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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

7540

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.

7542

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.

7543

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.

7544

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.

7546

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.

7547

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.

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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.

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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.

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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).

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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.

7586

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.

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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.

7617

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

7620

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.

7622

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.

7639

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.

7640

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.

7643

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.

7662

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.

7663

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.

7666

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.

7667

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.

7668

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.

7671

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.

7674

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.

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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.

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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.

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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.

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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.

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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.

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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.

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"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.

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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.

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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.

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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

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

7851

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.

7852

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.

7853

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.

7854

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.

7855

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.

7856

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.

7857

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.

7858

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.

7859

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.

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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.

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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.

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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.

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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.

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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.

7877

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.

7880

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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

7918

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.

7920

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.

7921

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.

7922

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.

7923

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.

7924

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.

7925

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.

7926

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.

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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.

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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.

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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.

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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.

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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.

7958

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.

7959

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.

7960

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.

7961

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.

7990

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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.