traumatic brain injury (n = 7). Among volunteers exposed to mefloquine, the rs141942830 ADORA2A variant was potentially over-expressed among volunteers who had either long-term or short-term AEs compared to those who did not. Two additional variants were under- or over-represented relative to the comparable gnomAD population frequency, suggesting differences from reference controls. MTFHR was enriched for variation for volunteers who had long-term side effects compared to those with short-term or no side effects. A pharmacogenomics approach may help develop a mechanism to integrate test data and clinical findings to guide safer mefloquine use. These non-silent variants may serve as mediators to alternate pathways for signal transduction or drug metabolism, which may be future routes of research.

6099

OPTIMAL DOSING OF SINGLE LOW DOSE PRIMAQUINE FOR TRANSMISSION BLOCKING OF P. FALCIPARUM IN CHILDREN.

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Single low dose primaquine (SLDPQ) to block the transmission of artemisinin-resistant Plasmodium falciparum and curtail its spread was first recommended in 2012 but insufficient data at that time precluded the WHO from suggesting age- and weight based dosing tables. Dosing in young children is challenging because limited if any suitable paediatric forms are available at the right tablet strength and a lack of pharmacokinetic data mean that approximation methods used for children, notably, allometric scaling are used to derive regimens. However, such regimens may not be optimal and require tablet fractions. Our group is developing child-friendly paediatric primaquine, in the form of flavoured uncoated tablets of 2.5, 3.75, 5, 7.5 & 15 mg, for optimal dosing regimens for transmission blocking and radical cure. Pharmacokinetic data from age dosed SLDPQ were analysed and models developed to predict primaquine maximum concentrations and exposures as surrogates of the bioactive oxidative metabolites that are gametocytocidal and haemolytic in G6PD deficiency. Analysis is ongoing and we will present optimal weight-based SLDPQ regimens for stand-alone use and adapted to the different dosing bands of the artemisinin based combination therapies in common use.

6100

ASSESSMENT OF PLASMODIUM VIVAX BURDEN IN A MALARIA PRE-ELIMINATION CONTEXT AMONG HARD-TO-REACH POPULATIONS: P. VIVAX SEROLOGY AND PCR AMONG CLANDESTINE GOLD-MINERS IN THE GUIANA SHIELD (2015-2019)

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In a context of malaria pre-elimination in Suriname and French Guiana, residual transmission persists among hard-to-reach and mobile populations such as illegal gold miners. Plasmodium falciparum has been adressed by specific strategies but P. vivax (Pv) is particularly challenging, due to high proportion of asymptomatic carriers and low access to radical treatment leading to relapse. Our work aims to estimate the burden of Pv in the gold miner population in this region and its evolution between 2015 and 2019. Data derived from two cross-sectional surveys, conducted in 2015 and 2019 at the border between Suriname and French Guiana. Illegal gold miners having returned for less than 7 days from a gold mining site located in French Guiana were enrolled (questionnaire and collection of a venous blood sample). Samples were analyzed by qualitative polymerase chain reaction (PCR) according to the Snounou method. A serology specfic for Pv (described by Longley et al. In 2020) was used to identify individuals who had probably presented with Pv infection during the last 9 months. A total of 411 individuals were included in 2015, 378 in 2019. Among them, 36 (8.7%) had PCR detected Pv parasitemia in 2015 and 15 (3.9%) in 2019. For serology, a threshold corresponding to 63% sensitivity and 90% specificity was identified as the most appropriate for the study population: under these conditions, 45% of the participants in 2015 and 28% in 2019 had probably had a recent acute Pv infection, and were therefore potentially carriers of hypnozoites. In total, 40 (13.9%) of the 288 seropositive individuals had a positive PvPCR. Among the 51 positive PvPCR, 78% were Pv seropositive. In a context of low malaria prevalence, the proportion of individuals with serological markers of recent exposure to Pv remains significant. This species represents a major challenge for malaria elimination, and must targeted by tailored interventions. Moreover, these biological methods could be used as evaluation methods for new strategies for Pv elimination.

6101

IMPLEMENTATION OF MALARIA COMMUNITY CASE MANAGEMENT (MCCM) IN TANZANIA: SUCCESSES, CHALLENGES, AND WAY FORWARD

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The World Health Organization recommends community case management of malaria to improve access to prompt, effective testing and treatment by trained community members living in proximity to patients. In Tanzania, many rural areas with high malaria endemicity are difficult-to-reach with malaria health services; however, Tanzania's new 2021 policy restricts community-based malaria testing and treatment only to licensed medical personnel called Community-Owned Resource Persons (CORPS), not Community Health Workers (CHWs). To evaluate the implications of this policy, the National Malaria Control Program conducted a pilot of malaria community case management (mCCM) between June and December 2022 in 311 villages across 10 councils with high malaria burden and low access to health services. One CORPS per village was recruited; following placement, CORPS conducted malaria rapid diagnostic testing (mRDT) for patients with suspected malaria and provided treatment for uncomplicated malaria following national guidelines. Cases exhibiting severe malaria were referred to the nearest health facility. During the pilot, 35,409 patients sought health services from the CORPS. Of these, 33,030 (93.3%) were tested by mRDT, and 10,631 (32.2%) were positive. Initially, only 104 CORPS could be recruited because of the licensing requirement, and only 77 (74.0%) of these CORPS were retained during the pilot, serving only 24.8% of the 311 villages. The most cited reason for leaving CORPS duties was other employment opportunities. Of the 77 CORPS, 23 (29.9%) were not residents of their assigned village, and among these 8 (34.8%) faced poor acceptability from the community. Meanwhile, there were 434 CHWs who also resided in the 311 villages. Studies in Tanzania have shown CHWs are widely accepted within their communities. Coverage of malaria diagnosis and treatment achieved by relying on CORPS was lower than expected. Further evaluation might identify successes in the provision of services and reasons for limited coverage and attrition of CORPS to help expand access to community case management.

6102

LESSONS LEARNED FROM MADAGASCAR NATIONAL MALARIA PROGRAM PERFORMANCE REVIEW 2022

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To reduce the malaria burden in Madagascar and accelerate to elimination, the National Malaria Program (NMP) in collaboration with partners have implemented several interventions including free distribution of insecticide-treated bed nets (ITNs), targeted indoor residual spraying (IRS), prompt diagnosis and treatment, malaria surveillance, monitoring and evaluation (SME) between 2018 and 2022. The NMP and technical partners carried out a desk and document review of annual reports, specific study reports, from 2018-2022 to document progress and inform the development of the national strategic plan 2023-2027. Regarding reporting system performance, the completeness of reporting increased from 94.4% in 2018 to 97.9% in 2022, while timeliness of reporting increased from 46.7% (2018) to 90.4% (2022). The use of artemisinin combination therapies for treatment of confirmed malaria cases increased from 81% in 2018 to 96.6% in 2022, although this remained under the national target of 100%. The coverage (%) of three courses of Intermittent preventive treatment in pregnancy increased from 32.96% (190397/577582) in 2018 to 42.5% (302803/711426) in 2022, although below the national target of 60%. Overall, malaria incidence per 1,000 persons increased from 36.7 in 2018 to 81.9 in 2021, then decreased to 63.8 in 2022. Three regions (Atsimo Atsinanana, Anosy and Atsimo Andrefana) accounted for 60% of the malaria cases. The objective of reducing malaria morbidity by 30% by 2022 was not achieved; however, incidence decreased by 29% between 2021 and 2022. Regarding malaria mortality, a reduction of 69% was reported between 2018 (927 deaths) and 2022 (287 deaths). This review was useful to document progress toward the NMCP's objectives over the past five years. It also identified the main challenges to consider in the national strategic plan 2023-2027, which emphasize on subnational actions on hotspots and strategies to accelerate malaria elimination in Madagascar.

6103

GENERATION OF PLASMODIUM-RESISTANT ANOPHELES GAMBIAE

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The vector-born parasite Plasmodium falciparum is the major etiological agent of human Malaria, causing more than 200 million clinical diseases per year and accountable for the majority of the deaths (~0.6 million per year globally). Vector control strategies like insecticide-treated nets (ITNs) or indoor residual spraying (IRS), have been the only effective approach leading to lasting malaria eradication. The reduction in efficacy of insecticides and parasite drug-resistance call for new tools to be developed to stop the transmission of the parasite. Advances in mosquito gene drive technologies has opened the door to develop the new approaches for malaria control. Our current strategies involve CRISPR-Cas9 mediated knockout (KO) of mosquito host factors that facilitate the parasite and transgenesis-based overexpression, or CRISPR-Cas9 mediated knock-in (KI), of effector molecules targeting malaria parasites at essential Plasmodium life cycle stages. One challenge with targeting the early parasite stages in the mosquito blood bolus using transgenic technology is the expression of effectors that can reach those parasites immediately upon ingestion of infected blood. Towards this goal, we are exploring the expression of early parasite stage -targeting effectors in the saliva that can be ingested, and blended, with the gametocyte-containing blood in the mosquito midgut. Here we discuss this approach along with other transgenic parasite-blocking approaches that show prominent reduction in prevalence and ookinetes number after an infectious blood meal.

6104

ENTOMOLOGICAL MONITORING IN ZANZIBAR TO SUPPORT MALARIA ELIMINATION EFFORTS

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Zanzibar is in the malaria pre-elimination phase with multiple ongoing vector control interventions, including the distribution of insecticide-treated nets (ITNs) and indoor residual spraying (IRS). The Zanzibar Malaria Elimination Program has 10 sentinel sites (6 in Unguja and 4 in Pemba) established for entomological monitoring of the malaria vector population and bionomics to track the impact and for timely adjustment of vector control strategies. Between October 2021 to September 2022, adult Anopheles mosquitoes were collected during two consecutive nights per month from each sentinel site. Methods for collecting mosquitoes included indoor and outdoor human landing catch, indoor CDC light-trap, pyrethrum spray catch, and pit trap. A total of 3,206 female Anopheles mosquitoes were collected (1,628 from Unguja and 1,578 from Pemba), with an average of 94% composed of Anopheles gambiae sensu lato, and the remaining a mixture of An. funestus s.l, An. coustani, and An. rufipes. Of the 2,813 successfully amplified specimens of An. gambiae s.l., 2,714 were An. arabiensis, dominating on average 96% of species across the two Islands, with An. merus and An. gambiae sensu stricto contributing the remaining proportion. An. arabiensis exhibited early peak biting time before typical sleeping hours (before 9:00 PM), and predominantly outdoor feeding. These feeding behaviors were generally consistent across sentinel sites. An. arabiensis is the predominant malaria vector in Zanzibar, and its early and predominantly outdoor biting behaviors may be attenuating the impact of personal protection provided by ITNs and IRS. This calls for complementary vector control strategies coupled with social behavioral change to address the risk of outdoor malaria transmission.

6105

USING EVIDENCE-BASED RESEARCH TO IMPROVE TIMELY DETECTION, DIAGNOSIS, AND TREATMENT OF MALARIA IN GUATEMALA'S PUSH FOR ELIMINATION

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Since 2012, reported malaria cases in Guatemala have fallen by nearly 70%, totaling fewer than 1,900 in 2022. In a 2021 surveillance assessment, the National Malaria Control Program (NMCP) estimated that only 44% of cases began treatment within the WHO-recommended 72 hours of symptom onset. To address this gap, the NMCP sought to describe the barriers and facilitators that cases experience in successfully starting treatment within three days of symptom onset. We conducted a mixed-methods study in 2022 in Alta Verapaz, Escuintla, and Izabal - Guatemala's

three most endemic regions comprising 89% of cases nationwide. We administered a cross-sectional survey to 160 randomly selected cases from the NMCP's 2021 database. We also conducted 60 semi-structured interviews with key stakeholders, including cases, vector control technicians (VCTs), and community health workers (CHWs). Our survey results showed that 41% of cases self-medicated with analgesics, antimalarials, or other medications prior to seeking care. Those who self-medicated were 37% less likely to initiate treatment within 72 hours compared to those who did not ($p < 0.02$). We also found that CHWs conducted just 9% of tests but captured 57% of all cases. However, cases captured by CHWs experienced more extreme delays in starting treatment compared to those captured by VCTs (median: 1 vs. 2 days; range: 0-42 vs. 0-16 days). Self-reported treatment completion was high (98%) and most cases (87%) received direct observed therapy (DOT) for the entire 14-day treatment scheme. In interviews, VCTs reported challenges with DOT and CHW supervision due to funding gaps for vehicles and fuel, while CHWs reported frequent stock outs of rapid tests. Cases reported that feeling too ill to leave home was their primary barrier to seeking care. Some did not associate their symptoms with malaria. Others delayed care seeking due to a fear of being tested or vaccinated for COVID-19. As Guatemala pushes towards their 2025 malaria elimination goal, there is an opportunity to use evidence-based research to plan targeted education campaigns, improve commodity access, and strengthen CHW supervision.

6106

CLUSTERING OF ASYMPTOMATIC MALARIA INFECTIONS IN NEIGHBORING HOUSEHOLDS: REACTIVE CASE DETECTION REVIEW AND META-ANALYSIS FROM 2010 TO 2022

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Progress toward malaria elimination is increasing as many countries near zero indigenous malaria cases. In elimination settings, interventions will be most effective at interrupting transmission when targeted at the residual foci of transmission. These foci may be missed due to asymptomatic infections. To solve this problem, the World Health Organization recommends reactive case detection (RACD) triggered in response to index cases. The rationale of RACD is that local transmission potential is higher around index case households, leading to infection clustering. To test this hypothesis, pooled data from different RACD studies were utilized to determine the average risk of malaria among index case households and neighbors. Published studies between January 2010 - September 2022 were identified through PubMed and Google Scholar. Search terms included malaria and RACD, contact tracing, focal screening, case investigation, focal screen and treat. MedCalc Software was used for data analyses and the pooled studies' findings were analyzed using a fixed effect model. Summary outcomes were presented as forest plots and tables based on 54 studies reviewed. Of these studies, 7 met the eligibility criteria based on the risk of malaria in individuals living with an index case < 5 years old, 13 met the eligibility criteria based on the risk of malaria in an index case household member compared with a neighbor of an index case, and 29 met the eligibility criteria based on the risk of malaria in individuals living with index cases and were included in the meta-analysis. Individuals living in index case households with average risk (odds ratio 2.58; 95% CI 2.54 - 2.61) were more at risk of malaria infection and showed pooled results of high variation heterogeneity chi-square = 235.60, ($p < 0.0001$) $I2 = 98.88$ [97.87-99.89]. The pooled results showed that neighbors of index cases were 0.35 [0.30-0.41] times more likely to have a malaria infection relative to index case household members and this result was significant ($p < 0.001$). Evidence to support infection clustering in neighborhoods that necessitates the inclusion of neighboring households in RACD was presented.

6107

ACCESS TO MALARIA DIAGNOSIS AND TREATMENT IN ZAMBIA IN THE CONTEXT OF SCALING-UP COMMUNITY CASE MANAGEMENT

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The National Malaria Elimination Centre (NMEC) launched a pilot of community case management (CCM) for malaria in Southern Province, Zambia in 2009, and CCM was later scaled-up in an incremental fashion at national level between 2013-2020. The goal of this study was to: 1) examine the impact of CCM on treatment seeking behaviors among individuals of all ages with a febrile illness; and 2) assess the proportion of children less than five years old with malaria (defined as a positive rapid diagnostic test plus fever in the past two weeks) that received the first line malaria treatment artemether-lumefantrine (AL). We analyzed changes in these outcomes and their determinants over time using data from the Zambia Malaria Indicator Surveys (2012, 2015, 2018, and 2021) combined with distance to the nearest malaria provider at the time of survey from data on volunteer community health worker (CHW) expansion, as well as travel time from a friction surface from the Malaria Atlas Project. While results showed there was no significant increase in treatment seeking from 2012 to 2021 (overall seeking rate: 57.1% [52.7%, 61.0%]), time from fever onset to treatment seeking decreased significantly from 2.42 days [2.27 - 2.58] in 2012 to 1.71 days [1.56 - 1.86] in 2021. Children <5 with a fever in the previous two weeks were significantly more likely to have been taken for treatment compared to older age groups (ORs: 1.26 [1.12 - 1.42] for 5-19 years old and 1.48 [1.32 - 1.66] for 20 years and older). Respondents with a fever in the past two weeks who had access to a malaria provider (either CHW or health facility) within a 30-minute walking distance were significantly more likely to seek treatment compared to those further away (OR = 1.47 [1.29 - 1.67]). Across all survey rounds, among children with malaria and fever, 58.6% [51.2% – 65.5%] did not receive AL. Among children who had malaria and fever, those within a 30-minute walking distance to a malaria provider were significantly more likely to receive AL compared to those further away (OR = 1.59 [1.03 – 2.44]). While CCM in Zambia has been successfully scaled-up, gaps remain in malaria treatment access, especially in remote areas.

6108

HALT THE MARCHING OF ANOPHELES STEPHENSI IN AFRICA: FOLLOW INDIA'S INTERVENTION STRATEGIES

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Anopheles stephensi was reported from village Ellichpur (now Achalpur), Amravati district, Maharashtra, India. South Asia and the Arabian Peninsula is the home of this malaria vector. Now this species has been detected in Djibouti (2012), Ethiopia (2016), Sudan (2016), Sri Lanka (2017), Somalia (2019), and most recently in Nigeria (2020), Yemen (2021) and Ghana (2023). A recent modelling study using marine cargo traffic indicates that it may invade in more than half of the African countries. Since 2019 World Health Organization (WHO) to ASTMH 71st Annual Meeting at Seattle in 2022, and recently RMB Vector Control Working Group in Accra, Ghana

(6 to 8 February 2023) and WHO Regional Response meeting in Addis Ababa, Ethiopia (8 to 10 March 2023) have echoed the threat of perineal malaria transmission especially in urban settings. This species has three variants i.e. Type, Intermediate and mysorensis. They behave differently in terms of vector competence, bionomics and response to insecticides. Genomic studies and molecular diagnosis of these variants are possible developing isofemale homogenized lines. It is important to carry out detailed site-specific studies to plan strategic intervention strategies. Our study in Mangalore city, India revealed case-centric vector control response using smart digital surveillance devices brought down malaria at the lowest level leading to malaria elimination. Similar strategies would find a solution to prevent marching of Anopheles stephensi in Africa involving Indian scientists.

6109

REBOUND IN THE PLASMODIUM FALCIPARUM RESERVOIR FOLLOWING THE DISCONTINUATION OF INDOOR RESIDUAL SPRAYING AND IMPLEMENTATION OF SEASONAL MALARIA CHEMOPREVENTION IN NORTHERN GHANA

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It is now understood that the large reservoir of asymptomatic Plasmodium falciparum infections in all ages sustains malaria transmission in sub-Saharan Africa. If we are to achieve malaria elimination, the impact of current interventions to reduce this reservoir must be investigated. Here we present one of few contemporary studies to assess the efficacy of short-term indoor residual spraying (IRS) with non-pyrethroid insecticides and seasonal malaria chemoprevention (SMC) to reduce the reservoir of infection in all ages. Using data collected from an interrupted time series study in northern Ghana (2012-2020), involving four surveys each of ~2,000 participants, we examined the impact of two sequential interventions, IRS and SMC in combination with long-lasting insecticide-treated nets (LLINs), on the P. falciparum reservoir. We showed that the addition of IRS to LLINs reduced the size of the P. falciparum reservoir as measured using PCR, with participants of all ages being significantly less likely to be infected post-IRS in 2015 (41.6%) compared to baseline in 2012 (73.8%). Despite this reduction, in 2017, 32-months after IRS was discontinued, there was a rebound in prevalence to 64.2%. This rebound in the size of the P. falciparum reservoir was found in all age groups, except for the younger children (1-5 years) directly targeted by SMC. In 2020, over five years after IRS was stopped, but during the continued implementation of SMC and LLINs, P. falciparum prevalence remained high (50.0%) with younger children still being significantly less likely to have an infection compared to the older age groups. This rebound was also associated with higher median P. falciparum densities in 2017 and 2020, suggesting a loss of immunity in all ages due to reduced exposure to infection during the IRS. Molecular surveillance data will also be discussed. These results show that if high-burden countries, like Ghana, are to achieve a 90% reduction in the burden of malaria by 2030, they must develop strategies that can both reduce clinical disease and target the P. falciparum reservoir.

6110

"DON'T WAIT FOR SYMPTOMS!": INCREASING ROUTINE MALARIA TESTING AMONG FOREST-GOERS IN CAMBODIA

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Malaria transmission in Cambodia is highly localized among forest-goer populations. The Cambodia National Malaria Treatment Guideline includes systematic diagnostic testing for forest-goers exiting forests. Formative research indicated that adoption of routine malaria testing may be influenced by social norms and social support from family members to test. An SBC intervention was designed with communities to increase perceived social norms and social support among forest-goers for malaria testing after leaving the forest. Activities were implemented through various channels in 50 high-risk villages in three provinces under the slogan "Don't Wait for Symptoms!". Interpersonal communication was delivered by Village Malaria Worker (VMW) visits to forest-goer households to increase the positive social norm of testing and increase malaria risk perception. Additional behavioral nudges (banners, posters, audio messages) were delivered via placement close to forest exits and within forest-goer communities. Cross-sectoral surveys were conducted with random samples of forest-goers (n=360) from 50 villages before (May 2022) and after (December 2022) implementation to evaluate differences in perceived social norms and self-reported testing behaviors. No control group was interviewed, but routine data were compared with reports from non-intervention villages over the same period. Routine data recorded 12,338 VMW-performed community-wide tests of forest-goers upon returning from forest work during the intervention period, increasing 76% compared to the same period the previous year. VMWs in villages in the same catchment areas but not covered by the intervention recorded a 26% increase in testing. Survey data showed the percentage of forest-goers who believe other forest-goers consistently seek a malaria test when leaving the forest increased from 67% to 96% ($p<0.001$); self-reported malaria testing increased from 27% to 90% ($p<0.001$). Key messages reinforcing the social norm of malaria testing should continue, and explicit emphasis should be added on improving social support for forest-goer testing among family members.

6111

AN ONLINE SURVEY OF MALARIA ON MOBILE AND MIGRANT POPULATION AMONG INDONESIAN MALARIA MANAGERS: MINERS

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Miners are one of the malaria high-risk populations since they do outdoors activities and have poor access to health facilities. We conducted online survey from February to September 2022, with 514 district health managers as our participant, to determine their understanding of malaria problem in miners. The survey, which was developed in SurveyMonkey, inquired about the presence of miners with malaria issues, including but not limited to population size, distribution, malaria detection and diagnosis, vector control, obstacles, and future control programs. From the responses gathered, 114 (22.1%) districts reported having mining sites, with 29 (25.4%) of those experiencing malaria problems among the workers. Workers who contracted malaria received treatment from nearby primary healthcare and were mostly diagnosed using RDT. The types of mining minerals that had malaria problem at the sites were gold, coal, nickel, and tin. The distance to the sites varied, but they typically had to travel on rocky, damaged, and muddy roads to reach the sites. Majority of the districts also have influx of workers from other districts who could stay for more than three months at the sites. However, their departure and arrival times was unknown due to the uncertainty of mining projects in the area. More

than half of the districts had implemented interventions to control malaria with the most common being distributing long-lasting insecticidal nets (LLINs), health promotion, and vector control with larvaciding. LLINs were reported as the most effective intervention. Poor access to the sites and lack of funding were among many reasons that hampered malaria control efforts in miners. District health managers planned to build a cross-sectoral collaboration, train cadres, and conduct more migration surveillance in the future. This study provides insights into the level of perception, knowledge, malaria control strategy and efforts among the miners. The study findings will support in reformulating strategies to address potential obstacle and contribute to the National Plan to Eliminate Malaria in 2030.

6112

SAVING LIVES FOR CHILDREN UNDER FIVE YEARS THROUGH STRENGTHENING COMMUNITY TO HEALTH FACILITY LINKAGE; A CASE OF ICCM IMPLEMENTATION IN NORTHERN UGANDA

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Malaria Consortium is supporting 11 districts in Northern Uganda to improve community to health facility Linkage since September 2021. Several interventions have been undertaken and these include, among others, orientation of Village Health Teams (VHTs) Supervisors and VHTs on the new revised ICCM guidelines to manage HIV,AIDS,TB,Malaria,D iarrhorea,Pneumonia in the community and supporting quarterly VHTs coordination meetings with Health Facility health workers. Implementation is district led approach where District Health Teams (DHTs) are supported and facilitated to implement. Ministry of Health and TASO give technical support to ensure implementation according to the standard guidelines and policies. Community Data from District Health Information System 2 (DHIS 2) was downloaded and computations for selected ICCM indicators were done. Community reporting increased from 60.4% in September 2021 to 88.0% by the end of December 2022; the number of children under 11 months reportedly dying in the community decreased by 58.5%, from 270 to 112 children; the percentage of children with fever and danger signs reduced from 2.9% to 2.1%; the number of children under five years seen by the VHTs in the community every quarter increased from 120,281 to 350,890; the number average number of children seen by a VHT in a quarter increased from 11 to 33 children; the percentage of children with malaria treated within 24 hours increased from 59% when we started to 89% by the end of 2021. There have been challenges in stocks availability that have led to continuous low malaria testing rates (consistently below 80%) and significant referrals from the community, consistently at 15% - 16%, as reported previously. The results show that lives have been saved through interventions to strengthen health facility to community linkage in Northern Uganda. Demand and access to health services for children under five years from VHTs increased significantly during implementation. Gaps in stocks availability should be addressed to ensure access to quality services by the unreached vulnerable groups.

6113

CLINICAL PLASMODIUM FALCIPARUM DURING THE DRY SEASON IN AN ENDEMIC AREA OF MALI, TORODO.

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Plasmodium falciparum (Pf) clinical malaria is rare during the dry season in endemic countries, were the transmission mediating mosquitoes (Anopheles) are not prevalent at that time. Regarding all the effort made during transmission season and slow moving of the disease control and elimination program, additional strategies need to be explored to contribute to the existing one. Indeed, we addressed the following research question within one of our cohort studies: Can, Pf asymptomatic infected or non-infected individuals at the beginning of the dry season develop the disease at that period? Thus, from our cohort study of 250 participants (2 to 16 years old) in Torodo, 74 individuals (~29%) out of the 250 participants, were infected at the baseline (February 2022). Female represented ~44% of the positive group and the age group 7-11 years were more infected (13,2%). Looking at to the hemoglobin levels (which is one of the major indicators of Plasmodium falciparum acute or asymptomatic infection), it was higher in the negative group with a means around 11.5g/dl compared to the positive group (around 10.5). To track Pf clinical malaria during dry season we followed both group (Pf asymptomatic infected and non-infected groups) actively and/or passively from February to May 2022. During the follow-up, we observed 20 cases of Pf clinical malaria after PCR correction and 17 and 3 cases were respectively in the infected and non-infected groups from the baseline. These finding highlights that carrying asymptomatic Pf infection at the beginning of dry season can favor Plasmodium falciparum clinical malaria through all the dry season period, but also some new cases can happen in non-carriers, suggesting that an effort need to be addressed regarding malaria control and elimination program during that period.

6114

NEW SURVEILLANCE STRATEGIES FOCUSED ON ELIMINATION IN SOUTHERN ANGOLA

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Malaria incidence in southern border districts of Angola has seen a steady decline over the past years. This decrease in malaria cases is the result of joint efforts to reduce transmission and contribute to malaria elimination in neighbouring Namibia. As transmission declines, new surveillance approaches are required to tackle focal transmission. The objective of this study is to report the implementation of new surveillance strategies focused on elimination in southern Angola and to characterize transmission in line with case classification made. The implementation of case classification strategies started in November 2022 across 5 health facilities of Cunene and Cuando Cubango provinces. These health facilities have been shortlisted because they registered 5 or less cases per month on average over the past 3 years. Case classification was done for RDT/MO confirmed malaria cases using a structured questionnaire applied at health facility level focused on travel patterns and use of malaria preventive measures. Overall, 100% of the positive cases were classified (26). Of these, all were local, particularly 21 (81%) were considered as local L1 (own house) and the remaining L4 (out of usual accommodation but in the same province). Local cases had the following characteristics: 10 (38%) less than 15 years old, 16 (62%) more than 15 years old, 9 (35%) were females. It is likely to identify 12 foci of transmission based on the local guidelines that point out a focus of transmission to be the presence of more than 1 local case within a month. The data presented, the first of its kind in Angola, showcases the high proportion of local cases in areas targeted. Foci investigation, classification and response are key to tackle local transmission and gradually eliminate these scattered points of local transmission in the south.

6115

MATHEMATICALLY MODELLING THE IMPACT OF CASE MANAGEMENT AT BORDER AREAS ON MALARIA TRANSMISSION IN THE MOZAMBIQUE, SOUTH AFRICA AND ESWATINI REGION

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Eswatini and South Africa are in the path of malaria elimination but however, they share borders with Mozambique who has a high incident rate of malaria. Studies conducted show that most of the malaria cases recorded in both South Africa and Eswatini are imported cases from Mozambique. For these countries to attain their goal of malaria elimination, they need

to prioritise case management at border areas as their main strategy of malaria elimination. Will the use of rapid antigen tests at the border gate areas accelerate the elimination of malaria in the MOSASWA region? What impact will border management have on the malaria transmission in these countries? A Nonlinear stochastic ordinary differential equation model is used to simulate the impact of case management at border areas on malaria transmission in the MOSASWA region which consists of eastern Eswatini, the southern Mozambican provinces of Maputo, Gaza and Inhambane, and the north-eastern districts of the South African provinces of KwaZulu-Natal, Mpumalanga, and Limpopo. The results show us that malaria transmission can be reduced significantly if rapid antigen tests are conducted at the borders in the MOSASWA region. The results show us that malaria cannot be eliminated by this intervention but can reduce the malaria burden significantly in Eswatini and South Africa endemic regions. Border control is a vital strategy for malaria elimination in South Africa and Eswatini. However, malaria cannot be eliminated and hence this intervention combined with other interventions can contribute towards malaria elimination in the region.

6116

THE UGANDA HOUSING MODIFICATION STUDY - ASSOCIATION BETWEEN HOUSING CHARACTERISTICS AND MALARIA BURDEN IN A MODERATE TO HIGH TRANSMISSION SETTING IN UGANDA

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Scale up of proven malaria control interventions has not been sufficient to control malaria in Uganda emphasizing the need to explore innovative approaches. Improved housing is one such promising strategy. We describe the housing characteristics and their association with malaria burden in a moderate to high transmission setting in Uganda. In October-November 2021, a household survey was conducted in 1500 randomly selected households in Jinja and Luuka districts. Information on demographics, housing characteristics, use of malaria prevention measures, and proxy indicators of wealth were collected for each household. A finger-prick blood sample was obtained for thick blood smears from all children aged 6 months to 14 years in surveyed households. Febrile children were tested for malaria by rapid diagnostics test (RDT) and positive cases were managed per national guidelines. Hemoglobin (Hb) concentration was assessed in children aged 2-4 years, with anemia defined as Hb < 8 g/dL. Mixed effect models adjusted for age and wealth were used to estimate association between malaria burden and house type. Forty-four percent of households lived in modern houses (defined as built with finished roofs/walls/floors materials combined with closed eaves); the rest lived in traditional houses built with unfinished/natural materials. While most houses had closed eaves (85.5%), the use of other protective features like window and vent screens and having ceilings installed was limited (0.4%, 2.8%, and 5.2%, respectively). Malaria prevalence was 31.4% in 3443 children with smears collected. RDT test positivity rate was 56.6% among 1851 children with fever. Participants living in modern houses had a significantly lower parasite prevalence (adjusted prevalence ratio [aPR]=0.80; 95% confidence interval [95%CI] 0.71-0.90) and RDT test positivity rate (aPR=0.90; 95%CI 0.81-0.99) compared to those in traditional houses, with no significant impact on anemia. Our study found that even after adjusting for wealth, higher quality housing had a moderate protective effect against malaria, on top of the protection already afforded by recently distributed nets.

6117

IMPACTS OF ARMED CONFLICT FOR MALARIA PREVENTION AND ELIMINATION PROGRAMS IN ETHIOPIA: A TIME-SERIES ANALYSIS

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Ethiopia has experienced several conflicts during the last several years that have negatively impacted its health systems. This study aims to assess the impact of the conflicts in Northern Ethiopia on malaria prevention and elimination efforts, as well as the malaria surveillance system. We used routine district health information system data to quantify the changes in the levels of malaria prevention and control services from 2019 to 2021. We used interrupted time-series analysis and descriptive statistics to estimate the changes in intervention levels within the conflict-affected and surrounding districts. The routine malaria surveillance data showed that the reported national malaria cases increased by 20% from 2019 to 2021. Disruptions were found to vary across zones and districts with clear patterns by the intensity and duration of the conflict. There was a significant difference in test and incidence rates between affected areas and surrounding affected/not affected areas. In conclusion, While data limitations made it difficult to describe the level of disruptions to malaria prevention and elimination measures during the conflict (particularly in conflict-affected areas), these findings highlight a strong variation in the malaria incidence between conflict-affected and unaffected areas. Our study highlights the importance of peace and stability and preserving a functioning health system to sustain Ethiopia's progress toward malaria elimination targets.

6118

SURVEILLANCE OF PLASMODIUM MALARIAE INFECTION AMONG INHABITANTS AND ANOPHELES' MOSQUITOES IN RURAL AREAS OF SOUTHERN BENIN

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Among the Plasmodium species that infect humans, P. falciparum has been widely studied in malaria-endemic areas. However, P. malariae infection is less documented among the human population and mosquitoes. This study aimed to investigate the prevalence and distribution of P. malariae in southern Benin. A cross-sectional survey was conducted in Ouidah and Kpomasse from June to October 2019. At the time of blood collection from the participants and at the same time, mosquitoes were collected from the participants' households. Data on malaria infection were obtained by microscopic diagnosis and nested PCR in participants. In addition, the collected mosquitoes were identified morphologically and molecularly, and the infection status of Plasmodium species was investigated by qPCR. Considering the participants, according to microscopy, the prevalence of P. malariae mono-infection and P. falciparum/P. malariae co-infection was

2.3% and 1.2% respectively in our study area. This prevalence was higher ($P < 0.01$) than that reported ten years ago in the same study area with 0.7% and 0.3% of P. malariae and P. falciparum/P. malariae, respectively. Based on PCR analysis, the prevalence of P. malariae was 14.1%, of which 5.2% were mono-infected and 8.9% mixed with P. falciparum. Regarding the mosquito data, of the 415 mosquitoes collected, three species of Anopheles were identified with a predominance of An. gambiae s.l. (61%). Molecular speciation of this species revealed that An. coluzzii was the majority species 59.2% and 98.5% in Ouidah and Kpomassè respectively. The infection rate of Plasmodium spp. in An. gambiae s.l. revealed that 4.4% were infected with a predominance of P. falciparum (75%), followed by P. malariae (25%), and only An. coluzzii mosquitoes were infected. These results provide valuable evidence of the increasing prevalence of P. malariae infection and that An. coluzzii is the mosquito responsible for the spread of this parasite. This highlights the need for national malaria control programs to take P. malariae into account when designing future measures for effective malaria control and treatment.

6119

EVALUATING THE EFFECTIVENESS OF TRIMETHOPRIM-SULFAMETHOXAZOLE PROPHYLAXIS IN PREVENTING MALARIA IN PREGNANCY

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In sub-Saharan Africa, malaria in pregnancy remains a critical health concern for mothers and their babies. The WHO recommends sulfadoxine-pyrimethamine (SP) for the prevention of malaria during pregnancy. However, pregnant women living with HIV infection receive daily trimethoprim-sulfamethoxazole (TS) prophylaxis and therefore cannot safely also take SP. Previous studies have produced conflicting evidence as to whether TS prophylaxis adequately prevents malaria during pregnancy in women with HIV infection. We had the opportunity to evaluate the effectiveness of intermittent preventative treatment of malaria in pregnancy using sulfadoxine-pyrimethamine (IPTp-SP) in pregnant women without HIV infection compared to daily TS prophylaxis in pregnant women with HIV infection. We screened pregnant women with and without HIV infection for malaria enrollment in a clinical study and collected placental blood at the time of delivery from a cohort in a semi-rural area at one clinical site in southern Malawi. Dried blood spots from the enrollment visit in the second trimester paired with dried blood spots from the placenta after delivery underwent extraction and qPCR for 18S ribosomal DNA. Among 290 samples from pregnant women with and without HIV, we detected no Plasmodium falciparum infection. Our findings suggest that IPTp-SP and TS prophylaxis are equally effective in preventing placental malaria infection. We are currently testing enrollment samples from this cohort to characterize the burden of malaria infection when pregnant women initiate antenatal care. This will allow us to determine if the interventions prevented placental infection or if malaria transmission in the area was lower than anticipated.

6120

SPATIOTEMPORAL CORRELATION OF MALARIA INTENSITY AND VECTOR ABUNDANCE IN A PRE-ELIMINATION SETTING OF CHOMA DISTRICT, SOUTHERN ZAMBIA

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Choma District in Southern Province, Zambia, with malaria parasite prevalence by rapid diagnostic test of 2%, has long been targeted for elimination. However, low-level transmission with seasonal outbreaks has persisted, perhaps exacerbated by infectious secondary vectors. Previous geospatial risk maps of the area derived from remotely sensed data found that parasitemic individuals tended to be clustered in areas near streams at lower elevations. In this way, spatiotemporal analysis of low-level parasite prevalence and vector abundance has been critical in informing strategies targeting malaria elimination. This study aimed to produce malaria risk maps by assessing the spatial and temporal correlation of individuals with parasitemia by quantitative polymerase chain reaction (qPCR) and vector breeding sites within rural health center (RHC) catchment areas. Malaria case and entomological data were collected in 2022 and 2023 in Macha, Mapanza, and Simaubi RHCs. Passively-reported index case households and neighboring households within 250 meters of the index case household were surveyed from April 2022 to April 2023. Residents were tested for parasitemia using qPCR from dried blood spots. In October 2022, entomological surveillance began at 38 sentinel households, where each household was visited bimonthly. CDC light traps were set indoors and outdoors at each house and larval breeding sites within 500 meters were sampled. All households and larval breeding sites were geolocated. Intensity maps were created of the households of qPCR-confirmed parasitemic residents and confirmed breeding sites using kernel estimation with optimized bandwidths. Clustering was assessed using the K-function. We further compared the two intensity maps and clustering patterns with each other using the cross-K function. Analysis was done in R and ArcGIS. We will present the results of the malaria intensity mapping, K-functions for clustering, and cross-K function, and expect the results will inform further malaria risk mapping and targeted interventions in this pre-elimination setting.

6121

PLASMODIUM FALCIPARUM MALARIA IS ASSOCIATED WITH INCREASED KSHV SEROPOSITIVITY AND HIGHER KSHV ANTIBODY BREADTH AND MAGNITUDE: RESULTS OF A CASE-CONTROL STUDY FROM RURAL UGANDA

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We previously showed that children with asymptomatic Plasmodium falciparum (Pf) malaria infection had higher Kaposi sarcoma-associated herpes virus (KSHV) viral load, increased risk of KSHV seropositivity, and higher KSHV antibody levels. In the current study, we investigated the association between clinical malaria and KSHV seropositivity and antibody levels using an expanded immunoassay. Sick children (aged 5-10 years) presenting at a clinic in rural Uganda were enrolled in a case-control study. Pf was detected using malaria RDT and subsequently with qPCR. Children with malaria were categorized into two groups; RDT+/Pf PCR+ and RDT-/Pf PCR+. The seroprevalence of KSHV was 60% (47/78) among children who did not have malaria (RDT-/PfPCR-), 79% (61/77); among children who

were RDT-/PfPCR+ (Odds Ratio [OR] 2.41, 95% CI 1.15-5.02) and 95% (141/149) in children who were RDT+/Pf PCR+ (OR 10.52, 95% CI: 4.17-26.58; P (trend)<0.001). Furthermore, RDT+/PCR+ children followed by RDT-/PCR+ children had higher KSHV antibody levels and reacted to more KSHV antigens compared to malaria-uninfected children. Malaria infection in children is associated with both increased KSHV seroprevalence and antibody magnitude suggesting that malaria is affecting immunity to KSHV.

