoms can include diarrhea, but infections are often subclinical. Disease transmission occurs by ingestion of infectious cysts in contaminated food or water. In developing countries, giardiasis is one of the leading causes of growth stunting in children under two years old. Changes in intestinal barrier integrity have been shown to contribute to impaired nutrient absorption, thereby leading to growth stunting in children. Although intestinal barrier defects have been linked to infection, there is limited understanding of barrier repair dynamics post-infection. Previous studies have demonstrated that *Giardia* infection is associated with dysbiosis in humans and animals. Because Aryl hydrocarbon receptor (AHR) signaling has been shown to promote intestinal repair in other systems, we are exploring the role of AHR in barrier repair following a *Giardia* infection. We quantified specific microbiome-derived AHR ligands in the plasma of infected C57BL/6 mice and observed a reduction of indole-3-ethanol and indole-3-pyruvic acid at 21 days post-infection. Since IL-22 signaling can also promote barrier repair, we quantified IL-22 transcripts by RT-PCR and found significantly increased levels of IL-22 mRNA in infected mice. Animals fed a diet with 20% calories from protein had elevated expression of IL-22 while animals on 2% protein did not. We also observed changes in certain barrier repair markers post-infection. This data suggests that *Giardia* can reduce barrier repair through altering levels of AHR ligands and that IL-22 may contribute to successful repair in mice fed a normal diet. Our current data can give a better understanding of possible dietary interventions to prevent growth restriction in *Giardia*-infected children.

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UNWINDING THE IRONY OF SEVERE ANEMIA IN ANTIMONY-RESISTANT *LEISHMANIA DONOVANI* INFECTION AT THE NEXUS OF OXIDATIVE OUTBURST AND IRON PURSUIT

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Pentavalent antimonials (SbV), the mainstay for treating Visceral leishmaniasis (VL) caused by an intracellular protozoan parasite, *Leishmania donovani* (LD), have been discontinued from the Indian sub-population for decades due to rising antimony-resistance. Despite the withdrawal of SbV, recent clinical LD field isolates showed antimony resistance (LD-R) pointing towards genetic adaptation that underpins its evolutionary persister nature and superiority over drug-sensitive strains (LD-S). The highlight of this study is understanding how LD-R has tackled antimony pressure which is paramount for unveiling the underlying signaling contributing to severe anemia and chronic hepatosplenomegaly resulting from parasite overburden observed in LD-R infection. Strikingly, the common mode of action of both SbV and host-defense-arsenal includes Reactive-oxygen species (ROS) outburst which is successfully exploited by LD-R. To thrive in high ROS, LD-R is equipped with enriched reducing equivalents, also, high ROS boosts iron production, a crucial component that is critically flawed in these parasites since LD are heme-auxotrophs. To interpret the cause of severe anemia in LD-R-infection, we unveiled that LD-R has devised a strategy to produce and rapidly propel host-iron inside parasitophorous-vacuole (PV) of murine macrophages through re-orientation of macrophage surface iron exporter-Ferroportin around PV membrane. Higher iron utilization to support aggressive proliferation of LD-R leads to iron deficiency which is compensated by inflated erythrophagocytosis due to the SIRPα degradation. Cleavage of SIRPα results in loss of discriminatory signal between CD47-enriched live RBCs and CD47-deficient senescent RBCs resulting in aggravated erythrophagocytosis of both live and senescent RBCs. This poses a question of how SIRPα is degraded. Stay tuned for the epilogue of a complex diad of 2 proteases that drive SIRPα cleavage! Taken together, this study provides key insights into the emergence of drug unresponsiveness in LD and related heme-auxotrophic pathogens and offers directions for refining therapeutic strategies.

8423

UNIQUE IMMUNE AND TISSUE REPAIR MARKERS IN CONGENITAL CHAGAS

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It remains unclear why 5% of Chagas-infected mothers transmit *Trypanosoma cruzi* to their baby (Transmitter). No molecular biomarkers are available to predict transmission risk, and the understanding of this pathogenesis is hindered by limited analyses of human-derived placenta tissue analysis. Understanding the molecular mechanisms associated with T. cruzi transmission is essential for the proper management of congenital Chagas.Here, we analyze the transcriptome of placenta tissue and peripheral blood that were collected upon delivery to detect local and systemic RNA expression changes, respectively. Differentially expressed genes (DEG) between transmitter and non-transmitter were identified using a cutoff of adjusted p-value ≤ 0.05 and absolute fold change ≥ 1.5. Placenta tissue analysis revealed a total of 298 DEG (64 decreased, 234 increased). A gene set enrichment analysis (GSEA) showed that several processes such as immune receptor activity, cellular response to IFN-γ, response to other organisms, and IgG immunoglobulin complex were implicated, probably suggesting an increased localized inflammatory response in transmitting mothers. In the peripheral blood, no DEGs were detected, but a GSEA analysis highlighted that transmission was significantly associated with distinct pathways, including increased T-cell receptor signaling and humoral immune response, higher endopeptidase activity, and decreased collagen-related protein and extracellular matrix remodeling. We highlight upstream regulators and central gene modulators that could inform the risk of transmission. Our analysis suggests that transmitting mothers exhibit unique gene expression patterns indicative of tissue damage, remodeling, and an increased inflammatory response to the parasite. We suggest that peripheral blood could be valuable for assessing congenital Chagas transmission risk. Further studies analyzing blood samples during pregnancy may be suited to validate gene-level biomarkers.