6122

TACKLING ASYMPTOMATIC MALARIA INFECTION IN PREGNANCY AS INTERVENTION TO IMPROVE PREGNANCY OUTCOMES IN BURKINA FASO

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Malaria in pregnancy is assumed to be asymptomatic in endemic area. The national malaria control program (NCMP) recommends to treat all malaria cases after confirmation either by microscopy or rapid diagnostic tests (RDT) before treatment. Asymptomatic infections have no clinical manifestation and thus remain undetected and untreated. Even asymptomatic, malaria infections are potentially harmful for both women and their offspring's. We therefore, sought to determine the prevalence of asymptomatic malaria infection among pregnant women at their first antenatal care (ANC) and the risk factors associated. A cross-sectional study was conducted in Nanoro district and all pregnant women attending the first ANC visit were recruited. Blood samples were collected to assess malaria infection using microscopy as gold standard and haemoglobin level using HemoCue®. Among the 418 pregnant women recruited, 318 were asymptomatic. The overall prevalence of asymptomatic malaria infection during first ANC was 25.5% (95% CI: 21.1 - 30.4) with a geometric mean parasite density of (95% CI): 790 (602 - 1036) parasites/µL. From the 86 pregnant women infected with malaria, those at the third trimester gestational age were significantly more prevalent 21.3% (13/61), followed by the second trimester 25.6% (66/258) and the first trimester 38.8% (7/18), P<0001. Younger age was associated with significantly higher odds of asymptomatic malaria compared to elder women. Furthermore, primigravida had 3.09 (95% CI: 1.52 – 6.26; p = 0.002) and secundigravida 3.02 (95% CI: 2.00 – 5.34; p = 0.001) folds higher risk than multigravida women. The mean haemoglobin concentration was 10.56 ± 1.55 g/dL and the prevalence of anemia was 59.1% (95% CI:53.9- 64.7). In multivariate analysis, asymptomatic malaria increased two times the likelihood of having anemia (AOR 2 95% CI:1.1-3.4; p < 0.001). Our findings highlight the importance of integrated strategies such as systematic screening with sensitive rapid diagnostic tests and treatment with effective malaria drugs during the first ANC to clear residual parasitaemia and thus improve pregnancy outcomes.

6123

INSIGHTS ABOUT MALARIA BURDEN AND CARE IN MALARIA-ENDEMIC, INDIGENOUS COMMUNITIES UNDER THE COVID-19 PANDEMIC USING CONVERGENT-PARALLEL APPROACH

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In Peru, the interruption of the malaria control program due to the COVID-19 pandemic increased the number of cases in urban areas. However, the impact on the burden and care in remote, indigenous areas was unknown. In this mixed-method study, we investigated malaria prevalence using molecular diagnosis and factors associated with malaria infections in indigenous communities in the Peruvian Amazon. Moreover, we explored the population's perceptions of the COVID-19 impact on malaria burden and care. We performed population surveys (2021 and 2022) and semi-structured interviews with inhabitants and local health workers (2022) in four indigenous communities of the Amazonas region. We identified the factors associated with malaria infection through multivariate modeling and assessed the participants' perceptions through a thematic analysis. The convergent parallel approach served to merge the quantitative & qualitative components through a pillar integration process resulting in a joint display. The overall prevalence of malaria varied between 2021 and 2022 (17.6% and 25.5%, n=528 participants). Living in some communities (OR=0.70) and having experienced previous malaria episodes (OR=0.07) reduced the likelihood of malaria infection.On the contrary, experiencing chills (OR=38.4) was associated with higher odds of malaria infection. Inhabitants and health workers pointed out the prioritization of COVID-19 interventions, leaving malaria control activities aside and affecting malaria prevalence. On the other hand, the population's behavior toward malaria prevention did not change during the pandemic. However, the participants highlighted the limited access to healthcare facilities during the pandemic and the absence of health posts in the two communities, which increased the likelihood of experiencing malaria (OR=0.19-0.47). The novel mixed methods approach facilitated the integration of quantitative and qualitative data to explain the malaria situation in indigenous areas better. Our findings provide relevant information to improve the current interventions for malaria control and elimination in Peru.

6124

TEMPORALITY AND MODALITY OF FIRST HEALTH CARE SEEKING AMONG MALARIA PATIENTS IN THE REPUBLIC OF GUINEA

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The temporality and modalities of seeking care are crucial in the fight against malaria. In Guinea, malaria is a public health problem, with a morbidity of 39.91% in health facilities. The prevalence among children under five of age was 17% in 2021. In addition, there are many opportunities to manage malaria, with conventional and non-conventional offers. The aim is to analyze the temporality and modalities of first health-seeking for malaria patients. This is a partial analysis of data from a cross-sectional study conducted between December 2022 and March 2023 in the health facilities of nine (9) health districts randomly sampled in the eight administrative regions. The data were collected using an Open Data Kit system and analyzed with R software. Early care-seeking was defined within 24 hours and late after 48 hours. The conventional modalities are the public and private health facilities and community health walkers, while the non-conventional are constituted by other offers not recommended by the national policy of malaria management. A total of 3300 confirmed malaria cases, of which 1632 (49.45%) were female, were interviewed in 60 health facilities. 1132 were less than 5 years old (34.30%) with a mean age of 27 months (SD=16). For the group of 5 years and older the mean age was 27 years (SD=18.7). Early care-seeking for all modalities was 53.2%, 95% CI [0.52-0.55]. With 63.60%, 95% CI [0.61-0.66] in the under 5 years and

47.83%, 95% CI [0.46-0.50] in the 5 years and older. The median time to first care-seeking was 24 and 48 hours, respectively. Early and appropriate seeking behavior was different in the age groups (p<0.0001) with 33.66% and 25.88% respectively. The median cost of the first referral varied according to age group, 54000 GNF and 49000 GNF, and referral modality, 110000 GNF for conventional and 6000 GNF for non-conventional. The partial analysis of this cross-sectional study shows proportions of early and appropriate care-seeking in the first intention, below 50%. This result demonstrates the importance of the next steps in this project whose goal is to provide evidence on patterns of malaria management service consumption and determinants.

6125

ANOPHELES MOSQUITO BITE EXPOSURE TESTING TO ASSESS THE IMPACT OF VECTOR CONTROL INTERVENTIONS IN THE COLOMBIAN PACIFIC REGION

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Previous studies have demonstrated that IgG antibodies against mosquito salivary proteins are a reliable tool to measure arthropod bite exposure and disease risk. In Colombia, Anopheles vectors belong to subgenus Nyssorhynchus (An. albimanus and An. darlingi) and subgenus Anopheles (An. pseudopunctipennis) among others. Thus, we measured IgG antibodies against four peptides designed from immunogenic salivary proteins of An. albimanus (Peroxi-P3 and Transferrin-2), An. darlingi (AnDar-Apy2) and the salivary biomarker gSG6-P1 to determine the degree of exposure to bites from mosquito species from subgroups other than Nyssorhynchus. In the first phase of the study, blood samples were collected from two regions of Cauca Department on the Pacific Coast of Colombia where two different malaria control interventions [insecticide treated bednets (ITNs) and indoor residual spraying (IRS)] are being implemented. To compare exposure to bites with previous exposure to Plasmodium parasites, we also determined the levels of IgG antibodies against Plasmodium vivax (PvCSP and PvMSP1) and P. falciparum (PfCSP and PfMSP1). The second phase of this study is underway, but our preliminary results from phase 1 showed a significant positive correlation between age and Peroxi-P3, Transferrin-2 and gSG6-P1 in people using bed nets. This correlation was not observed in people living in houses treated with insecticide suggesting that the type of mosquito control intervention shapes bite exposure dynamics in the population. So far in both study sites, we have observed a significant positive correlation between all salivary peptides and Plasmodium antigens suggesting an important association between exposure to mosquito bites and immune responses against Plasmodium in this area. Our results highlight the relevance of using antibodies against salivary proteins as an indirect tool to measure efficacy of vector control interventions in malaria endemic areas to support malaria elimination efforts.

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EPIDEMIOLOGIC RISK FACTORS TO URBAN MALARIA IN WESTERN AND COASTAL KENYA

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Most countries in Sub-Saharan Africa are reporting an increase in urban population growth. With Kenya still reporting a high endemicity of malaria in various urban regions, it is not known how urbanization will affect vector populations, disease transmission and control measures. Our prospective cohort study was conducted at two urban towns in Coastal (Ukunda) and Western (Kisumu) Kenya with demographic and risk factor surveys administered every 6 months between December 2019- February 2022. Participants were also interviewed any time they had a fever during the duration of the study. Blood samples were collected during the community survey and febrile (sick) visits for the detection of malaria by microscopy. Only survey responses at enrollment were considered in this preliminary risk factor analysis due to a high attrition rate and non-response during the follow up periods. The overall study prevalence for malaria in our study was 12.8 % (578/4534) with a significantly higher seroprevalence in Kisumu (20.1%,518/2521) than in Ukunda (3.0%, 60/2013) ,(OR=8.42, 95% CI =6.40-11.08;(p<0.01). 63.3 % (366/578) of all confirmed malaria diagnosis were from a febrile (sick) visit, 29.8%(172/578)were detected during the community survey, and 6.9% (40/578) during both the community survey and sick visit. Among the malaria-positive patients, 98.6% (570/578) of them were positive for Plasmodium falciparum, and 1.4 % had mixed infections of P. falciparum and P. malariae. There was an increased likelihood of malaria among children (<16 Years), (OR =1.43,95% CI =1.20-1.70 ; P < 0.01), those who had moved from their primary residence 6 months prior to the administration of the survey (OR =9.5, 95% CI =7.28-12.35 ; P < 0.01),and those with indoor occupations (OR =1.43,95% CI =1.20-1.70 ; P < 0.01).There was a decreased likelihood of malaria among households that had window screens, (OR =0.30, 95% CI = 0.22-0.41 ; P < 0.001).Gender, water collection, and insecticide use were not associated with malaria positivity in our study.Further studies are still needed to understand the epidemiology of malaria in urban settings in Sub-Saharan Africa.

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MAXIMIZING THE USE OF HUMAN POPULATION MOVEMENT DATA FOR MALARIA CONTROL AND ELIMINATION

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Malaria transmission through human population movement (HPM) poses a major obstacle to malaria elimination. We hypothesize that the collection of routine surveillance data on travel patterns of malaria patients in a country nearing malaria elimination could be used to maximize the use of HPM data for malaria elimination. From May 2017 to December 2021 we enrolled 6320 malaria patients from 107 health facilities Lao PDR. We obtained information on demographics, travel patterns, mobile phone use and ownership and collected dried blood spots. 27% were females, 73% males. Median age was 19 years. 58% had Plasmodium vivax, 40% P. falciparum, 1% mixed P. falciparum and P. vivax, 0.02% P. knowlesi and

0.02% P. ovale. The proportion of malaria patients travelling increased from 55% to 85%. Travel to the forest was most common, increasing from 53% to 75%. Attapeu was the most popular destination for inter-province travel (44-100%). During COVID, travel concentrated to Attapeu (from 46% to 60%) and Phouvong (from 26% to 53%), while inter-province and inter-district travel elsewhere decreased. The demographics of forest visitors remained unchanged. Males 25-49 years comprised the largest proportion of forest visitors and farmers remained the most popular occupation (59-69%). Visitors tended to stay overnight in the forest (71%). While mobile phone use in the general population was high (according to census), 24% of malaria patients owned or used a mobile phone. At district level, API was weakly negatively correlated with mobile ownership proportion (R2= 0.3, p-value= 0.005). Mobile phone ownership and use in both genders was significantly lower when compared to the general population (p<0.001), regardless of province, gender separated by province, age group and age groups separated by gender (P<0.001). In conclusion, routine collection of detailed travel surveys from malaria patients provide rich information to inform activities and future national malaria programmes. Low mobile phone ownership among malaria cases suggests use of cell phone data to analyze travel patterns will be relatively uninformative and travel surveys should be prioritized.

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POLICIES, KNOWLEDGE, ATTITUDES AND PRACTICES RELATED TO MALARIA, HELMINTHS AND SCHISTOSOMIASIS AMONG PREGNANT WOMEN IN GHANA: AN ETHNOGRAPHIC STUDY IN TWO GHANAIAN REGIONS

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The sub-Saharan African Region is burdened with high prevalence of malaria, helminth infections and schistosomiasis, which makes pregnant women within this region susceptible to infections. The study sought to explore policies on dealing with infections during pregnancy in health facilities and to describe knowledge, attitudes and practices among pregnant women related to malaria, helminths infection and schistosomiasis. This ethnographic study was carried out in two administrative regions in Ghana. It employed non-participant observation, in depth interviews (IDIs), focus group discussions (FGDs) and key informant interviews. Two sets of data were collected: (1) IDIs with health workers and health managers and (2) community key informant interviews with gatekeepers, IDIs with husbands and FGDs with pregnant women and lactating women. NVivo Version 12 was used to support thematic coding and analysis of data. All the health facilities implemented treatment guidelines on malaria during pregnancy based on WHO recommendations, however there were no uniform guidelines on treatment of helminths and schistosomiasis. Most of the study participants in the communities had knowledge on the causes and effects of malaria in pregnancy, but had little knowledge on the causes and effects of helminths infections and schistosomiasis in pregnancy. They mentioned health facilities as the place to seek treatment for malaria. FGD participants claimed that when they were pregnant or during their current pregnancy, they were not given dewormers and medicine to treat schistosomiasis at the ante natal clinic, so they did not view helminths infection and schistosomiasis as serious health issues needing attention. It was revealed that some pregnant women visited multiple sources such as health facilities for the treatment of malaria and other illnesses, but if they still felt unwell, they visited herbalists or self-medicated. Education on other infections that can have a negative effects on pregnancy should be intensified. The health service authority needs to provide clear guidelines for dealing with parasitic infections during pregnancy.

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INCREASING PATTERN OF MALARIA CASES IN LOW ENDEMIC DISTRICTS IN RWANDA

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Malaria remains a public health priority in Rwanda with the whole population being at risk of malaria infection. In 2016, Malaria stratification based on malaria incidence identified four epidemiological strata across the 30 districts of Rwanda. Since then, following core interventions have been deployed accordingly and based on availability of funds: early diagnosis and treatment both at health facility and community level, long Lasting insecticidal nets, indoor residual spraying in 12 high endemic districts, and information, education and communication as cross-cutting intervention. At National level, from 2020 to 2022, based on malaria cases reported from Health Management Information System, malaria incidence reduced from 114 to 76 per 1,000 persons with a 33% of reduction. While Rwanda malaria reduced in the last two years in high burden districts covered with core vector control interventions mainly IRS, low burden districts such as Musanze, Nyabihu, Burera and Gakenke mainly of Northern Province reported more malaria cases. Throughout this period, malaria incidence increased from 10 to 16 malaria cases per 1000 persons in these formerly lowest endemic districts, the number of malaria cases increased by 62% from 16,383 in 2020 to 26,591 cases in 2022. In Burera, malaria incidence remained constant at 5 per 1000 persons while in Gakenke malaria incidence increased from 25 to 41 per 1000 persons. Malaria incidence increased by 93% in Musanze and 67% in Gakenke. It was also found that malaria cases were heterogeneously distributed in sub-district in few sectors per each district. While the focus of malaria control over the last six years has been on high endemic districts, in low burden districts, malaria increase may not take adequate attention to malaria managers and pause a really threat to the population and sustainable of achievement in high endemic district. Therefore, it is important to continuously analyze data especially at sub-district levels, the sector, in order to determine most affected sub-areas and any changes in malaria epidemiology so as to deploy appropriate interventions in a timely manner

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THE ASSOCIATION BETWEEN MALARIA PARASITAEMIA, INTESTINAL PARASITE AND ANEMIA IN CHILDREN LESS THAN 6 MONTH IN SENEGAL: A CROSS SECTIONAL SURVEY

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Although malaria is declining in many countries in Africa, malaria and anaemia remain frequent in children. This study was conducted to assess the relationship between malaria parasitaemia, intestinal worms, and anaemia, in children under 6 months of age living in low transmission area in Senegal. A cross sectional survey was carried out in Lamarame in the central part of Senegal. A random sampling method was used to select study participant. Children under 6 months were enrolled after informed consent. For each child, blood thick and smear tests were performed, haemoglobin concentration was measured with HemoCue, and stool samples were collected and examined using the Ritchie technique. A total of 162 children were recruited. Malaria parasite prevalence was 0.75% (0.7-2.6); anaemia was found in 16.7% (11.3-23.3), while intestinal parasites and stunting represented 25.4% (18.5-33.4) and 22% (18.6-25.5), respectively. In a logistic regression analysis, anaemia was significantly associated with malaria parasitaemia (aOR= 6.3 (1.5-53.5)) and stunting (aOR = 2 (1.2-3.1)); The association was found between intestinal parasites and anaemia (OR=1.1(0.5-3.4). Malaria and anaemia remain closely associated

even when malaria is declining. Scaling up antimalarial interventions may contribute to eliminate malaria and reduce the occurrence of anaemia among children.

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SEASONAL DYNAMICS OF COMPOSITION AND DENSITY OF CO-ENDEMIC PLASMODIUM FALCIPARUM AND P. VIVAX IN ELIMINATION SETTING, SOUTH ETHIOPIA: IMPLICATIONS FOR ELIMINATION

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Malaria elimination requires targeting all remaining infections including the ones that do not elicit symptoms. It is important to evaluate the magnitude and parasite density of residual malaria in terms of species composition and season in elimination-targeted settings. To appraise these, longitudinal data were collected for one year between 2019 and 2020 covering major and minor transmission seasons and the dry season. Three elimination-targeted low transmission settings: Dilla town, Wonago, and Yirgacheffe were included. In each season, 504 individuals from 168 households were sampled. Microscopy, RDTs, ELISA, and 18S-based qPCR were performed. Overall, parasite prevalence was 7.3%, 6.8%, and 17.5% by microscopy, RDT, and qPCR, respectively. Microscopy (10.4%) and RDT (10.7%) missed infections detected by qPCR. The PvAMA1/PvMSP1/PfMSP1 antibody prevalence was 20.2%-30.4% based on the K-means algorithm. qPCR-based parasite prevalence showed seasonal variation with 12.5%, 18.3%, and 21.8% during the minor, peak, and dry seasons respectively ($p<0.05$). Of these, Plasmodium vivax infections were dominant during the minor (54.0%, 34/63) and dry (64.5%, 71/110) seasons. The highest malaria case burden was reported in the urban setting, Dilla town (29.6%, 149/504). High parasitemia was detected for both P. falciparum (median 159,44518S copies/µL) and P. vivax (median 140,321) for all seasons. A significant density of parasitemia was observed during the peak rain season ($p<0.05$). From the GEE model, study site, anemia, clinical status and bed net utilization ($p<0.001$) showed significant association with malaria. The over-dominance of P. vivax in two seasons implicates control measures need to consider tailored approaches. The considerable missing cases by conventional methods, even those parasite densities above the detection threshold of microscopy, may pose a challenge to elimination progresses. The noticed high malaria burden in urban settings and all seasons need spatial and year-round interventions through the elimination program. Also, the stratification of some settings as low transmission areas needs to be reconsidered.

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ASSOCIATION BETWEEN ANAEMIA AND PLASMODIUM FALCIPARUM AND HELMINTH INFECTIONS AMONG CHILDREN AND YOUNG ADULTS LIVING IN RURAL AREAS OF GABON, CENTRAL AFRICA

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The objective of this analysis was to describe in a cohort of school-aged children and young adults the profile of anaemia and its association with malaria and helminth infections. The study was longitudinal where participants were followed for 15-months. However, the present analysis was performed on data collected at six months follow-up. Blood samples were collected for the determination of haemoglobin parameters using an automated haematology analyzer, for the detection of malaria parasites using thick blood smear microscopy, and for the diagnosis of filariasis using leucoconcentration technique. Stool samples were collected for the diagnosis of soil-transmitted helminths (STH) while urine samples were collected for the diagnosis of schistosomiasis. Anaemia and its severity were defined using the WHO criteria for the level of the sea. General linear regression was used to assess factors associated with anaemia. A total of 217 participants were included in the present analysis. Of them, 73% (160, 95%CI: 67 - 79) were anaemic. Among the anaemic participants, most had a normal MCV value (42%, 95%CI: 34 - 50), compared to low (27%, 95%CI: 20-35) or high (31%, 95%CI: 24-39) values of the MCV. A low value of MCH (66%, 95%CI: 58 - 73) and MCHC (70%, 95%CI: 62 - 77) was observed in more than half of the participants. Anaemia was associated with Plasmodium infection (p-value=0.04) but not with STH infections (p-value=0.16), schistosomiasis (p-value=0.12) or filariasis (p-value=0.59). After multivariate analysis adjusted for age, sex, and helminth infections, participants with Plasmodium parasites had an adjusted odd of 2.44 (95%CI: 1.07 - 6.13), compared to those without Plasmodium infection. In conclusion, the prevalence of anaemia in children and young adults is high in rural areas surrounding Lambaréné, making anaemia a significant public health issue in our community. We reported malaria as the main parasitic infection associated with anaemia in the area also known to be endemic for STH infections, schistosomiasis, and filariasis. Our results, therefore, call for more interest in anaemia in the general population.

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ASSESSMENT OF THE BURDEN AND DETERMINANTS OF MALARIA TRANSMISSION IN SELECTED URBAN SETTLEMENTS IN NIGERIA

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Nigeria is the highest-burden malaria country. Unplanned urbanization may result in environmental conditions that promote heterogeneities in malaria risk. Identifying urban settlements with high malaria transmission risk will guide better targeting of interventions. We are conducting field epidemiological and entomological studies to understand the variations and drivers of malaria risk in formal and informal settlements, and slums in Kano and Ibadan cities. The design of our epidemiological and entomological assessments is informed by formative research. Study sites were chosen based on findings from multistakeholder dialogues which helped in defining and identifying settlement types. Focus group discussions, key informant interviews, and cognitive interviews were conducted to inform the design of quantitative instruments for epidemiological surveys. Our epidemiological surveys aim to estimate malaria prevalence and identify related factors among all ages, and pregnant women. To achieve this, we are conducting household and health facility cross-sectional surveys during the wet and dry seasons. We are also conducting 12-month longitudinal surveys to assess malaria seasonality and drivers among children under the age of 10 years. Dry and wet season entomological surveys (mosquito collection using CDC light trap and Pyrethrum Spray catches) are being conducted to establish the presence or absence of local transmission using various entomological indicators. Preliminary findings from the multi-stakeholders dialogue revealed that having a settlement plan, social amenities, and population densities were key factors useful for categorizing settlement types into formal, informal, and slums. During dry season entomological surveys, we captured two main malaria vectors - Anopheles Gambiae and Anopheles Funestus between the hours of 6 pm and 5 am in all settlement types, although most vectors were found in informal settlements. Results from the wet season cross-sectional surveys and early findings from the longitudinal surveys will be available for presentation at the annual meeting.

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PLACENTAL MALARIA AND BLOOD PRESSURE AT AGE FOUR YEARS: EVIDENCE FROM THE GHANA RANDOMIZED AIR POLLUTION AND HEALTH STUDY

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In sub-Saharan Africa, malaria and hypertension are one of the commonest causes of morbidity and mortality in children and adults respectively. Although previous studies have shown that malaria in pregnancy may increase the risk of gestational hypertension, the effect of placental malaria (PM) on blood pressure (BP) in childhood has not been well studied. The Ghana Randomized Air Pollution and Health Study recruited N=1414 non-smoking women prior to 24 weeks gestation in the Kintampo North Municipality and Kintampo South District of Ghana. PM was assessed by placental histology of full-thickness biopsies obtained at delivery. PM was first dichotomized as no infection or evidence of any infection followed by a more detailed classification: no infection, acute infection, chronic infection or past infection. At age four years, a subset of study children underwent two resting BP measurements, spaced five minutes apart after a 10-minute rest, using the digital OMRON BP742N BP monitor (OMRON Healthcare, CA, USA). We employed multivariable linear regression models to examine associations between PM and childhood systolic and diastolic BP. Of the N=1306 livebirths at 28+ weeks gestation, N= 639 had both valid PM and blood pressure data. The prevalence of PM was 24%. The mean systolic BP (SBP) and diastolic BP (DBP) at age four was 90.2 mmHg and 64.2 mmHg respectively. Following adjustment for child sex and BMI, maternal age and parity, wealth index and ethnicity, PM (any infection) trended towards increased DBP (β=1.51 mmHg; 95% CI -0.20 to 3.22; p=0.08) compared with no infection. Similarly, evidence of past PM showed a trend towards increased DBP (β=1.78 mmHg; 95% CI -0.27 to 3.82; p=0.09) compared with no infection. There was no evidence of an association between PM and SBP. PM may be associated with increased diastolic BP in early childhood. Given that childhood BP tracks into adulthood, larger longitudinal studies are needed to understand the effects of in-utero exposure to malaria and the risk of hypertension in childhood and whether this risk in sustained to adulthood.

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EVALUATION OF THE SEASONALITY OF MALARIA TRANSMISSION THROUGH ROUTINE DATA FROM HEALTH FACILITIES IN BURKINA FASO

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Malaria transmission is strongly seasonal peaking in the rainy season.in Burkina Faso and the country counts for the “high burden to high impact” initiative launched by WHO and the roll Back Malaria Partnership. Despite combined effective control measures include large scale distribution of long-lasting insecticide treated bed nets, the chemoprevention in pregnant women and the seasonal malaria chemoprevention in children 3-59 months, prevalence and incidence of malaria remain high, even though high proportion of diagnosed malaria are unconfirmed (either microscopy or rapid diagnosis test) despite continued effort to confirm malaria diagnosis. Thus, in this project, we aimed to investigate how the diagnosis of malaria in the absence of microscopy or Rapid Diagnosis Test confirmation is impacting malaria seasonality appraisal. Through the ACCESS-SMC project, we conducted a retrospective extraction of routine data from 40 randomly-selected health facilities in 8 different health districts spread all over the country from 2012 to 2016. Data collected included gender, age, clinical signs (fever, vomiting, diarrhea and other signs suggestive of malaria), the performance of rapid diagnosis test or not and the final diagnosis along with the treatment administrated. Overall, 826,199 consultations for suspected malaria were recorded over the study period. There was 36,34% increase in the testing rate between 2012 and 2016 (43.32 versus 79.66%). January to June considered as the low transmission period there were respectively 59.21% [range: 58.79%-59.64%] and 46.34% [range: 45.89%-46.8%] of unconfirmed malaria recorded while July to December considered as the highest transmission period, we recorded respectively 33.63% [range: 33.29%-33.96%] and 46.64% [range: 46.22%-47.06%]. Comparing these periods, the proportion of confirmed malaria is different between the two periods compared to the unconfirmed cases.

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MEASURING IMPACT OF SEASONAL MALARIA CHEMOPREVENTION ON MALARIA CASE DISTRIBUTION FROM ROUTINE DATA SOURCES COMPARED TO MODELLED PREDICTIONS IN BURKINA FASO

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Clinical trials assessing effectiveness of seasonal malaria chemoprevention (SMC) show high impact preventing around 80-85 percent of uncomplicated cases of malaria in children under 5. However, when implemented at scale, SMC programmes have not shown the expected impact in routine and administrative data. We are using a mathematical model to develop a framework for assessing impact of SMC programmes by bringing together relevant data such as prevalence, rainfall, health management information system (HMIS) case data, other interventions, implementation of SMC. We calibrated a malaria transmission model to malaria prevalence (Demographic Health Surveys [DHS]) over time for selected health districts in Burkina Faso using maximum likelihood methods by varying mosquito density. We simulated clinical cases in under 5’s during implementation of SMC in each district including rainfall, net use (Malaria Atlas Project), and treatment seeking (DHS). We compared model predictions of the proportion of clinical malaria cases in children under 5 out of children under 15 to district level rapid diagnostic test confirmed cases from the HMIS. The age distribution of cases aligns well with model simulations prior to SMC, however, model predictions show a larger change after SMC and this change varies by baseline transmission. This could be due to non-malarial fevers presenting at the health facility affecting seasonal patterns in routine data. We will present modelling analyses assessing the effect non-malarial fevers have on seasonal patterns and the extent to which these may mask the impact of SMC seen in routine data.

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MOLECULAR SCREENING SUGGESTS ANTAGONISM BETWEEN PARASITEMIA WITH PLASMODIUM FALCIPARUM AND P. OVALE IN TANZANIA

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Even as Plasmodium falciparum burden has declined in parts of sub-Saharan Africa in recent years, the prevalence of non-falciparum species, such as P. ovale, appears to be rising in the same populations. We employed cross-sectional molecular screening of over 6000 participants >5 years of age residing in coastal Bagamoyo, Tanzania, to examine rates of mono- and co-infection with P. falciparum and P. ovale and investigate possible cross-species interactions. Specifically, we calculated the prevalence ratio of ovale parasitemia between individuals who were positive and negative for falciparum parasitemia using a binomial logistic regression adjusting for age, sex, and seasonality. Of 6,258 participants screened between October 2018 and November 2021,1,929 (31%) were positive for P. falciparum and 644 (10%) were positive for P. ovale. These distributions show evidence of an antagonistic interaction, with individuals positive for P. falciparum having 0.67 (95% CI: 0.56, 0.82) times the probability of also having P. ovale compared to falciparum-negative individuals. This finding of fewer mixed infections than expected by independent assortment was detected in all age groups except adolescents, with age-stratified P. ovale prevalence ratios (95% CI) comparing falciparum-positive to falciparum-negative participants of 0.71 (0.52, 0.97), 1.14 (0.76, 1.74), 0.44 (0.28, 0.69), and 0.62 (0.42, 0.92) among participants ages 6-12, 13-18, 19-30, and >30, respectively. Potential explanations for these results could be that cross-protective immunity or competitive inhibition from the more-common falciparum malaria reduces detected co-infection by decreasing P. ovale susceptibility or parasitemia, or by suppressing ovale relapse infections. We plan to replicate this analysis using data from other molecular surveys in Tanzania and elsewhere in sub-Saharan Africa; if replicated, this interaction may help explain the relative resilience of non-falciparum species amidst declining falciparum burden.

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INTRA-HOST CLONAL DYNAMICS SHAPE CHRONIC PLASMODIUM FALCIPARUM INFECTIONS THROUGH THE DRY SEASON

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Plasmodium falciparum can persist in asymptomatic individuals for extended periods of time, which is particularly relevant in regions where malaria transmission is almost entirely interrupted by a long dry season. In Mali, up to 30% of children carry P. falciparum throughout the dry season without symptoms, comprising a genetic reservoir that bridges two transmission seasons. Our data show that the decreased virulence of the parasite during the dry season is likely not influenced by sensing of seasonal cues, but rather by the timing of inoculation and number of replicative cycles that individual parasite clones undergo within a host. We applied amplicon sequencing of a highly polymorphic gene (apical membrane-antigen 1) on longitudinal samples collected fortnightly in Kalifabougou, Mali, from gender-and-age matched individuals during one transmission season that maintained P. falciparum persistent infections during the 6-month dry season (n=92) or that cleared them due to either treatment during the season or to natural clearance (n=38). We observed that children with persisting parasites had a higher overall within-host diversity (measured by Shannon evenness of clonal abundance), even when taking into account differences in complexity of infection or parasite density, than those who did not. The ability of children with dry season persistent infections to control parasites more broadly suggests that immunity plays a role in structuring this diversity, and that clonal abundance is a predictor of persistence. We apply these data to inform mathematical models and intra-host simulations to determine drivers of persistence throughout and evaluate our predictions with longitudinal data collected monthly during the dry season in Torodo, Mali (n=74). Our findings highlight how the within-host clonal dynamics over time promote persistence and may inform new strategies for elimination in areas with highly seasonal transmission.

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EVALUATING MALARIA PREVALENCE IN NON-HOMOGENEOUS FOR MAL AND INFORMAL COMMUNITIES IN FREETOWN SIERRA LEONE: A MULTIPHASE CROSS SECTION SECTIONAL STUDY

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Limited resources for malaria, including in Sierra Leone, require national programs to stratify activities within urban areas. Simultaneously urbanization and changing transmission dynamics require innovative approaches for malaria control in urban areas. Catholic Relief Services (CRS) and the College of Health and Allied Sciences undertook a cross-sectional study from July 2021 to November 2022 to determine the prevalence of malaria in children 6-59 months old in four separate communities within Freetown. Two communities were identified as formal (Wilberforce and Hill Station) and two informal (Kolleh Town and Cockle Bay). Freetown, has two peak transmission seasons in May and the second in October/November, however, changing weather patterns have delayed rains in recent years. The three cross-sectional surveys were conducted within the four communities based on rainfall in the low transmission season (RD1, August 2021), mid-year transmission season (RD2, June/July 2022), and peak transmission seasons (RD3, November/December 2022). We observed a consistently higher malaria prevalence in the formal settlements [μ=14% - 11.1% RD1, 13.6% RD2 & 17.4% RD3] than informal settlements [μ=11.3%- 10% RD1, 8.7% RD2 & 15.2% RD3]. In formal areas 36% of houses were identified to be 'traditional' in construction suggesting that increased urbanization is leading to blended (non-homogeneous) formal areas. Other factors such as housing type, ITN ownership, and wealth quintile were variable in predictive association for malaria among households in formal and informal areas. The results demonstrate that increased urbanization has resulted in non-homogeneous areas of Freetown, and that malaria rates are higher than reported in national malaria surveys. New approaches including improved WASH, housing, and vector control are needed within urban areas to help stratify available malaria resources.

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HIGH-THROUGHPUT GENOTYPING OF PLASMODIUM VIVAX IN THE PERUVIAN AMAZON VIA MOLECULAR INVERSION PROBES

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Genomic epidemiology has enabled in-depth, high-throughput study of Plasmodium populations, antimalarial resistance, and importation. Molecular inversion probes (MIPs) have enabled efficient and affordable high-throughput genotyping of Plaasmodium falciparum populations in African contexts, but application to other species has lagged. P. vivax is the most widespread human malaria species and is an emerging threat in many areas with successful P. falciparum control. As such, there has been a recent proliferation in global P. vivax genomics studies facilitated by the superior PvP01 genome assembly. Leveraging the success of P. falciparum MIPs, we developed four P. vivax MIP panels covering: 1) known genes of interest (e.g. reticulocyte binding proteins, Duffy binding proteins, potential vaccine targets, potential drug resistance genes, and diversity markers); and SNPs identified in globally distributed (including Africa) whole genome sequences that are 2) highly geographically differentiating; 3) neutral and rare; and 4) neutral and common. We used these panels to study the population structure of 689 Peruvian P. vivax samples collected by NAMRU between 2011 and 2017 in the region around Iquitos. The panels consistently perform well with isolates at ≥ 200 p/µL, with some isolates <100 p/µL also performing well in initial sequencing. Across both our SNP panels and our genes of interest (e.g. RBP2), we detect a lack of rare alleles (Tajima's D > 2), which could indicate balancing selection in genes associated with RBC invasion that are under immune selection. Assessment of directional selection signatures in the population are ongoing, including evaluation of putative drug resistance alleles. Overall, we find minimal large-scale geographic or temporal structure among these samples based on PCA, consistent with a long-term panmictic population. However, at the local level we detect clusters within the same city and year that may represent local outbreaks and warrant further investigation. The new P. vivax MIP panels provide a high-throughput genotyping approach to interrogate genome-wide SNPs as well as genes of biological interest.

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PLASMODIUM VIVAX SHOWS HIGH GENETIC DIVERSITY AND RAPID LOCAL ADAPTATION IN A REMOTE COMMUNITY FROM THE PERUVIAN AMAZON REGION

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There is no a lot of information about Plasmodium vivax malaria transmission and parasite genetic diversity in remote hard to reach areas from the Peruvian Amazon that represent a challenge to achieve the long-awaited malaria elimination. The main objective of this work was to evaluate the P. vivax population genetics changes over time in the community of Santa Emilia, province of Loreto. Weekly active case detection and monthly screening were performed in 2013 and 2015-2016. A prevalence of 49% [IC 43-55] by microscopy and 82% [IC 77- 86] by PCR was found during all the surveillance activities. In addition, 350 out of 529 total samples were genotyped using sixteen neutral microsatellite markers. The result showed high genetic diversity (0.70 ± 0.10 in average) over time, high population differentiation (Fst> 0.5) between 2013-2015 and 2013-2016, and 40% of polyclonal infections. Additionally, we found the absence of a recent bottleneck in the population, with the presence of new alleles, supported by 14% of genetically unrelated parasites. Bayesian inference indicates that four more likely clonal populations (ΔK = 4) were circulating during this period of time. In conclusion, our results suggested that P. vivax had rapid adaptation and expansion in Santa Emilia and this community presents a high vulnerability to the importation of new parasites that support local transmission and high genetic diversity maintenance. This scenario may be due to the local human mobility, that should be better studied in these remote areas. This information is relevant to focalize or adapt the elimination strategies, already in place, mainly in remote communities.

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GENETIC ANALYSIS REVEALED HIGHLY RELATED LOCAL TRANSMISSION OF PLASMODIUM FALCIPARUM IN THE ISLAND OF SÃO TOMÉ

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The Democratic Republic of Sao Tome and Principe (STP) is approaching malaria elimination and aiming to eliminate it by 2025. However, continuous transmission and increasing cases have been seen in the past few years. To target effective control strategies, it is crucial to characterize local transmission and identify risk factors of transmission. Here, we collected 419 samples on the island of São Tomé between 2015 and 2016 and applied a multiplexed amplicon sequencing approach targeting 165 diverse microhaplotypes to obtain genetic data for each sample. To quantify transmission intensity and identify transmission clusters, we used MOIRE to estimate complexity of infection (COI) and within-host parasite relatedness, and Dcifer to estimate inter-sample relatedness. Preliminary results from 120 samples showed a very high proportion of monoclonal infections (96.7%, 116/120; average COI = 1.08) and high relatedness among a large proportion of samples. Most samples from 2016 (76.4%; 68/89) and a few from 2015 (9.7%; 3/31) were part of a single, predominant genetic cluster with high relatedness (range of pairwise relatedness from 0.9 to 1.0). The predominant cluster was transmitted throughout 2016 and sustained in Agua Grande (67.6%, 46/68) and Lobata (23.5%, 16/68) districts. Most 2015 samples outside the predominant cluster also showed a significant pairwise relatedness (> 0.5) to one or more samples from 2016. Overall, our results demonstrate extreme bottlenecking of parasite diversity in 2016, suggestive of sustained but low local transmission with limited importation of Plasmodium falciparum in the island of São Tomé. We are currently working with case surveillance data to identify risk factors of transmission, which may further guide targeted elimination strategies.

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GENOME STRUCTURE OF PFHRP2/3-DELETED PLASMODIUM FALCIPARUM: DELETION BREAK-POINTS AND CONSEQUENCES OF THE DELETION

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Deletions in Plasmodium falciparum histidine-rich proteins 2 and 3 (pfhrp2/3) cause false-negative RDT results, threatening malaria control efforts. These deletions occur as spontaneous rearrangements in P. falciparum, but the mechanism, break-points, and the extension of the deletions into flanking regions are not well-described. It is also unknown what impact these genome rearrangements have on the parasite genome, and on the phenotypic diversity and environmental adaptability of the parasite. In this study, we investigated the genome structure of P. falciparum with pfhrp2/3 deletions to understand how the deletions occur and the impact of the deletions on chromosome architecture. We derived whole genome sequence for two pairs of clinical and culture-adapted isolates using high-quality short-read genomic sequencing and carried out de novo assembly to investigate genome rearrangement. The genomes were annotated and synteny maps generated against the 3D7 reference genome. Genomic rearrangements including duplications, inversions and translocations were common in the sub-telomeric regions of most of the chromosomes in all parasite lines, suggesting this is a relatively common process in P. falciparum which can lead to pfhrp2/3 deletions. There is a clear common break-point for pfhrp2 at a location adjacent to it, spanning the distal 25-50 kb at the right end of chromosome 8. By contrast, pfhrp3 occurs at the end of a deletion block spanning 600 kb at the right end of chromosome 13. These differences may suggest that pfhrp2 deletion is a recent positive selection event but pfhrp3 deletion could be a passive consequence of genetic hitchhiking. The majority of genes deleted together with pfhrp2 and pfhrp3 encode variant surface antigens (VSA), possibly altering the parasite's immune evasion repertoire. We also observed gene deletions broadly involved in sexual cycle proteins predicted to impact the transmissibility of the parasites. Understanding whether the parasites acquire any advantage linked with deletions can aid in planning appropriate control strategies.

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DISTRIBUTION OF PLASMODIUM FALCIPARUM APICAL MEMBRANE ANTIGEN 1 CLUSTER ONE LOOP HAPLOTYPES AND THEIR ASSOCIATION WITH MALARIA SYMPTOMS IN BANDIAGARA, MALI

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Although overall malaria incidence has decreased sharply over the past two decades, progress has stalled since 2015. Vaccination is a control strategy that could limit malaria burden. While multiple malaria vaccines have been tested in phase 2 or phase 3 trials, and only one progressing to phase 4 trials, no vaccine has induced an overall clinical efficacy greater than 50% except the R21 vaccine. Understanding the parasite genetic factors playing a role in malaria pathogenesis could help identify essential proteins and aide in the design of an effective malaria vaccine. We hypothesize that clinical malaria phenotypes are a function of parasite density, genetic makeup of both parasite and host, starvation, co-infection, environmental factors, and potentially parasite and host epigenetic factors. To investigate the relationship between parasite genetics and clinical phenotypes, we have focused on apical membrane antigen 1 (AMA1), a parasite antigen involved in red blood cell invasion, which contains a cluster one loop (c1L) fragment that interacts with anti-AMA1 antibodies. Using ama1 gene sequences generated from samples collected from 425 children during a three-year malaria incidence study conducted in Bandiagara, Mali, we assessed the relationship between individual haplotypes and clinical malaria symptoms and disease phenotypes of those presenting with clinical malaria symptoms. AMA1 haplotype dynamics showed a gene under balancing selection. After adjusting for study participant location, using logistic regression, c1L haplotypes were not associated with malaria symptoms or disease phenotypes. None of the most frequent haplotypes were linked to clinical malaria, defined as any temperature greater than 37.5 degree Celsius and a parasitemia greater or equal to 2,500 parasites per microliter. Our findings suggest a lack of association between AMA1 haplotypes and symptomatic malaria. Likely, multiple factors are related to malaria symptomatology.

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A NOVEL PROBABILISTICALLY MODEL BASED ON GENETIC DATA FOR ESTIMATING PLASMODIUM VIVAX RELAPSES AFTER RADICAL CURE TREATMENT

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The diverse potential origins of recurrent infections after treatment against Plasmodium vivax make it difficult to estimate treatment anti-relapse efficacy. However, the genetics of parasite populations can support a more realistic estimation of the anti-relapse efficacy. Hereby, we developed a probabilistic statistical framework based on P. vivax microsatellite genotyping data from a cohort treated with chloroquine and primaquine in the Peruvian Amazon, aiming to estimate relapse events after treatment translated into anti-relapse efficacy. First, we performed multiple imputations to deal with missing microsatellite data using polytomous logistic regression models. Then, we proposed a probability of relapse integrating the prevalence of allelic profile and allelic dissimilarity index (multilocus comparison of pre-/post-treatment isolates). This informed to the binomial probability process to randomly impute the recurrent status (i.e., either reinfection or relapse), and multiply repeated to evaluate the uncertainty. Finally, Rubin's rules were applied to the final pooled estimates. Of 302 participants, 197 (65.2%) had at least one P. vivax recurrence during the 2-year follow-up. The pooled mean Nelson-Aalen cumulative hazard estimate of first heterologous recurrences was 4,0% at day 28 and increased gradually up to 2 years after treatment (45.7% at 6 months, 66.7% at 1y, and 88.5% at 2y). On the contrary, the first homologous recurrences only occurred from day 52 (0.35%) and were less frequent afterward (11.5% at 6 months, 13.5% at 1y, and 15,0% at 2y). The final pooled 6-month and 2-year cause-specific cumulative incidence function of first relapses after treatment were 0.22 (95% CI 0.17-0.28) and 0.29 (95% CI 0.23-0.35) for the overall study population. Our study proposes a statistical approach to identify the origin of P. vivax recurrences after treatment with a comprehensive assessment of the treatment's efficacy considering the parasite population's genetic features and the probability of relapse.

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MOLECULAR SURVEILLANCE OF MALARIA PARASITES IN AN INDIGENOUS COMMUNITY IN THE PERUVIAN AMAZON

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Hard-to-reach communities represent Peru's last challenge for malaria elimination, but information about epidemiology and transmission is scarce. We investigated the transmission dynamics/population genetics, drug resistance markers, and pfhrp2/3 deletions of Plasmodium vivax (Pv) and P. falciparum (Pf) in Nueva Jerusalén (NJ). NJ is a remote indigenous community in the Loreto region (~50 km from the Ecuador border) with persistent malaria transmission. We performed population surveys in 3 weekly consecutive active case detection (ACD) visits in November 2019 and by passive case detection (PCD) from December 2019 to May 2020. We analyzed a representative sample of positive-PCR isolates (Pv=70, Pf=64) using AmpliSeq NGS assays.The Pv population was genetically homogeneous during the study and had modest genetic diversity (He=0.27). In contrast, the Pf population had low diversity (He=0.08) and 3 clusters (one generated an outbreak).Moreover, Pf parasites carried resistance mutations in pfcrt (100%), pfdhfr (94%), and pfdhps (48%). No artemisinin resistance variants were found in pfK13. In addition, the most frequent haplotype was hrp2-/hrp3+ (62%). Compared to other remote areas, NJ's Pv parasites were highly differentiated from the ones from Yavari (district next to the Brazilian border, >480km distant from NJ) (Fst=0.45) but little differentiated from Mazan (riverine district, >350 km far away) (Fst=0.08). On the other hand, Pf in NJ had modest to high genetic differentiation with Santa Emilia (riverine community, >260 km from NJ) (Fst=0.19) and Mazan parasites (Fst=0.34). The Pf resistance markers and pfhrp2/3 haplotypes were similar among the areas, except in Mazan, where the double deletion was predominant. In this first report about malaria genomic surveillance in Peruvian indigenous communities, Pv & Pf population structure in NJ were different between them and also among other areas, highlighting the importance of performing regular surveillance in these communities in terms of imported infections and spread of drug resistance to promptly recommend the adaptation of the malaria elimination strategy in Peru.

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COMPARISON OF MOLECULAR SURVEILLANCE METHODS TO ASSESS CHANGES IN THE POPULATION GENETICS OF PLASMODIUM FALCIPARUM IN HIGH TRANSMISSION

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A major motivation for developing molecular methods for malaria surveillance is to measure the impact of control interventions on the population genetics of Plasmodium falciparum as a potential marker of progress towards elimination. Here we assess three established methods (i) single nucleotide polymorphism (SNP) barcoding (panel of 24-biallelic loci), (ii) microsatellite genotyping (panel of 12-multiallelic loci), and (iii) varcoding (fingerprinting var gene diversity, akin to microhaplotyping) to identify changes in parasite population genetics in response to a short-term indoor residual spraying (IRS) intervention. Typical of high seasonal transmission in Africa, multiclonal infections were found in 82.3% (median 3; range 1-18) and 57.8% (median 2; range 1-12) of asymptomatic individuals pre- and post-IRS, respectively, in Bongo District, Ghana. Since directly phasing multilocus haplotypes for population genetic analysis is not possible for biallelic SNPs and microsatellites, we chose ~200 low-complexity infections biased to single and double clone infections for analysis. Each genotyping method presented a different pattern of change in diversity and population structure as a consequence of variability in usable data and the relative polymorphism of the molecular markers (i.e., SNPs < microsatellites < var). Varcoding and microsatellite genotyping showed the overall failure of the IRS intervention to significantly change the population structure from pre-IRS characteristics (i.e., many diverse genomes of low genetic similarity). The 24-SNP barcode provided limited information for analysis, largely due to the biallelic nature of SNPs leading to a high proportion of double-allele calls and a view of more isolate relatedness compared to microsatellites and varcoding. Relative performance, suitability, and cost of the methods relevant to sample size and local malaria elimination in high-transmission endemic areas will be discussed.

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DIFFERENTIAL REGULATION OF PFMDR2 AND PFK13 TRANSCRIPTS IN KENYAN CHILDREN WITH SEVERE MALARIAL ANEMIA: POTENTIAL IMPACT ON ARTEMISININ-BASED COMBINATION THERAPY RESPONSES

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Severe malarial anemia (SMA: Hb≤6.0 g/dL, with any density parasitemia) is a common clinical manifestation of severe malaria in children under five in holoendemic Plasmodium falciparum transmission regions, such as Siaya County, western Kenya, and a primary cause of morbidity and mortality. To explore the impact of parasite-derived factors on malarial disease severity, we performed transcriptomic analyses on whole blood collected from children (3-36 months) with non-SMA (Hb>6.0 g/dL, n=40) and SMA (n=20) prior to treatment with artemisinin-based combination therapy (ACT). Next-generation sequencing was performed at a depth of >20 million high-quality mappable reads using Illumina NovoSeq and subsequently mapped to a reference genome for a Kenyan P. falciparum isolate (pfKE01) using the HTSeq platform. This resulted in the annotation of ~3200 distinct P. falciparum transcripts. RNA reads for each sample was normalized by calculating transcripts per kilobase million (TPM) per transcript. There were 688 differentially expressed P. falciparum genes between the SMA and non-SMA groups (P<0.05): 649 upregulated and 39 downregulated. Two P. falciparum transcripts related to ACT treatment responses were differentially regulated. Specifically, children with SMA had upregulated levels of multidrug resistance protein 2 (MDR2; Log2foldChange=1.33) and downregulated levels of kelch protein K13 (Log2foldChange=-0.47). These results suggest that children with SMA may have altered susceptibility profiles to ACTs. Further research is required to determine if altered gene expression patterns for MDR2 and K13 affect drug effectiveness and if

the driving force behind these observed patterns is due to pressure from the human host immune response and/or inherent genetic changes in the parasite.

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SPATIAL CONNECTIVITY, IMPORTATION AND TRANSMISSION FLOW OF PLASMODIUM FALCIPARUM IN MOZAMBIQUE USING MICROHAPLOTYPE DATA

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Malaria genomics represents a promising tool to improve current surveillance systems and tailor malaria control and elimination interventions. The GenMoz (Plasmodium falciparum genomic intelligence in Mozambique) project aims to operationalise a functional malaria molecular surveillance system in Mozambique to inform programmatic decisions on the use of effective diagnostic and treatment tools, targeted strategies for malaria elimination and effective intervention combinations to maximise burden reduction. For this purpose, a novel amplicon sequencing panel was developed to generate 272 genetic microhaplotypes targeting 250bp regions that are highly informative of diversity, misdiagnosis and drug resistance mutations, allowing precise estimates of relatedness for polyclonal infections. We studied the spatial structure of genetic connectivity of P. falciparum populations in Mozambique to assess the potential of genomics to characterise transmission flow and quantify the contribution of imported cases in low-transmission settings. We used the R package Dcifer to estimate identity-by-descent between sample pairs from various provinces, studying isolation-by-distance in a wide range of geographical distances, using Mandel tests. We quantified the contribution of imported cases in two low-transmission areas from the fraction of highly related pairs between samples from these areas and from other areas, correlating the statistics with travel history surveys. We found strong spatial genetic distinction across the country, with higher fractions of highly related pairs within regions (north-north or south-south) than between regions (north-south). The Mandel tests confirm strong isolation-by-distance at large scales (between provinces), but no statistical significance at small scales (within province). Few highly related pairs between samples in the targeted low-transmission areas and samples from different provinces of Mozambique were found, with no significant correlation with their travel history data, suggesting no significant contribution of imported cases in the low-transmission areas studied.

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EXPANDING THE GLOBAL WHOLE GENOME SEQUENCE DATASET OF PLASMODIUM FALCIPARUM

Richard D. Pearson on behalf of MalariaGEN

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Malaria control and elimination requires decision making regarding the use of vaccines, diagnostics and treatments, all of which can be informed by genomic surveillance of the parasite. Whole genome sequencing can play an important role in detecting new molecular markers associated with drug resistance, identifying regions of the genome that are under selection, and better understanding host-parasite interactions. We previously released the largest global resource of genomic data on Plasmodium falciparum, comprising over 20,000 samples from 82 partner studies in 33 countries. Since then, we have released further whole genome sequence data to MalariaGEN partners. We are working towards publicly releasing an expanded set of curated genotype data. As with previous releases, this will include genotypes at SNPs and short indels genome-wide, in addition to copy number variation calls at genes related to drug resistance and failures of rapid diagnostic tests. The latest release will include sample QC, identification of populations and characterisation of samples by inferred resistance status to major frontline anti-malarial drugs. In addition to an expanded set of samples, we aim to enhance the value of this data resource by making jupyter notebooks of typical analyses publicly available using a free-to-use cloud-based platform.

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PREVALENCE OF CYP2C8 POLYMORPHISM IN CHILDREN AGED 3 TO 59 MONTHS IN BOBO DIOULASSO, BURKINA FASO

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Cytochrome P450 2C8 (CYP2C8) is a key enzyme responsible for the metabolism of many drugs such as amodiaquine (AQ), which is a component of artemisinin-based combination therapy (ACT) and seasonal malaria chemoprevention (SMC) drugs. Polymorphisms present in this gene may have an impact on the pharmacokinetics (PK), efficacy and safety of this antimalarial. The objective of this study was to determine the prevalence of CYP2C8 mutation, associated with Plasmodium falciparum in children under 5 years of age in Bobo Dioulasso, Burkina Faso. Dried blood spots were collected from 1083 participants and extracted using the Qiagen kit (DNeasy Blood & Tissue Kit). The prevalence of the human CYP2C8*2 and CYP2C8*3 genotypes were determined by PCR-RFLP, and the identification of P. falciparum was done by the microscopy. The prevalence of P. falciparum was 7.20% (i.e. 78/1083) and the prevalence of CYP2C8*2 was 28.72% (i.e. 311/1083) in the study population. homozygous (*2/ *2) and heterozygous (*2/*1) participants for the CYP2C8*2 were 26.41% (i.e., 286/1083) and 2.31% (i.e., 25/108) respectively. The proportion of participants with the CYP2C8 mutation and with positive for P. falciparum was 0.74% (i.e. 8/1083). The influence of these CYP2C8 mutations on the metabolism of antimalarial drugs, in particular amodiaquine (AQ), needs to be further evaluated.

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INFERRING FOR CE OF INFECTION FROM MOLECULAR-BASED ESTIMATES OF MULTIPLICITY OF INFECTION IN FALCIPARUM MALARIA WITH AN APPLICATION TO INTERVENTION IN NORTHERN GHANA

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Force of infection (FOI), defined as the number of new Plasmodium falciparum infections acquired by an individual host over a given time interval, is a direct measure of exposure to Plasmodium falciparum blood-stage infection. It reflects risk of infection and clinical episodes, and relates local variation in malaria burden to transmission. It is thus suitable for monitoring the impact of antimalarial interventions and assessing vaccine or drug efficacy in clinical trials. Despite being recognized as

a key epidemiological parameter, FOI remains difficult, expensive, and labor-intensive to accurately measure, either directly via cohort studies or indirectly via the fitting of epidemiological models to repeated cross-sectional surveys. Molecular advances to sequence and type the var multigene family encoding for the major surface antigen of the blood stage of infection, provide a basis to estimate a sister "static" quantity, the multiplicity of infection (MOI, the number of genetically distinct parasite strains co-infecting a single human host), typically under sparse sampling schemes. Having extended this approach to a Bayesian framework to account for measurement error, we propose a general approach to obtain FOI on the basis of MOI. We specifically adapt two methods from queuing theory to derive FOI, and evaluate these with numerical simulations with a stochastic agent-based model. We then apply the methods to longitudinal surveys from northern Ghana before, during, and after a three-round IRS (Insecticide Residual Spreading) intervention. Both methods give accurate and consistent FOI estimates across various simulated scenarios. Their application to field surveys shows that despite a pronounced 60% reduction in FOI during IRS, transmission intensity rebounds almost completely in 32 months following IRS interruption. The methods should be applicable to many geographical locations where cohort or frequently-sampled cross-sectional studies are lacking but single-time-point surveys under sparse sampling schemes are available. They should also apply to other infectious diseases for which MOI has been obtained.

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POPULATION DYNAMICS AND GENOTYPIC VARIATION OF PLASMODIUM VIVAX IN A LOW-ENDEMICITY AREA OF SOUTH AMERICA BETWEEN 2012 AND 2020

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Ecuador is one of the countries that is part of the E-2025 initiative and would be able to eliminate malaria in the coming years. Nevertheless, elimination efforts have fallen short and cases have been increasing, particularly in the Amazon of the country. Plasmodium vivax is the main malaria parasite affecting the Ecuadorian population but little is known about the populations of P. vivax circulating in the country. We used nine microsatellite markers in 150 samples of P. vivax from the Ecuadorian Coast and Amazon regions collected between 2012 and 2020 to characterize their origin, distribution and population dynamics. We found that in Ecuador, there is higher genetic diversity and multiclonality of P. vivax in the Amazon region than in the coast of the country. In addition, there was evidence of gene flow and moderate genetic differentiation between Amazonian localities, but little gene flow between the Coast and Amazon. The coast of Ecuador shared lineages and had low/moderate genetic differentiation with coastal Colombian localities. Similarly, Amazon localities shared lineages and had low/moderate genetic differentiation with Peruvian Amazon localities. This study suggests a recent increase in P. vivax multiplicity of infection and diversity in the Amazon of Ecuador because of increased transmission. It confirms the importance of the Andes as a geographical barrier and underlines the importance of geographic corridors through the Pacific coast of South America and the Amazon rivers that help sustain malaria in the region and hamper elimination.

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GENETIC CONNECTIVITY AND TRANSMISSION METRICS OF PLASMODIUM FALCIPARUM IN ZAMBEZI REGION, NORTHERN NAMIBIA

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As malaria transmission declines, an increasing proportion of the parasite reservoir is clustered in subpopulations with shared risk factors and spatial hotspots. While the WHO recommends a targeted response in high-risk populations, there is limited evidence quantifying transmission between populations and the impact of targeted interventions. As part of a population-based evaluation of targeted malaria interventions in seasonal agricultural workers in northern Namibia (2019-2020), epidemiological data and samples were collected from cases at agricultural sites (n=35) and those presenting to nearby health facilities (n=511). All samples with parasite density ≥10 parasites/μL of blood by qPCR were sequenced using amplicon deep-sequencing panels including 175 highly diverse and differentiated loci. Population level and within-host genetic diversity measures, including effective complexity of infection (eCOI) and within-host relatedness were estimated by population (nationality and worker/community) and study arm, using an MCMC based approach. Preliminary results are reported from 25 cross-sectional and 280 incident cases. There was no difference in eCOI between agricultural workers and communities in control and intervention areas at either time point, but non-Namibians had a higher eCOI than Namibians, potentially indicating parasite importation from or increased connectivity with higher transmission settings. At endline, eCOI was lower in the intervention arm within both worksites and surrounding communities (median = 1.14 (95% CI: 1.13-1.16) and 1.16 (1.15-1.18)) compared to the control arm (1.21 (1.20-1.22) and 1.22 (1.21-1.23)). A similar, non-significant trend was observed for within-host relatedness and proportion of polyclonal infections in agricultural workers. Results suggest an impact of the intervention on transmission at worksites that may have spilled over to communities. Additional analyses will include data from all cases and evaluate genetic relatedness between infections using identity by descent and transmission networks within and between subpopulations at different spatial scales.

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BENCHMARKING IDENTITY-BY-DESCENT CALLERS FOR PLASMODIUM FALCIPARUM

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Genomic surveillance combined with traditional epidemiological analyses is important for identification of at-risk populations for targeted intervention in support of malaria control/elimination efforts. Identity-by descent (IBD) is one population genetic metric used to study genetic relatedness, effective population size (Ne), migration and population structure, and drug resistance-related selection in Plasmodium falciparum (Pf). Despite the wide use of IBD as a metric of genetic relatedness, a comprehensive evaluation of available tools for the identification of IBD segments in Pf has not been performed, and valuable information conveyed by individual IBD segments is not always well exploited. To date, existing IBD quality assessments either focus on the human genome (rather than Pf), use a loose definition of IBD accuracy or are biased toward long segments from pedigree-based simulations. In this study, we performed population-based simulations that account for the high recombination rate and shrinking Ne of Pf, and examine IBD segments spanning a wide length distribution. We benchmarked several IBD callers, including probabilistic (hmmIBD, isoRelate), Identity-By-State-based (hap-ibd, TPBWT), or other (Refined IBD, tree-based) methods, by comparing inferred IBD with genealogy-based true IBD. Our simulations suggest that hmmIBD-inferred IBD segments tend to be less biased for the determination of pairwise total IBD, length-specific population total IBD, and IBD-based demography estimates while remaining sensitive to IBD positional enrichment due to positive

selection. However, hmmIBD suffers from a high rate of false positive short IBD segments (<4cM), which should be excluded in sensitive analyses such as IBD-based Ne inference. Ongoing work will focus on the validation of benchmarking results in an empirical dataset with over 7000 worldwide Pf samples (including MalariaGen Pf6 and an in-house dataset) by evaluating the ability of different IBD callers to capture known selection signals and generate Ne and population structure estimates consistent with existing knowledge for each geographic region.

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THE RISK OF VACCINE GENOTYPE REPLACEMENT FOR PLASMODIUM FALCIPARUM

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Malaria vaccines represent a vital new tool in the fight against Plasmodium falciparum. Vaccines administered to children aim to prevent morbidity, while deploying vaccines to all ages aims to reduce morbidity and transmission, thus accelerating elimination. The first malaria vaccine, RTS,S/AS01, was recently approved, and many anti-infective (AIV), blood-stage (BSV), and transmission-blocking (TBV) vaccine candidates are under development or early clinical trials, such as R21. If targets of these vaccines are not conserved, there is a risk that vaccines confer variable protection between parasite genotypes due to antigen diversity. The risk of spreading vaccine-resistant or partially resistant P. falciparum is unknown, as are the factors promoting this spread. We adapted an individual-based model of malaria transmission to assess the spread of parasites partially or fully resistant to AIV and BSV when deployed to children and the spread of parasites resistant to an AIV when deployed alone or in combination with a TBV to adults or the whole population. For each vaccine type and use case, we assessed which biological, epidemiological, vaccine properties, and deployment factors drive the spread of resistant parasites and the impact of this spread on vaccine effectiveness. We estimated that even genotypes with low degrees of resistance could spread quickly for both use cases. Therefore, developing vaccines targeting conserved antigens and monitoring allele frequency and vaccine efficacy in implementation settings is essential. The estimated spread was faster for BSV than AIV and faster for more efficacious vaccines having longer half-lives and higher initial efficacies. Moreover, while favouring vaccine effectiveness, resistance spread is faster with a higher frequency of vaccine deployment and more extensive population coverage. Deploying a drug with a vaccine both increases the public health impact and reduces resistance spread. Additionally, deploying a TBV with an AIV to the whole population strongly delays the spread of AIV-resistant genotypes and increases the chance of elimination in some settings.

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INFLAMMATORY MARKERS ASSOCIATED WITH IN-HOSPITAL MORTALITY IN CHILDREN WITH SEVERE MALARIA

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Despite treatment with efficacious antimalarial therapy, severe malaria (SM) in children is associated with high mortality. The contributions of different pro- and anti-inflammatory cytokines and chemokines to mortality in severe malaria (SM) is not fully characterized. To better understand the pathogenesis of SM, we evaluated serum levels of 40 markers of inflammation, angiogenesis and chemotaxis by a Luminex assay in 596 Ugandan children 6 months - 4 years of age with severe malaria (SM) and 120 community children (CC). Children with one or more of the 5 most common forms of SM in Uganda (cerebral malaria, respiratory distress, malaria with multiple seizures, severe malaria anemia and prostration) were enrolled in the study. Levels of 21 of the 40 markers tested differed significantly between children with SM and CC ($p<0.00125$). To evaluate which markers were associated with mortality in SM, we compared levels of these 21 markers in children with SM who died (n=43) vs. those who survived (n=553) during the initial admission. Five markers were significantly elevated in children with SM who died compared to the children who survived ($p<0.0024$): a pro-inflammatory cytokine (IL-6), an anti-inflammatory cytokine (IL-1ra), a soluble programmed cell death ligand involved in immune suppression (sPD-L1), and chemokines involved in eosinophil (CCL11) and lymphocyte (CCL20) chemotaxis. In-hospital mortality increased (adjusted odds ratio [95% confidence interval] with natural log increase in the levels of IL-1ra (2.7 [1.57, 4.64]), IL- 6 (1.3 [1.11, 1.55]), sPD-L1 (2.7 [1.58,4.63]), CCL11 (5.2 [2.72,9.95]) and CCL20 (1.94 [1.51,2.49]). The study findings suggest that a complex combination of factors that regulate inflammation and cell chemotaxis contribute to severe disease and death in malaria.

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SEVERE THROMBOCYTOPENIA IS ASSOCIATED WITH AUTOANTIBODIES TO PHOSPHATIDYLSERINE IN *PLASMODIUM VIVAX* INFECTION.

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One of the most frequent hematological findings during Plasmodium vivax infections is a decrease in platelet count. One of the pathophysiological mechanisms proposed to mediate this hematological alteration is the production of autoantibodies directed against components of platelets, in particular phosphatidylserine (PS), which is exposed in the membrane of activated platelets during infections such as malaria. We hypothesized that platelet elimination may be a consequence of a previously described autoimmune response during P. vivax infection that includes anti-PS antibodies (PMID: 32687495). The purpose of this study was to determine the association of anti-PS antibodies in thrombocytopenia during P. vivax infections. An analytical, cross-sectional study was carried out between 2017 - 2019 an endemic area of Tierralta, Córdoba, Colombia. 163 patients monoinfected by P. vivax with different levels of thrombocytopenia were included (P. vivax + mild thrombocytopenia n=42; P. vivax + moderate thrombocytopenia n=53; P. vivax + severe thrombocytopenia n=31; P. vivax without thrombocytopenia n= 37) and 60 healthy volunteers without malaria or thrombocytopenia. Determination of anti-PS antibodies in the plasma of patients was performed by indirect ELISA and confirmation of PS exposure in platelets was determined by flow cytometry using Annexin V. It was found that the levels of anti-PS antibodies in the P. vivax patient group without thrombocytopenia were significantly lower compared to the group with severe thrombocytopenia ($p<0.05$). When comparing all patients in the cohort, the correlation between platelet counts and anti-PS antibodies was inverse ($r= -0.19$, $p<0.05$), with higher PS exposure in platelets from patients with severe thrombocytopenia. The results suggest that anti-PS antibodies binding to PS exposed on platelet membranes during P. vivax infection may be one of the pathophysiological mechanisms mediating the onset of severe thrombocytopenia in patients.

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MULTI-STAGE HUMORAL IMMUNITY TO PLASMODIUM FALCIPARUM MALARIA IN A LONGITUDINAL COHORT OF CHILDREN

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Acquired humoral immunity to Plasmodium falciparum prevents clinical illness. It predominantly targets the blood stages, but antibodies are also acquired to the pre-erythrocytic stage. The relative contributions of antibodies to different life stages in acquired immunity is not well understood, nor whether antibodies to different stages can act additively or synergistically to prevent malaria infection or illness. We have quantified antibodies to merozoites, parasitized RBCs, and sporozoite antigens in a longitudinal cohort of children in Papua New Guinea. We analyzed their acquisition and associations with protection, as well as the relationships between acquired responses. We quantified antibody magnitude as well as functional activity including complement-fixation and activation, antibody interactions with Fc-receptors and phagocytic functions, and growth inhibitory activity. Antibodies to merozoites, including antibodies with Fc-mediated functional activities, were more strongly associated with protection from symptomatic malaria than antibodies to parasitized RBCs, PfEMP1 on the surface of pRBCs, or sporozoite antigens. Associations with protection varied for different antigens, and for different functional antibody response types. Functional antibodies to sporozoites were acquired more slowly and substantial functional activity was only observed among a minority of children. However, higher magnitudes of Fc-mediated functional activities to the most abundant sporozoite antigen (CSP) were significantly associated with a reduced risk of malaria. Further statistical analyses and modelling is investigating potential synergistic effects of antibodies to multiple stages and antigens. These findings provide new insights into protective acquired immunity across the life-cycle of P. falciparum and may help inform the development of multi-stage vaccines for malaria.

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ASSOCIATION OF NOVEL IGG3 ALLOTYPE WITH MALARIA IN CHILDREN FROM SEPIK REGION OF PAPUA NEW GUINEA

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Malaria is a global health burden causing death and severe illness in children under five years of age in malaria endemic regions. Recent work has established the importance of malaria-specific IgG3 in malaria immunity. IgG3 via Fc region binds to Fcγ-receptors (FcγRs) on immune cell surface to instigate immunological defense against malaria. Changes in the amino acid sequences due to single nucleotide polymorphisms (SNPs) of IgG3-Fc regions give rise to IgG3 allotypes which can modulate IgG3 functions. A novel IgG3 allotype, G3m29, was recently reported in pregnant women from Sepik, Papua New Guinea, and has been shown to have enhanced affinity to FcγRIIa. We hypothesized that the prevalence of G3m29 in this population was associated with possible protection from severe or uncomplicated malaria in children. Here, we amplified the Fc region of IgG3 genes by polymerase chain reaction using heavy chain constant domains 2 and 3 specific primers, in a longitudinal study cohort of children aged 1 to 3 years (N=203) with multiple malaria episodes. We performed Sanger sequencing to identify SNPs and compared to the reference alleles of immunogenetics (IMGT) database. We identified that 78% of children in the cohort were either heterozygous (n=82, 40%) or homozygous (n=77, 38%) for G3m29 allotype. We also found a significant decrease in the total number of Plasmodium infections in children with G3m29 allotype compared to non-G3m29 allotype carriers (β= -1.736, 95% CI [-3.39, -0.079], p <0.05) via linear regression. This effect was most pronounced for effects of P. vivax infections. We are presently examining the relationship between allotypes and the levels of antimalarial antibodies and presence of anaemia in these children. Since polymorphisms arise in ethnic and isolated groups and persist in the population because of natural selection, the high prevalence of G3m29 allotype in Sepik region and its association with the number of malaria infections confirms that it is indeed under positive selection and might have a possible role in malaria immunity.

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A CONSERVED EPITOPE IN VAR2CSA IS TARGETED BY CROSS-REACTIVE ANTIBODIES ORIGINATING FROM PLASMODIUM VIVAX DUFFY BINDING PROTEIN

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In placental Plasmodium falciparum infection, VAR2CSA is expressed on the surface of infected erythrocytes (IEs) and mediates their sequestration in the placenta. Antibodies to VAR2CSA are largely restricted to women infected during pregnancy. These antibodies protect women in subsequent pregnancies but in an allele-specific manner. We discovered that VAR2CSA antibodies could also be elicited by P. vivax Duffy binding protein (PvDBP). We proposed that infection with P. vivax in non-pregnant individuals can generate antibodies that cross-react with VAR2CSA. To better understand the specificity of these antibodies, we took advantage of a mouse monoclonal antibody (3D10) raised against PvDBP that cross-reacts with VAR2CSA and identified the epitopes targeted by this antibody. We screened two peptide arrays that span the entire ectodomain of VAR2CSA from the FCR3 and NF54 alleles. Based on the array data, we designed a 34 amino acid synthetic peptide called CRP1 that maps to a highly conserved sequence in DBL3X and overlaps a previously defined CSA binding site. We showed by Isothermal Titration Calorimetry that this peptide can bind directly to CSA, and antibodies to CRP1 raised in rats significantly block the binding of IEs to CSA in vitro. In our Colombian cohorts of pregnant and non-pregnant individuals, at least 45% were seroreactive to CRP1. Most exciting, antibody reactivities to CRP1 and the 3D10 natural epitope in PvDBP region II, subdomain 1 (SD1), were strongly correlated in both cohorts. These findings suggest that antibodies arising from PvDBP may cross-react with VAR2CSA through the epitope in CRP1. These antibodies could contribute to protection against VAR2CSA by blocking a CSA binding site in DBL3X.

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THE PRESENCE OF DUFFY BINDING PROTEIN II PEPTIDES-SPECIFIC CD4+ T CELL RESPONSES IN PLASMODIUM VIVAX PATIENTS

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Plasmodium vivax Duffy Binding Protein region II (PvDBPII) is a leading vaccine candidate against blood-stage vivax malaria. Anti-PvDBPII antibodies potentially block parasite invasion by inhibition of erythrocyte binding. However, knowledge of PvDBPII-specific T cell responses is limited. Here, to assess immunogenicity of PvDBPII epitopes for induction of memory T cell responses in natural P. vivax infections, three cross-sectional

studies were conducted in recovered subjects. In silico analysis was used for potential T cell epitope prediction identified total 492 predicted peptides, which were further selected to obtain 29 peptides with lowest percentile rank. PBMCs from P. vivax subjects were stimulated with selected peptides and examined for cytokine production by ELISPOT or intracellular cytokine staining. From our analysis, six dominant T cell epitopes were identified. Peptide-driven T cell responses showed effector memory CD4+T cell phenotype, secreting both IFN-γ and TNF-α cytokines. Single amino acid substitutions in three T cell epitopes altered levels of IFN-γ memory T cell responses. Further analysis of antibody response to PvDBPII in individuals enrolled for detection of PvDBPII-specific T cell responses showed that 27.8% (5/18) displayed both IFN-γ T cell and antibody response, while 66.7% (12/18) exhibited only IFN-γ T cell response. Altogether, these findings demonstrate the response of CD4+ T cells and antibody to PvDBPII in natural infection. The knowledge of antigenicity could facilitate development of an efficacious vivax malaria vaccine.

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DYNAMICS OF NEUTROPHILS ACTIVITIES ACCORDING TO MALARIA INFECTION STATUS

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Neutrophils are the highest population in human leucocytes. They are considered to be the front-line fighters of the immune system against any invading pathogens including malaria parasites. Over the recent years, more insight has been gained from their role in inflammation. In addition to their phagocytizing property, it has now been admitted that activated neutrophils produce variety of pro-inflammatory cytokines and surface molecules. Recent technology advancement allows haematology analysers to go beyond the simple counting of neutrophils. Their activation status would it be their metabolic activity (cytokines production) represented by their reactivity intensity (Neut-RI) as well as their density or complexity (phagocytosis), represented by the cell's granularity (Neut-GI) can be differentiated. To elucidate that question, we assessed the neutrophils activation status in healthy, asymptomatic and symptomatic malaria in children aged between 3 months to 14 years. Blood samples were collected for full blood count and malaria microscopy. Among the 902 participants recruited, the prevalence of asymptomatic malaria (AM) cases, no malaria (NM) and clinical malaria (CM) were respectively 42.57% (384/902), 38.47% (347/902) and 18.96% (171/902). Regarding the neutrophils metabolic activity, Neut-RI were significantly ($p<0.001$) higher in CM compared to both AM and NM as well as in AM compared to NM ($p<0.001$). For the phagocytizing activity, the Neut-GI were significantly ($p<0.001$) higher in CM compared to both AM and NM participants while the difference was not significant ($p=0.3$) between NM and AM groups. There was a significant positive correlation ($\rho=0.30$, $p=0.0001$) between the metabolic or cytokines production activity with malaria parasite density in clinical malaria (CM) while this was not the case for Neut-GI ($\rho=0.04$, $p=0.6$). The metabolic activity of neutrophils is enabled regardless of the symptomatic status of malaria, whereas their phagocytizing activity is primarily seen in symptomatic cases. Furthermore, the metabolic activity is positively correlated with parasite density in malaria clinical manifestations

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BRAIN SEQUESTERED M1-LIKE MACROPHAGES EXPRESS ABUNDANT LEVELS OF CD163 DURING EXPERIMENTAL CEREBRAL MALARIA IN MICE

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Brain sequestered macrophages are one of the mediators of the pathogenesis of experimental cerebral malaria in mice. Likewise, accumulation and sequestration of macrophages in the brain during human cerebral malaria has also been reported. Despite their prominent role in cerebral malaria, the macrophage population(s) involved in malaria pathogenic processes remain poorly defined. Macrophages polarize into proinflammatory classically activated M1 macrophages or anti-inflammatory alternatively activated M2 macrophages. We examined macrophage polarization by measuring the expression of M1 markers (CD80 and CD86) and M2 markers (CD163 and CD206) on brain sequestered CD11b+F4/80high macrophages during the cerebral phase of a Plasmodium berghei ANKA infection in mice. Flow cytometric analysis showed that 82% of brain sequestered macrophages coexpressed the M1 markers CD80 and CD86. However, the majority (93%) of these CD80+CD86+ brain sequestered macrophages also expressed CD163, a scavenger (mainly hemoglobin/haptoglobin) receptor and a known marker for immunosuppressive M2c macrophages. In contrast, a minority (7.3%) of CD80+CD86+ brain sequestered macrophages expressed CD206, the mannose receptor and a known marker for immunomodulatory M2a macrophages. Our results suggest that brain sequestered macrophages may have an intermediate phenotype with mixed M1 and M2 features and CD163 may function to diminish the inflammatory response of M1-like (CD80+CD86+) brain sequestered macrophages because of its ability to produce anti-inflammatory heme metabolites. Lastly, due to exclusive expression on the monocytic lineage and abundant expression on macrophages at sites of inflammation, CD163 is currently being assessed as a target of immunotherapy for cancer and autoimmunity and also warrants consideration as a target of adjunctive therapy for cerebral malaria.

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IMPACT OF PLASMODIUM FALCIPARUM MALARIA ON SARS-COV-2 ANTIBODY RESPONSES IN KENYA AND BURKINA FASO (MALCOV)

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To investigate the impact of malaria co-infection on serological responses to SARS-CoV-2, we enrolled a cohort of 708 COVID-19 patients in Kenya and Burkina Faso, 139 (20%) of whom also had malaria. Median age was 33 years (IQR 24, 46), 10% were under age 15. We measured IgG antibody response against SARS-CoV-2 nucleoprotein (NP) and receptor binding domain (RBD) on days 1, 3, 7, 14, and 28 with a multiplex bead assay. Antibody responses with median fluorescence intensity (MFI) of ≥5000, >2000-5000, and ≤2000 were considered positive, intermediate and negative, respectively. At enrolment, 16.5% were positive for IgG against

both antigens simultaneously, 3% intermediate, 40% negative, and 40% had mixed responses to the different antigens. By Day 28, these were; 65% positive, 0.7% intermediate, 6% negative, and 29% mixed responses. Overall seropositivity at Day 28 was higher for NP than RBD (84% vs 67%) and lower in patients with recent or sub-patent (rapid diagnostic test-HRP2 positive, microscopy-negative) or patent malaria infection (microscopy-positive) than in malaria negative patients: 53%, 49% and 71%, respectively. The difference was mainly seen for RBD (NP: 75%, 77% and 88%; RBD: 53%, 49%, and 73%, respectively). There was no difference in the magnitude of antibody response in seropositive patients by malaria status. SARS-CoV-2 seroconversion occurred within one month in 35% of patients, regardless of the antigen. Persistent seropositivity, starting and remaining seropositive, was similar for RBD and NP (34% vs 29%), but persistent seronegativity was higher for RBD (15% vs 3.6%). Malaria co-infection had a limited impact on seroconversion. The largest observed difference was in the seroconversion to NP between patent malaria and malaria-negative patients: 45% vs 37%, respectively. Overall, antibody responses to SARS-CoV-2 RBD were lower than to NP. The effect of malaria on SARS-CoV-2 antibody response was dependent on antigen; there was no discernible effect on the response to NP, but responses to RBD were lower in individuals with patent or recent/sub-patent malaria.