8424

CO-DELIVERY OF IL-12 AND LEISHMANIA PEPCK AS A VACCINATION STRATEGY TO INCREASE EXPRESSION OF SKIN HOMING MOLECULES AND RESIDENT MEMORY T CELL DEVELOPMENT

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Cutaneous leishmaniasis is a neglected tropical disease associated with a wide spectrum of clinical presentations which are often difficult to treat. Currently, there are no vaccines for human leishmaniasis which is likely due to the inability to generate long-lived memory T cells. However, we found that *Leishmania major* infection in mice generated long-lived CD4+ dermal resident memory T cells (dTrm) and that these dTrm provide protection against rechallenge. Furthermore, we found that subcutaneous immunization with a leishmania-conserved antigen, phosphoenolpyruvate

carboxykinase (PEPCK), generated long-lived dTrm cells. Importantly, this vaccine not only induced dTrm cells that were present at the immunized (inflamed) site but were also globally seeded in the skin. However, the level of protection was not at the level induced by infection-induced immunity. Therefore, our goal is to enhance vaccine-induced immunity by increasing the generation of PEPCK-specific dTrm cells, using both tetramer staining and PEPCK TCR transgenic T cells to track the responding T cells. The first step in dTrm development is licensing T cells to enter non-inflamed skin, which is dependent upon high expression of skin home molecules, such as P and E selectin ligands (PESLs), by T cells early after activation in the lymph nodes (LNs). PESLs are induced by IL-12 signaling, and we tested if administration of IL-12 with the PEPCK vaccine would enhance PESL expression by T cells in draining LNs and lead to increased T cells entry into non-inflamed skin. We found that co-delivery of IL-12 mRNA-LNP particles with a PEPCK vaccine significantly enhanced the expression of PESLs in the draining LNs and dramatically increased the number of PEPCK-specific T cells that were present in non-inflamed skin. These results suggest that administration of IL-12 mRNA-LNP particles at the moment of immunization may enhance the generation of dTrm cells.

8425

IMMUNE SIGNATURES PREDICT TREATMENT RESPONSE IN CUTANEOUS LEISHMANIASIS PATIENTS

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Cutaneous leishmaniasis (CL) caused by *Leishmania braziliensis* is characterized by an exaggerated inflammatory response that leads to parasite control, but it is also the cause of tissue damage and ulcer formation. The first-line treatment for CL in Brazil is pentavalent antimony, and we have documented that failure to therapy may occur in up to 50% of the patients. Here, we evaluated in a prospective cohort if the immune response at the lesion site can predict therapy failure with pentavalent antimony. This study was performed in Corte de Pedra, an endemic area of CL with high *L. braziliensis* transmission, located in Bahia state, Brazil. Participants were CL patients (N = 53) with classical ulcers and the diagnosis was confirmed through the detection of the DNA of *L. braziliensis* by PCR in biopsied tissues. The failure rate was 52% (N = 28) during follow-up. Cytokines production in supernatants from lesion biopsies were assessed before therapy by ELISA. Patients who fail therapy displayed higher levels of cytokines (IL-1β, TNF, IL-17, IL-10, Granzyme B, and IL-15), and chemokine (CCL2). We found a strong positive correlation between these cytokines and healing time and receiver operating characteristic (ROC) analysis showed that levels of IL-1β, Granzyme B and IL-10 can predict treatment outcome with high accuracy. Moreover, Subjects with a high IL-1β, Granzyme B, IL-10, IL-17 and CCL2 production exhibited a delayed response to therapy. Finally, clinical cure was associated with high levels of IFN-γ and CXCL9. This work identified molecules that can predict responsiveness to treatment and bring an advancement in the field as identification of patients at high risk of failing antimonial therapy, allowing earlier introduction of alternative therapy regimes such as Miltefosine or Amphotericin B.