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LOCAL GUT MICROBIOTA TOLEROGENIC HOMEOSTASIS NEGATIVELY IMPACTS ANTI-PLASMODIUM SYSTEMIC IMMUNITY

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Our laboratory researches the relationship between severe malaria and gut microbiome in mice. For that, we use Plasmodium yoelii and C57BL/6 mice from different vendors, which is sufficient for presenting diverse phenotypes in severity terms, recapitulated by introducing cecal or fecal material from the hyper-susceptible into the regular mouse, as well as onto germ-free mice. Although the causality is well established, the mechanisms are yet to be completed. Recently, we have shown that hypersusceptible mice present early contraction of germinal centers and consequently the lower quality of antibodies, leading to a parasitemia curve of 28 days instead of 14 and reaching up to 80% parasitemia instead of 20%. Tregs and T follicular regulatory cells are increased in the Peyer Patches and spleens of hyper-susceptible mice compared to the regular mice. Although both mice produced IL-10 on the serum and spleen on days 5-7 post-infection, the susceptible mouse failed to produce IFN-g, whereas the regular mice have a classic IFN-g/IL-10 ratio. To further evaluate the tolerogenic nature of the microbiota in the hypersusceptible mouse, we used sub-colitis doses of DSS, and they presented resistance to weight loss. In contrast, the regular mice showed weight loss and blood in their feces. Purified IgA-bound bacteria from the susceptible mice can recapitulate the phenotype in the regular mice. 16S sequencing of the IgA-bound bacteria presents an enrichment of invasive bacteria capable of causing septicemia in humans and rodents. These results provide insights into the impact of the gut microbiota on systemic immunity, an essential factor to consider in developing optimal malaria treatment and vaccines.

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ROLE OF IGE RESPONSE AGAINST MALARIA INFECTION IN CHILDREN UNDER FIVE YEAR OLD, LIVING IN MALARIA ENDEMIC RURAL AREA OF BURKINA FASO

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Despite these various measures, malaria remains one of the major health problems in the world, mainly due to the various forms of Plasmodium, as well as to the increase in resistance of vectors to insecticides and parasite to antimalarial drugs. The understanding of IgE responses dynamic, in children living in endemic area may help to optimize design interventions tools that could be used in malaria vaccine development. This study aimed to assess the relationship between IgE responses to Plasmodium falciparum and incidence of clinical malaria in children naturally exposed to malaria infection in Saponé (Burkina Faso) It was a secondary analysis of blood samples collected in 2007. Samples were collected during malaria low transmission season and at the peak of the high transmission season in malaria endemic area of Saponé, Burkina Faso. Sandwich ELISA was used to quantify IgE antibodies. Thick drop and blood smear were used for microscopic diagnosis of malaria. We combined levels of IgE to P. falciparum in plasma samples from 325 children with age, P. falciparum density, malaria transmission season and incidence. IgE quantification shows that IgE responses were higher among the parasitized children compared to non-parasitized. The means of IgE were respectively 1079.924 IU (CI95%= 943.8103 -1102.744) for parasitized children and 899.1933 IU (CI95% =718.0199 – 918.5753) for non-parasitized (p=0.045). In additional, the results show a statistically significant difference in IgE production during the two malaria transmission seasons. The mean IgE were respectively 993.25 IU (CI 95% =986.74- 1169.76) during low transmission and 854.37 IU (CI 95%=692.98-885.77) for high transmission season (p= 0.000134). IgE responses increased with age in both low and high malaria transmission seasons with respective p=0.00196 for low transmission and p=0.0531 for high transmission. In conclusion, IgE antibodies were produced in malaria infection. Its responses were associated with P. falciparum density, malaria transmission season and age. Key words: malaria, IgE, age, season of transmission and P. falciparum density.

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COMPARATIVE ANALYSIS OF PLASMODIUM FALCIPARUM TRANSCRIPTOME PROFILES REVEALS UPREGULATION OF HEAT SHOCK PROTEINS AND KINASES IN PEDIATRIC SEVERE MALARIAL ANEMIA

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The rapid emergence of resistance to anti-malarial therapy calls for the exploration of more anti-malarial drug targets to boost existing therapies. This can be achieved by harnessing vital pathways for the survival of Plasmodium parasite, the causative pathogen of malaria, in both the arthropod vectors and human host. Heat shock proteins (HSPs) and their co-chaperones are components of such vital pathways in P. falciparum parasites. The HSPs regulate the folding and stabilization of their client proteins that are essential for the parasites to survive temperature changes in the host during febrile illness. Among the client proteins of these HSPs are kinases, which have been shown to play roles in mediating the motility of sporozoites towards the liver cells and the subsequent attachment and entry into the hepatocytes. In addition, the egress of merozoites, infection of red blood cells and the adherence of the parasites in the endothelial vessels are equally dependent on kinases. To determine if parasite gene

expression levels of these proteins are associated with severe malarial anemia [SMA, hemoglobin, Hb, ≤6.0g/dL] pathogenesis, we examined P. falciparum transcriptome profiles derived from whole blood samples from two groups of pediatric malaria patients in Siaya County Referral Hospital, Kenya: SMA (n=20) and non-SMA (Hb>6.0g/dL, n=40). Our data reveal significant (P<0.05) upregulation of transcripts for the following P. falciparum HSPs and kinases in children with SMA: HSP110 (Log2foldChange=1.19), HSP90 (Log2foldChange=2.26), HSP60 (Log2foldChange=4.2), HSP40 (Log2foldChange=1.67), guanylate kinase (Log2foldChange=2.13), serine/threonine protein kinases (Log2foldChange=1.19), pyruvate kinase 2 (Log2foldChange=2.35), and phosphoglycerate kinase (Log2foldChange=1.58). Collectively, these findings provide novel information about the differential regulation of Plasmodium HSPs and kinases in SMA pathogenesis, and have the potential to facilitate the identification of new therapeutic targets, particularly for severe cases.

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PERIPHERAL BLOOD TRANSCRIPTOME PREDICTS ALTERED UBIQUITINATION PROCESS IN KENYAN CHILDREN WITH SEVERE MALARIAL ANEMIA

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Malaria remains one of the leading causes of childhood morbidity and mortality and manifests as severe malarial anemia [SMA, hemoglobin (Hb)<6.0g/dL] in western Kenya. Our recent studies revealed differential gene expression profiles of the host ubiquitination process in children with malarial anemia and temporal expression changes following ingestion of malarial pigment (hemozoin) by peripheral blood mononuclear cells. We extend these findings by determining the host transcript profiles of human ubiquitination process genes in children with non-SMA (Hb≥9.0g/dl, n=41) and SMA (n=25) presenting at Siaya County Referral Hospital in western Kenya. Total RNA was isolated from peripheral blood collected upon presentation at hospital for acute malaria prior to treatment. RNA sequencing was performed with coverage of >20 million high-quality mappable reads using the Illumina NovoSeq platform. Sequence reads were mapped to the human genome (GR-Ch38) using the STAR software. Differential gene expression analysis between the two clinical groups was performed using the EdgeR package. A MetaCoreTM network-building algorithm was used to identify direct functional interactions of significantly differentially expressed genes (DEGs). Results revealed 40 ubiquitination process DEGs (Padjust≤0.050) of which 26 were up-regulated and 14 were down-regulated in children with SMA. Specifically, 3 genes displayed a magnitude ≥1.5 fold-change (up-regulation) in SMA: UBE2H (Padj.=4.68E-19), RNF123 (Padj.=2.47E-10), and DDB1; (Padj.=9.73E-15). Functional analysis identified the βTrCP-MDM2-UBE2D2-UBE1L2-UBE2D1 network with UBE1L2 and MDM2 as central divergence and convergence hubs, respectively, both with 6 direct interactions. The top gene ontology process that emerged was Protein Ubiquitination (P=1.79e-60). Collectively, these results reveal DEGs in ubiquitination processes in children with SMA, suggesting that altered ubiquitination appears central to the pathogenesis of severe Plasmodium falciparum malaria.

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DIFFERENTIAL ANTIBODY RESPONSES TO DUAL-BINDING PFEMP1 ANTIGENS IN MALIAN CHILDREN WITH SEVERE MALARIA USING A CUSTOM PROTEIN MICROARRAY

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Plasmodium falciparum erythrocyte membrane protein-1 antigens (PfEMP1s) play an important role in virulence and immune evasion. Antibodies against PfEMP1s have been associated with protection from severe malaria, and distinct gaps in antibodies have been shown in children with cerebral malaria (CM) and severe malarial anemia (SMA) compared to uncomplicated malaria. We conducted a case-control study of severe malaria in Mali, West Africa, including cases of CM, SMA, and concurrent CM + SMA matched to uncomplicated malaria controls with and without a history of severe malaria. Controls were matched on age, sex, ethnicity, and date of presentation. We have recently found that cases of severe malaria had higher expression of PfEMP1s that bind both endothelial protein C receptor (EPCR) and intercellular adhesion molecule 1 (ICAM-1). We tested the hypothesis that children with severe malaria lack antibody responses to these dual-binding PfEMP1s. Sera was collected at the time of acute illness, during convalescence at day 21, and in the dry season after illness. We fabricated a custom protein microarray containing 158 PfEMP1 fragments from the 3D7 reference genome and 78 fragments from PfEMP1s associated with severe malaria. We selected PfEMP1 fragments containing consecutive domains from domain cassettes (DCs) previously associated with severe disease, including DCs 1, 4, 5, 8, 13, and 15 from the lab strains IT4, HB3, and Dd2 as well DCs 8 and 13 from clinical isolates collected from Malian children. Serological responses to these fragments were measured in 88 cases of severe malaria, including 57 that were matched to uncomplicated cases of malaria. Serological responses were also compared at the time of acute illness to day 21 of convalescence and to the dry season following infection. The results of this study could inform the design of vaccines and treatments against severe malaria.

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ASSOCIATION BETWEEN THE GUT MICROBIOME AND MALARIA INCIDENCE IN INFANTS LIVING IN MALAWI

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Studies in infants living in malaria-endemic regions have suggested a role for the gastrointestinal microbiome in establishment of Plasmodium infection, disease progression, and severity of infection. We hypothesize that malaria infection impacts the developing microbial community in infancy and, conversely, disruptions in the gastrointestinal microbiome may predispose infants to infections. Using 16S rRNA amplicon sequencing, we characterized the gastrointestinal microbiota in a longitudinal birth cohort in Malawi with active and passive surveillance for malaria infection and clinical disease from birth up to 2 years of age. Clinical malaria was defined as symptoms of malaria and a positive rapid diagnostic test (RDT), and malaria infection as any visit with P. falciparum DNA detected from dried blood spots by qPCR. Rectal swab samples were collected every 6 months, starting at 6 months of age. To identify whether the gastrointestinal

microbiota was associated with occurrence of clinical malaria, we compared the microbial species diversity, as measured by the Shannon Diversity Index (SDI), at 6 months of age in children who had subsequent malaria infections to those who did not. Among 60 children included in the study, 24 had clinical malaria between 6 and 12 months of age with a mean SDI of 2.69 (SD = 0.62) compared to a mean SDI of 2.85 (SD = 0.47) among those without malaria (p = 0.28). To account for the time between measurement of SDI and occurrence of malaria, survival analysis, adjusted for month of year and length-for-age Z score (a predictor of malaria) identified SDI at 6 months as associated with a non-significant decrease in the hazard of clinical malaria during the next six months (HR = 0.71, 95%CI = 0.33,1.54). Further analysis will identify temporal changes in the gastrointestinal microbiota associated with incidence and symptoms of malaria infection in this cohort. Our findings highlight the need to better understand the association between onset of malaria and microbial communities to develop novel strategies to reduce malaria susceptibility in infants.

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DEFINING THE PLASMODIUM PIPECOLIC ACID PATHWAY AND ROLE IN CEREBRAL MALARIA

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Cerebral malaria (CM) is a clinical syndrome and a leading cause of death from malaria, with a fatality rate between 15% to 30% in African children. CM occurs when Plasmodium falciparum infected erythrocytes accumulate within the cerebral microvasculature and cause vaso-occlusion, which is associated with high brain swelling, coma and seizures. The etiology of the coma is not well understood. Our prior studies demonstrated elevated blood pipecolic acid (PA) levels in children with CM and a corollary increase in PA in the brain lysate of mice during experimental cerebral malaria (ECM). PA is a non-proteinogenic amino acid metabolite of the lysine degradation pathway. PA has been associated with neuromodulation in humans and in animal models. Although Plasmodium generates PA, the parasite metabolic pathway is unknown. From this data, we will knock out pathway enzymes and measure pipecolic acid production to confirm the pathway model. Here, we will first confirm the production of PA in P. falciparum under in vitro growth conditions, using a quantitative liquid chromatography-mass spectrometry (LC-MS). Our second goal is to define lysine degradation pathway in P. falciparum using 13C labelled lysine in vitro to trace labeled pathway intermediates that gives rise to PA. Our preliminary data identified three 13-C labelled lysine pathway metabolites: (1) amino adipic semialdehyde. 2) piperideine-6-carboxylic acid and (3) pipecolic Acid. We mapped our model of lysine degradation pathway onto canonical KEGG pathway database which suggested that pyrroline-5-carboxylate reductase 1 (PF3D71357900) enzyme is involved in PA production in P. falciparum. To confirm the role of PF3D71357900 in PA production, we will use pargyline to inhibit PF3D71357900 in vitro. We will use the same labelling strategy to confirm this pathway model in vivo in P. berghei ANKA infected ECM model. This study informs our knockout strategy of pathway enzymes to disrupt PA production and examine the effect of PA on the neurological decline in ECM model.

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MALARIA- INTESTINAL PARASITES CO-INFECTION AMONG CHILDREN IN A LYMPHATIC FILARIASIS ENDEMIC REGION OF GHANA

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Malaria- intestinal parasites (IPs) co-infections are a major problem in tropical regions of the world including Ghana. This is mostly as a result of an overlap in their geographical distributions. Malaria and IPs are a major cause of morbidity in children, having severe consequences on their cognitive development and growth. This study was conducted to determine the prevalence of Malaria and IPs coinfections amongst children in the Ahanta West District of Ghana, a Lymphatic filariasis (LF) endemic region. The Study was done in the dry season where malaria transmission is expected to be low. Again, this region had ceased Mass drug administration for LF control for three years prior. The study utilized malaria rapid diagnostic tests (RDTs) such as NexTek, Bioline and First Response and microscopy to examine stool samples for IP. Out of 113 participants with a mean age of 12.10±2.3, 60 (53.1%) had malaria, 81 (71.7%) had IP, and 45 (39.8%) had malaria-intestinal parasite coinfection. Notably, 22.1% of participants had received malaria treatment three months prior to the study, and 66.4% had dewormed in the past three months. The overall prevalence of malaria, intestinal parasites and malaria-intestinal parasites coinfection were 60 (53.1%), 81 (71.7%) and 45 (39.8%), respectively. This high prevalence of asymptomatic malaria even during the dry season, may hinder current elimination strategies and drive malaria transmission. The impact of Malaria-IP coinfection is multifactorial, therefore, combatting parasitic infections simultaneously is essential to improve the health of these children.

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UNRAVELLING VAR COMPLEXITY: RELATIONSHIP BETWEEN DBLA TYPES AND VAR GENES IN PLASMODIUM FALCIPARUM

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The enormous diversity and complexity of var genes that diversify rapidly by recombination has led to the exclusion of assembly of these genes from major genome initiatives (e.g., Pf6). A scalable solution in epidemiological surveillance of var genes is to use a small 'tag' region encoding the immunogenic DBLα domain as a marker to estimate var diversity. As var genes diversify by recombination, it is not clear the extent to which the same tag can appear in multiple var genes. This relationship between marker and gene has not been investigated in natural populations. Analyses of in vitro recombination within and between var genes have suggested that this relationship would not be exclusive. Using a dataset of publicly-available assembled var sequences, we test this hypothesis by studying DBLα-var relationships for four study sites in four countries: Pursat (Cambodia) and Mae Sot (Thailand), representing low malaria transmission, and Navrongo (Ghana) and Chikwawa (Malawi), representing high malaria transmission. In all study sites, DBLα-var relationships were shown to be predominantly 1-to-1, followed by a second largest proportion of 1-to-2 DBLα-var relationships. This finding indicates that DBLα tags can be used to estimate not just DBLα diversity but var gene diversity when applied in a local endemic area. Epidemiological applications of this result are discussed.

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TRANSCRIPTOME ANALYSIS OF BLOOD-STAGE PLASMODIUM FALCIPARUM REVEALS UP-REGULATED PFHSP70 AND HISTONE TRANSCRIPTS IN SEVERE MALARIAL ANEMIA

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Malaria-related morbidity and mortality remain as significant health burdens in sub-Saharan Africa, accounting for 95% of 247 million cases and 96% of 619,000 global deaths. In Siaya, western Kenya, a holoendemic Plasmodium falciparum transmission region, severe malaria in children <5 years primarily manifests as severe malaria anemia [SMA, hemoglobin (Hb)≤6.0 g/dL]. Although the P. falciparum genome contains multigene families that influence parasite survival, it is largely unclear how differential expression of parasite genes influence human malaria severity. As such, the entire P. falciparum transcriptome was captured in whole blood prior to antimalarial treatment in children (3-36 months) who presented at hospital with non-SMA (Hb>6.0 g/dL, n=40) or SMA (n=20). Next-generation sequencing was performed at a depth of >20 million high-quality mappable reads using the Illumina NovoSeq platform. Reads were mapped to a Kenyan isolate reference genome (pfKE01) using the HTSeq platform, revealing ~3200 distinct P. falciparum transcripts. Differential expression analysis revealed 688 significantly differentially expressed genes in SMA (P<0.05) for which 3 heat shock protein 70 genes and 3 histone genes were upregulated: PfKE01_110038600 (PfHSP70-3, Log2foldChange=1.01), PfKE01_080037100 (Log2foldChange=0.51), PfKE01_090022300 (Log2foldChange=0.70), PfKE01_060023900 (histone PfH2A, Log2foldChange=1.51), PfKE01_110009800 (PfH2B, Log2foldChange=1.40), and PfKE01_060016500 (PfH3, Log2foldChange=1.97). Previous studies illustrate that the PfHSP70 family facilitates parasite proteostasis and protection from cytotoxic drugs, thus mediating parasite survival and potential pathogenesis. The P. falciparum histone family regulates parasite gene expression associated with its developmental stages, with the release of parasite histones into circulation stimulating pro-inflammatory mediators known to influence the pathogenesis of SMA pathogenesis. Collectively, these results support the PfHSP70 and PfHistone families as targets for small molecule inhibitors for novel therapeutic development.

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SINGLE CELL SEQUENCING OF BRAIN SEQUESTERED CD8+ T CELLS DURING EXPERIMENTAL CEREBRAL MALARIA

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Brain-sequestered CD8+ T cells play a prominent role in the pathogenesis of experimental cerebral malaria (ECM) in mice. A recent study has also shown that CD8+ T cells target the cerebrovasculature in children with cerebral malaria caused by Plasmodium falciparum. CD8+ T cells accumulate in the brain during the effector phase of a P. berghei ANKA (Pb-A) infection in mice and promote pathogenesis by inducing apoptosis of endothelial cells of the blood brain barrier. However, the molecular events associated with this CD8+ T cell-mediated pathogenesis remain poorly understood. To better characterize how brain-sequestered CD8+ T cells exert their pathogenic effect, we performed single cell sequencing of the transcriptome of CD8+ T cells isolated from perfused brain tissue of Pb-A infected moribund and non-moribund C57BL/6 mice and uninfected C57BL/6 mice. A single cell whole transcriptome library was prepared from RNA isolated from approximately 50,000 brain sequestered leukocytes that was also labeled with cell (TCRβ, CD3ε, and CD8α) and sample (mouse) specific antibody oligonucleotide conjugates. Approximately 2-2.5 billion clusters were then paired-end sequenced on a NovaSeq S4 PE100 flow cell and bioinformatic analysis was subsequently performed. Genes transcriptionally altered in brain sequestered CD8+ T cells and bioinformatic analyses-based biological pathways associated with the effector phase of ECM will be presented.

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IMPORTANCE OF INSULIN-LIKE GROWTH FACTOR : IGF-1 IN PLASMODIUM VIVAX MALARIA

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Malaria is a public health problem that causes millions of deaths a year. Plasmodium vivax is the most widely distributed etiological agent of malaria in the world. Malaria has been shown to have some relationship to insulin-like growth factor 1: IGF-1 is an important indicator of malnutrition, and acts as an acute phase reactant in infections and inflammation. The objective of this study was to evaluate the plasma concentration of IGF-1 and its relationship with fibrinogen, C-reactive protein CRP, body mass index, and anemia in patients with malaria caused by Plasmodium vivax. 23 individuals with malaria and 20 healthy individuals were included. This research was descriptive and analytical cross-sectional. Study zone: Tierralta, Córdoba, Colombia in a period of six months in the year 2022. Plasma fibrinogen concentration and IGF-1 were determined by ELISA and C-reactive protein was determined by latex agglutination in microtiter plates, using Anthro and Anthro Plus software, individuals were characterized according to height and body mass index according to age. The hemoglobin concentration was determined from automated blood table 7 of IV generation. A thick smear was made to calculate the density of parasites. The fibrinogen concentration increased significantly in patients with malaria (324.03± 59.87 mg/dl, compared to the control group 224.74± 34.88 mg/dl. The CRP increased significantly in patients infected with malaria 21.52± 35.59 mg/l compared to the control 2.43± 0.97 mg/l and the concentration of IGF-1 decreased 45.01± 0.53 significantly in malaria patients, who had a low body mass index, compared to controls. In conclusion, this study suggests that in patients with P. vivax malaria, a greater production of fibrinogen, C-reactive protein is induced, which promotes a decrease in IGF-1, associated with malnutrition and anemia.

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NON-FALCIPARUM SPECIES INFECTIONS AND MALARIA SEVERITY: PRELIMINARY FINDINGS IN HIGH TRANSMISSION SETTINGS IN SENEGAL

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In sub-Saharan Africa, non-falciparum species circulate at low prevalence and density of parasitemia, predominantly in co-infections with the dominant malaria Plasmodium falciparum species. The problematic diagnosis of non-falciparum parasites remains a challenge to accurately estimating their prevalence, contribution to the disease's burden, and potential role in severe malaria. This study assessed the contribution of non-falciparum parasites to malaria severity in Senegal. The study analyzed blood samples of 273 malaria patients (48,4% severe and 51,6% uncomplicated cases) enrolled in 2015, 2017 and 2020 from health facilities in Kolda, Tambacounda and

Kedougou, the three regions of Senegal with the highest malaria incidence. The Plasmodium positivity and Plasmodium species specific composition were determined by molecular methods. R Software was used for statistical analysis of non-falciparum species distribution concerning patients' demographics (age, sex), clinical malaria status (uncomplicated and severe), and the odds ratios of the relative risk of the disease severity associated with non-falciparum species infections. Non-falciparum species i.e P. ovale, P. vivax and P. malariae were retrieved at proportions of 37.36%, 28.20% and 1.83%, respectively, in tested samples. Among the non-falciparum species, P. ovale and P. vivax accounted for 6% of unique infections. Severe and uncomplicated cases are evenly distributed in age groups and gender. P. ovale infection was associated with a significant (OR=0,12) three-fold reduction of severe malaria, while P. vivax in co-infection increased, though non-significant (OR>1), the risk of malaria severity. These preliminary findings support a role of non-falciparum parasites species in the burden of malaria and potentially the severity of the disease in Senegal, and call for immediate attention from the control programs to sustain the limited success gained to date concerning malaria control in the areas.

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ACCEPTABILITY OF TECHNOLOGICAL INNOVATION IN MALARIA VECTOR CONTROL IN MALI: THE CASE OF ATTRACTIVE TARGETED SUGAR BAIT IN THE HEALTH DISTRICT OF KATI MALI

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Malaria is the leading cause of morbidity and mortality in Mali and it's among the ten countries with the highest number of malaria cases and deaths, accounting for 3% of cases and deaths worldwide and 6% of cases in West Africa. In Mali Malaria is endemic, where about 90% of the population is concentrated. Given the increase in resistance to the current generation of insecticides and the behavioral plasticity of the vectors that result in continued transmission of malaria despite the use of insecticide-treated nets (ITNs) or indoor residual spraying. Insecticides with new modes of action are needed, hence the need for Attractive Targeted Sugar Bait (ATSB). This qualitative research explores and assesses the perceptions and community acceptability on ATSB in Mali. Focus group discussions (12) and in-depth interviews (10) were conducted, and a mapping of distrust was done. Data were analyzed using Sphinx software. The results provided an understanding of the factors influencing the supply and community acceptability of ATSBs. Our data also show that ATSBs are perceived in different ways. On the one hand, they are an alternative to vector control. On the other hand, they are subject to mistrust regarding possible long-term environmental risks. Interpersonal communication with community authorities is a guarantee of the acceptability of ATSBs. Some ideas and strategies have been developed for the introduction of ATSBs on a sub-regional scale. The use of ATSBs offers hope in the fight against malaria in malaria-endemic areas. As with any innovation, its full and complete adoption requires a period of appropriation by the users.

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EFFECT OF SEASONAL MALARIA CHEMOPREVENTION ON ASEXUAL PLASMODIUM FALCIPARUM INFECTION IN CHILDREN AGED 5 TO 14 YEARS IN DANGASSA, MALI

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The effectiveness of seasonal malaria chemoprevention (SMC) in reducing malaria-related mortality and morbidity has been demonstrated through several studies. However, its effect on parasite clearance in asymptomatic carriers needs more investigation. This study aimed to determine the effect of SMC on the prevalence of Plasmodium falciparum infection. A secondary analysis was performed using the data from an open randomized study conducted in children 5-14 years in Dangassa to estimate the effect of an additional fifth round to the current SMC regimen (four rounds). A monthly follow up was done from July to December to collect data on parasitemia using smear microscopy in both intervention and control groups. Binomial generalized linear mixed regression was performed to estimate the reduction in the prevalence of P. falciparum infection in children under SMC adjusted on the age groups and the use of long-lasting insecticidal nets (LLINs) with a threshold at 5%. At baseline, the prevalence of P. falciparum infection was similar between the two groups (12.5% for the control group vs 13.4% for the intervention group, p=0.942). After adjusting for age groups and long-lasting insecticidal nets (LLINs) usage, a reduction of 60% in the prevalence of P. falciparum infection was observed in the intervention group (OR = 0.40, 95%CI [0.30 to 0.54], p<0.0001) compared to control group. Stratified by age groups, the same trend was observed with 58% and 61% reduction in prevalence, respectively in children aged 5 – 9 years (OR = 0.42, 95%CI [0.28 to 0.63], p<0.0001) and 10 – 14 years (OR = 0.39, 95%CI [0.26 to 0.58], p<0.0001). Our finding demonstrated the effectiveness of SMC in the reduction of asymptomatic parasitemia carriage among older children in Dangassa. Nevertheless, a large-scale study is warranted to assess the contribution of SMC in malaria transmission.

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FACTORS AFFECTING PREGNANT WOMEN'S ADHERENCE TO INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN THE NANORO HEALTH DISTRICT

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Malaria in pregnancy is still a public health issue despite progresses in case management and prevention. The later includes use of long-lasting insecticide treated nets (LLINs) together with administration of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP). The national malaria control program (NMCP) has recommended at least 3 doses of IPTp-SP but available information suggests that only 30% of eligible women received this in 2016 despite observed high levels of antenatal care (ANC) attendance. Importantly, adherence to IPTp-SP may be affected by perceptions, acceptability and contextual factors that need to be understood and thus improve the effectiveness of health interventions. Therefore, we conducted a qualitative study to explore the socio-cultural factors limiting pregnant women's adherence to IPTp-SP in Nanoro, Burkina Faso. We have carried out 43 individual interviews and 4 focus groups with 84 people, direct observations between August 2021 to June 2022, targeting pregnant women, husbands, mothers in-low, traditional healers, community health workers and health workers. Participants were selected purposively. Interviews were audio-recorded and transcribed. Data were coded and thematic analysis was conducted using Nvivo 12. The results indicate that although pregnant women have popular beliefs about the causes of malaria, they still rely on medical treatment and do not use traditional care. Adherence to IPTp-SP is compromised by pregnant women's late initiation of ANC visits because they believe that pregnancy does not need biomedical care, as long as they are healthy, they do not need care. Also, the lack of awareness of IPTp-SP, the low perception of the seriousness of malaria during pregnancy by pregnant women, the difficulties related to the supervised intake and the stock-outs of SP are other reasons that explain the low adherence of pregnant women to IPTp-SP. To improve

IPT-SP coverage, awareness for early initiation of ANC should be increased and the conditions of the health facilities offer in terms of maternal health should be improved.

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LARGER FAMILIES ARE LESS LIKELY TO ACHIEVE UNIVERSAL LONG-LASTING INSECTICIDAL NETS COVERAGE IN ETHIOPIA

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In a population with a high risk of malaria infection, using long-lasting insecticidal nets (LLIN) is an essential malaria prevention method. Ethiopia has been distributing LLIN for free. However, ensuring sufficient access and use of LLINs requires close monitoring and evaluation. Hence, this study assessed ownership of LLINs in the Sidama Region in Southern Ethiopia. A community-based cross-sectional study was conducted in February and March 2023. Multi-stage cluster sampling was used to select representative households. We estimated LLIN coverage in terms of WHO's universal LLIN coverage (at least one LLIN for every two people) and national LLIN targets, which aim at 100% LLIN coverage of the population at risk with one LLIN per sleeping space. In addition, the LLIN distribution depends on the family size, with one LLIN for a family size of 1-2, two LLINs for a family size of 3-5, three for 6-7 and four for eight or more family members. We did not assess the quality of the LLIN. A total of 1647 households were included in the study. Most households were led by males (89%), farmers (63%) and persons who were unable to read and write (55%). The ownership of at least one LLIN per household was 85% (95% CI 83.5 - 86.9%; 1405 of 1647 households). About two-thirds (66%) of households had at least one LLIN for every sleeping space, and about half (49%) had the required LLIN per family size. Only 36% of households had universal access to LLIN. Moreover, only 33% of households with children less than under-five years of age or pregnant women had universal access to LLIN. Homes with larger families (Adjusted Odds Ratio (AOR): 8.14 [6.26, 10.58]) and female-headed households (AOR: 3.08 [1.47, 6.43]) were more likely to have unmet universal LLINs coverage. We conclude that the LLIN coverage was low compared to WHO-recommended universal LLIN coverage and national LLIN targets per sleeping space and family size. The National LLINs distribution standard should consider additional LLIN for larger families.

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CAREGIVER KNOWLEDGE AND CONFIDENCE IN SMC EFFECTIVENESS IN NIGERIA

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In 2012, the World Health Organization (WHO) issued a policy recommendation for seasonal malaria chemoprevention (SMC) as an intervention against Plasmodium falciparum malaria. It is aimed to protect children by clearing existing infections and preventing malaria infections during the season of greatest malaria risk. Caregivers are provided with basic information on the purpose of SMC, eligibility of targeted children, importance of SMC doses, duration of treatment and timing of the intervention. Caregivers with more information are likely to adopt positive behavioral change attitudes. Overall confidence in SMC was measured as caregivers' whose children received day1 dose of Sulphadoxine Pyrimethamine+Amodiaquine (SPAQ), importance of day 2/3 doses of Amodiaquine (AQ), what to do if their children experience any adverse drug events, and caregivers who reported confidence in the efficiency of SMC. We assessed knowledge of caregiver against their overall confidence in SMC. Data was extracted from 2022 end-of-round SMC coverage survey and analyzed data of 11,880 caregivers - child peer of sample from nine SMC implementing states of Nigeria. Mixed-effects multivariable logistic regression models were fitted to explore the association between SMC knowledge and caregivers' confidence in SMC. The proportion of caregivers with overall knowledge of the four SMC knowledge indicators assessed was low (56.6%) however, there were high odds of confidence of SMC among caregivers with knowledge of the purpose of SMC (OR: 1.7, 95% CI: 1.3 - 2.4, p<0.001), SMC age eligibility (OR: 1.4, 95% CI: 1.1 - 1.9, p=0.013), importance of receiving day 2/3 doses (OR: 5.0, 95% CI: 3.7 - 6.7, p<0.001), and what to do if their children experience any adverse drug event (OR: 2.1, 95% CI: 1.7 - 2.5, p<0.001). The study shows direct relationship between SMC knowledge and caregiver's confidence in SMC. Therefore, there is need to review SMC messaging either through orientation or direct social behavior change (SBC) intervention to ensure the right information and knowledge permeates the entire community space. This will have a positive influence on effective delivery of SMC.

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UTILIZATION OF LONG-LASTING INSECTICIDAL NETS AT HOUSEHOLD AND INDIVIDUAL LEVELS IN SIDAMA REGION, SOUTHERN ETHIOPIA

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Malaria is an increasing public health problem in Ethiopia, sometimes occurring as epidemics. The utilization of long-lasting insecticidal nets (LLIN) is an essential malaria prevention tool, and there is limited information on its utilization in the Sidama Region in Southern Ethiopia. This study aims to assess LLIN use in rural Sidama. Using multi-stage cluster sampling, a cross-sectional study was conducted in two districts in February and March 2023, including 1,647 households with 8,054 individuals. LLIN utilization was measured by the self-report of sleeping under LLINs the day preceding the survey and was estimated at household and individual levels. Descriptive statistics and binary logistic regression were performed. The mean age of house members was 23 years; half of the participants were males, and 47% could not read and write. Of 1647 households, 85% (95% CI 83 - 87%) owned at least one LLIN, from which 78% (95% CI 76 - 80%) used at least one LLIN the preceding night. However, the individual-level LLIN use showed that only 31% slept under a bed net the previous day. Females (Adjusted Odds Ratio (AOR): 1.5 (1.4, 1.7)) and members from large families (AOR: 1.3; 95% CI 1.1, 1.4) were more likely not to sleep under LLIN. Meanwhile, literate household members (AOR 1.2; 95% CI 1.1, 1.4) were likelier to sleep under bed nets than those who couldn't read and write. Our study shows that the proportion of the population in a malaria-endemic area who slept under LLIN the previous night was far below what is required to control malaria. Furthermore, our study shows that measuring individual LLIN use may give more appropriate information for control than using the household as a unit, as often recommended.

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IMPACT OF SCALING UP SEASONAL MALARIA CHEMOPREVENTION ON COVERAGE AND QUALITY OF IMPLEMENTATION IN KARAMOJA REGION, UGANDA

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Uganda scaled-up seasonal malaria chemoprevention (SMC) using sulfadoxine-pyrimethamine and amodiaquine (SPAQ) to eight districts in Karamoja region, where malaria transmission is highly seasonal targeting 209,405 children under five. This followed a pilot in 2021 that targeted 73,464 children in two districts. Delivery was through a door-to-door approach by village health teams (VHTs), supervised by health workers. In three districts, four cycles were delivered because of delays in finalizing funding arrangements. In five districts, five cycles were implemented in line

with the duration of peak transmission season. This study documented the impact of SMC scale-up on intervention fidelity. We assessed coverage, quality of delivery and beneficiary perceptions through end of round household surveys conducted before and after scale-up. A total of 1863 SMC eligible households were surveyed in 2021 and 1404 in 2022. Review of SMC implementation and adaptation processes and documents were conducted. In 2022, full coverage (proportion of eligible children who received all delivered cycles and the complete 3-day treatment course) was 78.2 % (95%CI: 76.0 - 80.3) across eight districts. Among eligible children who received day 1 SPAQ, 93.1% (95%CI: 91.6 - 94.4) received directly observed treatment (DOT). These were comparable to 2021 when 87.2% (95%CI: 85.2 - 89.1) of eligible children received all five cycles of SPAQ in the two districts, and 97.4% (95%CI: 96.4 - 98.3) received day 1 SPAQ by DOT. Similar to 2021, 98.0% of caregivers reported having heard of SMC in 2022, with VHTs a predominant source of information. Majority (> 90.0%) of caregivers knew the purpose, eligibility criteria, justification for giving SPAQ only to children under five, importance of amodiaquine doses on days 2 and 3, and how to respond when a child experienced an adverse event. Overall, 99.1% and 98.2% of respondents in 2021 and 2022 respectively, felt the program was effective in malaria control. SMC was successfully scaled-up in Karamoja region, increasing its access to beneficiaries at high coverage and quality, while adhering to the adapted implementation model.

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STAKEHOLDER PERSPECTIVES ON INCORPORATING A NEW VECTOR CONTROL TOOL INTO THE KENYA NATIONAL MALARIA VECTOR CONTROL POLICY

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New vector control tools are needed to reduce malaria transmission. It is essential to ensure the new tools reach the market as soon as possible and are accompanied by evidence-based policy recommendations. To complement a trial of the efficacy of a spatial repellent for malaria control, key informant interviews with national malaria control policy stakeholders were conducted. The national policy stakeholders were individuals or organisations that make and/or influence vector control policy and had first-hand knowledge about review, licensing, adoption, and distribution of vector control products. The interviews investigated the factors influencing policy adoption and the role that actors and evidence play in the policymaking process, to draw lessons to help accelerate the uptake of new vector control tools. The interviews were audio-recorded, transcribed, and analysed thematically. Stakeholders outlined the strengths and limitations of existing core interventions comprising long-lasting insecticidal nets, indoor residual spraying, and larval source management. The roles of various individuals and institutions in the processes of formulating vector control policies were also revealed. Upon submission of evidence of efficacy and safety of a proposed new tool, national experts and stakeholders hold discussions and critically analyse its strengths, weaknesses, opportunities, and threats. Additional considerations such as cost, acceptability, usability and complementarity to existing mosquito vector control tools, advocacy and buy in at various decision-making levels and source of funding are also key aspects influencing the adoption and integration of new vector control tools. This study provides insights into the nature of potential problems and solutions for adopting and integrating a new mosquito vector control tool into the national malaria control sphere.

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FACTORS ASSOCIATED WITH INSECTICIDE TREATED BED NET ACCESS AND USE IN SUSSUNDENGA, MOZAMBIQUE

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Insecticide treated bednets (ITNs) are the key malaria prevention tool used in endemic areas. However, there are several barriers to access and use of ITNs in many countries and particularly in rural areas. Mozambique has the fourth highest prevalence of P. falciparum malaria worldwide. Malaria incidence and prevalence follow a gradient of lowest in the south to highest in the north. Manica Province is located in the center of the country and has historically high malaria prevalence with seasonal peaks in incidence following the rainy season. The use of ITNs is the primary malaria prevention method available in this area. The aim of our study was to quantify access and use of ITNs in Sussundenga village, Manica Provice and determine factors associated with both access and use. Ninety-eight (98) households with 302 residents completed the study. The overall malaria prevalence by rapid diagnostic test (RDT) was 31%. Sixty-five percent (65%) of participants reported sleeping under an ITN the previous night. The primary reason given for not sleeping under an ITN was not having any in the household, or not having sufficient numbers for all of the residents of the household. ITN use the previous night was significantly associated with decreased risk of malaria infection measured by rapid diagnostic test (RDT). We constructed several generalized estimating equation (GEE) logistic regression models to quantify individual level and household level factors associated with access and ownership of ITNs, and use of an ITN the previous night. These finding are relevant for informing malaria control campaigns in the area to increase ITN ownership and usage. In 2020 this area was target with a large-scale ITN distribution, aiming to achieve universal coverage in Manica Province. The findings of this study can be used to improve use by identifying factors associated with regular use of ITNs.