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MALNUTRITION CONTRIBUTES TO VISCERAL LEISHMANIASIS SEVERITY BY EXACERBATING LIVER PATHOLOGY

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Protein malnutrition is a common risk factor for developing visceral leishmaniasis (VL) since it disrupts immune mechanisms that control parasite replication in the target organs of the disease. Because malnutrition contributes to alterations in intestine function and microbiota, we hypothesized that chronic malnutrition also enhances disease severity in VL by disturbing the homeostasis of the gut-liver axis. To study the consequences of chronic malnutrition on VL pathogenesis, we used a polynutrient-deficient diet (deficient protein, energy, zinc, and iron), which mimics moderate human malnutrition for six weeks, followed by *Leishmania infantum* infection. The 16S sequencing of stool samples demonstrated that the polynutrient-deficient diet alters the intestinal microbiota composition and worsens dysbiosis over time. Also, we detected 16S DNA in the liver of polynutrient-deficient diet-fed mice by qPCR. Granuloma formation was limited in the liver and malnourished-infected mice exhibited severe liver pathology characterized by steatosis, diffuse inflammation over the parenchyma, and inflammatory cell infiltration around the veins suggestive of intestinal bacterial translocation. Kupffer cells are specialized resident liver macrophages equipped with innate immune receptors and are positioned at the sinusoids to prevent the systemic spread of microorganisms translocated from the intestine. Flow cytometric analysis revealed that the polynutrient-deficient diet-fed mice had enhanced expression of Toll-like Receptors by Kupffer cells and increased hepatic levels of IL-1beta. Collectively, our findings suggest that malnutrition contributes to VL severity by disturbing the intestinal microbiota leading to enhanced liver pathology.

8427

HUMAN FILARIAL INFECTION RESHAPES THE TRANSCRIPTIONAL AND FUNCTIONAL PROGRAMMING OF CD8 T CELLS AT HOMEOSTASIS AND IN RESPONSE TO CYTOMEGALOVIRUS (CMV) IN FILARIAL/CMV COINFECTED INDIVIDUALS

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We have previously demonstrated that filarial infection drives a distinct population signature of $CD8^+$ T cells (CD8's) at homeostasis and following antigen stimulation. To characterize the heterogeneity and function of these CD8's we performed multiparameter flow cytometry from PBMCs collected from 44 CMV- infected individuals with (Fil+; n=29) or without (Fil-; n=15) concomitant filarial infection at homeostasis and in response to CMV antigen. At baseline, CD8's from Fil+ (compared to Fil-) showed higher frequencies of $CD8^+$ cells expressing IFN-γ, TNF-α, IL2, or IL17 and increased frequencies of $CD8^+CD107a^+$ cells - known to reflect cytotoxic activity. After re-stimulation with CMV, CD8's from Fil+ subjects had diminished expression of the type 1 cytokines, TNF-α; IFN-γ, and reduced frequencies of antigen experienced ($CD137^+$) cells. $CD8^+CD137^+$ effector cells from Fil+ showed diminished frequencies of IFN-γ, TNF-α, IL2, and GrB producing cells as well as multifunctional T cells (e.g. $CD8^+CD137^+IFN^+TNF^+IL2^+$) compared to Fil- subjects. Using multidimensional profiling and clustering algorithms, the Fil+ group at homeostasis had marked expansion of several unique populations, most notably $CD8^+CD45RA^+CD57^+GrB^+Perforin^+$ - shown to be associated with high levels of differentiation. In response to CMV, Fil+ subjects showed a decrease in prevalence of $CD8^+CD45RA^+CD57^+CD137^+GrB^+Perforin^+IFN^+TNF^+$ cells compared to Fil- subjects, confirming that antigen experienced cells are diminished in Fil+ individuals. Since the population of $CD8^+CD45RA^+CD57^+$ appears to be associated with filarial infection both at baseline and after CMV re-stimulation, we performed cell sorting and mRNA sequencing to understand the transcriptionally-based nature of this population (analysis in progress). Our data suggest that filarial infection is associated with activation of CD8's; but when stimulated with CMV antigen the subpopulations fail to produce key cytokines for viral control. These findings are likely important to understand the nature of bystander suppression of viral specific responses induced by filarial infections.

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LATENT CYTOMEGALOVIRUS INFECTION DISRUPTS INNATE AND ADAPTIVE IMMUNITY TO *PLASMODIUM FALCIPARUM* DURING PRIMARY MALARIA INFECTION

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Latent Cytomegalovirus (CMV) infection has widely reported immunomodulatory effects on the immune system, leading to altered responses to vaccination or infection within an individual. However, the impact of CMV on the immune response to the malaria parasite, *Plasmodium falciparum* is unknown. We studied the impact of latent CMV infection on immune response to *P. falciparum* malaria during Controlled Human Malaria Infection (CHMI). We assessed the influence of CMV on parasite multiplication rates and cellular and humoral immunity. Cell responses were analysed by spectral flow cytometry, and the magnitude and function of induced antibodies was quantified. We found CMV infected individuals had reduced control of parasite growth and reduced clinical symptoms compared to CMV negative individuals. Parasites control is mediated by innate cells including NK cells, monocytes and Vd2+ γδ T cells. We found, CMV infection associated differences in malaria control to be mediated by changes to NK cells. Latent CMV infection was associated with an expansion of phenotypically senescent and regulatory NK cells expressing CD57, TIGIT and PD1, and a reduced responsiveness to malaria parasites, with reduced CD107a, granzymeB and IFNγ. Additionally, latent CMV infection was associated with reduced adaptive immune responses, specific infected individuals had reduced induction of IgG1, and other functional antibodies including C1q, FcγRII, FcγRIII. In malaria, within T-helper follicular cells, only Tfh2 subsets are associated with the induction of protective antibodies. Consistent with this, latent CMV infected indivuals had a skewed Tfh compartment with expanded Tfh1 cells before and during CHMI, and the proportion of Tfh1 cells was negatively associated withantibody responses. Taken together, latent CMV infection impacts both innate and adaptive responses to malaria infection. These altered innate and adaptive immune responses may have particular importance in malaria endemic countries where CMV infection is almost universal and acquired early in life.