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PREDICTING MALARIA INFECTION AND ANEMIA IN PREGNANCY AT FIRST ANTENATAL CARE ATTENDANCE

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Malaria in pregnancy is responsible for adverse effects both on mothers and their offspring's. To tackle these adverse events, WHO recommends the promotion and use of long-lasting insecticide treated nets (LLINs) together with administration of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP) and appropriate case management through prompt detection and effective management. At least, 4 antenatal care visits (ANCs) and 3 doses of IPT-SP are recommended before delivery. Unfortunately, all these interventions are delivered through the antenatal care (ANC) channels. Knowing the characteristics of pregnant women attending ANC for the first time can help to customize interventions towards this specific group. We therefore, sought to determine the prevalence of malaria infection in pregnant women attending their first ANC visit and the risk factors associated. We conducted a cross sectional survey in 4 health centers of the district of Nanoro and all pregnant women attending their first ANC visit were recruited. Blood samples were collected to assess malaria infection using microscopy as gold standard and haemoglobin level using

HemoCue®. From the survey, less than 14% and less that 7% of pregnant women attended ANCs during the first and third trimester respectively. The prevalence of malaria infection and anemia were respectively 28.2% (n=118/418) and 70% (n=253/416). Being a primigravidae (Adj. OR=3, 95% CI:1.65-5.40) and at the first trimester of pregnancy (Adj. OR=0.28, 95% CI:0.08-0.91) were associated with higher risk of malaria infection. In addition, being primigravidae (Adj. OR=2.00, 95% CI:0.88-4.76), in the second trimester of pregnancy (Adj. OR=1.38, 95% CI:0.55-3.38) and malaria infection (Adj. OR=2.07, 95% CI:1.17-3.73) were strongly associated with the anemia. Socio-anthropologic studies with the objective to understand low and late ANC attendance should be performed and intervention strategies developed accordingly. Scale-up of these interventions is a key entry point for the effectivity of malaria prevention and control in pregnancy.

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IMPACT OF INDOOR RESIDUAL SPRAYING AT THE END OF THE RAINY SEASON IN A HOLOENDEMIC MALARIA TRANSMISSION SETTING IN NORTHERN ZAMBIA: A DEMONSTRATION PROJECT

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Nchelenge District in northern Zambia experiences holoendemic, perennial malaria transmission. Pre-rainy season indoor residual spraying (IRS) has been deployed annually since 2008 with distribution of insecticide-treated nets, yet Plasmodium falciparum prevalence by microscopy remains above 30%. Anopheles funestus is the most abundant vector and peaks in the dry season (May-July). We conducted a pilot trial to assess the effect of adding IRS at the end of the rainy season to the current IRS program on parasite prevalence. Four clusters of households were selected and two were sprayed with clothianidin pre- and post-rainy season; the remaining two clusters were sprayed only pre-rainy season. A total of 401 residents among 65 households were surveyed monthly from March to September. The primary outcome, measured monthly, was the presence of a parasite-positive episode by microscopy. Multilevel logistic regression with adjustment for socio-demographic and geographic variables found no significant difference in the odds of a microscopy positive episode comparing sprayed and unsprayed clusters pre- and post-rainy season spray (adjusted ROR 0.11, 95% CI: 0.01-1.19, p = 0.07). This same model found no significant difference in odds comparing pre- and post-spray at the end of the rainy season (adjusted OR 5.5, 95% CI: 0.57-52.6, p = 0.14). A time to infection analysis using a log-rank test and a Nelson-Aalen Cox proportional hazards model with baseline risk stratification found a statistically significant difference in hazards of a microscopy positive event across the sprayed and unsprayed clusters (log-rank test p<1x10-5). While the second round of IRS reduced hazard rates, we did not find a measurable impact on overall parasite prevalence. Given the limitations of this analysis and the p-value associated with relative odds of parasite prevalence comparing sprayed and unsprayed clusters pre- and post-spray (p=0.07), further investigation is warranted. Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.

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FREE-LISTING OF MOSQUITO CONTROL STRATEGIES IN BUSIA COUNTY, WESTERN KENYA

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Additional mosquito vector control interventions are needed, and their potential effectiveness will be improved if user perceptions and practices regarding existing strategies are integrated into their design. To complement a trial of the efficacy of a spatial repellent for malaria control, listing of existing mosquito control products and behaviours was included. The free-lists allowed inferences to be made about the cultural salience of the strategies in the participants' mosquito control domain. Listed products and behaviours will be ranked to help the project understand perceptions of existing mosquito prevention measures. The data obtained will inform the potential and strategies for introducing the spatial repellent at scale. Using a free-listing approach, 61 participants were asked to name all the mosquito control strategies they know. The individual lists were entered into Excel to generate frequencies for each mentioned product. The generated list will be a basis for further inquiry about the items such as when, where, why, how, and by whom these items are used in a ranking exercise. In all, 317 products/behaviours were coded into 47 categories. Participants often mentioned insecticide treated bed nets, mosquito coils, draining stagnant water, creating smoke, and clearing the compound. Other less commonly mentioned mosquito control strategies included spraying insecticide and closing doors/windows early, applying mosquito repellent, and clearing the compound of garbage. The most frequently mentioned strategies were eleven, each mentioned by more than 10% of the sample. Because the spatial repellent is a supplementary tool to existing mosquito control strategies, its introduction must be carried out in a way that optimizes the use of the recommended strategies. The data gathered from the free-listing shows the more widely used strategies and ranking will provide specific insights on characteristics that make those strategies popular. This information will be considered for designing and large-scale distribution of the spatial repellent.

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FEASIBILITY AND ACCEPTABILITY OF GROUP ANTENATAL CARE FOR MATERNAL HEALTH CARE PROVIDERS AND SUPERVISORS IN RURAL HEALTH CENTERS IN BENIN

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Group antenatal care (GANC) is a model in which prenatal counseling and services are delivered monthly to groups of 8-15 pregnant women of the same gestational age starting in second trimester. This allows women to learn while building supportive social networks. GANC can increase uptake of key pregnancy interventions. We examined factors affecting the feasibility and acceptability of GANC for providers and their supervisors in rural Benin, in the context of a study assessing the effect of implementing GANC on uptake of antenatal care under routine programmatic conditions. Six health zone officials and 2-3 ANC providers (midwives, health aides) in each of 20 facilities with ~20-130 new ANC clients/month were trained on

GANC in 2021. Nine months after implementation began, semi-structured interviews (45-90 minutes long) were conducted with purposively selected supervisory health staff (7) and GANC providers (14) from 6 health centers selected to represent both low and high performing facilities with regard to GANC implementation. Data were analyzed through qualitative framework analysis. All participants expressed support for continued implementation and eventual scale-up of GANC. Providers appreciated the opportunity to build closer relationships with patients. They found GANC implementation challenging, particularly scheduling and reminding pregnant women about meetings, starting meetings on time, and accommodating late arrivals. Staffing shortages resulted in GANC meetings being disrupted so facilitators could attend to labor and delivery activities. Supervisors contended that additional supervisory personnel were required to support implementation, especially where there were shortages of qualified providers. Some facilities might need changes to physical layout, to make space for meetings. Providers appreciated the GANC model. Having an adequate number of providers is critical to implementation. Feasibility depends on identifying efficient GANC reminder systems, shortening meetings, and ensuring adequate personnel to support both meeting facilitation and care for emergencies and labor and delivery.

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INFLUENCE OF SEASONAL MALARIA CHEMOPREVENTION ON THE PREVALENCE OF MALARIA INFECTION, PLASMODIUM FALCIPARUM GENETIC DIVERSITY AND RESISTANCE PROFILE IN CHILDREN LIVING IN RURAL AREAS OF BURKINA FASO

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Seasonal Malaria Chemoprevention (SMC) is recommended since 2013 by WHO for the preventive treatment of malaria with sulfadoxine pyrimethamine (SP) plus amodiaquine (AQ) during periods of high or moderate transmission in endemic areas. Chemoresistance and genetic diversity of the parasite are among the major challenges in malaria control. The aim of this study was to assess the impact of SMC on the prevalence of malaria infection, Plasmodium genetic diversity and the prevalence of P. falciparum resistance molecular markers in rural children in Burkina Faso. The study consisted of 222 children participating in the SMC in the Saponé health district. Blood samples were taken for thick drop for microscopic diagnosis and blood spots for molecular analysis at Centre National de Recherche et de Formation sur le Paludisme molecular laboratory. Parasite DNA was extracted using Qiagen kits, the prevalence of malaria infection and genetic diversity were determined by nested PCR while molecular resistance markers were analysed by PCR/RFLP. The prevalence of malaria infection determined by PCR during SMC was 19.7%. The study of genetic diversity revealed a high polymorphism of the parasite during SMC. The prevalence of mutations associated with resistance to SP+AQ was very low in our study. However, the Pfdhfr59 mutation was very high in the study and averaged 92.31% respectively. These results showed a reduction in the mutation prevalence of Pfcrt genes associated with antimalarial drug resistance in Burkina Faso after the implementation of SMC. In addition, SMC contributes to the reduction of the prevalence of malaria infection, affects the genetic diversity of P. falciparum and the distribution of molecular markers of antimalarial drug resistance.

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ASSESSING THE IMPACT OF GROUP ANTENATAL CARE ON INTERMITTENT PREVENTATIVE TREATMENT IN PREGNANCY (IPTP3) UPTAKE IN ATLANTIQUE DEPARTMENT, BENIN: A CLUSTER RANDOMIZED CONTROLLED TRIAL

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In 2020, an estimated 33.8 million pregnancies occurred in malaria endemic areas of sub-Saharan Africa. WHO recommends HIV-negative pregnant women in malaria endemic areas receive at least 3 doses of intermittent preventative treatment in pregnancy (IPTp3). However, coverage remains low at 32%. Group Antenatal Care (GANC) is a service delivery model in which 8-15 women are assigned to a group at their first ANC visit, and subsequent care is provided in the group setting. GANC has been associated with higher quality and greater retention in ANC care. We conducted a cluster-randomized controlled trial in Atlantique Department, Benin, to assess whether GANC improved retention in ANC and uptake of IPTp3. Forty purposively selected health facilities (HF) were randomized 1:1 to control or GANC. Cross sectional household surveys were conducted before and after implementation, among randomly selected women who had given birth in the previous 12 months from each HF catchment, to measure uptake of ANC and IPTp. Changes in coverage were assessed using a difference in difference approach, adjusting for HF clustering. At baseline (N=1259), coverage of at least 4 ANC visits (ANC4) and IPTp3 was 52.8% and 48.0%, respectively, in the intervention arm catchment areas and 44.9% and 49.4% in the control catchment areas. At endline (N= 1280), coverage of ANC4 improved in both arms, to 56.7% in the intervention and 46.1% in the control. Accounting for baseline differences, the increase in the intervention arm was not significant (p = 0.51). Coverage of IPTp3 also increased, to 53.2% (intervention) and 49.7% (control) but was not significant (p=0.26). Only 140 women reported participating in GANC- 99 (15.6%) from intervention and 41 (6.5%) from control arm. Participation in GANC improved coverage of both ANC4 (65.0% vs 50.5%, p=0.002; Odds ratio (OR) 1.9, 95%CI 1.4-2.5) and IPTp3 (64.0 vs 50.6%, p=0.004; OR = 1.8, 95%CI 1.2-2.6). Among women who participated, GANC improved retention in ANC and IPTp3 uptake, but participation was limited. Understanding and addressing the barriers to participation will be critical if GANC is to be used more widely to improve IPTp coverage.

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COMPARING THE DURABILITY OF SYNERGIST LONG-LASTING INSECTICIDAL NETS PERMANET®3.0 AND CONVENTIONAL NETS YORKOOL© IN SOUTHEAST BENIN REPUBLIC AFTER NATIONAL MASS CAMPAIGN IN 2020

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Long-lasting insecticidal nets (LLINs) based on pyrethroids have been important in significantly reducing malaria cases in Africa, but insecticide resistance in Anopheles mosquitoes threatens their impact. The synergists

could help control insecticide-resistant populations. The LLIN PermeNet 3.0 (pyrethroid-piperonyl butoxide (PBO)) is an example. However, the longevity of PBO nets in Benin is not well known. To provide the National Malaria Control Program with evidence of physical and insecticidal durability, two of the LLIN brands deployed in similar districts, Massè (PermaNet®3.0), Adja-Ouèrè (Yorkool®) and Adingnigon (PermaNet®3.0) in the southeast during the 2020 mass campaign were evaluated. This is a prospective cohort study enrolling a representative sample of households six months after distribution. Over a 21-month period, all nets from the campaign in these households were marked and monitored. The primary outcomes were the "proportion of nets in good condition" based on measures of integrity and attrition in years. Insecticide results were determined by bioassay using the WHO cone test. A total of 1559 campaign nets (109% of target) from 546 households were included in the study. Final results could be determined for 70% of the nets in the cohort in Massè, 54% in Adja-Ouèrè and 74% in Adingnigon. After 21 months, all-cause attrition was 31% in Massè, 13% in Adja-Ouèrè and 37% in Adingnigon (p=0.199) and attrition due to wear and tear was 2% in Massè, 5% in Adja-Ouèrè and Adingnigon (p≥0.05). Survival in use at the last survey was 39% in Massè, 53% in Adja-Ouèrè and 45% in Adingnigon (p≥0.05). The multivariate Cox proportional hazards models suggest that the difference between sites was not primarily attributable to LLIN brand. Insecticidal efficacy was optimal for 100% of PermaNet®3.0 tested compared to 67% for Yorkool© after 21 months. In the southeast Benin environment, the PermaNet®3.0 polyester LLIN performed significantly better than the Yorkool LLIN, but both were below a three-year survival rate. Improved net usage behavior should lead to increased physical durability.

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PERENNIAL MALARIA CHEMOPREVENTION (PMC) INTEGRATION INTO MOZAMBIQUE'S ROUTINE HEALTH SYSTEM: A PLUS PROJECT CASE STUDY

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Malaria is endemic in Mozambique, accounting for 42.9% of cases among children under five in 2021. To develop a perennial malaria chemoprevention (PMC) model for Mozambique and discuss how PMC could be integrated into Mozambique's routine HMIS, the NMCP led a cascade of multi-day co-design meetings with participation from stakeholders and representatives from various health programs. In November 2022, Mozambique's Ministry of Health (MoH) adopted an overarching malaria chemoprevention strategy, which included PMC. In parallel with the design of a Mozambique-specific model of PMC resulting from the June workshop, additional work was required to fully integrate PMC into Mozambique's routine health system, which included updating paper-based data collection tools and the online HMIS database. A week-long workshop was held in September 2022 to adapt the existing healthy child consultation (HCC) data collection and reporting tools to include PMC data elements. The workshop was also spent discussing monitoring and evaluation plans, such as deciding on key performance indicators (% of sulfadoxine-pyrimethamine (SP) doses administered to target population, % of target population receiving one or more SP doses, % of PMC health facilities reporting no stockout of SP, and number of adverse events notified). Additional technical questions must still be resolved before PMC is fully integrated into the reporting system, such as the time it takes to fill SP information in the new register book column and plans for production of updated HCC register books. Integrating PMC reporting alongside routine health reporting is a vital step to ensuring timely data collection, accurate documentation, and comparable data sharing for this newly approved malaria chemoprevention policy. Results from this case study can be used by other provinces in Mozambique and other countries implementing PMC to ensure compatible data collection and sharing processes.

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EXPLORING NET USAGE, PREFERENCES, AND REPAIR HABITS: A QUALITATIVE STUDY ON MALARIA PREVENTION STRATEGIES IN KONONGO, GHANA

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Understanding insecticide-treated net (ITN) usage and net care and repair (NC&R) are vital for enhancing prevention strategies. There is currently a lack of research on current net usage and NC&R inhibitors, especially among non-net users. This study explored factors affecting ITN usage, preferences, and repair behaviors in Konongo, Ghana. By understanding NC&R habits, overall net retention methods can be improved We conducted 60 in-depth interviews with maximum variation purposive sampling. Participants consisted of 30% non-net users and 70% net users. Interviews covered net usage habits/preferences, NC&R habits/messaging, net damage, and malaria incidence, then qualitatively analyzed using MaxQDA. Average net age and household net count indicated nets were not lasting long and were below the recommended amount. Experiences with net damages were common, with few users attempting repairs. Quantitatively, 40% of net-using households reported net repair inhibitors such as lacking materials or knowledge on how to repair, or exposure to repair messaging. Furthermore, only 13% of families have been exposed to any form of repair messaging. Because of this, the majority of participants expressed a desire for a net repair kit, highlighting a potentially unmet need. A preference for polyester over polyethylene nets suggests comfort and usability impact usage. Non-users cited net damage, heat, and irritation as reasons, revealing areas for improvement in net design, distribution, and education.: In conclusion, To increase net use, it is crucial to address net use, repair, and maintenance inhibitors, and their concerns about heat and irritation. Understanding these factors can also guide targeted interventions and behavior change communication strategies, ultimately increasing overall net retention. Further research is necessary to explore the potential benefits of integrating the provision of materials and education on net repair into standard net distribution programs.

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EMPOWERING COMMUNITY LEADERS TO INFLUENCE ACTIONS AGAINST MALARIA AT HOUSEHOLD LEVEL. LESSONS FROM MOYO DISTRICT, WEST NILE REGION, UGANDA

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Over 90% of Uganda's population is at risk of contracting malaria. The West Nile Region, with an estimated population of 3,404,800 has one of the highest malaria prevalence rates in Uganda at 22% as reported in the Malaria Indicator Survey 2019. Moyo District hosts approximately 23,000 registered refugees, and an unknown number of self-settled refugees, mainly from neighboring South Sudan and Democratic Republic of Congo, posing unique vulnerability to malaria and other diseases. Improving risk perception, building structures, and implementing targeted malaria prevention interventions to empower communities to own the response process requires intense leadership engagement at the grassroots. The USAID PMI Uganda Malaria Reduction Activity (MRA), implemented by JSI, identified high burden villages using HMIS data. Malaria interventions were implemented in 318 households in Lefori and Laropi sub counties in Moyo District. Community leaders were empowered to improve malaria prevention

at household level. Monthly data review meetings were held at the village level led by the community leaders to track progress in malaria response activities. Household malaria response plans were developed, awareness and knowledge on malaria prevention improved. A total of 214 households were followed up ; 85% of the household had children under five sleep under mosquito nets, 80% of the households had pregnant women who attended antenatal care. Data enabled stakeholders to harmonize interventions and implementation approaches, contributing to more effective resource allocation. Community leaders addressed negative myths and misconceptions and social norms that limited community access to correct malaria information and health services. Involvement of leaders, community and health service providers formed an important structure for a supportive environment for households most affected by malaria.

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"AFTER A LONG DAY OF PLAY, I GET TIRED AND FOR GET TO UNFURL MY BEDNET": EXPLORING BARRIERS AND FACILITATORS OF BEDNET USE IN EASTERN UGANDA

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Insecticide-treated bednets are the most common form of malaria prevention throughout the world and understanding the factors that affect their use is critical. Self-reported use may not accurately measure actual practice due to social desirability bias and temporal variations in use. Electronic bednet monitors can provide more precise measures of use. Households in Tororo and Busia districts who were enrolled in an ongoing study with electronic bednet monitors underwent in-depth interviews about bednet use. Household members aged 8 and older were eligible. A survey guide was developed using an Information-Motivation-Behavioral (IMB) framework. A simplified guide was used for children under age 15. Thematic analysis was done using the IMB framework to categorize the data according to barriers and facilitators of use. Fourteen participants from 4 households were interviewed, including 7 adults (mean age: 42 years) and 7 children (mean age: 11 years; range 8 to 17). Ten of 14 participants (64.3%) were female. Facilitators of bednet use included knowledge of bednets as a low cost way to prevent malaria, more rooms in a house and more stable sleeping arrangements. The presence of the electronic monitoring devices was noted to promote bednet use, as were habits such as unfurling the bednet before bed time. Age was a moderating factor, with older people more likely to use bednets compared to the younger children. Barriers to use of bednets included ignorance about the cost of treatment, excessive heat and tiredness after a long day of play for the children. Children depended on parents for bednet use, leading to non-adherence when parents were unavailable. In this qualitative study of individuals undergoing observation with electronic monitoring of their bednet use, multiple factors were identified with heterogeneity between age groups that may present targets for improving bednet use in this population at risk of malaria.

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PREDICTORS OF ACCESS TO SEASONAL MALARIA CHEMOPREVENTION MEDICINES OUTSIDE HOUSEHOLD VISITS IN NIGERIA IN 2021

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In Nigeria, Seasonal Malaria Chemoprevention (SMC) medicines are typically delivered to children under five door-to-door through household visits by SMC community distributors during the high transmission season. Despite this recommended approach, some households access SMC through other means, including fixed point distributions, health facilities and private purchase. However, until now, analysis of access to SMC outside household visits has been limited. Our study aimed to identify household characteristics associated with access to SMC outside household visits. We analysed data from Malaria Consortium's 2021 Nigeria SMC end-of-round coverage survey, covering seven states. We described sources of SMC medicines using weighted percentages and performed univariate and multivariate logistic regression analyses to identify predictors of access to SMC outside household visits. We estimated adjusted odds ratios (AOR) with 95% confidence intervals (95% CIs). Of the 9,491 caregivers of eligible children included in our analysis, 96.32% received SMC, of which 1.36% accessed SMC outside household visits. The three most common alternative sources of SMC medicines were health facility personnel (36.29%), informal distribution in public by SMC distributors (25.81%), and family or friends (16.94%). Univariate model results showed that caregivers with higher educational attainment, being non-partnered, having less SMC-related knowledge, and not using indoor residual spray or mosquito nets were more likely to access SMC outside household visits. In the multivariate analysis with mutual covariate adjustment, we found higher levels of caregiver educational attainment are a positive predictor of accessing SMC outside household visits (AOR 2.30, 95% CI: 1.08–4.89 for post-secondary vs. none/informal) and having a household head born in the local state (AOR 0.46, 95% CI: 0.24–0.86) was a negative predictor. This analysis will be expanded to identify predictors of access to SMC via specific sources, and to explore the potential impacts of different SMC sources on caregiver SMC knowledge and adherence to the full course of SMC medicines.

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THE ROLE OF COMMUNITY DRUG DISTRIBUTORS IN THE QUALITY OF SEASONAL MALARIA CHEMOPREVENTION DELIVERY IN NIGERIA

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Seasonal malaria chemoprevention entails the door-to-door distribution of four or five monthly cycles of sulfadoxine-pyrimethamine and amodiaquine (SPAQ) to children 3 - 59 months as a malaria prevention strategy delivered by community drug distributors (CDD). CDDs are responsible for ensuring the first dose of SPAQ is given as a Directly Observed Treatment (DOT) informing the caregiver how to administer subsequent doses of amodiaquine (AQ) of days 2 and 3 and what to do in the event of any adverse reaction. Adherence to the three-day complete course of SPAQ is a measure of quality of implementation and is critical to the impact of the intervention in reducing malaria morbidity and deaths in children. We analyzed reported CDDs compliance with protocol against caregivers' adherence to subsequent SMC doses. Data were collected from 11,188 primary caregivers of eligible children randomly sampled from nine SMC-implementing states in Nigeria during the 2022 end-of-round household survey. Of the 94.8% (10,606) caregivers visited by CDDs, 89.0% (9957) reported CDDs' directly observed them giving the children SPAQ on day 1, 82.1% (9185) of caregivers received information on how to administer days 2 and 3 doses of AQ and 81.1% (9073) on what to do in the event of adverse drug reaction. When CDD-related factors predicting adherence to days 2 and 3 AQ doses among caregivers were analyzed, after controlling for other confounders such as caregiver's background demographics and female peer influencers' visit, caregivers whose SPAQ administration on day 1 was supervised by CDDs were almost 3 times more likely to adhere (aOR = 2.75, 95% CI = 1.69 -4.47 p<0.001), there was no association between those who received information on what to do in the event of adverse drug reactions (aOR = 0.950, 95% CI = 0.53 -1.69 p=0.86) or those who were informed on how to administer Days 2 and 3 doses (aOR=0.89, 95% CI=0.54 - 2.39 p=0.72). The study underscores the importance of CDDs observance of directly observed treatment in caregivers' adherence and highlights the need for further studies on the content and delivery of key messages to caregivers to determine its effectiveness and benefits.

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PERCEIVED FACTORS IMPACTING COMMUNITY HEALTH WORKERS' CAPACITY TO IMPLEMENT SEASONAL MALARIA CHEMOPREVENTION ACROSS DELIVERY SETTINGS: QUALITATIVE SECONDARY ANALYSIS FROM RECENT STUDIES IN MOZAMBIQUE, NIGERIA, SOUTH SUDAN AND UGANDA

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Seasonal malaria chemoprevention (SMC) is the intermittent administration of antimalarials to children from age groups at risk of severe infection in areas of seasonal transmission. Since 2012, Malaria Consortium has been implementing SMC at scale in the Sahel region of Africa as recommended by the World Health Organization (WHO). More recently, SMC implementation has been expanded to new geographies, including countries in East and Southern Africa. During the SMC round, corresponding to the peak transmission period, monthly courses of antimalarials are administered to age-eligible children. Community health workers (CHWs) play a role in SMC campaigns across implementing countries, either as community distributors, in the case of Boma Health Workers (BHWs) in South Sudan and Village Health Teams (VHTs) in Uganda, as community-based support to caregivers, in the case of lead mothers (LMs) in Nigeria, or in other key intermediary roles such as Agentes Polivalentes Elementares (APEs) in Mozambique. Previous studies have looked at the role of CHWs in SMC, however, questions around what factors impact CHWs' capacity to implement SMC across different delivery settings have remained relatively unaddressed. Aiming to bridge this gap, we conducted secondary analysis of recent (2021/2022) qualitative SMC studies in Mozambique, Nigeria, South Sudan and Uganda, comprising of focus group discussion (FGDs) and key informant interviews (KIIs) with stakeholders at various levels of the health system, including CHWs. Thematic analysis is ongoing and preliminary results point to some factors affecting CHWs' capacity to implement SMC across countries: CHWs' proximity to, and rapport with community members and/or caregivers; feasibility of, and synergies between multiple tasks performed by CHWs; level of motivation; areas to cover and number of CHWs; remuneration and allowances; selection criteria. Complete results from this secondary thematic analysis will be presented, focusing on identifiable commonalities and points of differences across delivery settings, to support the development of improved engagement strategies at community level.

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POPULATION DIFFERENCES IN VACCINE RESPONSE: THE ROLE, REVERSIBILITY AND MEDIATORS OF IMMUNOMODULATION BY CHRONIC INFECTIONS IN THE TROPICS PROTOCOL B: THE EFFECT OF INTERMITTENT PREVENTIVE TREATMENT FOR MALARIA WITH DIHYDROARTEMISININ-PIPERAQUINE ON RESPONSE TO VACCINES AMONG RURAL ADOLESCENTS

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Vaccines are key tools for infectious disease control, but several important vaccines differ in immune responses induced, and in efficacy between populations. We hypothesized that malaria infection suppresses responses to unrelated vaccines and that this effect can be reversed, at least in part, by monthly intermittent preventive treatment (IPT) of malaria in high-transmission settings. A randomized, double-blind, placebo-controlled trial was conducted to assess the effect of monthly intermittent preventive treatment of malaria with Dihydroartemisinin-Piperaquine (DP) on vaccine responses. Adolescents 9 to 17 years were recruited from primary schools in Jinja district, Uganda, where malaria is highly endemic, and randomized to monthly DP versus placebo. The DP/placebo was administered monthly, including twice prior to the first immunization. Participants received a standard portfolio of BCG, Yellow Fever (YF-12D), oral typhoid (Ty21a), HPV, and tetanus/diphtheria (Td) vaccines. There were three main immunization days (week 0 (BCG), week 4 (YF - 12D, Ty21a, and HPV), and week 28 (Td)). Primary outcomes were BCG-specific interferon-gamma ELISpot response at 8 weeks post-immunization, vaccine-specific IgG responses to YF - 17D, Ty21a, HPV at four weeks, and Td at 24 weeks post-immunization. The trial was conducted from May 2021 to August 2022. 341 participants were enrolled, 170 in the DP arm and 171 Placebo arm. 145 (85.3%) participants in the DP arm and 140 (81.9%) in the placebo arm were followed up to week 52. At enrolment, 60% of participants had malaria on PCR, this reduced to <5% among participants in the DP arm. The geometric mean ratio of BCG-specific interferon-gamma response at week 8 was 1.19 (95% CI 0.99-1.42) P = 0.064. There was no effect of DP versus placebo on IgG responses to TT (geometric mean ratio (95% CI) 1.12 (0.84-1.48), p=0.44), DT 0.97 (0.83-1.12), p=0.66), Ty21 (1.037 (0.82-1.32), p=0.76). Outcomes for YF-17D and HPV are being processed. IPT significantly reduced malaria in the DP arm. With exception of BCG, IPT did not affect immune responses to Td and Oral typhoid vaccines.

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COMMUNITY PERCEPTIONS ON FEASIBILITY AND ACCEPTABILITY OF SEASONAL MALARIA CHEMOPREVENTION IN AWEIL SOUTH COUNTY NORTHERN BAHR EL GHAZAL STATE SOUTH SUDAN

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Seasonal malaria chemoprevention (SMC) is an effective intervention to prevent malaria infection in children. SMC was implemented in Aweil South County in South Sudan targeting 17,000 children aged 3-59 months. With boma health workers (BHWs) already active in the area, acting as community distributors, children received courses of sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) in five monthly cycles from July to November 2022. A qualitative study to assess the feasibility and acceptability of SMC was conducted at the end of SMC campaign round. We held key informant interviews with national ministry of health officials (3), gender experts (2), community leaders (4), health facilities in-charges (4) and state ministry of health officials (4). We also conducted focus group discussions with caregivers of SMC age-eligible children (6) and BHWs (4). Thematic analysis using an inductive approach was conducted. Most respondents perceived positive impacts of SMC through reduction of malaria cases in children aged 3-59 months. Many reported that acceptance increased over time due to the perceived effectiveness of SMC and use community distributors from the same community. Majority of the key stakeholders cited proper sensitization of caregivers, commitment of the service providers, proper planning, timely logistics supplies, community engagement through sensitization meetings, adequate number of boma health workers to cover vast geographical distances between households, and proper training of boma health workers as key determinants for successful implementation of SMC. Some respondents reported need for gender inclusiveness in household's healthcare seeking behaviors, quoting women as chief decision makers for children healthcare unlike men for non-health related issues in a household. While most stakeholders spoke of the successful implementation of SMC, some implementation challenges were outlined, including the effects of floodings in the area and long distances between households. Many of the respondents asked for SMC to be extended and scaled up to additional areas.

6204

ASSESSING THE IMPACT OF EXTENDING SEASONAL MALARIA CHEMOPREVENTION TO FIVE CYCLES: FINDINGS FROM AN ANALYSIS OF ROUTINE DATA OF 19 DISTRICTS IN BURKINA FASO (2015-2021)

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Seasonal malaria chemoprevention (SMC) typically involves administering antimalarial medicines to eligible children over four monthly cycles, coinciding with the rainy season and period of high malaria transmission. In 2021, five monthly SMC cycles were introduced in some areas with longer high transmission seasons, including 19 of the SMC-eligible districts in Burkina Faso. There is not yet any evidence on impact of the additional cycle under programmatic conditions since 2021. We compared trends and estimates of key malaria outcomes between periods of four and five SMC cycles using routine health facility data (2015 to 2021) of 19 districts that transitioned from four to five SMC cycles in Burkina Faso. Newey-West interrupted time-series analysis (ITSA) was used to explore district-level monthly trends in malaria incidence and deaths from the period of four SMC cycles to that of five cycles. Negative binomial regression models were fitted to compare estimates of mean malaria incidence and deaths between four-cycle and five-cycle years. The models generated estimates of the impact of five SMC cycles relative to four cycles, in terms of incidence rate ratios (IRRs) and their corresponding 95% CIs, while controlling for district-level, time-varying factors such as population growth, health-seeking behaviour, health system capacity and seasonal trends in the outcomes of interest. ITSA trends showed a decline in the peak incidence of RDT-confirmed malaria cases in 2021 following the introduction of the fifth cycle. Compared with the four-cycle years, incidence of RDT-confirmed malaria was 10% lower in the five-cycle years, IRR 0.90 (95% CI: 0.84 - 0.97, p= 0.004). A more substantial decline in malaria-related deaths was observed in the five-cycle years relative to the four-cycle years, IRR 0.06 (95% CI: 0.04 - 0.08, p=0.001). The study provides early evidence on the additional impact of introducing the fifth SMC cycle in areas with longer high transmission seasons. Further research with more robust data over a longer period is needed for a better understanding of impact.

6205

EVALUATION OF THE LEVEL OF SATISFACTION OF AN INTEGRATED MALARIA INFORMATION SYSTEM USERS IN MOZAMBIQUE

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In 2019, the Mozambique National Malaria Control Program (NMCP) developed and has been implementing an Integrated Malaria Information System (SIIM/iMISS) that enables all NMCP staff to monitor key indicators, assess the impact of interventions and provide evidence for decision making. The study evaluated the level of satisfaction of the SIIM/iMISS among users at provincial, district and health facilities level. A cross-sectional study with data collected using a self-administered online Google survey with the link sent to all 645 active and inactive users. Data collected included access; ease of navigation; impact in improving quality malaria data reporting timeless, completeness and accuracy and usefulness in decision making. The study explored satisfaction of the platform among users and associated factors. Descriptive statistics were used to summarize results and logistic regression was used to examine factors influencing satisfaction. 415(64.3%) users completed the online survey. Majority of respondents (63%) were from the district level. 92.5% are active users. Among active users, 19% were data entrants and over 81% had access to all visualizations and automated analyses (data users). Most user; data entrants (92%) and data users (88.9%) reported SIIM/iMISS to be easy to use and simple to operate. 74.5% of the active users agreed that the use of the SIIM/iMISS has had an impact on the quality of malaria data reported with 99.7% active users reporting that it is useful for decision making. Overall, satisfaction was high with 69.5% of active users reported being satisfied and 24.5% very satisfied. Factors significantly associated with satisfaction included features accessed, and whether the users reported fast data update. Data users were more likely to be satisfied compared to data entrants (OR 3.87) and those who reported no fast data updates were less likely to be satisfied compared to those who reported (OR 0.37). Further improvement to achieve more satisfaction can focus on ensuring access to visualization features even to data entrants.

6206

COMMUNITY DATA USE; PIVOTAL TO IMPROVING THE UPTAKE OF MALARIA SERVICES BY PREGNANT WOMEN AND THE RESILIENCE OF COMMUNITY HEALTH SYSTEMS - THE CASE OF PHCS IN CROSS RIVER STATE NIGERIA

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Accurate, timely, and accessible health data is crucial for data use and evidence-based improvements of essential healthcare services during pregnancy. This study investigates the correlation between the change in some malaria indicators and the establishment of data quality and use teams. The teams were established across 20 high-volume facilities randomly selected in 7 LGAs of Cross River, Nigeria and trained on data quality and use in November 2021. Each team which comprised heads of facilities, record officers, representatives from all service delivery units, and the Ward Development Committee (WDC) held monthly meetings to present data and review the performance of malaria indicators. These routine meetings revealed issues such as low uptake of antenatal care services (ANC) and stock out of Sulphadoxine-Pyrimethamine (SP) in health facilities. The WDC used the data to engage communities on identified issues leveraging community development and religious meetings, and targeted advocacy on SP procurement to key stakeholders. These engagements helped communities mobilize pregnant women (PW) to attend ANC and further donate 10200 doses of SP to 15 out of 20 facilities, demonstrating ownership and resilience. A pre and post (twelve-month before and after the intervention) Wilcoxon signed rank test at 95% confidence level with an alpha value of 0.05 was conducted to assess malaria services uptake indicators for PW drawn from the National Health Management Information System. The findings revealed a significant improvement in PW receiving intermittent preventive treatment in pregnancy - second and third dose (IPTp2 & IPTp3) from 51% to 82% (p =0.008) and 27% to 51% (p=0.005) respectively. Similarly, the proportion of PW attending first ANC before 20 weeks and ANC 4th visit improved from 22% to 32% (p=0.009) and 27% to 40% (p=0.02) respectively suggesting an improved ANC early attendance and retention. The findings of this study support the hypothesis that data-driven community engagement may further improve the acceptability, accessibility, and uptake of ANC services with the potential to address and prevent health and gender inequities.

6207

MENTORSHIP IMPROVES QUALITY OF MALARIA IN PREGNANCY SERVICES IN PMI-SUPPORTED REGIONS IN TANZANIA

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Malaria Services and Data Quality Improvement (MSDQI) supportive supervision assesses the quality of services and competence of health workers at service delivery points including Reproductive and Child Health (RCH) clinics. It is expected that the competence gaps in the provision of quality services during antenatal care visits (ANC) identified during MSDQI assessments can be addressed through mentorship between MSDQI assessments. The PMI Impact Malaria project supported the regional and district health management teams to implement MSDQI at 512 health facilities in Lindi, Mtwara, and Katavi in Tanzania in 2021 using the RCH checklist and identified 47 facilities performing <50% in the key competence indicators of assessment of danger signs, clinical history taking and physical examination, laboratory testing, diagnosis and treatment, and counseling and communication. These facilities were later visited once by trained mentors to strengthen capacity. On average, the MSDQI visits in 2022 following mentorship revealed improvements in indicators from 2021 to 2022: assessment of danger signs (45% vs. 88%); clinical history taking and physical examination (35% vs. 82%); laboratory testing (43% vs. 76%); counseling and communication (65% vs. 82%); and diagnosis and treatment (35% vs. 88%). Facilities with high performance during MSDQI assessments in 2021 that received subsequent MSDQI visits in 2022 without intervening mentorship maintained performance in assessment of danger signs (78% vs. 79%), clinical history and physical examination (75% vs. 76%), laboratory testing (71% vs. 79%), and counseling and communication (91% vs. 90%); overall diagnosis and treatment performance increased from 79% to 90%. In poor performing facilities, mentorship led to improved competence in provision of malaria services to pregnant women.

6208

QUANTIFYING THE ADDED BENEFIT TOWARD MALARIA ELIMINATION BY COMMUNITY CASE MANAGEMENT IN THE DOMINICAN REPUBLIC

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A strong surveillance system is required to achieve certification of malaria elimination. As part of the elimination strategy in the Dominican Republic (DR), community health workers (CHWs) perform community case management in malaria outbreak-affected foci to supplement the passive surveillance system. We present a novel application of the previously reported "Freedom from Infection" (FFI) framework-- a set of surveillance methods adapted to malaria elimination settings that allow: (i) the estimation of the sensitivity of a surveillance system to detect cases in the community (SSe) and (ii) the probability that zero reported malaria cases effectively reflect the absence of transmission (Pfree). We aimed to estimate the added value of CHWs on the health system's ability to detect malaria. Routine malaria surveillance data from passive case detection (PCD) from 2018 to 2022 was collected in 47 health facilities, 9 of which included CHW data. Based on the results of the FFI model with the PCD data only, several facilities exhibited a high degree of uncertainty in the estimated SSe. Despite the high uncertainty, the preliminary results suggest that in some areas, malaria freedom is likely with 21/34 (0.62, 95%CI 0.44, 0.78) health facilities reaching Pfree equal to 1 in at least 1 month of observation based on the PCD data alone. However, where a high Pfree was achieved, it was only sustained between 1 to 50 of the 50 months of observation. When the CHW data was added, two additional facilities reached a high Pfree, and overall, the facilities with CHW data sustained Pfree from 48 to 52 months. The difference in the precision of estimates when CHW data was added to the model was 0.28, or a 0.4-fold increase in precision. Overall, results suggest that the addition of CHW data generally improves the sensitivity of a malaria surveillance system to detect infections if they are present.

6209

OPTIMAL STRATIFICATION STRATEGIES IN THE SELECTION OF SENTINEL SITES FOR AN INTEGRATED MALARIA SURVEILLANCE IN BENIN

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Despite massive investments in recent years, malaria remains the leading cause of care seeking in Benin with an incidence that has plateaued around 20% for several years and high mortality rate among children under 5 and pregnant women. This stagnation questions the effectiveness of current strategies and calls for a paradigm shift towards the improvement of the targeting of interventions. This is the rational of ongoing discussions around the selection of a set of sentinel sites that will allow for an integrated monitoring covering entomological, epidemiological, climatological… dimensions. This research is a contribution to these discussions. It aims to propose a stratification strategy based on the spatial distribution of malaria transmission risks, allowing for a data-informed choice of sentinel sites that ensures the representativity of the entire country in an integrated surveillance system. The methodology used, is based on the World Health Organization's conceptual framework for the control of Malaria from which, we selected several variables deemed to be determinants for malaria transmission. We then estimated a set of linear mixed-effects models on longitudinal data for all the country's districts over the period from January 2017 to December 2021, to confirm the validity of these determinants. Finally, using a hierarchical ascending classification consolidated with the k-means method, we classified the districts of the country, into reasonably homogeneous blocks that can shelter each, a sentinel site. The main contribution of this study is therefore to use statistical methods to propose a dynamic classification tool that allows the user to pick a number of sentinel sites to be operationalized, likely taking into account resource constraints, and to obtain in return, the optimal slicing with the selected number of geographical areas. Crafted on a rational basis, such optimal slicing of the national territory is expected to foster a well-tailored integrated surveillance system generating a better targeting of the interventions, for an effective reduction of the burden of the disease.

6210

IMPROVING MALARIA EPIDEMIC SURVEILLANCE THROUGH ACTIVE ENGAGEMENT OF DISTRICT LEADERS. LESSONS FROM BUSOGA REGION IN EASTERN UGANDA

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The World Health Organization surveillance guidelines 2018 consider transformation of malaria surveillance into a core intervention as one of the pillars of the global technical strategy. In 2001, Uganda adapted and began implementing the Integrated Disease Surveillance and Response developed by WHO for African region member states. However, human resource challenges and technical glitches with the online reporting system as well as stock out of HMIS tools have weakened malaria epidemic surveillance in Uganda. The PMI Uganda Malaria Reduction Activity implemented by JSI, works with the Ministry of Health to strengthen malaria prevention and response efforts at all levels in the five highest-burden regions of Uganda. A broad range of interventions to ensure data completeness, timeliness, and quality are implemented. In Busoga region, beginning in April 2022, technical assistance was provided to twelve districts to improve HMIS reporting rates and address existing data quality gaps. Weekly, surveillance data was shared on reporting rates, malaria diagnosis, case management and malaria commodities stock status. District health, administrative and political leaders from 12 districts were engaged to lead the process of following up with 517 health facilities to address reporting and data quality gaps. Monthly reporting rates improved from 76% between April and June 2022 to 99% between October and December 2022. The weekly surveillance reporting rates further increased from 55% in week 22 of 2022 to 84% in Week 37 and rose to 91% in week 48. As of 2023, in week 3 and week 4, the reporting rate peaked at 93%. District leaders made data reporting a key performance indicator for health facility managers in 9 of the 12 districts. Active participation of district leaders in data management triggers health workers to improve performance. Using data to inspire leaders to be involved in malaria epidemic surveillance and deploying the tools available is a critical approach in settings where human resources are less motivated to document and report quality malaria data.

6211

PLASMODIUM FALCIPARUM MALARIA MOLECULAR INDICATORS IN SOUTH WEST BURKINA FASO: COMPARISON OF ACTIVE AND PASSIVE CASE DETECTION

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The aim of this study was to compare the molecular indicators of P. falciparum during active and passive case detection. Samples of children aged from 1.5 to 12 years were collected from October 2020 to Mars 2021. Children below 5 years benefited on the National seasonal malaria chemoprophylaxis (SMC). All study participants received either supervised curative doses of artesunate (AS) or dihydroartemisinin-piperaquine (DHAPQ) to clear existing parasites prior their enrolment. Active and passive case detection methods were combined to capture all malaria clinical episodes during the follow up. Blood spots were collected and DNA extracted; alleles frequencies and msp-2 genes diversity investigated by nested polymerase chain reaction. A total of 458 (403 for active and 55 for passive cases) P. falciparum isolates collected from 176 participants (38.43%) were genotyped. The mean values of MOI were 2.91 [2.74-3.07] for active and 3.52 [3.04-4.00] for passive visit respectively (p=0.01) and those of FOI in active visit was 1.95 [1.76-2.15] versus 2.38 [1.75-3.01] in passive visit (p=0.16). No statistically significant difference in FOI values (p=0.92) was found between subjects who were on SMC (1.98 [1.57-2.39]) and those who were not (2.00 [1.82-2.18]). On average, 2.98 [2.83-3.14] clones parasitized our subjects during each infection and there was no statistically difference (p=0.75) between subjects on SMC (3.03 [2.69-3.38]) and the other group (2.97 [2.79-3.15]). This study shows that the molecular indicators of P. falciparum were higher in isolates from subjects with symptomatic malaria. Despite the current malaria control tools deployed in young subjects, variant patterns in young subjects, allelic variant profiles identical to those of subjects without SMC coverage are still observed. This may support the current hypothesis that school children should also be the target of malaria control tools.

6212

THE YELLOW FEVER OUTBREAK SHEDS LIGHT ON THE MISSED THREAT OF MALARIA IN ISIOLO COUNTY, KENYA 2022

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Malaria and Yellow Fever can be difficult to differentiate based on symptoms and signs, leading to delayed diagnosis and increased morbidity and mortality. In March 2022, in a suspected febrile illness outbreak in Isiolo, some samples collected were confirmed malaria. We investigated by retrospectively reviewing patient records, conducting malaria data quality audit and surveillance capacity in 16 randomly selected facilities from October 2021 through March 2022. A suspected case was any patient's record that had presented with fever and any of the following - headache, backache, chills, sweat, myalgia, nausea, and vomiting in Isiolo County during the review period, a confirmed malaria case was any patient's record tested positive for malaria through a blood smear test or rapid diagnostic test within the same period. We abstracted data on age, sex, visit date, diagnostic test, and laboratory results. Data Quality Assessment (DQA) evaluated timeliness, completeness, and data. Descriptive statistics utilized means, medians, frequency and proportions. We reviewed 5,527 records from three sub-counties; Garbatula contributed 45.03% (2,489) of the cases, Isiolo 46.35% (2,562) and Merti 8.61% (476) cases. Median age was 15 Years (IQR 5 - 30). Attack rate for ages under five was 6.54% (86/1.315), and above five was 10.87% (458/4,212). Approximately 10.3% (571/5527) cases tested positive — a case attack rate of 2.08 per 1000 population for Isiolo county. Garbatula had highest case positivity rate — 57% (323/571) an attack rate of 4.64 cases per 1000 Population, Isiolo was 1.26 cases per 1000 population and, Merti was 1.01 cases per 1000 population. Undetected case upsurges to alert thresholds noted on the 3rd, 4th and 5th epidemic weeks of 2022. Data completeness was 83% and timeliness 71%. At least 25% (4/16) facilities had significant stock-outs of mRDTs and antimalarials. Weak surveillance systems could have contributed to the missed upsurge of cases. We recommend strengthening support supervision, improving mRDTs access in facilities without laboratories, and redistributing antimalarials to strengthen malaria control and surveillance

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PIONEERING ELECTRONIC FORMS AND REPORTING IN SEASONAL MALARIA CHEMOPREVENTION IMPLEMENTATION AMID INSECURITY IN ZAMFARA STATE

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Malaria is the leading cause of morbidity and mortality in children under the ages of five (CU5) in Nigeria. In Zamfara state, SMC has been implemented among CU5 since 2015. SMC implementation contends with difficulties around payment of SMC personnel (Community Drug Distributors [CDD], health facility workers and Local Government teams) and incomplete submission of data, specifically, with heightened security risks. E-accountability tools - CDD nomination, CDD attendance, call-in data, and in-process monitoring forms were introduced in 2021 to overcome these challenges, and SMC personnel were provided practical training on their use. Throughout SMC implementation, monitoring and supervisory support was provided by state trainers on use of these tools. This assessment compared the SMC implementation processes and outcomes before (2020) and after the introduction of the e-tools in 2021. Deployment of CDDs e-nomination forms reduced the number of days for CDD selection and engagement from 6 to 2 working days, while deployment of the e-attendance increased CDDs daily attendance submission from 5% to over 85%. The daily call-in data received from health facilities on delivery of the SMC drugs increased from 14% to 80% and the field supervisors' submission of in-process monitoring reports increased from 35% to 100%. The duration of personnel replacement reduced from 20 to 3 working days, due to the establishment of a replacement protocol aided by the unique ID numbers linked to every registered personnel. The timeline for payment of SMC actors reduced from 30 to 3 working days. The e-tools improved microplanning by facilitating the inclusion of and provision for CU5 in internally displaced persons (IDP) camps and hard to reach communities. The introduction of e-tools during SMC implementation had a positive impact on overall program management, monitoring, commodity availability, personnel management, and payment processes. This has also contributed to the increased availability of real time data for prompt decision making, cost efficiencies throughout the process and improved SMC delivery including in security challenged area.

6214

INTEGRATING ANTENATAL CLINIC-BASED MALARIA SCREENING DATA AND MATHEMATICAL MODELLING TO CAPTURE THE TRAJECTORY OF MALARIA TRANSMISSION IN WESTERN KENYA IN THE CONTEXT OF THE COVID-19 PANDEMIC.

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In Siaya county, western Kenya, pregnant women are routinely screened for malaria at their first antenatal care (ANC) visit. Since 2016, screening has occurred alongside an all-age continuous household Malaria Indicator Survey (cMIS), providing a unique opportunity to understand how malaria infection trends at ANC map to general population prevalence, a metric by which ~85% of the world's malaria burden is estimated. As with much population-based disease surveillance, cMIS was halted in 2020 in the context of the emerging COVID-19 pandemic. Meanwhile, an insecticide treated net (ITN) campaign scheduled for mid-2020 was delayed to March 2021. In contrast, ANC surveillance remained ongoing and largely unaffected in 2020-2021. We assessed the relationship between ANC and population prevalence using binomial regression. We then incorporated this relationship within an existing dynamical malaria transmission model, using particle Markov Chain Monte Carlo to estimate transmission trends throughout the study period. Through k-fold cross-validation, we show that ANC-based surveillance accurately captured a rapid decline in population malaria prevalence from around 50% to 20% immediately after an ITN campaign in 2017. Our estimates suggest a near thirty-fold reduction in transmission from an entomological inoculation rate (EIR) of ~30 to ~1 during this period. By early 2020, both population prevalence and our estimates of transmission had rebounded to their pre-ITN peaks. During the pandemic, both ANC-based prevalence and our transmission estimates remained near their study-level peak throughout the year-long delay in ITN distribution, declining rapidly from March 2021 when ITNs were eventually distributed. This highlights the utility of ANC-based indicators in providing more granular estimates of population-level trends and as a data source likely to remain more robust to external shocks such as pandemics than other forms of population-based surveillance such as cMIS. These results also provide a quantitative example of the indirect impact the pandemic is likely to have had upon malaria control, transmission, and burden.

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TRACKING PROGRESS OF PROPORTIONAL USAGE ANTIMALARIALS FOR TREATMENT OF PLASMODIUM FALCIPARUM INFECTIONS IN CHILDREN, TWO DECADES OF ARTEMISININ-BASED COMBINATION THERAPY (ACT) POLICY IMPLEMENTATION

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A policy shift to Artemisinin-based combination therapy (ACT) for managing malaria cases contributed substantially to the reduction of malaria burden globally. Unfortunately, in the past few years progress stalls and that plateau trend continues. Possible explanation for the slowing down could be inequalities in the uptake of interventions in specific transmission foci and sector specific performances. Studies suggest that unregulated private sector may allow the use of ineffective antimalarial medicines resulting to poor clinical outcomes. Additionally, undetected poor performance at subnational levels may mislead correct allocation of control strategies, hence, slowing down the progress in malaria control. This work assessed the public-private share and geographical variations of the proportional use of ACT in treatment of uncomplicated P.falciparum infections in children in malaria endemic countries two decades since the recommendation of the policy. Utilizing data from demographic health surveys, hierarchical Bayesian modelling framework were developed and deployed to estimate country-year, sector-specific and subnational distribution of the usage. The models were adjusted for treatment seeking rates, health system, socio-demographic, and environmental factors. Our findings indicate that rural and low-wealth areas have lower uptake of the ACT policy, despite an overall increase in the public sector's share of malaria services from 46.7% in 2001 to 61.8% in 2022. Overtime, use of ACT has significantly improved within both sectors. Over two decades, 79.8% of children treated in public sector received ACT contrary to 67.2% in private sector. Private sector increases in ACT use outpaced public sector increases by 75.6% to 64.5%. Regional, national and subnational variations exist, with the public sector dominating in provision of malaria services in most. SSA countries. In Nigeria, private sector is treating most cases mostly with ACT, however, in the Democratic Republic of Congo, despite public sector treating most almost a third receiving non-ACT.

6216

SPATIAL AND TEMPORAL VARIATION OF MALARIA CLINICAL INCIDENCE IN CHILDREN UNDER 10 YEARS OF AGE IN KOULIKORO, MALI

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Despite the wide deployment of malaria control interventions during the last decades, we are observing over the last 5 years a plateauing of the number of cases in many endemic countries like Mali. Thus, it is necessary to review and redirect malaria interventions specifically in low and middle-income countries with more malaria. The cost-effectiveness of malaria interventions will depend on the area' level of endemicity and seasonality of transmission. Spatiotemporal analysis of malaria burden variation in Koulikoro health district of Mali was used to determine the variation in malaria indicators such as incidence among children less than ten years of age.A total of 2,916 children were enrolled in July 2021 and followed up to April 2022 (a ten-month period). Households of participants were geolocated at enrolment and for the purpose of spatial analysis, locations were aggregated to 1km2 grid cells to calculate cumulative incidence rates (CIRs) per 100 persons. To assess the temporal variation of malaria both hot spots and cold spots within the study area, we used the Fish Model on SaTScan. To reduce the dimensions of environmental variables and avoid collinearity between environmental factors, we performed a principal component analysis (PCA) in the FactoMiner. Data were collected from all children visiting health care facilities for malaria symptoms using digital tablets. Overall, malaria incidence rate was 4.1 children per month in October and 70% of children had at least one malaria episode during the follow-up period. Peak of malaria incidence was observed in September and November and the maximum number of malaria episodes a child experiences was 4 over 10 months. Recurrent malaria events were frequently observed in villages along the Niger River with a heterogeneous distribution during the transmission season.

6217

THE VALUE OF END-USE VERIFICATION SURVEYS ON THE AVAILABILITY OF ANTIMALARIAL COMMODITIES IN MADAGASCAR, 2022

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To monitor the availability of quality health commodities in Madagascar, the Malagasy Ministry of Public Health (MOPH) has implemented end-use verification (EUV) surveys—a USAID-funded standardized methodology for assessing the storage conditions and inventory management of antimalarial and other commodities. The USAID Improving Market Partnerships and Access to Commodities Together (IMPACT) project has been supporting the MOPH in conducting the EUV surveys and implementing corrective actions and recommendations in response to survey findings since 2020. EUV surveys are conducted every 6 months in around 100 randomly sampled health facilities: 3% hospitals, 17% district pharmacies (Pha-G-Dis), 64% basic health centers (CSBs) and 15% community health workers in USAID-supported regions with higher malaria incidence. Findings of each assessment are discussed among stakeholders at each administrative level and actions defined to address the challenges. The results of the malaria EUV survey in December 2022 in 109 facilities show that, on the day of the visit, 35% of 23 Pha-G-Dis had an appropriate stock of artemisinin combination therapy (ACTs) for infants, compared to 13% of 18 in May 2022; and 31% of Pha-G-Dis had an appropriate stock of injectable artesunate, compared to 21% in May 2022. From September to November 2022, all 109 structures recorded 0% stock out of ACTs for adolescents compared to 20% in May 2022; 0% stock out of ACTs for adults compared to 14% in May 2022; and 0% stock out of malaria rapid diagnostic tests compared to 7% in May 2022. At the health facility level, 81% of 72 facilities (both CSBs and hospitals) had a formulation of ACTs for children under 5 years old (compared to 76% of 70 facilities in May 2022) and the stock out rate of adult ACTs was 7% (compared to 12% in May 2022). The action plans developed and implemented by regional and district supply chain actors after reviewing EUV survey results have contributed to improvements in subsequent surveys. IMPACT continues to support the Madagascar MOPH in effective use of data for evidence-based decision making.

6218

ENGAGING HEALTH FACILITY TEAMS TO IMPROVE MALARIA DATA QUALITY, USE, AND SERVICE DELIVERY IN AKWA IBOM STATE

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The National Health Management Information System (NHMIS) is one of the six building blocks of health systems that integrates data collection, processing, reporting, and use (WHO, 2010). Data is critical to delivering high-quality malaria services and guides malaria elimination efforts in Nigeria. This study examines the utilization of health facility (HF)-based data quality teams set up in five high-volume HFs in Akwa Ibom state in July 2021. The objective of the data quality teams was to enable HFs to generate and use quality data for improvement of malaria services. The teams were trained and supervised for the first 6 months of implementation and their responsibilities included coordinating facility data validation and triangulation and conducting monthly HF data review meetings. A descriptive quantitative analysis of NHMIS data on the proportion of fever cases tested for malaria and confirmed uncomplicated malaria treated with artemisinin-based combination therapy (ACT) was conducted in the selected HFs for a 3-year period (January 2019 - December 2021). Data availability across the HFs improved from 91% in 2019 to 100% between July-December 2021 when the data quality team meetings were set up and conducting monthly data reviews. The data also showed an improvement in malaria service delivery. In 2019, 72% of data records of fever cases tested for malaria deviated from the national target of 100%; this dropped to 8% between July - December 2021. A similar pattern was reported for the proportion of confirmed uncomplicated malaria cases treated with ACTs, where service delivery gaps reduced from 55% in 2019 to less than 2%. Continuous review of data using HF-based data quality teams presents a sustainable and scalable approach for HFs, fosters continuous use of data to identify gaps, and supports adaptive and improved adherence to standards of care. Implementing this strategy should take into consideration factors that support sustainability and ownership, such as skills transfer from members of the data quality team to all relevant HF staff and continuous on-the-job mentoring from government supervisors to HF teams.

6219

MALARIA MOLECULAR SURVEILLANCE IDENTIFIES CLONAL PARASITE POPULATION STRUCTURE IN DIOURBEL SENEGAL THAT REVEALS TRANSMISSION PATTERNS TO INFORM OPERATIONAL ACTIVITIES

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Ongoing national surveillance of Senegal Plasmodium falciparum infections provides emerging threat detection including drug resistance to inform transmission patterns that can guide intervention use by the Senegal National Malaria Control Program (NMCP). Parasite genetic metrics such as the frequency of clonal and multiple strain (polygenomic) infections, and genetic relatedness are emerging as key indicators for both monitoring transmission trends and identifying transmission patterns for tailoring subnational intervention stratification. We surveyed parasite genetic parameters from Diourbel, a site of moderate transmission (annual incidence ~25 cases/1000/year). Genotyped samples were collected through passive case detection (PCD) at health facilities from 2018 to 2020 (n = 412) and active case detection (ACD) at large residential schools called Daaras in 2020 (n = 120). Based on the PCD samples, infections in Diourbel were unusually clonal and inbred relative to its reported incidence levels. Between 2018 and 2020, we did not observe an increase the frequency of polygenomic infections (0.13 [0.08, 0.20] in 2018 to 0.10 [0.07, 0.15] in 2020). Despite this, infections in Diourbel have become increasingly clonal and inbred over time. The proportion of monogenomic samples infected with a shared clone increased from 0.48 [0.39, 0.58] to 0.83 [0.76, 0.88]) and the relatedness of strains (measured with RH) within polygenomic infections increased from 0.03 [0, 0.08] in 2018 to 0.40 [0.35, 0.46] in 2020. Five persistent clonal parasite lineages were observed across multiple sampling years. This unusual clonal and inbreeding structure was not observed in nearby Touba, which has a similar incidence. Genetic metrics collected through PCD and ACD were similar except for RH, which was 0.10 (0.03, 0.18; compared to 0.40 overall) in the ACD samples collected in 2020. We hypothesize that this unusual population genetic structure represents a unique focal spatial structure in Diourbel and are working with the Senegal NMCP to map the spatial structure of clonal parasite populations to identify transmission sources for intervention targeting.

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IMPROVING MALARIA SURVEILLANCE DATA: INSIGHTS FROM SOUTHERN ANGOLA

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Malaria in SADC region has significantly reduced over the last decade. As countries progress towards elimination, it is key to turn surveillance as a core programmatic component not only for first line elimination targeted countries but also for the second line countries which adequate control is essential to sustain elimination goals. In 2020, Angola started to implement aggressive activities focused on improving surveillance for elimination practices in southern border districts with Namibia. Surveillance activities integrated a combined approach that included support to routine collection of monthly reports, on site data quality assessments and on the job supportive supervision. The objective of this work is to highlight the achievements in core surveillance indicators achieved in 3 years of programmatic implementation. Reporting coverage was retrieved from National Health Information System to analyse progress of health facility reporting coverage over time. Information from data quality assessments was extracted from a database and simplified data quality indicators were analysed to understand trends in data quality over time. Results show that none of the 7 border districts targeted for intensive surveillance interventions had an annual reporting coverage above 90% in 2018, 1 in 2020 while all seven targeted districts had reporting coverages above 90% in 2022. Data quality shows that, in 2020, 58% of health facilities had incompletely filled reports whereas in 2022 this proportion dropped to 13%. In 2020 the accuracy of data between the consultation books and monthly reports was 93% but was improved to 99% in 2022. In 2020, 25% of the health facilities visited reported stock out of monthly reporting forms and 39% of consultation books. In 2022, those proportions changed to 5% and 17% respectively. A strong malaria surveillance system is highly dependent on availability and quality of data. Implementation of intense activities focused in improving data accessibility and quality showcase that it is possible to improve the system and sustain those gains over time.

6221

DEFINING PCR-DETECTED PARASITEMIA THRESHOLDS FOR CLINICAL MALARIA FROM ACTIVE AND PASSIVE CASE DETECTION

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Historically, clinical malaria was defined as fever and a blood smear positive for Plasmodium parasites above a defined density threshold. Blood smears have since been replaced by rapid diagnostic tests for diagnosis and more sensitive molecular diagnostic tests for research purposes. Thus, sensitive and specific definitions of clinical malaria using parasite density thresholds based on molecular diagnostics in the absence of blood smears are needed in 1) clinical settings where they must account for community prevalence of infection and 2) community-based surveillance to quantify disease among those not seeking treatment. We calculated the threshold of PCR-detected P. falciparum parasitemia that indicated clinical malaria disease among 1) individuals seeking treatment at health care facilities, and 2) individuals included in active case detection (ACD). Infection was detected by qPCR (18SrRNA) in a cohort of 962 Malawians of all ages who were followed for one year, using monthly active, and continuous passive case detection. ROC curves for the total population and by age were used to identify the qPCR-detection thresholds for 1) clinical care-seeking with fever and positive RDT, and 2) fever measured or reported during ACD. Among 1949 episodes of infection without recent antimalarial treatment, median age was 11y (IQR = 7, 19); median parasitemia was 16.21 parasites/ul (IQR = 2.23, 350.15). There were 283 clinical episodes, with an AUC of 0.89, and the parasitemia threshold identified was 427/ul, with sensitivity and specificity = 0.88 and 0.76. During ACD, there were 487 febrile episodes, with an AUC of 0.72, and the parasitemia threshold was 519/ul, with sensitivity and specificity = 0.88 and 0.51. Thresholds were higher among children under age 5 (634 and 904/ul for the two case definitions, respectively) and significantly lower among individuals over age 15 (40 and 70/ul). Results on predictors of care seeking by age and season will also be presented. While

these thresholds are likely to be specific to our transmission setting, our results highlight the importance of age-specific parasite density cut-offs for clinical disease.

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INTEGRATED AND INNOVATIVE DECENTRALIZED MALARIA RESURGENCE RESPONSES IN THE SOUTH EAST OF MADAGASCAR

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The Ministry of Health (MOH) sub-national team, supported by the National Malaria Control Program (NMCP) and partners conducted a package of response activities to address malaria resurgence in the districts of Farafangana and Vangaindrano in the South East region of Madagascar. The incidence of malaria cases increased from 63 per thousand inhabitants in Farafangana in October-December 2021 to 99.9 per thousand in 2022 in the same period. In Vangaindrano, incidence increased from 188.4 per thousand to 217.4 cases per thousand inhabitants from 2021 to 2022 for the same periods. The response package included: 1) mass behavior change communication; 2) active mass screening and treatment (MSAT); 3) Outreach Training Supportive Supervision (OTSS+) for targeted health facilities;4) in-service training on malaria case management. During the MSAT in Farafangana, 1,808 people of all ages were tested by malaria Rapid Diagnostic Test (RDT). The RDT test positivity rate was 47% and 84% were asymptomatic. In Vangaindrano district, 1,686 were tested by RDT. The RDT test positivity rate was 46.5% and 88% were asymptomatic. Most of these 1808 people tested received sensitizations on the prevention of malaria. In the four health facilities visited in Farafangana, the OTSS+ checklist showed the biggest gaps were register completeness (49%) and simple malaria case management competency (51%). The highest performance was on RDT competency (85%). In the three health facilities visited in Vangaindrano, the biggest gap was simple malaria case management competency (45%). Register completeness (60%) and RDT competency (86%) were slightly higher. Two in service medical training sessions for public and private providers were then conducted and tailored to address the subjects that OTSS+ showed poor performance on. The innovative decentralized response package to the malaria outbreak was accepted by health workers and the population. Malaria services delivery could be evaluated and strengthened through OTSS+. Community level can feasibly conduct mass active response to control malaria transmission in the context of high asymptomatic malaria cases rate.

6223

USING DATA INTEGRATION AND VISUALIZATION TO STRENGTHEN THE MALARIA SURVEILLANCE SYSTEM IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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A robust malaria surveillance system is the backbone of malaria control and elimination. Data integration and visualization are critical components of enabling the use of large volumes of data and answering analytical questions. Integration consolidates data from different sources into a single database. Visualization allows for more intuitive manipulation and interpretation of large and complex datasets. In 2021 in DRC, Bluesquare's open-source data platform, OpenHEXA, was used to create an integrated database using routine data from the National Health Information System's DHIS2, weekly surveillance data from the Integrated Disease Surveillance and Response platform, and environmental data. DRC is now capable of automatically running data integration routines to ensure the most recent version of each data source is used at all times. Analytics dashboards using Tableau software were also developed, allowing an interactive exploration and use of the integrated data. Dashboards include a weekly National Malaria Control Program (NMCP) epidemiological bulletin; analytics down to the health area level to monitor malaria trends, commodities, and data quality; and monitoring of environmental data. Institutionalization of these tools included training Ministry of Health (MoH) staff at all levels of the health system to analyze, interpret, and use malaria data. Changes in data utilization were observed since the introduction of these dashboards at the government stakeholder level, including using dashboards for evidence-based planning of supervision, decision-making on rapid outbreak response, distributing malaria commodities, internal redeployment of malaria commodities between health facilities, identifying data outliers, active monitoring of indicator performance, providing feedback on data quality and on malaria case management data, and reducing data validation violations. Key next steps include integrating entomological data into the data integration and analytics platform, improving spatial granularity down to the health facility level, and improving coverage of trained MoH staff on the NMCP dashboards.

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MODEL-BASED ESTIMATES OF LONG-TERM AND SEASONAL MIGRANTS IN NORTHWESTERN DISTRICTS OF ETHIOPIA

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Human mobility represents a major driver of the spread and persistence in Ethiopia's malaria epidemiology. Large scale movements of seasonal workers between areas of low and high malaria transmission have complicated efforts to reduce disease burden at both ends. In resource-poor farming settings where road transport or mobile-phone based data or large-scale population surveys are lacking, long-term migration patterns correlate with seasonal migration patterns and thus have been suggested for use in quantifying seasonal migration patterns. In this study, we used a five-year (2009-2013), survey-based internal migration dataset covering 78 zones in Ethiopia to develop a spatial-interaction model, and down-scaled estimates of migration to a finer spatial scale, in 816 districts (woredas). We also used the estimates to infer seasonal migration to woredas in northwestern Ethiopia identified as development corridors hosting seasonal workers. Accordingly, there were an estimated 1.53 million (95% CI: 1.51 - 1.56 million) long-term migrants crossing zonal borders annually, while 1.76 million (95 CI: 1.72 - 1.80 million) migrants crossed woreda borders, among them 10.6k (10.2 - 11k) migrated to the northwestern woredas. Based on our association model, this meant 294k (95% CI: 94k - 735k) seasonal migrants arriving at the northwestern woreda annually, which, according to reported prevalence of Plasmodium falciparum among seasonal migrants, translates to 37k (95% CI: 12k - 93k) positive cases returning to their home woredas annually. By applying a previously developed spatial downscaling approach and using secondary data on seasonal migration and prevalence of P. falciparum, our study inferred seasonal migration between a larger set of sources and destinations, thus filling a critical data gap. Results from this study are being used to inform meta-population disease transmission

models crucial in the identification of effective malaria control interventions in the presence of seasonal migration. This work constitutes an important part of the strategic plan aiming at malaria elimination in districts of moderate and low transmission risks.

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A SECOND BLOOD MEAL ELEVATES THE PLASMODIUM VIVAX SPOROZOITE LOAD IN ANOPHELES DIRUS SALIVARY GLANDS

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Anopheles mosquitoes become infectious with Plasmodium sporozoites by taking blood from an infected human. The parasites undergo a series of developmental changes in the mosquito and mature to sporozoites capable of infecting the next human. The time duration required by the parasites to develop within the mosquito to become infectious sporozoites, known as the extrinsic incubation period (EIP), is a key determinant of the vectorial capacity of the mosquitoes. During their life span, mosquitoes naturally feed multiple times in order to complete gonotrophic cycles. Previously, our group examined the impact of the second blood meal on P. vivax sporogonic development and observed significantly larger oocysts and shorter EIP in twice-fed mosquitoes. In this study, we further investigated the influence of the second blood meal on the number of salivary gland sporozoites and evaluated the infectivity of these sporozoites. Salivary gland sporozoites were inoculated to a hepatocyte-derived cell line, HC-04, then the number of the liver stage parasites were counted at day 4 and day 7 post inoculation. With the same number of sporozoites per well, there was no significant difference in the number of infected hepatocytes between single and twice fed mosquitoes. From these results, we conclude that the additional blood meal not only accelerates the sporogonic development of the parasite within the mosquito, but also led to a higher number of sporozoites with unaltered hepatocyte infectivity.

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CLONAL TRANSMISSIBILITY AND FACTORS INFLUENCING HUMAN-TO-MOSQUITO TRANSMISSION OF ASYMPTOMATIC PLASMODIUM FALCIPARUM INFECTIONS OVER THE COURSE OF ARTEMISININ-BASED COMBINATION THERAPIES IN MALI

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Plasmodium falciparum malaria infections in high-transmission areas often consist of several distinct parasite clones. Few studies have directly investigated the complexity of Plasmodium falciparum malaria infections in both humans and the mosquitoes they infect. Molecularly undetectable circulating parasite clones were previously found to transmit to mosquitoes, leading to a high complexity of infection in mosquitoes post-feeding. This is likely due to asexual parasite clones being more abundant in peripheral blood than gametocyte clones, the parasite stages responsible for human-to-mosquito transmission. Artemisinin-based combination therapies (ACTs) are the first-line treatment for uncomplicated P. falciparum malaria and eliminate asexual parasites rapidly but have limited activity against mature gametocytes. It is unclear whether certain gametocyte clones persist longer than others post-ACT and whether there are any genetic characteristics that may influence their transmissibility. Using next-generation multiplex amplicon sequencing targeting heterozygous regions in Pfcsp and Pftrap, we analysed complexity of infection in human blood samples at six timepoints over the course of an ACT and in the midguts of the mosquitoes that became infected in membrane feeding experiments using the same blood material at these different timepoints. We found that after the elimination of asexual parasites by the ACT, parasite clones in human blood and cognate mosquito midguts largely match, although there is still some transmission of molecularly undetected circulating clones. In addition, data will be presented on genetic factors that may influence the level of transmission, such as molecular markers of drug resistance in Pfcrt, Pfmdr1, Pfdhps, Pfdhfr and PfK13 and genetic variability in the P. falciparum surface protein Pfs47 and the Pfs47 midgut receptor, by which parasites that express a compatible Pfs47 haplotype can evade the mosquito immune system.

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STUDY OF AN IMPORTANT GENE FOR SEXUAL REPRODUCTION OF PLASMODIUM BERGHEI AS A POTENTIAL TARGET FOR BLOCKING MALARIA TRANSMISSION

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Through advances in genomics, proteomics and transcriptomics, currently studies analyzing these tools in search of new targets for potential drugs and vaccines are increasingly present in academia. Important targets to be studied are proteins involved in the life cycle of the protozoan Plasmodium, the malaria-causing agent, for potential vaccine formulations, such as vaccines with the transmission-blocking strategy. Recently, our research group identified a group of genes from P. berghei, conserved in different Plasmodium species, as essentials for the fertilization of the protozoan during its sexual reproduction phase. This project aims to deepen the studies on one of these genes and the protein it encodes, producing it recombinantly for antibody production, with the purpose of studying whether these antibodies would be able to inhibit protozoan fertilization, thus characterizing the protein as a potential candidate for the development of a transmission-blocking vaccine. Previously, a P. berghei ANKA knockout parasite was constructed for the studied gene. This knockout was carried out in a parasite previously constructed in the laboratory that has the luciferase gene linked to its ookinete formation process (PbOokluc). After obtaining the knockout, the characterization of the parasite phenotype was carried out through tests of parasitemia and gametocythemia curves, ookinete conversion and exflagellation assays. After these results, it was observed that the knockout parasite has a lower ookinete formation rate when compared to the Ookluc parasite. To obtain the recombinant protein for antibody production in mice, protein expression was performed in cultures of E. coli BL21 bacteria, and the protein is currently being purified so that it can be inoculated in mice for antibody production. After this step, it is expected to use these antibodies in P. berghei Ookluc parasites submitted to conversion assays to observe whether these antibodies are capable of inhibiting the sexual reproduction of the parasites.

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EVALUATION OF THE ACTIVITY OF ESSENTIAL OILS OF HYPTIS SPICIGERA LAM. AND OCIMUM AMERICANUM L. IN THE MALARIA TRANSMISSION BLOCKING

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Medicinal plants are widely used, and many of them have already proven their therapeutic effects through scientific studies. African populations in developing countries rely greatly on medicinal plants for their healthcare. Malaria remains a global public health concern, with 247 million cases registered in the world in 2022 and 95% of which occurred in Africa (WHO, 2022). Control methods are developed continuously because of resistances observed with antimalarial drugs and insecticides. In the present study, we

assessed the antimalarial activity of essential oils from two medicinal plants of Burkina Faso.Hydrodistillation was performed on fresh leaves of Hyptis spicigera Lam. and Ocimum americanum L. collected in the Hauts-Bassins region of Burkina Faso. In a Direct Membrane Feeding Assay, lab-reared mosquitoes were fed with gametocytemic blood supplemented with the essential oils; control group only received plain gametocytemic blood. Seven days later dissection was performed, and oocysts prevalence and density were determined. H. spicigera had a density of 1 and a prevalence of 1.42%. O. Americanum had a density of 0.72 and a prevalence of 3.13%. As for the control group, density was 33.8 and prevalence was 54.5%. The transmission blocking activity was 97.17% and 92.22% for H. spicigera and O. americanum respectively.These results confirm the potential of medicinal plants in malaria control.

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MALARIA VECTOR NUTRITION PREDICTS RATE OF PLASMODIUM FALCIPARUM DEVELOPMENT AND INFECTIVITY

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The malaria parasite Plasmodium falciparum must complete an intricate series of cell traversal and differentiation steps within the mosquito to enable transmission to the human host. This complex journey from the mosquito midgut to the salivary glands involves multiple parasite developmental stages and is fueled by mosquito nutritional resources that vary by environment. The rate of parasite development in the mosquito is a key determinant of malaria transmission because mosquito lifespan is short. Here we used single-cell RNA sequencing and in vitro hepatocyte infection to evaluate developmental progress of salivary gland sporozoites as a function of adult mosquito nutrition. Salivary gland sporozoites represent the final stage of parasite transcriptional and translational preparation for human liver infection. We specifically compared parasites developing in Anopheles gambiae mosquitoes provided with a single infectious blood feed (1BF) vs. an additional non-infectious blood feed 3 days post-infection (2BF). These treatments mimic natural mosquito gonotrophic variation. Our results demonstrate that transcriptional states of salivary gland sporozoites vary within and across treatments at 11 days post-infection. A marked transcriptional transition is observed during occupancy of the glands, and progress across this transition is significantly advanced in the 2BF treatment. 2BF sporozoites show significantly higher expression of genes associated with human infection whereas 1BF sporozoites show significantly higher expression of genes associated with earlier sporozoite functions. 2BF sporozoites also show upregulation of genes involved in lipid and fatty acid metabolism. Importantly, 2BF sporozoites show significantly higher rates of hepatocyte infection (1.9x rate of 1BF). Together, these results suggest that malaria parasites are not maximally effective at hepatocyte invasion upon initial arrival to the mosquito salivary glands, but undergo an additional maturation phase. Time to final parasite maturity also appears sensitive to mosquito feeding variability common to many malaria settings.

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PLASMODIUM FEMALE GAMETE SURFACE HSP90 IS A KEY DETERMINANT FOR MOSQUITO INFECTION

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Plasmodium female gamete surface HSP90 is a key determinant for mosquito infection Sung-Jae Cha1, Dingyin Tao1,2, Heather M. Kudyba3, Marcelo Jacobs-Lorena1, and Joel Vega-Rodriguez31 Johns Hopkins Bloomberg School of Public Health, Department of Molecular Microbiology and Immunology and Malaria Research Institute, 615 N. Wolfe St., Baltimore, MD, 21205, USA 2 Current address: National Center for Advancing Translational Sciences, National Institutes of Health, 9800 Medical Center Drive, Rockville, Maryland 20850, United States.3 Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD 20852, USA Abstract

Plasmodium fertilization is required for the development of the malaria parasite in the mosquito and is considered a prime target for strategies to block malaria transmission. Using phage peptide display screening we identified MG1, a peptide that binds to male gametes and inhibits mosquito infection, presumably blocking fertilization by competing with a female gamete ligand. Anti-MG1 antibodies bind to the female gamete surface and by doing so, inhibit oocyst formation in the mosquito. We determined that this antibody specifically recognizes HSP90 on the surface of Plasmodium female gametes. Our findings establish Plasmodium HSP90 as a potential target for the development of a transmission-blocking vaccine.