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HOST DIRECTED THERAPY TO IMPROVE ANTI-PARASITIC IMMUNITY IN VOLUNTEERS EXPERIMENTALLY INFECTED WITH BLOOD STAGE MALARIA

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Slow immune development to malaria is linked to immunoregulatory mechanisms that are induced by infection. These regulatory responses include development of Type 1 regulatory (Tr1) CD4 T cells, which emerge early in infection after Type I IFNs signaling and JAK1/2 activation. We hypothesized that blockade of this pathway would modulate the development of malaria induced immunoregulatory responses and boost protective anti-parasitic immunity.We tested the immune boosting potential of the licensed, oral JAK1/2 inhibitor ruxolitinib, in a randomized double-blind placebo controlled human malaria infection trial. Participants were inoculated with blood-stage *Plasmodium falciparum* and randomized in a 1:1 ratio at day 8/9 to receive the anti-malarial drug artemether/lumefantrine in combination with either ruxolitinib or placebo. Participants were also re-inoculated 3 months after their first inoculation. Modulation of cell signaling was investigated by measuring phosphorylation of STAT3 following *ex vivo* stimulation of peripheral blood mononuclear cells with IFNβ. Cell phenotypes and functions were assessed by CyTOF, spectral flow cytometry and scRNAseq, and parasite specific responses measured following parasite stimulation or by quantifying parasite specific antibodies. Ruxolitinib treatment modulated cell signaling pathways during primary infection, and increased circulating IFNy/IL10 ratios, increased activation of T-follicular helper (Tfh) cells and the frequencies of malaria specific Tfh cells. Further, treated individuals had a modulated memory responses during secondary infection across multiple lymphoid subsets, including changes in T and B cell subset composition, and cytokine production. Results show that host directed therapy during infection can reduced regulatory responses associated with slow immune acquisition.

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DIFFERENT MICRORNA PROFILES IN THE CIRCULATING CD4+T CELLS ARE ASSOCIATED WITH DIFFERENT CLINICAL PRESENTATIONS OF *LEISHMANIA DONOVANI INFECTION*

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Visceral leishmaniasis (VL) and post kala-azar dermal leishmaniasis (PKDL), caused by the intracellular protozoan *Leishmania donovani*, cause significant morbidity and mortality in the Indian subcontinent. Several microRNAs (miRNAs) associated with the outcome of leishmaniasis in murine models or human cell lines are reported, but studies of miRNAs in human VL patients are lacking. Most circulating miRNAs are found either in circulating blood cells or packaged into freely circulating microvesicles called exosomes. Because of their documented involvement in modifying immune responses, we investigated the roles of miRNAs in circulating exosomes and CD4+T cells of patients with VL or PKDL or healthy, endemic controls from Bihar, India. First, the plasma was isolated from whole blood and then PBMCs were extracted from the rest of the blood using density gradient separation followed by CD4+T cell isolation. We first screened all 827 reported human miRNAs using NanoString profiling in CD4+T cells, followed by data analysis and second, significant miRNAs were evaluated by TaqMan assays. Expression of miR-23a was decreased in CD4+T cells of VL patients compared to EC and PKDL ($p<0.05$), whereas miR-29 was decreased only in CD4+T cells of VL patients compared to EC. Nanostring profiling of miRNAs of CD4+T cells revealed many significantly upregulated and downregulated miRNAs in VL subjects compared to EC, but only few differentially regulated miRNAs in PKDL subjects compared to EC. Notably, miR-146a was significantly regulated in both plasma and CD4+T cells of VL subjects. we can infer from our study that the plasticity of T cell proliferation and differentiation in human VL is contingent upon microRNA-mediated gene regulation. Differential expression of miRNAs might provide prognostic marker to predict subjects who will develop PKDL as a complication of VL. We hypothesize these miRNAs may be critical determinants of immune response like macrophage polarization, suppression of T cell responses to *L. donovani* infection.

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ISOLATION AND CHARACTERIZATION OF α-GAL-CONTAINING EXTRACELLULAR VESICLES FROM *TRYPANOSOMA CRUZI*: UNVEILING NEW BIOMARKERS FOR CHAGAS DISEASE

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Chagas disease (CD), caused by the protozoan parasite *Trypanosoma cruzi*, remains a significant public health issue, predominantly affecting impoverished regions and resulting in considerable morbidity and mortality. The disease's complexity is further compounded by the parasite's sophisticated evasion mechanisms, including the secretion of extracellular vesicles (EVs) that facilitate host immune system evasion and pathogen persistence. This study aims to isolate and characterize α-Gal-containing EVs from three major *T. cruzi* genotypes: TcI (Colombiana strain), TcII (Y strain), and TcVI (CL Brener clone), highlighting their potential role as novel biomarkers for CD. EVs were purified from tissue culture cell-derived trypomastigotes (TCT-EVs) by affinity chromatography and separated into two fractions: α-Gal(-) (flow-through) and α-Gal(+) (eluate). Proteomic analysis of these fractions revealed a rich repertoire of glycosylphosphatidylinositol (GPI)-anchored proteins, including *trans*-sialidase (TS), mucin-associated surface proteins (MASP), and gp63 in the α-Gal(-) fraction. On the other hand, the α-Gal(+) TCT-EV fraction contained mainly GPI-anchored mucins of the TcMUC II family, which is abundant in TCTs and targets lytic protective anti-α-Gal antibodies. Notably, by chemiluminescent ELISA, isolated α-Gal(+) TCT-EVs demonstrated strong specific reactivity with sera from chronic CD (CCD) patients across multiple geographic regions, underscoring their potential as sensitive and specific biomarkers for diagnosis and chemotherapy follow-up. This research opens new avenues for the early diagnosis and therapeutic monitoring of CD, offering a promising strategy for tackling one of the most neglected tropical diseases.

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EXTRACELLULAR VESICLES FROM *TAENIA SOLIUM* DAMPENS PI3K-AKT-MTORC1 SIGNALING AND AMELIORATES DSS-COLITIS IN MICE

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Neurocysticercosis (NCC) is a neurological infection caused by the larval stage of *Taenia solium*, it accounts for up to 30% of acquired epilepsy in endemic areas. *T. solium* cysticerci in viable stage modulates host immune response and induces predominant type II (anti-inflammatory) immune response. Cysticerci secretes a plethora of molecules during the infection, which interact with host immune cells and suppresses them. *T. solium* cysticerci were grown in serum free medium and extracellular vesicles (EV) were isolated via ultracentrifugation-based protocol. Here, for the first time we report that *T. solium* cysticerci release EV that are readily internalized by macrophages in a dose dependent manner. In the metabolomic analysis we identified that EVs are rich in metabolites that are associated with the negative regulation of AKT signaling. We found that the EV induced anti-inflammatory gene expression in macrophages, indicating an immunodominant role of EVs in maintaining anti-inflammatory state during viable cysticercosis infection. Further, we investigated that EV induced degradation of AKT and mTORC1 proteins via autophagy mediated pathway and increased lysosomal activity in the macrophages. To investigate the therapeutic role of EV, we developed colitis in mice via 3% DSS in drinking water. We found that EVs significantly lowered the disease severity in DSS+EV groups. In the histopathology scores, EV rescued altered colon morphology induced by DSS and protected the mice in both the pre- and post-EV stimulation groups. On further analysis, pAKT level was high in the DSS only group which was suppressed upon EV stimulation. LC3 protein expression was increased after EV stimulation, henceforth activating the autophagy. In conclusion, these findings suggested that the EV from *T. solium* parasite can suppress the PI3K-AKT-mTORC1 pathway and suppress inflammation. Our study has provided the novel aspect of *T. solium* EV as potential therapeutic agents.

8433

A SPECIALIZED RIBOSOME PROMOTES HOST-TO-VECTOR TRANSMISSION IN THE HUMAN MALARIA PARASITE

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Ribosomal RNA (rRNA) in eukaryotes is encoded by repetitive gene clusters. In contrast, genomes of Plasmodium species contain only a few individual rRNA-encoding genes that are divergent in their primary sequence and located on different chromosomes. The expression pattern of these rRNAs is tightly developmentally regulated, making Plasmodium one of the most compelling instances of ribosome heterogeneity. In addition to the two known classes of rRNAs in P. falciparum, here we report on a third, highly divergent rRNA type with a deep evolutionary origin among primate-infecting Plasmodium. This 'O-type' rRNA does not include an 18S, features a 1.5x longer 28S that is processed into three fragments, and is predominantly expressed in the early stages of parasite development in the mosquito. We used RNA-RNA interaction sequencing to reconstruct the O-type 28S secondary structure, identifying a conserved ribosome core outfitted with extensive expansion segments. We showed that O-type rRNA assembles with 18S rRNA of different ribosome types and interacts with multiple other rRNA-associated ncRNAs including tRNA and snoRNAs that guide a distinct rRNA modification pattern. Importantly, knock-out of the O-type 28S led to an arrest of parasite development in early gametocytogenesis, suggesting a specialized function that cannot be compensated for by another cytoplasmic ribosome. Moreover, comparative ribosome profiling revealed that O-type ribosomes are responsible for the efficient translation of a subset of mRNAs during gametocyte development. Altogether, we report on the structural, compositional, and functional heterogeneity of a new ribosome type with a specialized role during host-to-vector transmission of P. falciparum.