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INVASION OF RED BLOOD CELLS BY PLASMODIUM MALARIAE: UNRAVELING INTRA-ERYTHROCYTE DEVELOPMENT AND MOLECULAR MECHANISMS

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The frequent low parasitemia in Plasmodium malariae natural infections, the common occurrence of co-infections with mainly P. falciparum, and the impossibility of long-term in vitro culture has limited the information available for this species. In particular, but not limited to, there are large gaps of knowledge on specific molecular mechanisms of red blood cell (RBC) invasion and on host-cell preference of differentially mature RBCs present in circulation. In this study we aim to address some of these issues using P. malariae parasites collected from infected individuals aged 1-14 years in Mali. Host cell preference was measured taking advantage of a fluorescently labelled anti-CD71 antibody and, both, a DNA and a mitochondrial dye. A robust assay that allows quantification of new invasions in vitro, permitted to characterize invasion phenotypes using enzymes, which differentially cleave receptors from the RBC surface, and also the blocking effect of antibodies against known essential and non-essential RBCs receptors in other Plasmodium spp (Basigin, CD55, Duffy Antigen, CD71, Band 3 and Glycophorin A, CR1 and Sema7A). Our results show this parasite displayed a clear preference for reticulocytes, opposite to current knowledge. Also, treatment of RBCs with different enzymes (i.e. neuraminidase, trypsin and chymotrypsin) showed a significant but not complete reduction in invasion with all enzymes tested. None of the three antibodies tested, some with known blocking effects in other Plasmodium spp, hampered RBC invasion.

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THE ROLE OF THE PLASMODIUM FALCIPARUM ACETYL-COA SYNTHETASE IN GAMETOCYTOGENESIS AND TRANSMISSION

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Acetyl-CoA synthetase (PfAcAS) catalyzes the synthesis of acetyl-CoA, a key metabolite and histone acetylation donor in Plasmodium falciparum, the most lethal malaria parasite. Previous studies have shown that PfAcAS is essential for blood-stage growth and survival, and that specific

inhibitors of PfAcAS prevent growth by depleting cellular acetyl-CoA and disrupting histone acetylation. However, the role of PfAcAS in other parasite stages remains unknown. Here we investigated the function of PfAcAS in gametocyte and transmission stages using genetic manipulation, chemical inhibition, and functional assays. Using the NF54-iGP2 inducible gametocyte producing line, we generated highly synchronous gametocyte cultures to profile how PfAcAS inhibitors affect parasite viability and histone acetylation throughout gametocytogenesis. We found that inhibition of PfAcAS disrupted the development of early and late-stage gametocytes, and that histone acetylation was reduced in early gametocyte stages, consistent with previous observations in asexual-stage parasites. Using DDD9309, an optimized analogue of the PfAcAS inhibitor MMV019721 with improved biochemical and cellular potency (PfAcAS enzyme IC50 16 nM; 3D7 EC50 40 nM), we selected for resistance in the NF54-iGP2 line, and identified a novel T648A mutation in PfAcAS that conferred high level resistance to multiple PfAcAS inhibitors. We further characterized the ability of PfAcAS-T648A parasites to produce viable gametocytes and undergo transmission through mosquito stages of the parasite's lifecycle. Immunofluorescence assays showed that PfAcAS has a dynamic localization, changing from predominantly nuclear to cytosolic and back during gametocyte maturation, indicating that PfAcAS may perform multiple functions in gametocytes. Our study suggests that PfAcAS plays a role in the epigenetic regulation of gametocyte development, and reveals the essential role of PfAcAS in malaria parasite transmission stages. We propose that targeting acetyl-CoA biosynthesis could be a novel strategy to block malaria transmission.

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MOUSE ERYTHROCYTE BASIGIN INTERACTS WITH PLASMODIUM YOELII ERYTHROCYTE BINDING LIKE PROTEIN

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Malaria merozoites invade host erythrocytes through multiple interactions between parasite and erythrocyte surface proteins. Erythrocyte-binding-like (EBL) proteins, type I integral transmembrane proteins released from the merozoite micronemes, are known to play an important role in the formation of tight junctions between the merozoite and the erythrocyte surface. In human malaria, Plasmodium falciparum encodes 4 EBLs (PfEBA175, PfEBA140, PfEBA181, and PfEBL1) and P. vivax 2 EBLs (PvDBP, PvEBP2). Therefore, it is difficult to elucidate the functions by the loss-of-function approach because they may compensate each other. In contrast, P. yoelii encodes only a single EBL protein, PyEBL, and a single amino acid substitution (C351Y) in the N-terminal cysteine-rich Duffy binding-like region 2 (R2) of PyEBL drastically changed the virulence of P. yoelii parasites suggesting the usefulness of P. yoelii for the functional discovery of EBL proteins. In this study, we sought to elucidate the erythrocyte receptor of PyEBL that mediates its role as an invasion ligand. First, using the eukaryotic wheat germ cell-free system, we developed a protein library consisting of 237 mouse erythrocyte surface proteins and screened the library with native PyEBL protein as a ligand using AlphaScreen technology. We found that PyEBL interacts with mouse basigin, an erythrocyte surface protein. Using surface plasmon resonance, we further confirmed that PyEBL-R2 is the binding region with basigin, and the C351Y mutation did not affect the binding capability. These results are consistent with previous results that the R2 of P. vivax and P. falciparum EBLs interact with their erythrocyte receptors. The identification of basigin as the putative PyEBL receptor offers new insights into the role of this molecule and provides an important base for in-depth studies toward developing novel interventions against malaria.

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TRANSMISSIBILITY OF PRIMARY AND RECURRENT PLASMODIUM VIVAX INFECTIONS AND THE ROLE OF TRANSMISSION MODULATING IMMUNITY IN ETHIOPIA

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The prevalence of antibodies against sexual stage Plasmodium vivax parasites determines the success of transmission to mosquitoes, but their dynamics is not well characterized in homologous and heterologous recurrent infections. We evaluated the kinetics of transmissibility to mosquitoes and level of transmission blocking and enhancing antibodies among P. vivax infected patients (n=155) using direct membrane feeding assays (DMFAs) in 12 months follow up in Ethiopia. Of the 399 DMFAs done using 47,880 mosquitoes, 68% feeds were infectious with no difference between recruitment (67%, 169/252) and recurrent (70.7%, 104/147) infections. Of the feeds that involved serum replacement (n=146) using 23,993 mosquitoes, more feeds were infectious when naïve sera were used (80%) than feeds with patient's own sera (73%). Transmission reducing activity (TRA) >80% was observed in 16% (24/146) of these feeds. The mean oocyst density was higher in infected mosquitoes fed on naïve serum (42; 1-321) compared to autologous sera (21; 1-272; $p<0.001$). The proportion of infected mosquitoes associated with total (18S based qPCR) parasite ($\rho=0.32$; $p<0.001$) and gametocyte (sex specific RT-qPCR) densities ($\rho= 0.35$; $p=0.001$). Antibody responses against a panel of P. vivax gametocyte antigens are being quantified using ELISA. From a preliminary observation, antibodies against Pvs47, Pvs230 and Pvs25 were associated with reductions in mosquito infections and PvsHAP2 or Pvs47 antibodies were produced more likely in samples with TRA. The very high transmissibility of recurrent infections strengthens the need to implement radical cure strategies in P. vivax endemic settings. The sustained transmission blocking activity in recurrent infections hints the additional benefit transmission blocking interventions could add. Samples from patients at recruitment and recurrence were sequenced using short amplicon Next Generation Sequencing (NGS) using a panel of 100 P. vivax microhaplotype. We will apply a modelling framework that uses genotyping to determine the likelihood that recurrent infections derive from new (reinfection), recrudescent or relapse.

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A TWO PATCH MODEL FOR MUTASA AND NYANGA DISTRICTS IN MANICALAND PROVINCE ZIMBABWE INCORPORATING CLIMATIC CONDITIONS

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In Zimbabwe more than 50% of malaria cases are concentrated in Manicaland province, where seasonal malaria epidemics occur despite intensified control strategies. Understanding the local epidemiology of malaria, particularly diverseness across time and space is crucial to achieving control and elimination. Elimination and control efforts need to take cognisance of mobility patterns as well as climatic conditions as these can significantly influence prevalence and transmission of malaria. A two-patch model of non-linear differential equations for Mutasa and Nyanga district within Manicaland province is formulated and used to assess how variability in temperature and rainfall as well as mobility patterns affect the transmission dynamics of malaria in a population. The model is fitted using number of malaria cases, mean monthly temperature and rainfall data for the period 2005-2020. Sensitivity analysis using temperature and rainfall data highlighted that mosquito carrying capacity, and transmission

probability per contact for susceptible mosquitoes influence malaria transmission dynamics in the patches. The malaria burden within the two districts increases with increases in mean monthly temperature and mean monthly rainfall (|17-250C| and |32-110mm|) respectively. Numerical simulations reveal that mobility accounts for endemicity of the disease in both patches, in particular if biting intensity of the mosquitoes is high then infection prevalence increases with mobility. Incorporating variability in climatic conditions and mobility in the patch model helps forecast malaria transmission patterns and highlights which areas need interventions. The numerical simulations highlighted that perturbations as a result of major climatic changes also affect mobility patterns, therefore there is need to continually monitor and evaluate the implications of these changes.

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DESCRIPTION OF PLASMODIUM FALCIPARUM TRANSMISSION ASSOCIATED HAPLOTYPES

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Malaria is the deadliest mosquito-borne parasitic infection worldwide, with one parasite, Plasmodium falciparum (Pf), accounting for the majority of deaths, especially in Africa and Asia. Despite its tremendous impact on public health, much remains to be characterized in global populations of Pf, including existing structural variation among Pf genomes. Recent observations, based on whole genome sequencing data from Pf samples from Africa and Southeast Asia (SEA), suggest that the vector may have an underappreciated impact on Pf evolution. In particular, we have identified (nearly) fixed nonsynonymous SNPs in loci preferentially expressed during transmission-related stages of the life cycle. Now, based on whole genome assemblies for 19 Pf samples from countries in Africa and SEA, we have also identified fixed structural differences between African and SEAn Pf populations. AP2-G, a key transcription regulator of sexual stage commitment, harbors a 200 bp deletion at the 3' end of the gene in all African Pf samples, including the reference Pf3D7. This deletion spans the in-frame stop codon found in SEAn Pf strains, as well in outgroup Plasmodium species, resulting in a longer and quite different C-terminal AP2-G sequence in African strains. Here, we investigated if there are other genomic variants in allelic association with the AP2-G deletion, which could contribute to modulate its function. In addition to 4 additional genes containing fixed structural variants, there are 28 nonsynonymous SNPs, identified among 12 genes, in strong linkage disequilibrium (r2 >= 0.7) with the observed AP2-G deletion. These genes are enriched in biological processes such as responses to defenses of host. Most of these genes are primarily expressed in Pf sexual life-cycle stages. We are investigating possible interactions between these genes and AP2-G. Finally, several of these genes are transmission-associated loci targeted by vaccines currently in the developmental pipeline, including Pfs47 and the gene encoding TRP1, providing region-specific Pf transmission-associated haplotypes, which may be important to consider in vaccine formulations.

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DYNEIN HEAVY CHAINS IN PLASMODIUM FALCIPARUM DURING GAMETOCYTES DEVELOPMENT

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Plasmodium falciparum is the deadliest among the malaria causing parasites. The sexual conversion into the gametocyte and development (gametocytogenesis) is crucial step for the successful transmission of parasite in the mosquitos. Further, the gametocytogenesis is a response of the parasite to cope up with the continuous stresses that it faces during the asexual intra-erythrocytic development cycle (IDC) in the human host. In our previous genetic phenotype piggyBac mutagenesis screen we found that one of the Dynein Heavy Chains gene (DHC) Pf3D7_1122900, a microtubule associated protein, manifests the increased sensitivity to stress response pathways during IDC upon heat shock and Dihydroartemisinin (DHA) stress. Orthologs of these proteins known to act as the ATP dependent motor proteins on the microtubules for the cellular transportation of the cargos, positioning of the organelles and the structural integrity of the cells. However, these genes remain uncharacterized in the P. falciparum. Here we report the piggyBac screening for the gametocytogenesis and found that several piggyBac DHC mutants are involved in the induction of gametocyte conversion and the development. In order to characterize their functions, we used Lox-Pint mutagenesis and generated conditional Knock-out mutants for these genes. Dynein heavy chains and their associated proteins play an important role in the transport and structural integrity of the cells that is also an essential mechanism for the gametocytes to attain their specific falciform shape in order to get transmitted successfully. Therefore, functional characterization of this family would provide new drug targets to mitigate the malaria pathogenesis by inhibiting the transmission of parasite from human to mosquitos through breaking the survival chain of the parasite.

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LOSS OF FUNCTION OF THE PLASMODIUM FALCIPARUM PROLINE TRANSPORTER MFR4 MEDIATES HALOFUGINONE RESISTANCE BUT RESULTS IN OOCYST DEVELOPMENTAL DYSFUNCTION.

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Halofuginone (HFG) is a potent antimalarial targeting the cytoplasmic proline-tRNA synthase of Plasmodium falciparum. We have previously demonstrated that resistance to HFG can be mediated through two distinct mechanisms: the Adaptive Proline Response (APR) and mutations in the active site of the target gene. In asexual parasites, the APR is characterized by accumulation of cytoplasmic proline that confers low level (20-fold) resistance to HFG by competing for binding the target protein. Whole genome sequencing identified frameshift and nonsense mutations in the major facilitator superfamily related protein 4 gene (pfmfr4, also known as ApiAT2) associated with the APR phenotype. Metabolic labelling experiments were used to demonstrate that during asexual blood-stages, MFR4 functions to export proline derived from hemoglobin degradation and biosynthesis from arginine. To understand whether HFG resistant parasites are transmissible, infectious bloodmeals containing drug-selected ΔMFR4 parasites were fed to Anopheles gambiae mosquitoes. ΔMFR4 parasites show no defect in infectivity to mosquitoes, but are dysfunctional in their development as oocysts. While ΔMFR4 parasites cannot complete development to sporozoites, a subset of the oocyst population demonstrates growth at a reduced rate. Previous work in the Plasmodium

berghei/Anopheles stephensi experimental system pointed to an essential role of MFR4 in transmission. Our data suggest that proline transport and metabolism play a critical, yet unknown role in the transmission stages of P. falciparum development, revealing a novel target for mosquito-based transmission blocking interventions.

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A SINGLE FULL-LENGTH VAR2CSA ECTODOMAIN ELICITS HETEROLOGOUS FUNCTIONAL ANTIBODIES IN AOTUS NANCYMAAE

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Malaria caused by Plasmodium falciparum continues to be a global problem with devastating consequences. Pregnancy malaria is associated with poor outcomes including stillbirth, preterm delivery, and low birth weight. Placental malaria (PM) is caused by P. falciparum-infected erythrocytes that bind to the placental receptor chondroitin sulfate A (CSA) and sequester in maternal intervillous spaces. In first-time mothers, parasite sequestration in the placenta often induces a macrophage-rich inflammatory infiltrate associated with poor pregnancy outcomes. Women become resistant to pregnancy malaria as they acquire antibodies that target surface proteins expressed by placental parasites. VAR2CSA, a member of the PfEMP1 variant antigen family, is a surface protein of infected erythrocytes (IE) that mediates adhesion to CSA and is the leading target antigen for a vaccine to prevent PM. Here, we assessed the functional activity of antibodies raised against a recombinant full-length VAR2CSA ectodomain (NF54 variant). Plasma samples from Aotus (N=4) immunized with full-length VAR2CSA were tested in binding-inhibition assays that used freshly collected IE from 15 pregnant women in Ouelessebougou, Mali. All plasma samples inhibited IE binding to CSA (i.e., reduced the number of parasites bound >50%) in most isolates (range, 53-73% of isolates). These results suggest that a VAR2CSA vaccine using a single or limited VAR2CSA alleles can elicit broad heterologous functional activity.

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INITIAL EVALUATION OF THE PVS230D1-EPA CONJUGATE VACCINE CANDIDATE

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Pvs230, a pre-fertilization gametocyte/gamete antigen of Plasmodium vivax, is a promising malaria transmission-blocking vaccine (TBV) candidate. Pvs230 is expressed by parasite gametocytes in the human host and displayed on the surface of gametes in the mosquito host. To increase immunogenicity, the recombinant, Pichia pastoris-expressed domain 1 of Pvs230 (Pvs230D1M) was conjugated to the recombinant, non-toxic Pseudomonas aeruginosa ExoProtein A (rEPA) in conformance with current good manufacturing practices (cGMP). In order to meet regulatory requirements prior to clinical trials, extensive evaluations of the conjugate must be conducted. In this study, the cGMP Drug Product Intermediate (DPI) Pvs230D1-EPA conjugate was evaluated by the following analyses: purity by visual inspection (appearance); limulus amebocyte lysate (LAL) for endotoxin; microbial enumeration tests for bioburden; general safety and rabbit pyrogenicity test; strength (protein content) by UV spectrum (A280) and BCA protein assay; identity by amino acid composition; pH; SDS-PAGE with Coomassie blue staining (migration pattern); Western blot using conformation-dependent monoclonal antibody 1H3 and an anti-exotoxin A polyclonal antibody; and integrity by SDS-PAGE, reverse phase ultra-performance liquid chromatography (RP-UPLC), size-exclusion ultra-performance liquid chromatography (SEC-UPLC) and size exclusion chromatography with inline multi-angle light scattering (SEC-MALS). Our results indicate the cGMP grade Pvs230D1-EPA meets regulatory requirements and is suitable for use in human clinical trials.

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SYSTEMS SEROLOGY OF PFSPZ VACCINE REVEALS IMPORTANCE OF NON-PFCSP ANTIBODY IMMUNITY IN LONG-LASTING PROTECTION

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Malaria remains a major cause of morbidity and mortality across Sub-Saharan Africa as well as globally. PfSPZ Vaccine is a whole cell radiation attenuated Plasmodium falciparum (Pf) sporozoite (SPZ) vaccine that has demonstrated promising efficacy in multiple clinical trials. Previous work has suggested that liver resident CD8+ T cells are essential for long-last PfSPZ-mediated protection. Here we have applied high-dimensional antibody profiling to identify humoral correlates of long-lasting protection. Though Anti-PfCSP Ab titers and antibody-dependent complement deposition (ADCD) increase with PfSPZ vaccination and are associated with protection early on, their responses wane and are not central to long lasting-protection. Our machine learning and statistical methods showed a new role for non-PfCSP non-IgG and complement activity in PfSPZ-mediated long lasting protection and point to the importance of non-PfCSP functional antibody responses in pre-erythrocytic vaccine-mediated immunity.

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CHARACTERIZATION OF KENYAN PLASMODIUM FALCIPARUM FIELD ISOLATES FOR USE IN CONTROLLED HUMAN MALARIA INFECTION

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Controlled human malaria infection (CHMI) is a critical tool for evaluating drug and vaccine efficacy in a controlled setting. However, CHMI studies have been conducted with limited number of parasite strains isolated from human more than 40 years ago. This could lead to false inferences due to lack of parasite diversity inherent in present-day natural infections. Only two unique cloned strains are available for use (NF54/3D7 from Africa and 7G8 from Brazil). To fill this gap this study is designed to identify, down select parasites sensitive to chloroquine (CQ), quinine (QN), atovaquone (AV), primaquine (PQ), artemether (AR), artesunic acid (AS), amodiaquine (AMQ), artemisinin (ART), halofantrine (HAL), and tafenoquine (TAF). Isolates should produce infective gametocytes and genetically diverse. A total of 56 individuals from WRAIRs 2454 protocol presenting symptoms of uncomplicated malaria were screened for blood borne pathogens before enrollment, and a total of 40 individuals were excluded. Immediate ex vivo

analysis was done for sensitivity testing and molecular analyses to confirm species composition, genotypes, gametocytes and drug resistance marker profile. Serum and plasma for n (16) was processed and sent to WRAIR for blood borne pathogen confirmatory testing. Of n=16, 10 were tested and had the following median drug concentration (IC50s) 14 ng/ml (7.946-14.78) for chloroquine, 29.04 ng/ml (21.71-57.17) for quinine, 4.955 ng/ml (3.631-6.173) for atovaquone, 870 ng/ml (622.6-900.1) for primaquine, 3824 ng/ml (1527-6569) for doxycycline, 5.796 ng/ml(3.941-8.531) for artemether, 3.627 ng/ml (3.299-6.829) for artesunic acid, 1.457 ng/ml (0.9395-1.666) for amodiaquine, 5.796 ng/ml (3.941-8.531) for artemisinin, 19.69 ng/ml (16.45-27.74) for halofantrine and 423.4 ng/ml (141.2-859.4) for tafenoquine. Of the 16 samples, 87.5% harbored gametocytes, 68.75% had falciparum only, and 12.5% had co-infection of either P. falciparum with P. malariae or P. falciparum with P. o.wallikeri respectively. These findings prequalify and support the identification of new isolates for consideration in future CHMI studies.

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CROSS-SECTIONAL ASSESSMENT OF FACTORS DRIVING PARTIAL VERSUS FULL UPTAKE OF RTS,SAS01 MALARIA VACCINE AMONG CHILDREN IN RARIEDA SUB-COUNTY, WESTERN KENYA, 2021 TO 2022

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Following the 2015 World Health Organization (WHO) recommendation, pilot implementation of the 4-dose RTS,S/AS01 (RTS,S) malaria vaccine began in western Kenya in September 2019 as part of the routine childhood immunization schedule at 6, 7, 9, and 24 months of age. We used data from a continuous Malaria Indicator Survey (cMIS), a cross-sectional survey conducted from November 2021-July 2022 in 847 households, to assess RTS,S coverage and uptake 2 years post-introduction in Rarieda sub-county. Of 148 children, 71 aged 12-23 mo and 77 aged 27-38 mo, 66% had a home-based vaccination record documenting vaccination status (12-23 mo: 72% and 27-38 mo: 60%). RTS,S1, RTS,S2, RTS,S3, and RTS,S4 coverage was 90.2% (95% CI: 78.5-96.7), 84.3% (95% CI: 71.4-93.0), 80.4% (95% CI: 66.9-90.2), and 26.1% (95% CI: 14.3-41.1), respectively. Corresponding mean age at vaccination was 6.6 (95% CI: 6.0-7.1), 7.7 (95% CI: 6.9-8.6), 9.9 (95% CI: 9.3-10.6), and 23.3 months (95% CI: 19.4-27.1). Benchmark measles vaccine coverage (dose 1 - RTS,S3; dose 2 - RTS,S4) was 88.2% (95% CI: 76.1-95.6) and 56.5% (95% CI: 41.1-71.0). Odds of being fully vs. partially RTS,S vaccinated (<3 doses by 23 mo and primary series only by 38 mo) did not differ significantly by gender, household wealth, caregiver education, or bednet use. Of children 12-23 mo, those who were the only child under 5yrs in the household were 9.6 times (95% CI: 1.5-190.9) more likely to have received all 3 RTS,S doses compared to those in households with more than 1 under 5 yrs. Of children 27-38 mo, those with measles dose 2 were 9.9 times (95% CI: 1.5-199.9) more likely to be fully vaccinated with 4 RTS,S doses vs. those without the 2nd dose. While not significant, those who were fully vaccinated with core EPI vaccines per WHO guidelines were more likely to be fully vaccinated with RTS,S (OR: 1.8 [95% CI: 0.2-10.6]). Our study found high uptake and moderate dropout for the primary series. RTS,S4 may face similar uptake barriers as other second-year of life vaccines. If RTS,S vaccination schedules are revised, understanding populations at greater risk for dropout can guide vaccination roll-out strategy to ensure optimal coverage.

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FEASIBILITY EVALUATION OF RTS,S/AS01 MALARIA VACCINE PILOT INTRODUCTION IN WESTERN KENYA: COVERAGE SURVEY RESULTS 30 MONTHS POST-INTRODUCTION

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RTS,S/AS01 (RTS,S) malaria vaccine was introduced in western Kenya in September 2019 through the World Health Organization-initiated pilot to evaluate the safety, impact, and feasibility of integrating the 4-dose schedule (at ages 6, 7, 9, and 24 months) into routine immunizations. Three large household surveys assessed RTS,S uptake of doses 1-3 among children aged 12-23 months, and dose 4 in children 27-38 months in 46 pilot sub-counties before (HHS1, July-October 2019), and 18 (HHS2, May-July 2021) and 30 (HHS3, April-June 2022) months post RTS,S introduction. RTS,S coverage was measured by vaccination cards, available for 86%, 88%, and 89% of children in HHS1, HHS2, and HHS3, respectively; or caregiver recall for those with no cards. In HHS3, the coverage for RTS,S doses 1-3 was 82.7% (95%CI 78.6-86.1), 78.1% (95%CI 73.7-81.9), and 68.9% (95%CI 63.9-73.6), respectively, with an improvement from HHS2 in coverage (dose 1-3: 78.6%, 71.4%, and 62.3%) and dropout rates (9.2% to 6.0% dose 1 to 2; 20.7% to 16.9% dose 1 to 3). RTS,S dose 4 coverage was 32.7% (95%CI 27.9-37.9), with 52.2% dose 3 to 4 dropout, and lower uptake than measles dose 2 (58.9% (95%CI 55.3-62.4)) given 6 months earlier. RTS,S coverage was lower among children not sleeping under a bednet the night before, compared to those who did (dose 1: 57.6% vs. 84.2%; dose 2: 55.1% vs 79.4%; dose 3: 46.9% vs. 70.2%; $p<0.05$); and in areas with indoor residual spraying (IRS), than areas without IRS (dose 3: 55.1% vs. 73.3%; dose 4: 10.6% vs. 40.1%; $p<0.05$). No differences in RTS,S uptake were noted by sex, caregiver's age or parity, or residence (urban vs. rural). Caregivers with secondary or higher education were 2.1 times (95%CI 1.5-3.1) more likely to bring their child for all 4 RTS,S doses than those with primary education only, and uptake increased with wealth. No negative impact of RTS,S introduction on other malaria (bednet use) and childhood interventions (vitamin A supplements, deworming), or uptake of other vaccines was observed 30 months into the pilot. Our study found that coverage of the first 3 RTS,S doses and the dropout rates improved over time, while low uptake of the fourth dose remains a challenge.

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THE ADDITIVE VALUE OF RTS, S,AS01 MALARIA VACCINE IN REDUCING MALARIA INFECTION AMONG UNDER FIVE CHILDREN IN MALAWI

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The RTS, S/AS01 malaria vaccine was recently recommended by World Health Organization (WHO) for widespread use among under-five children in areas with moderate to high Plasmodium falciparum malaria transmission. As part of the Malaria Vaccine Implementation Program (MVIP), we estimated the additive value of RTS, S/AS01 in preventing malaria infection. We assessed prevalence of malaria in areas deploying: i) traditional mosquito nets, ii) Pyrethroid-piperonyl butoxide (PBO) or Interceptor G2 (IG2) nets only, iii) indoor residual spraying (IRS) only, vi) RTS, S/AS01 only, v) PBO/IG2 nets + RTS, S/AS01, vi) IRS + RTS, S/AS01. A total of 4,909 children aged 5-48 months were recruited for the survey. The mean age was 25 months (SD=11) and 2,456 (50.0%) were females. Out of the

enrolled children, 638 (13.0%), 1,256 (25.6%), 556 (11.3%), 323 (6.6%), 1,375 (28.0%) and 760 (15.5%) were from areas deploying traditional nets, with PBO/IG2 nets only, IRS only, RTS, S/AS01 only, PBO/IG2 nets + RTS, S/AS01 and IRS + RTS, S/AS01 respectively. Malaria prevalence was lowest in areas implementing PBO/IG2 nets + RTS, S/AS01 [4.8% (95% CI: 3.6%, 6.3%)], followed by PBO or IG2 nets only [5.4% (95% CI: 3.8%, 6.7%)], IRS + RTS, S/AS01 [13.8% (95% CI: 8.6%, 21.4%)], RTS, S/AS01 only [14.4% (95% CI: 4.6%, 37.2%)] then IRS only [23.2% (95% CI: 17.3%, 30.2%)] and highest in areas deploying traditional nets [25.2% (95% CI: 18.6%, 33.2%)]. To conclude, this survey has demonstrated that RTS, S/AS01 has substantial added value in reducing malaria infections when combined with existing standard vector control interventions such as the ITNs use or IRS. As malaria endemic countries are rolling out the RTS, S/AS01 malaria vaccine, policy makers and programmers should focus on promoting use of combined delivery of vector control interventions to rapidly reduce burden of malaria among children.

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RTS,S MALARIA VACCINE COMBINED WITH PYRETHROID-PIPERONYL BUTOXIDE-LONG-LASTING INSECTICIDAL NETS (PBO-LLIN) PROVIDES ADDED PROTECTION AGAINST PLASMODIUM FALCIPARUM INFECTION COMPARED WITH PBO-LLIN ALONE

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Both PBO nets and RTS,S vaccine have been shown to be independently effective against malaria in areas of high prevalence. However, the combined effects of these interventions have not yet been explored. The current study aimed to examine whether adding RTS,S to PBO nets is more effective in preventing Plasmodium falciparum infection compared with PBO nets alone. We analyzed data from 776 children aged 7 months to 10 years from a prospective community-based longitudinal study in Malawi. Index children aged 7-18 months received 3 doses of RTS,S, and PBO nets, while those aged 19 months to 10 years (siblings) received PBO nets only. Capillary blood samples were collected at enrollment (month 0), and at 2, 4, and 6 months thereafter, for detection and quantification of P. falciparum using qPCR targeting the 18s rRNA gene. The effect of adding RTSS+PBO nets compared to PBO nets only was estimated using multivariable generalized estimating equation models after adjusting for predictors including age. In total, 60% (469/776) of children received both PBO nets and RTS,S whilst 40% (307/776) received only PBO nets. In this analysis, all children contributed to 325 person-years of follow-up. There were 376 infection events/100 person-years at risk in the PBO nets alone group against 157 events/100 person-years at risk in the RTS,S+ PBO nets group. The adjusted incidence rate ratio (IRR) in children who had received only PBO nets was twice that of children who had received RTS,S+PBO nets (IRR: 2.11; 95% CI: 1.62-2.75). These results suggest that adding RTS,S vaccination to PBO nets intervention might be used to further reduce P. falciparum transmission and infection in areas where malaria is perennial.

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IMPACT OF RTS, S/AS01E VACCINATION ON PLASMODIUM SPECIES COMPOSITION IN INDIVIDUALS ENROLLED FOR AT BASELINE AND DURING THE SUBSEQUENT FOLLOW-UP PERIOD IN MALARIA ENDEMIC REGIONS OF WESTERN KENYA IN KISUMU COUNTY

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RTS, S/AS01E is a recombinant protein-based malaria vaccine that elicits the production of antibodies against the Plasmodium falciparum (Pf) circumsporozoites, thereby blocking the establishment of the infection in the liver cells. In 2014, a phase 3 trial showed that RTS, S had high efficacy in infants and young children, and based on this, the World Health Organization recommended the vaccine roll-out of in selected regions of Africa. However, information on the potential of the vaccine to protect against the acquisition of non-Pf species, such as P. malariae (Pm), P. ovale curtisi (Poc), and P. ovale wallikeri (Pow), is limited despite the rising frequency of non-Pf species infections, which account for 25% of imported malaria cases worldwide.A total of 125 samples from African adults with sub-clinical PCR positive parasitemia in Kombewa, Kenya participating in a RTS, S vaccine efficacy study were characterized for Plasmodium species composition at enrolment versus subsequent follow up time-points. Concurrently, 153 samples were obtained from symptomatic individuals visiting Kombewa Sub County Hospital within the same catchment and characterized for species composition of the infections was established using rt-PCR at enrolment as well as upon subsequent infection detection. Infections containing Pf were most frequent among the symptomatic individuals enrolled from the same catchment, with 76.19% followed by P. malariae, with 27.38%, P. ovale wallikeri, 17.86% while P. ovale curtisi was least prevalent at 10.0%. Analysis of species composition for the samples from individuals who received vaccines at the initial timepoint and at subsequent time-points during follow-up visits is underway

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EFFICACY OF THE RTS, S/AS01E MALARIA VACCINE ADMINISTERED ACCORDING TO DOSAGE REGIMEN UNDER CONDITIONS OF NATURAL EXPOSURE IN AFRICAN CHILDREN AGED 5-17 MONTHS: INSIGHTS FROM EXTENDED GENOTYPING-BASED ENDPOINT RESULTS AND MALARIA INFECTION STATUS AT FIRST VACCINATION FROM A PHASE 2B RANDOMIZED CONTROLLED TRIAL

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A phase 3 trial showed moderate vaccine efficacy (VE) of RTS,S/AS01E against clinical malaria in African children when administered according to a 0, 1, 2-month (M) primary schedule (M012) with a 4th dose given at M20. We present initial results deriving from PCR-based genotyping endpoints of an ongoing phase 2b open-label, randomized, controlled trial (NCT03276962) evaluating efficacy of RTS,S in multiple full vs fractional (Fx) dose regimens under conditions of natural exposure. A total of 1500 children aged 5-17M were randomized (1:1:1:1:1) to receive RTS,S (2 full-dose and 2 Fx dose regimens) or a rabies control vaccine (M012). We evaluated two molecular endpoints: the time to the first new molecular infection, and the total number of new molecular infections, each during 32 months post-dose-1 and 24 months starting at 14 days post-dose-3, using Illumina-based amplicon sequencing of the CS C-terminus and a control antigen. As in a previous analysis with shorter follow-up periods, we observed significant VE, in the 26%-42% range (95% CI union, 11%-53%), against the first molecular infection for all 4 RTS,S regimens vs. control across both follow-up periods. VE against the first molecular infection was similar across the 4 RTS,S regimens, with no significant differences. Each RTS,S regimen significantly reduced the number of new

molecular infections. We also tested the hypothesis that VE of RTS,S might be reduced in participants with evidence of existing baseline infections at the time of first vaccination from microscopy and/or PCR amplicon data. Contrary to expectation, VE of RTS,S against the first infection was significantly higher (P=0.0015) in participants who were malaria-infected (67.8%; CI 50.5-79.0%) vs. uninfected (31.3%; CI 17.5-42.9%) at the first vaccination. Higher VE in baseline-infected participants could suggest new strategies for highly efficacious malaria vaccine development or implementation.

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THE EFFECT OF RTS,S, AND SEASONAL MALARIA CHEMOPROPHYLAXIS (SMC) ALONE OR COMBINED ON ANTIMALARIAL ANTIBODY RESPONSES

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The combination of the malaria vaccine RTS,S and seasonal malaria chemoprophylaxis (SMC) has been shown to have a significant reduction in malaria incidence in children up to 5 years old compared with either intervention delivered alone. However, it is likely interventions will effect the development of naturally acquired immunity to malaria; understanding this effect may help predict and mitigate any post intervention effects on incidence in children as they age. Dried blood spots were collected in November, the peak transmission season, in 2019 and 2020 from study children who had received the combination of RTS,S and SMC together or separately in Mali and Burkina Faso. Samples were assayed against ~ 30 malaria specific antigens classified into representing historical & recent exposure and protection associated. Continuous antibody responses were analysed using principal components analysis (PCA). As expected, responses to the RTS,S vaccine components were significantly higher in those that received the vaccine (linear regression coefficient 1.97 for RTS,S alone vs SMC P<0.001 & 0.00 RTS,S/SMC vs RTS,S alone p=0.99).This included antibody responses to MSP5 an 'off target' antigen response that has previously been associated with RTS,S vaccination. For other antigen groups, responses were typically higher in participants from Burkina Faso than those from Mali reflecting differences in malaria transmission intensity. Overall, responses showed broadly similar patterns: lowest in children receiving the combined intervention and highest responses in those that received the vaccine alone (e.g protective associated - linear regression coefficient 0.03 for RTS,S alone vs SMC P0.05 & -0.09 RTS,S/SMC vs RTS,S alone p<0.001). This most likely reflects the mode of action of the different study interventions. Preliminary data on antibody avidity suggest antigen specific differences that may be linked to the development of protective immunity. How meaningful these antibody responses will be determined by the ability of children in each arm to be naturally protected from malaria in an ongoing prospective study.

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ESTABLISHING RTS,S/AS01 AS A BENCHMARK COMPARATOR FOR NEXT-GENERATION MALARIA VACCINES IN THE TGPB-PFCSP MOUSE CHALLENGE MODEL

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Mouse models using transgenic Plasmodium berghei sporozoite tgPb-PfCSP containing full-length P. falciparum CSP allow two assessments of efficacy: reduction in liver infection following IV challenge, and sterile protection against blood-stage infection following mosquito bite challenge. We introduce a clinically relevant benchmark for comparison of next-generation PfCSP targeted vaccines to the RTS,S/AS01E vaccine. We focus on reproducibility of antibody responses and functional activity in conjunction with robust statistical analyses. A 200-fold range of RTS,S was tested in a constant amount of AS01E adjuvant. Two or three doses were given intramuscularly at three-week intervals, with challenge two weeks after the last vaccination. Protection was highest with the three-dose schedule, but levels remained lower than those seen when potent anti-CSP mAbs, such as mAb317, are administered, indicating the range of this model is suitable for screening more potent vaccines. Induced sera anti-CSP antibody concentrations were also associated with activity: 141 µg/mL reduced liver infection by 50% relative to controls, whereas 300-350 µg/mL is required for 50% protection against blood-stage infection in the parasitemia model. These results provide guidance on using a mouse model of infection to compare vaccines against the only approved malaria vaccine to date. Accounting for assay variability, liver infection experiments are powered (80%) to detect a three-fold change in liver burden using at least eight mice per group and parasitemia studies are powered to detect a 35-40% improvement over three doses of RTS,S/AS01E using ten mice per group. With reasonable sample sizes, inter- and intra-assay variability remain within acceptable bounds for detecting improvement in vaccine function whether the result of greater levels or potency of the induced responses. This ability to compare advanced preclinical and clinical-stage CS-based vaccines to RTS,S/AS01 is now available to the broader malaria vaccine community.

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GENETIC PHYLOGENY OF DIARRHEAGENIC ESCHERICHIA COLI ISOLATED IN CHILDREN BELOW FIVE YEARS LIVING IN CLOSE CONTACT WITH FOOD ANIMALS, KISUMU COUNTY

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Diarrheagenic Escherichia coli strains they cause diarrhea infection in children below five years and food animals. Focus of the study; understand the genetic phylogeny of diarrheagenic E.coli isolated in children below five years and that isolated from food animals in Kisumu County, to establish possibility of zoonotic transmission, and determine their antibiotic resistance patterns. Two hundred children samples and animal samples were collected and processed using traditional culture methods. The molecular identification of pathotypes was assayed using primer-specific polymerase chain reaction (PCR) targeting three virulence genes (lt, st, bfpA, eae, aatA and aaiC) related to three DEC pathotypes (EPEC, EAEC and ETEC). The antimicrobial susceptibility testing was carried out using the Kirby-Bauer disk diffusion method. Colonies from 156 study subjects (100 diarrhea children and 56 diarrhea food animals) were positive for E. coli isolates. Subsequent PCR detection discovered that 26% of children and 10.7% of diarrhea food animals' isolates were positive for one or more virulence genes typical of particular strains. Among those EAEC [(11%), (2%)] ETEC,

[(4%), (0%)] and EPEC [(3%), (8.9%) Of the identified E. coli isolates, about (4%%) were found to be mixed infections. ETEC/EAEC (2%) and EAEC/EPEC (2%) strains this were better detected in children with close contact with diarrhea food animals than children with no contacts. Most antibiotic resistances were obtained towards trimethoprim sulfamethoxazole (95.8%), tetracycline (91.7%), and ampicillin (91.6%). ninety percent of isolates were resistant to a minimum of three categories of antibiotics. Diarrheagenic E.coli is the key contributor of diarrhea in children below five years, there is risk of severe diarrhea from known pathogenic strains hence emergence of resistance narrows options of treatment. Sequencing of isolates is ongoing.