8434

HIDE AND GO SEQ: CAPTURING THE ANTIBODY-VSG ARMS RACE DURING TRYPANOSOMA BRUCEI INFECTION

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Trypanosoma brucei, the protozoan parasite that causes Human African Trypanosomiasis (HAT) and Animal African Trypanosomiasis (AAT), continues to pose significant medical and economic burdens in endemic countries. T. brucei, an entirely extracellular parasite, is able to evade clearance using a sophisticated mechanism of antigenic variation. The parasite is covered in a dense coat of the antigenically variable Variant Surface Glycoprotein (VSG) and can switch expression of its VSG to avoid elimination by antibodies. T. brucei has access to a genomic repertoire of 1000s of VSG encoding genes that can be expressed or recombined into novel VSGs, giving the parasite a massive pool of antigens to choose from. With potentially hundreds of VSGs expressed during a single infection, the anti-VSG response is impossible to capture using standard low throughput techniques, and little is known about the in vivo anti-VSG response. Here, we aimed to elucidate the dynamics of the VSG-antibody interface during T. brucei infection in mice using high throughput methods. We combined VSG-seq, a targeted mRNA sequencing approach, with phage immunoprecipitation sequencing (PhIP-seq), a high throughput epitope mapping method. Using a phage display library of over 76,000 VSG peptides, we were able to track the dynamics and specificities of the anti-VSG response. With this longitudinal approach, we were able to visualize

the isotype specific kinetics of the anti-VSG response during infection. We were also able to identify and map peptide epitopes to expressed VSGs, providing insight into binding specificities and what VSG regions are accessible to different isotypes.

8435

ESTABLISHMENT OF A LABORATORY SYSTEM TO INTERROGATE TRYPANOSOMA CRUZI DEVELOPMENT WITHIN THE KISSING BUG VECTOR RHODNIUS PROLIXUS

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The single-celled eukaryote Trypanosoma cruzi alternates between insect and vertebrate hosts including humans, in which it causes Chagas disease. Endemic to Latin America, T. cruzi is estimated to chronically infect ~7 million people. While T. cruzi interactions with its vertebrate hosts are relatively well-characterized, factors affecting vector infection and transmission are poorly understood. To address this gap in our understanding of T. cruzi's basic biology, we established a model pathogen-host system using the kissing bug Rhodnius prolixus and the genetically tractable Y strain of T. cruzi. We first adapted rearing methods for efficient and high-throughput rearing of R. prolixus using custom 3D printed materials including an artificial feeding system. We next tracked T. cruzi colonization of different regions of the insect digestive tract using quantitative PCR and found that T. cruzi transiently passes through midgut regions but stably colonizes the hindgut long-term. Comparison of movement of inert fluorescent microspheres and parasites from anterior to posterior regions of the gut indicated that both arrive at the hindgut at circa 5 days post-ingestion, suggesting T. cruzi is passively carried to its preferred tissue by the peristaltic movement of the insect gut. Finally, we developed robust methods for isolation and purification of parasites released from insect excreta or from gut homogenates towards assessment of parasite transition from replicative to infectious stages. By establishing this easily cultured parasite-host model system, we are now well-positioned to begin interrogating the molecular basis for T. cruzi's colonization and transmission in its insect vector in future studies.

8436

CIRCADIAN RHYTHMS MEDIATE MALARIA TRANSMISSION POTENTIAL

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Malaria transmission begins when infected female Anopheles mosquitos deposit Plasmodium parasites into the mammalian host's skin during a bloodmeal. The salivary gland-resident sporozoite parasites migrate to the bloodstream, subsequently invading and replicating within hepatocytes. As Anopheles mosquitos are more active at night, with a 24-hour rhythm, we investigated whether their salivary glands are under circadian control, anticipating bloodmeals and modulating sporozoite biology for host encounters. Here we show that approximately half of the mosquito salivary gland transcriptome, particularly genes essential for efficient bloodmeals such asanti-blood clotting factors, exhibits circadian rhythmic expression. Furthermore, we demonstrate that mosquitoes prefer to feed during nighttime, with the amount of blood ingested varying cyclically throughout the day. Notably, we show a substantial subset of the sporozoite transcriptome cycling throughout the day. These include genes involved in parasite motility, potentially modulating the ability to initiate infection at different times of day. Thus, although sporozoites are typically considered quiescent, our results demonstrate their transcriptional activity, revealing robust daily rhythms of gene expression. Our findings suggest a circadian evolutionary relationship between the vector, parasite and mammalian host that together modulate malaria transmission.

8437

GENE-EDITING IN STRONGYLOIDES RATTI REVEALS THE NATURE OF HELMINTH SPECIFIC T CELLS

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CD4+ helper 2 (TH2) cells are key in driving parasitichelminth immunity and regulation of infection induced tissue pathology.However, the importance of antigen-specific vs. non-specific "bystander" CD4+T cell populations remains unclear. Our work describes a recently generated *Strongyloidesratti* mutant line using CRISPR-CAS targeting. This mutant, termed *Atilla,*contains an insertion of two copies of the immunodominant CD4+ T cell epitope2W1S, fused with FLAG and HA peptides into the astacin-likemetalloendopeptidase gene. Data show that *Attila* infection in C57BL/6mice induces marked expansion of trackable 2W1S+ specific CD4+ T cells in multipleorgans including: lung, spleen, mesenteric lymph nodes, and peritoneum. Uponrepeat inoculation, *Attila* specific 2W1S+CD62L-CD44+CD4+ T cellsco-expressed the transcription factor GATA3, the interleukin 33 receptor ST2and the chemokine receptor CXCR6. *In vitro* re-stimulation of splenocytesand lung cells from infected mice with the 2W1S peptide following induced significantlyincreased type 2 cytokine release in comparison to vehicle -treated controls.Notably, adoptive transfer of enriched 2W1S+CD62L-CD44+CD4+ T cells into mutantmice lacking alpha beta and gamma delta T-cell populations conferred host protection upon parasitechallenge as defined by significantly reduced fecal egg output burden andimproved survival kinetics as compared to mock-treated control mice. This work supportsa hypothesis that antigen-specific T cells serve an important role in helminthimmunity and limiting host pathology anddemonstrates that *Attila* is a robust exploratory tool forunderstanding helminth-specific T cellresponses.

8438

MRGPRA3 NEURONS DRIVE CUTANEOUS IMMUNITY AGAINST HELMINTHS THROUGH SELECTIVE CONTROL OF MYELOID CYTOKINES

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Skin employs interdependent cellular networks for barrierintegrity and host immunity, but most underlying mechanisms remain obscure. Herein, we demonstrate that the human parasitic helminth, Schistosoma mansoni,inhibits pruritus evoked by itch-sensing afferents bearing the Mas-related Gprotein-coupled receptor A3 (MrgprA3) in mice. MrgprA3 neurons control IL-17+γδ T cell expansion, epidermal hyperplasia, and host resistance against S.mansoni through shaping cytokine expression in cutaneous antigen-presentingcells (APCs). MrgprA3 neuron activation induces IL-1β and TNF in macrophagesand cDC2s partially through the neuropeptide calcitonin gene-related peptide(CGRP). Collectively, this work reveals a previously unrecognized mechanism ofintercellular communication

wherein itch-inducing MrgprA3 neurons initiate hostimmunity against skin-invasive parasites by directing cytokine expressionpatterns in myeloid APC subsets.

8439

IN VIVO SCREEN REVEALS *PLASMODIUM FALCIPARUM* TARGETS FOR MOSQUITO-BASED MALARIA INTERVENTION

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Progress against malaria has plateaued in recent years,necessitating new strategies to combat this deadly disease. We recentlydemonstrated that *Plasmodium falciparum* can be directly targeted withinthe *Anopheles* vector by allowing mosquitoes to land on surfaces coatedwith the antimalarial atovaquone. To discover additional inhibitors of mosquitostage *P. falciparum* that could be incorporated into mosquito bed nets,we performed an in vivo screen of 81 antimalarials by applying them onto thethorax of *Anopheles* females. This initial screen identified 22 activecompounds with seven distinct modes of action. Most compounds, however, werenot effective when mosquitoes had to actively take them up when landing ontreated surfaces, as they would when landing on bed nets. We therefore usedmedicinal chemistry approaches to introduce compound structural changes toincrease mosquito uptake upon exposure. This led to the generation of twohighly potent endochin-like quinolones (ELQs) targeting different sites (oxidizingand reducing) of cytochrome bc1. To assess the compatibility of these compoundswith bed net-like formulations, we incorporated them into low densitypolyethylene films. Brief contact exposure to these films completely ablated *P.falciparum* infection, and films fully maintained their antiplasmodialactivity over one year later. Importantly, mutant parasites generated via bloodstage selections showed severe defects during sporogony, and the two ELQcompounds did not show cross resistance. The potent activity of ELQs againstmosquito stage *P. falciparum* and the impaired transmissibility ofresistant mutants highlights the promise of using a combination of thesecompounds for vector-targeted antiplasmodial interventions.

8440

TICK INNATE IMMUNE RESPONSE TO PATHOGEN INFECTION AT SINGLE-CELL RESOLUTION

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Ticks rely on robust cellular and humoral immunity to control pathogen infection. However, a tick's innate immune system is a complex black box comprised of immune cells (called hemocytes), known to play a significant role in both cellular and humoral responses toward pathogens. Despite the importance of hemocytes in regulating microbial infection, understanding their basic biology and molecular mechanisms remains limited. A complete understanding of the immune factors involved in the interactions between ticks and tick-borne pathogens in hemocytes is crucial to elucidate their role in vector competence and to help identify novel targets for developing new strategies to block pathogen transmission. This study examined the tick hemocyte heterogeneity at the transcriptomic level. We used the 10X genomics single-cell RNA sequencing platform to analyze their transcriptome at a unique level in unfed, partially blood-fed, and pathogen-infected hemocytes. We were able to show the presence of seven distinct hemocyte transcriptomic populations in the tick vector. Our results revealed that clusters representing granulocyte and oenocytoids populations are increased with pathogen infection. This work opens a new field of tick innate immune biology to understand the role of hemocytes, particularly in response to prolonged blood-feeding (hematophagy) and tick-pathogen interactions.

8441

EXPANDING TOOLBOX FOR ODOR-BASED TSETSE FLY CONTROL IN EAST AFRICA

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Tsetse fly - transmitted Human AfricanTrypanosomiasis (HAT) and Animal African Trypanosomiasis (AAT) are among mostneglected tropical diseases in sub-Sahara Africa. Tsetse fly control strategiesconstitute cornerstones efforts in suppression and eradication of HAT and AAT.Tsetse fly lures that attract the flies to traps/insecticide-treated targetsand repellents that minimize contact between infective flies and theirvertebrate hosts can augment the strategies. We formulated a Novel AttractantBlend (NAB) comprised of ε-nonalactone, nonanoic acid, 2-nonanone and acetone) and Novel Repellent Blend (NRB) (δ-nonalactone, heptanoic acid,4-methylguaiacol and geranyl acetone) based on tsetse-refractory waterbuck odorconstituents, their structural analogues and attractant buffalo odor. Using two-choice wind tunnel in the laboratory and Latin square experimentaldesign in the field, we establish that 1) NAB is 2.4 times as attractive to *Glossina pallidipes* tsetse flies as POCA (3-n-Propylphenol,1-Octen-3-ol, 4-Cresol, and Acetone) blend routinely used in tsetse control and2) NRB is two-folds more efficacious than current commercial repellent blendagainst most savannah species. We microencapsulated the optimized NRB intoβ-cyclodextrin nano particles by kneading technique, evaluated responses of *G. pallidipes* tsetse to the microencapsulated blend andestablished kinetic release rates from the microcapsules under fieldconditions. We established significantly ($p<0.05$) lower release rate(5.35mg/h) in microencapsulated blend than the un-encapsulated control (11.82mg/h) and that the micro-capsulation did not significantly affect responses ofthe tsetse flies to traps. We assessed efficacy of NRB in livestock protectionusing randomized block experimental design and established at least 95%repellence of *G. pallidipes* from oxen by NRB. We successfully masked theNRB in fragrance for odor appeal (for potential use in security and hospitalityindustries) and are developing NAB and NRB into semiochemical prototypes forintegrated push-pull deployment in areawide control of tsetse flies in EasternAfrica.8442

8442

EFFECTIVENESS OF PYRETHROID-PIPERONYL BUTOXIDE NETS *VERSUS* STANDARD PYRETHROID-ONLY NETS IN PREVENTING MALARIA IN CHILDREN UNDER 10 YEARS LIVING IN KISANTU HEALTH ZONE, DEMOCRATIC REPUBLIC OF THE CONGO: A QUASI-EXPERIMENTAL STUDY

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The Democratic Republic of the Congo(DRC) is among the countries with the highest malaria incidence. Among the new generation of insecticide-treated nets(ITNs) with improved effectiveness of insecticides, ITNs treated with a combination of piperonyl butoxide(PBO)& pyrethroids appear promising for malaria control. This study evaluated the effectiveness of these ITNs under community conditions of use in DRC. A quasi-experimental study registered with ClinicalTrials.gov was carried out from January to December 2018, in Kisantu Health Zone. Thirty villages were randomly allocated as clusters(1:1) to receive one of two types of ITNs, ITNs treated with deltamethrin alone; or PBO with deltamethrin. After the intervention, the assessments were conducted monthly, quarterly&every six months for malaria infection, mosquito density&durability; respectively. The comparison of changes in different indices between the two groups was made using the ANOVA test for repeated measurements. A total of 1,790 children were included. There was a significant non-linear effect of time on the malaria infection incidence($p<0.0001$). The malaria infection incidence was higher in January–March, May-June&November. It remained higher in the control group compared to the intervention group($p<0.001$). Similarly, there was a significant non-linear effect of time on the density of both *Anophele(A) funestus* sl & *A. gambiae* sl. These densities decreased after the first month following the intervention&increased after time point 2. In cone bioassays at 12months post-distribution bio-efficacy was better in the intervention group ($p<0.001$). The nets treated with the combination of PBO&deltamethrin were found to be more effective for malaria control in the DRC.

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