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CHANGES IN GROWTH OBSERVED IN DIFFERENT ANTHROPOMETRIC INDICES AT 90-DAY POST-DISCHARGE FOLLOW-UP AMONG CHILDREN AGED 2-23 MONTHS REQUIRING READMISSION COMPARED TO THOSE WHO DID NOT REQUIRE READMISSION

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Due to availability of limited information on post-discharge growth follow-up among children requiring readmission, we sought to investigate whether post-discharge readmission at day-90 follow-up had any impact on growth in children aged 2 to 23 months. We conducted a case-control study and data extracted from “Antibiotic for Children with Diarrhea (ABCD)” trial which was a seven-country double-blind, randomized, placebo-controlled clinical trial. The Bangladesh site enrolled 1431 children aged 2 to 23 months who were dehydrated or severe stunted or moderately wasted or any combination of these. Among them, 145 children were readmitted to hospital (cases) within a 90-day post-discharge follow-up. Each cases were matched by age and sex to three controls (n = 435). Anthropometry of all children were measured at the time of enrolment and on the 90-day follow-up. The data were analysed using multivariate linear regression to assess the changes in growth at day-90 post-discharge follow-up. At 90 days of post-discharge follow-ups, the mean changes in growth among the cases using four anthropometric indices were found to be significantly reduced compared to the controls ($p<0.05$). After adjusting the potential factors, the anthropometric outcomes Δhaz (coef.-0.10, 95% CI -0.19, -0.01, p-0.036), Δwaz (coef.-0.22, 95% CI -0.32, -0.12, p-<0.001), Δwhz (coef.-0.21, 95% CI -0.35, -0.08, p-0.002) and Δmuac (coef.-0.15, 95% CI -0.28, -0.03, p-0.014) were found to have significant reduction of growth among the readmitted cases compared to their counterpart. In conclusion, the present study prevailed there was a significant reduction of growth in all anthropometric indices at day-90 post-discharge follow-up among children requiring readmission compared with those who didn`t require readmission. This finding underscores the importance of investigating the clinical and social risk factors of readmission that may help to design a post-discharge intervention that may further help to reduce the growth faltering by reducing post-discharge readmission.

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CLINICAL, SOCIO-ECONOMIC AND PATHOGENIC FACTORS OF WASTED AND OVERWEIGHT/OBESE UNDER-FIVE CHILDREN WITH DIARRHOEA: EXPERIENCE FROM AN URBAN HOSPITAL IN BANGLADESH

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Wasting (weight-for-height z score <-2 SD) and overweight/obese (weight-for-height z score >+2 SD) are two critical indicators of malnutrition. In recent years the burden of overweight (39 million) is increasing alongside a continuing problem of wasting, creating a “double burden” of nutrition-related health issues. Data are limited concerning the comparison of these two groups of under-five children with diarrhoea. Therefore, we aimed to compare the associated factors and outcomes of wasted children with overweight/obese children with diarrhea admitted to Dhaka hospital, icddr,b. Data from 15,795 children aged <5 years were extracted from the surveillance system of Dhaka Hospital between January 2012 and December 2021. After excluding the non-desired population (n=13,074), 2296 wasted and 425 overweight/obese children were analyzed. After adjusting age and sex, fever (aOR: 1.574, 95% CI:1.26,1.96, P<0.001), dehydration (aOR: 3.078, 95% CI:2.40,3.95, P<0.001), and use of IV fluid (aOR: 2.551, 95% CI:1.49,4.37, P=0.001) was more likely associated with wasted children compared to overweight/obese children. On the contrary father’s education (aOR:0.231, 95% CI:0.15,0.35, P<0.001), mother’s education (aOR: 0.260, 95% CI:0.16,0.42, P<0.001), antibiotic use before admission (aOR:0.520, 95% CI:0.39,0.69, P<0.001), use of sanitary latrine (aOR: 0.633, 95%CI:0.45,0.89, P=0.008), water purification (aOR: 0.737, 95% CI:0.60,0.91, P=0.004) were less likely associated with wasted children compared to their counterparts. Exposure to enterotoxigenic Escherichia coli (ETEC) (aOR: 2.603, 95% CI:1.12,6.04, P=0.026) was significantly associated with wasted children whilst rotavirus (aOR: 0.554,95% CI:0.37,0.83, P=0.004) exposure showed an opposite trend after adjusting age and sex. Clinical and microbiological presentations are different in these two nutritional groups of children with diarrhoea. This study may help the policy maker to establish better identification and management strategy for these vulnerable populations.

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TITLE: SOCIODEMOGRAPHIC AND CLINICAL DETERMINANTS OF DIARRHEA AFFECTED CHILDREN TREATED WITH ANTIBIOTICS EMPIRICALLY PRIOR COMING TO HEALTH CARE FACILITIES IN DEVELOPING COUNTRIES LIKE BANGLADESH

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Scarcity of evidence, children are receiving antibiotics empirically in acute watery diarrhea. This study explores the sociodemographic and clinical determinants of children who received antibiotics in acute watery diarrhea. Secondary Data were extracted from the” Antibiotic for children with diarrhea” trial, Bangladesh site database. ABCD study was a randomized multi-country, multi-site, double- blinded, placebo -controlled trial, conducted on seven countries from 1st July 2017 to 10th July 2019 among the 2-23-month-old children. Among 35137 screened participants, total 13630 children received antibiotics prior seeking treatment in health facility. The prevalence of using antibiotics (52%) by literature review, 384 are randomly taken who received antibiotics as case. Control was selected 2 times more, matched with age and sex. Children treated with antibiotics has 3- 5 times/day,6.77%, less dehydration 0.8% than control, 10.6% and 3.4% respectively and also has higher proportion of no sign of dehydration (99%) rather than control (96%), showing statistically significant. Mother’s aged ≥30 Years, well-educated and having one parity treated their children with antibiotics more likely (57%, 88.54% and 87.24%) than Control (50.13%, 80.8% and 79.9%). Logistic regression summarized that the odds of case [aOR:3.5, (95%CI:1.23,9.96); p-value: 0.019] were more likely severely stunted. children passing stool > 10 in a day has more in case [aOR:1.67, (95%CI:1.01,2.76); p-value: 0.044.]. mother’s age ≥30 Years and well educated has strong association with case [aOR:2.12, (95%CI:1.39,3.23); p-value:<0.001], [aOR:2.79, (95%CI:1.63,4.79); p-value: <0.001.]. Mothers having two parity [aOR:0.62, (95%CI:0.43,0.90); p-value: 0.012.] were less likely treated their child with antibiotics. After adjusting all covariates, by logistic regression we found that case had hospitalized more [aOR:1.17, (95%CI:0.40,3.43); p-value: 0.772.] than control. Despite

well education and less parity of mother, they treated their young child with antibiotics without considering its severity, needs awareness at community specially caregivers.

6255

DIARRHEA IN A MILITARY SETTING: EPIDEMIOLOGY, ETIOLOGIES AND IMPACT OF THE DISEASE IN MILITARY PERSONNEL DEPLOYED AT CAMP LEMONNIER, DJIBOUTI

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Diarrhea has immense impact on military operational readiness. Overseas military personnel are at increased risk of exposure to enteric infections. We studied the epidemiology of diarrhea among US military personnel stationed at Camp Lemonnier, Djibouti, the primary US base of operations in the Horn of Africa. From May 2021 to March 2023, 201 diarrhea cases were enrolled, answered a questionnaire, and provided a stool sample. Samples were tested using FilmArray (FA) GI panel. For comparative purposes, a subset of 109 samples was evaluated using published qPCR assays for the detection of pathogenic E. coli, Salmonella, Shigella, Campylobacter, and norovirus. The majority (79%) of the 201 enrollees were males. Participants were Reserve (34%), Active Duty (33%), or National Guard (28%). Acute diarrheal episodes ranged between 1 to 13 days with an average of 4.2 days and a median of three days. Most reported symptoms were abdominal pain/cramps (87%), fatigue (76%), and malaise (73%). Signs of dehydration were observed in about one third, while impact on work performance was reported by 55% and ranged between reduced performance (48%) and loss of duty days (7%). FA identified at least one pathogen in 84% of cases and co-infections, up to 5 pathogens, in 56%. ETEC (54%), EAEC (47%), EPEC (29%), and STEC (24%), had the highest infection rates. Other pathogens ranged between 0.5% to 13% with V. cholerae in 3%. In the 109 samples tested by both techniques, 10 (67%) of 15 Shigella positive cases by qPCR were missed by FA; confirmation of qPCR data was performed using multiple assays targeting ipaH, virB, wbgZ, rfpB, and rfc genes. Of 29 STEC positive by FA, 21 (72%) were not O157 and were not detected by qPCR assays. For ETEC positives, CS1 (59%), CS6 (56%) and CS21 (53%) were the most identified colonization factors; CS1CS3CS21 was the common combination. The existence of multiple pathogens in more than half of the cases is a barrier against administration of successful treatment and prevention strategies. Also, data describes the epidemiology of diarrhea and its significant impact on work performance in a military setting.

6256

ASSOCIATION BETWEEN ENTEROPATHOGENS, THE GUT MICROBIOTA AND BIOMARKERS OF ENVIRONMENTAL ENTERIC DYSFUNCTION IN RURAL MALAWIAN CHILDREN

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Environmental Enteric Dysfunction (EED) is a subclinical condition of the gut that is characterized by changes in gut morphology and function due to chronic inflammation triggered by exposure to toxins and enteropathogens. There is limited data examining the link between exposure to enteric infections and EED. We aimed to estimate the prevalence of enteropathogens in rural Malawian children with signs of EED and examine associations with gut microbiota diversity. We used archival total genomic DNA samples extracted from stool, and corresponding demographic data from a nested cohort study conducted within the framework of a randomized controlled trial (NCT02047981). We analysed 102 baseline samples from children aged 1-59 months. We used 16S rRNA gene sequencing to generate data on gut microbiota and enzyme-linked immunosorbent assay to quantify selected fecal biomarkers of EED (myeloperoxidase, neopterin, and alpha-1 antitrypsin). Additionally, we customized an enteropathogen Taqman array card that could test for 20 different enteropathogens simultaneously, including viruses, bacteria, helminths, and protozoa. Out of the 20 enteropathogens tested, 11 were detected, with Giardia (45%) and adenovirus (24%) being the most common. Giardia carriage was highest in children between the age of 13-24 months. We found no significant differences in fecal levels of biomarkers of EED between children who tested positive and negative for any of the enteropathogens. Similarly, the microbiota alpha diversity index did not differ between the two groups of children. Our findings suggest that Giardia and adenovirus are prevalent enteropathogens in rural Malawian children and they may represent regular exposures in EED. However, despite their prevalence, we did not find any associations between the carriage of these enteropathogens and either gut microbiota diversity or biomarkers of EED. Given the potential health implications of these enteropathogens, it is critical to conduct more comprehensive studies to investigate the long-term consequences of their fecal levels on the gut microbiota and EED biomarkers.

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HYPERGLYCEMIA IN DIARRHEAL CHILDREN; CAN WE PREDICT CLINICAL STATUS?

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A high blood sugar level is indicative of various clinical disorders and has crucial implications. Our objective was to determine the relationship between clinical and laboratory alterations and hyperglycemia in diarrheal children under the age of five. This is a retrospective study using the electronic data system of Dhaka Hospital, icddr,b from March 2019 to December 2021. Out of 10828 diarrheal children under age five, 2167 were hyperglycemic (RBS >7.0 mmol/L), and 8661 (RBS 2.5 mmol/L–6.9 mmol/L) were normoglycemic children on admission. We analyzed two groups of children using STATA software. After adjusting age, sex and dehydration status, hyperglycemia was significantly associated with fever on admission [aOR = 1.16 (95% CI: 1.04, 1.29); p=0.006], anemia [aOR = 1.16 (95% CI: 1.01, 1.33); p=0.036], leukocytosis [aOR = 1.49 (95% CI: 1.27, 1.75); p<0.001], thrombocytosis [aOR = 1.39 (95% CI: 1.12, 1.73); p=0.003], hypernatremia [aOR = 3.48 (95% CI: 2.89, 4.18); p<0.001], hypokalemia[aOR = 1.85 (95% CI: 1.58, 2.18); p<0.001], raised creatinine [aOR = 2.69 (95% CI: 2.20, 3.30); p<0.001]. Death was more than three times higher among hyperglycemic cases than normoglycemic cases. Hyperglycemic children were less likely to be breastfed [aOR = 0.88 (95% CI: 0.78, 0.98); p=0.021], severely malnourished [aOR = 0.82 (95% CI: 0.71, 0.93); p=0.003]. Our examination demonstrated that hyperglycemia can be a significant risk factor for critical illness and aberrant electrolyte imbalances upon admission. Diarrheal children with hyperglycemia should have a proper evaluation and an intense monitoring system to avoid a fatal outcome.

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EPIDEMIOLOGICAL AND LABORATORY INVESTIGATION TO IDENTIFY SOURCES OF A COMMUNITY OUTBREAK OF CHOLERA

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An outbreak of cholera with 76 microbiologically confirmed cases were reported between June and September 2022, from Kathmandu, Nepal. Identification of risk factors are crucial for control and prevention of cholera.

We conducted an outbreak investigation utilizing both epidemiological and laboratory methods to identify potential sources. A descriptive epidemiological study was followed by an analytical study. A semi-structured questionnaire was used to capture hygiene behavior, education level, water source, latrine use, and environmental conditions of the cases. Water samples from community sources consumed by the cases were collected, filtered, and tested for the presence of Vibrio cholerae. Inspection of drinking water storage, decontamination and treatment methods, and waste management was conducted. To find asymptomatic V. cholerae carriers, stool samples from patient's immediate household members were collected and tested using rapid diagnostic test (RDT) and culture techniques using selective media. Total 283 water samples (262 household water, 21 river water) were collected for environmental assessment. Presumptive V. cholerae were isolated from 14 household water samples (7 tap, 5 well, 2 jar) of confirmed cases whereas none were isolated from river water samples and stool samples of family members. In household surveys, 27.3% reported recent diarrhea among family members, while 18.2% reported illness resembling cholera. Most of the affected individuals (70.8%) had consumed raw fruits within 5 days before illness. Common symptoms included body ache (29.7%), headache (25.2%) and nausea (15.3%). Only 38% households reported treating water before use (boiled 58%, filtered 26%). Hand hygiene using soap and water after toilet use was reported by 95.5%. Most households disposed of waste through waste collectors (75%), burnt (12%), or dumped in river (4.5%). Most households had private toilets (69%). In conclusion, environmental contamination of water source and untreated drinking water are the likely causes of this cholera outbreak.

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CHARACTERISTICS OF 2-23 MONTHS OLD CHILDREN WITH PROLONGED DIARRHEA COMPARED TO THOSE WITH ACUTE DIARRHEA AND THEIR IMPACT DURING POST-DISCHARGE FOLLOW-UP AT DAY 90

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It is estimated that in 2019, about half a million under-5 children die annually due to causes attributed directly to diarrhea. A prolonged episode of acute diarrhea, defined as diarrhea lasting for 7–13 days, accounts for around 12 percent of all diarrheal episodes and over two-thirds of deaths associated with diarrhea. Here, we have compared the background characteristics of young children aged 2–23 months with acute diarrhea and prolonged diarrhea and also their impact at post-discharge follow-up at day 90. For this descriptive analysis, relevant data were extracted from the Antibiotics for Children with Diarrhea (ABCD) trial, which was a randomized, multi-country, multi-site, double-blind, placebo-controlled clinical trial. A linear regression model was used to compare the mean of the anthropometric outcome (ΔWLZ) across the two groups (prolonged diarrhea vs. acute diarrhea) in surviving children after adjusting for relevant covariates. A total of 8266 children were analyzed, of whom 756 had prolonged diarrhea and 7510 had acute watery diarrhea of <7 days duration. The overall prevalence of prolonged diarrhea was 9.15%. However, the highest prevalence was 15.7% in Pakistan, and the lowest was 1% in Tanzania. We observed that children aged 2–11 months who have more than three children under the age of 5 in their families and maternal illiteracy are at increased risk of developing prolonged diarrhea. At Day-90 follow-up, the children with prolonged diarrhea were found to have significantly lower weight for age Z score compared to those who suffered from acute diarrhea of <7 days duration, though their anthropometric indices were comparable at baseline. The mean± SD change in length-for-age z score from day 1 to day 90 was –0.09± 0.61 in the prolonged diarrhea group and –0.18± 0.60 in the acute diarrhea group ($p < 0.001$). There were 46 (6.1%) hospitalizations by day 90 in the prolonged diarrhea group compared with 335 (4.5%) hospitalizations in the acute diarrhea group ($p = 0.04$). Studies assessing the causes of prolonged diarrhea may be useful to predict children at risk and avert the long-term sequelae involving childhood growth.

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CLINICAL AND ENVIRONMENTAL EPIDEMIOLOGY OF VIBRIO CHOLERAE IN EASTERN DEMOCRATIC REPUBLIC OF THE CONGO, 2020-2022 (PICHA7 PROGRAM)

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Globally, there are an estimated 2.9 million cholera cases annually in cholera-endemic countries, which result in 95,000 deaths. The Democratic Republic of the Congo (DRC) is estimated to have 189,000 cholera cases each year, resulting in 7,100 deaths. The majority of cholera cases are found in cholera "hotspots", such as eastern DRC in the Great Lakes Region. However, there is limited longitudinal surveillance of cholera epidemiology in this region with most studies focusing on surveillance of suspected cholera cases rather than cases confirmed by bacterial culture. The objective of the Preventive Intervention for Cholera for 7 Days (PICHA7) program is to develop evidence-based water, sanitation, and hygiene interventions to reduce cholera in Eastern DRC. From March 2020 to December 2022, the PICHA7 program screened 644 diarrhea patients admitted to health facilities for cholera in urban Bukavu in South Kivu province of Eastern DRC. Diarrhea patient stool samples were collected within 24 hours of patient admission, and were analyzed by both rapid dipstick testing (RDT) using direct testing by the Crystal VC kit, and by bacterial culture for Vibrio cholerae. Both source and stored water samples were collected within 48 hours of patient admission for those patients confirmed to have cholera by RDT. Twenty six percent of diarrhea patients (166/644) had stool samples positive for cholera by RDT, and 21% (136/644) had stool samples positive for Vibrio cholerae by bacterial culture. The Crystal VC RDT by direct testing had moderate specificity and sensitivity compared to bacterial culture, 91% and 89% respectively. Nine percent of stored water samples (6/66) had detectable Vibrio cholerae by bacterial culture and 5% (3/64) of source water samples. These findings show a high prevalence of cholera among diarrhea patients presenting for treatment at health facilities in this cholera endemic setting in Eastern DRC and suggest that water is a transmission route for cholera infections in this setting.

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ACUTE FEBRILE ILLNESS IN PAKISTAN: ASSESSING CO-INFECTION OF MALARIA AND TYPHOID FEVER IN TERTIARY CARE FACILITIES IN KARACHI

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Acute Febrile Illness remains a major global public health threat. Historically, scholars have focused research on single disease etiologies, or exclude malaria-positive patients from further examination. To our knowledge, there have been few studies that investigated the co-infection of malaria and typhoid fever, and any related socio-demographic factors that might contribute to risk, in Pakistan. Furthermore, current diagnostic methods may represent a challenge in determining the exact etiology of acute febrile illness and can lead to misdiagnosis or improper differential laboratory diagnosis of these condition. Here, we present the result of a prospective cross-sectional study that evaluated the burden of malaria and typhoid fever single and co-infection. We also explored socio-demographic and cultural risk factors related to the occurrence of these two diseases. Overall, 550 participants (male:54%, female: 46%) aged from 2 to 80 years participated in our study and were screened using rapid diagnostic tests for typhoid and malaria. Among the study participants, 27.82% (153/550) were

typhoid positive (65 IgG and 153 IgM positive), P= 0.278, 95% CI [0.24-0.33]; and 4.91% (27/550), P=0.049, 95%CI [0.032-0.071] were malaria positive, constituting 6 cases of Plasmodium falciparum and 24 cases of P. vivax. The estimated co-infection rate for malaria and typhoid was 2.36% (13/550), P=0.24 95%CI [0.13-0.40]. Blood culture confirmed 49 typhoid cases (out of the 153 rapid test positives), of which 46 were identified as either extra- or multidrug resistant. The high prevalence of typhoid fever, and particularly drug resistant phenotypes, suggests the need for more research about risk factors contributing to typhoid transmission, and corresponding prevention strategies, in Pakistan. We observed a number of co-infections, highlighting the importance of comprehensive diagnostic testing to address multiple potential disease etiologies. We are conducting PCR testing and sequencing as next steps, which may help shed further light on risk factors and transmission dynamics.

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SIGNATURE OF EUKARYOTIC AND PROKARYOTIC GUT-MICROBIOME AMONG PATIENTS WITH GUT DISORDERS, SAUDI ARABIA

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Gut disorders are important health problems globally and in Saudi Arabia. They include irritable bowel syndrome (IBS), gut immune-mediated inflammatory diseases (IMID) and non-IBS/IMID diseases. Gut microbiota includes prokaryotic microbiota (bacteria and viruses) and eukaryotic microbiota (one-cell animals, including protozoa, and fungi). Variations in gut microbiota have several outcomes which are linked to gut health and disease.Stool specimens were collected from 2109 patients attending the KFHU. Stool specimens were microscopically examined for the parasites and their genomic DNA was extracted. Protozoal DNAs were amplified using PCR assays and PCR products were cut by restrictive enzymes and sequenced to determine genotypes and subtypes. Amplicon sequencing of extracted DNA for gut bacteria (targeting the 16S rRNA gene) and gut eukaryotes (fungi) (targeting the internal transcribed spacer (ITS) sequence) was done for bacterial and eukaryotic profiling, through analysis of BION data. Bacterial and eukaryotic diversity was measured in correlation with patient-related data.There is an unclear increase in the IMID in studies individuals. There is a clear signature of gut eukaryotes and prokaryotes profile that was linked to IBS, IMID and non-IBS/IMID gut disorders. Other than Blastocystis, parasitic infections were very rare among the study population. Gut eukaryotes, mainly Blastocystis were much less prevalent in IMIDs patients and very rare in patients with bacterial colonization. Bacterial diversity was higher in asymptomatic patients. Gut microbiota showed a pattern of distribution among different age groups and sex. The Saudi community share a unique lifestyle, genetic exposure and ethnic background which may influence the correlation between gut microbiota and gastrointestinal disorders. Gut-associated eukaryotes may reshape bacterial diversity and virulence/outcome of gut pathogens, by influencing both gut health and gut disorders.

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USE OF BIOMARKERS TO MONITOR TRACHOMA PREVALENCE AFTER IMPLEMENTATION OF MORE FREQUENT THAN ANNUAL MDA IN MAASAI COMMUNITIES IN NORTHERN TANZANIA

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Through implementation of mass drug administration (MDA), Tanzania reduced prevalence of trachomatous inflammation - follicular (TF) and met the criteria to stop MDA in 60/69 endemic councils. The remaining 9 endemic councils have persistent or recrudescent TF. Four of these councils - Longido, Ngorongoro, Monduli, Simanjiro - are located in remote geographies and largely inhabited by migrant populations. These characteristics contribute to low MDA coverage and continued trachoma transmission. As such, Tanzania is implementing strategies to better reach these districts, including more frequent than annual (MFTA) MDA. To monitor TF during MFTA MDA and understand the impact of seasonal population movement on trachoma transmission, we implemented trachoma sentinel site monitoring (SSM) in two districts receiving MFTA MDA (Longido and Ngorongoro) and two receiving annual MDA (Monduli and Simanjiro). We surveyed 10 sites per district before each MDA, randomly selecting 50 children, 1-9 years per site. We conducted clinical grading for TF and collected ocular swabs to detect Chlamydia trachomatis (Ct) infection and dried blood spots (DBS) to detect antibodies to the pgp3 antigen. Quesionnaires were completed to measure acceptability of sample collection, household occupation, household migratory patterns, and water and sanitation access. After, samples were transported to Muhimbili Hospital for processing, using rapid real-time PCR nucleic acid amplified test and pgp3 lateral flow assay. Preliminary results prior to and following the first round of MDA showed TF prevalence for Longido and Ngorongoro changed from 23.0% to 10.8% and 14.7% to 17.0% respectively and TF prevalence for Monduli and Simanjiro changed from 19.2% to 33.0% and 3.7% to 0.4%. We will present prevalence of Ct infection and pgp3 antibodies across all three rounds at ASTMH. We will draw conclusions on TF prevalence at three points in a ~12-month period in districts receiving MFTA MDA verses annual MDA. We will provide evidence on the usefulness of alternative surveillance approaches in trachoma endgame districts where population migration may be affecting programming.

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QUALITY OF TRACHOMATOUS TRICHIASIS SURGERY IN 25 DISTRICTS OF SOUTHERN NATIONS NATIONALITIES AND PEOPLE'S AND SOUTHWEST ETHIOPIA REGIONS: SUMMARY FINDINGS OF 31 SURGICAL AUDITS IN 2022

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The success of trachomatous trichiasis (TT) surgery in preventing blindness depends on maintaining quality surgical outcome in the operated eyelids. Unfortunately, surgical failure of TT after surgery cannot be zero. World Health Organization suggests Integrated Eye Care Workers (IECWs) aim for a surgical failure of trachomatous trichiasis rate less than 10% at 3-6 month follow up. The main objective of TT surgical audit was to measure actual surgical outcomes and compares them to a desired quality standard and to determine the post-operative trachomatous trichiasis (PTT) rate for the selected IECWs at 3-6 months period. The TT surgical audit was carried out in 25 districts of Southern Nations Nationalities and People's and Southwest Ethiopia regions in 2022. It was conducted by experienced eye care workers from Secondary Eye Care and Tertiary Eye Care Units. Purposeful sampling technique and systematic sampling were used to select IECWs and operated TT cases for those IECWs who had greater than 40 cases at 3-6 months period respectively. For IECWs who had less than 40 cases, all the operated cases were included into the surgical audit. A total of 31 IECWs were audited. A minimum of 26 eyelids and a maximum of 50 eyelids were audited per IECW. A total of 1,207 eyelids (on average, 39 eyelids were audited per IECW) were audited, and of these, 50 eyelids had post op TT which makes the overall PTT rate 4.1%. However, the PTT rate ranges from 0% to 10.0%. In conclusion, all the audited IECWs had low PTT rate at 3-6 months post op period compared to the WHO standard. Overall, only 50 (4.1%) eyelids had post op TT at 3-6 months which remarkably met the WHO quality standard for TT surgical outcome.

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UTILIZING MOLECULAR DIAGNOSTICS TO SUPPORT THE TRACHOMA CONTROL PROGRAM IN NAURU

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Trachoma is the world's leading infectious cause of preventable blindness, caused by the Chlamydia trachomatis bacteria. WHO simplified trachoma grading criteria are used to diagnose cases of trachomatous inflammation—follicular (TF) for field assessments of trachoma, including surveys to monitor progress toward elimination as a public health problem. Control of trachoma is through the SAFE strategy of surgery for trichiasis, antibiotic treatment for trachoma, promotion of facial cleanliness and implementation of environmental improvements. Recent reports of high TF in the absence of trichiasis, particularly in the Pacific region, suggest that TF presentations may be caused by infections other than C. trachomatis. Therefore, molecular diagnostic tools are required to confirm C. trachomatis infection to monitor the progress of eliminating trachoma as a public health problem. A baseline prevalence survey undertaken in 2019 found hyperendemic levels of trachoma in Nauru and 34.9% positive for C. trachomatis. Two rounds of MDA have been delivered, with the most recent survey reporting trachoma prevalence (TF) of 6.2%. In late 2022, the Nauru Ministry of Health, with the support of the Fred Hollows Foundation, Tropical Data and The Kirby Institute, undertook a trachoma impact study utilising the Tropical Data methodology. All consenting participants aged 1-9 years who were screened for TF were simultaneously asked to provide an ocular swab to be subsequently tested for the presence of C. trachomatis. DNA was extracted from the ocular swabs taken from one eye of the participants and tested for C. trachomatis via real-time PCR using the C. trachomatis/Neisseria gonorrhoeae (Ct/Ng) dual assay. Only C. trachomatis results were evaluated for this study. The samples of this study are still undergoing analysis and results are not ready at the time of this submission. This study will assess the impact of two rounds of MDA and whether trachoma continues to be a public health problem in Nauru. It is also anticipated that results will further support the growing supposition that molecular diagnostics is an important tool in trachoma elimination.

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NEARING ELIMINATION OF TRACHOMA AS A PUBLIC HEALTH PROBLEM IN AUSTRALIA

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Trachoma is an infectious disease of the eye, caused by Chlamydia trachomatis bacteria and is the world's leading infectious cause of preventable blindness. Australia is the only high-income country with endemic trachoma, found in First Nation populations in remote communities in central and northern Australia. The National Trachoma Management Program, initiated in 2006 follows national guidelines for the public health management of trachoma. The guidelines are based on the WHO SAFE strategy with key components being surgery for trichiasis, antibiotic treatment for trachoma, promotion of facial cleanliness and implementation of environmental improvements. First Nation children in remote communities previously identified at risk of trachoma are screened for clinical signs of trachoma, facial cleanliness, and treatment uptake. Data regarding trichiasis screening and surgery and implementation of health promotion activities are also collected at the community and regional levels by public health teams. These data are collated annually through programmatic reporting analysed to guide progress towards established targets. From 2007 to 2022, the number of remote communities identified as at risk of trachoma decreased from 229 to 84. The overall prevalence of trachoma in children aged 5-9 decreased from 14.3% to 2.2%. In 2007 65/123 communities screened reported trachoma prevalence above 5% compared to 30/84 in 2022. At the jurisdictional level, in 2007 prevalence's ranged from 13.5% to 15%, while in 2022 they were between 0% and 3.1%. With all jurisdictions now recording trachoma prevalence in at-risk communities below the WHO target of 5%, Australia needs to maintain these levels for 2 more years to be formally designated as having achieved elimination. Further, we need a plan to ensure trachoma prevalence continues to decrease, particularly in communities with ongoing endemicity, and elimination levels are sustained post-elimination

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OLDER AGE IN SUBARACHNOID NEUROCYSTICERCOSIS REFLECTS A LONG PRE-PATENT PERIOD

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Patients with subarachnoid neurocysticercosis (NCC) are usually older than those with parenchymal disease in all published series. Although it has been theorized that subarachnoid disease may have a prolonged incubation period, it is still unclear whether this age difference seen in clinical settings reflects an extended pre-symptomatic period or a delay in diagnosis owing to its insidious symptoms or poor healthcare access in endemic countries. Using available data from a large consecutive series of patients seen in a referral center in Lima, Peru, we compared the age at symptom onset between parenchymal and subarachnoid disease after adjusting for factors that could distort this relationship. Patients with mixed (parenchymal and subarachnoid) NCC or those with parenchymal cysts in different stages (viable and/or degenerating and/or calcified) were not included. From 408 eligible patients, we retrospectively compared the age at symptom onset in 140 patients diagnosed with parenchymal (pure viable or pure calcified) and subarachnoid NCC who had a confirmatory image available not more than two years after the beginning of symptoms. After controlling by sex and residence in rural endemic regions, the mean age at symptom onset in patients with subarachnoid disease was 13.69 years older than those with viable parenchymal disease (n = 140). Furthermore, our results showed consistency across all cut-off points of years between symptom onset and neuroimage evaluated in the total sample (n = 408). The design of this study allows an individual assessment of the contribution of the pre-patent period itself, adding evidence that this age difference seen on clinical grounds is not the product of delays in diagnosis, imaging, or access to care. Therefore, a long incubation period is a major contributing factor to older age at presentation in subarachnoid NCC.

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SEROPREVALENCE AND RISK FACTORS FOR NEUROCYSTICERCOSIS IN MEXICAN-AMERICANS IN STARR COUNTY, TEXAS

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Neurocysticercosis (NCC) is an invasive cestode infection caused Taenia solium. It is a leading cause of epilepsy and chronic headaches in endemic areas including Latin America, Africa, and Asia. The epidemiology of NCC has not been well-studied in the United States to date, but small epidemiological studies have demonstrated NCC in populations in the US who have immigrated from endemic regions. There is a population living in Starr County, Texas along the Texas-Mexico border in whom the presence of other neglected tropical diseases has been demonstrated due to the intersection of poverty, climate, and high rate of immigration. Our study was a serologic survey and risk factor analysis of NCC in a pre-existing cohort of Mexican-Americans in Starr County, Texas. Using a triplex enzyme-linked immunoassay (ELISA) against NCC-specific antigens, we identified an

overall seropositivity to T. solium in 7.4% (45/605) in the cohort which likely represents a combination of parasite exposure, T. solium disease outside of the central nervous system, old calcified NCC, and viable or degenerating NCC. We used self-reported survey data and neighborhood-level variables to conduct a risk-factor analysis. Female gender, specific occupation and indoor versus outdoor occupation were found to be significantly associated with NCC seropositivity. Twenty-six of the 45 positive cases were employed in healthcare, caregiving, or social service (p 0.009), and 42 of the 45 were employed in an indoor occupation (p <0.001). These occupations could pose a risk for T. solium acquisition. A geospatial analysis of cases at the census tract level showed increased percentage of seropositivity centered around urban cities Rio Grande City and Roma, as well as smaller city La Grulla and census-designated place Alto Bonito. There is a critical need to investigate these seropositive cases of NCC and confirm the diagnosis with imaging, as well as conduct an epidemiological investigation to determine if disease transmission is occurring in Starr County.

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THE POTENTIAL MECHANISTIC PATHWAYS LEADING FROM PARASITE INFECTION TO CHILDHOOD STUNTING

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In 2020, an estimated 149.2 million children under the age of 5 were physically stunted, defined as falling at least -2 standard deviations below the height-for-age World Health Organization (WHO) Child Growth Standards median. Stunting is a visible indicator of a deficient environment, the consequences of which include child morbidity and mortality, reduced and delayed neurocognitive development, and an increased risk of long-term chronic diseases. The underlying aetiology and pathophysiological mechanisms leading to stunting remain elusive, although parasites are thought to play a key role. Here, based on available studies, we present potential mechanistic pathways by which parasitic infection of mother and/or infant may lead to childhood stunting. The most well-recognised pathway to stunting is a 'vicious cycle' between deteriorating nutritional status and infection, which is evolving to encompass dysbiosis of the gut, local and systemic inflammation, alongside energetic, hormonal, and metabolic consequences. Anaemia, which is often presented as coexisting alongside stunting, may in fact be contributing. The bi-directional relationship between intestinal parasites and the microbiota in early life, and their combined effects, may also play a key role in stunting. Finally, epigenetic regulation of gene expression may link parasitic infections and poor gut health in early life to stunting. Guided by these plausible mechanisms, future multidisciplinary longitudinal studies and clinical trials should aim to elucidate the most influential factors, and synergies therein, that can lead to stunting, and ultimately towards finding solutions to successfully mitigate against it.

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PROTEOMIC AND IMMUNOINFORMATIC APPROACH TO IDENTIFY IMMUNE REACTIVE PROTEINS OF TAENIA SOLIUM CYSTICERCI FOR A POTENTIAL MULTIEPITOPE VACCINE CANDIDATE

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Metacestode larvae of Taenia solium is the causative agent for neurocysticercosis, which causes epilepsy. The unavailability of a vaccine against NCC for humans is a major cause for its widespread prevalence across the globe. Therefore, the development of a reliable vaccine against NCC is the need of the hour. We used proteomics along with immunoinformatics to develop a vaccine candidate. The immune reactive cyst fluid antigens (CF) of T. solium were identified by immune-blotting of two-dimensional gels with NCC patient's sera followed by Matrix-Assisted Laser Desorption-Ionization (MALDI) analysis. We performed a detailed proteomic study of these immune reactive proteins by using immune-informatics tools, identified the non-toxic, non-allergic, B-cell epitopes, and collected epitopes with the least sequence homology with human and other Taenia species. These epitopes were joined through linkers to construct a multiepitope vaccine. Different physiochemical parameters such as molecular weight (23.82kDa), instability (39.91), and aliphatic index (49.61) were calculated to ensure the stability of the linked peptides vaccine. The vaccine demonstrated stable interactions with different immune receptors like TLR4 and IgG confirming that it will effectively stimulate the host immune response. We anticipate that our designed B-cell linear epitope-based vaccine will show promising results in in vitro and in vivo assays. This study provides a platform that would be useful to develop other suitable vaccine candidates to prevent helminthic neglected tropical diseases in near future.

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NEUROCYSTICERCOSIS, NEUROLOGICAL DISEASE AND HIV IN THE EASTERN CAPE PROVINCE OF SOUTH AFRICA

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Neurocysticercosis (NCC), caused by the infection with larval stages of the tapeworm Taenia solium, is a leading cause of epilepsy in the Eastern Cape Province of South Africa. Human Immunodeficiency Virus (HIV) is also endemic in the Eastern Cape. Limited literature is available about the epidemiology of co-infections with these two pathogens. This study investigated the difference in prevalence of NCC between patients with different HIV and neurological statuses in the Eastern Cape in 2009-2012. A total of 146 patients were recruited from two local hospitals and categorised into four groups according to HIV and neurological status (epilepsy or headache). Patients were asked to provide blood samples for detection of active infection with T. solium larvae using the B158/B60 antigen ELISA. Patients in groups with HIV or neurological symptoms were offered a CT-scan to detect NCC lesions. Of the 127 patients providing a blood sample, 8 (25%) tested positive for active cysticercosis in Group 1 (HIV+ and neurological disease status +), a percentage significantly higher than all other groups in which 2 (7%), 0 and 2 (7%) tested positive in Group 2 (HIV- and neurological disease status +), Group 3 (HIV+ and neurological disease -) and Group 4 (HIV- and neurological disease -), respectively. Of the 70 patients who underwent CT-scans, 10 (44%) in Group 1 (9 calcified and 1 active, transitory and/or calcified), 12 (41%) in Group 2 (11 calcified and 1 active), and 9 (52%) Group 3 (7 calcified and 2 active) had NCC lesions. There were no significant differences in imaging in the three groups. CD4 counts below 200 cells per cubic millimeter were also not associated with a higher prevalence with the AgELISA or CT imaging. Despite substantial limitations caused by the socio-political climate in South Africa at the time of this study, we demonstrate the relatively high prevalence of NCC in this population with mainly calcified cysts and an increased risk of active T. solium infection among patients with HIV and neurological symptoms. This study highlights the need for improved cost-effective tests, and for further research on this neglected disease in vulnerable populations.

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CONSISTENT MEASUREMENT OF PARASITE-SPECIFIC ANTIGEN LEVELS IN SERA OF PATIENTS WITH NEUROCYSTICERCOSIS USING TWO DIFFERENT MONOCLONAL ANTIBODY (MAB)-BASED ENZYME-LINKED IMMUNOSORBENT ASSAYS

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Diagnosis of human neurocysticercosis (NCC) is complex due to the lack of specific clinical manifestations, because of that the development of new techniques based in serology constitutes a major issue for public health since NCC is one of the principal causes of neurological pathology in most developing countries. Monoclonal antibody (mAb)-based enzyme-linked immunosorbent assay (ELISA) is a complementary diagnosis technique for NCC, which detects circulating parasite antigen (Ag) indicating the presence of viable infection and Ag levels also correlate well with parasite burden. We assessed agreement between two Ag-ELISA techniques for detection of NCC, our in-house TsW8/TsW5 Ag-ELISA based on T solium mAbs and the reference Ag-ELISA for NCC B158/B60 Ag-ELISA for measuring antigen levels in sera from 113 patients with subarachnoid, parenchymal and calcified NCC. Concordance was demonstrated evaluating limits of agreement (LoA) stratified by type of NCC. Both ELISA's detected 47/48 (97.8%) subarachnoid NCC cases. In parenchymal and calcified NCC, the B158/B60 Ag-ELISA detected 19/24 (79.2%) and 18/41 (43.9%) cases, while the TsW8/TsW5 Ag-ELISA detected 21/24 (87.5%) and 13/41 (31.7%), respectively. Parenchymal and calcified NCC obtained a perfect agreement (100%), indicating that all sample results were within the predicted LoA, while for subarachnoid NCC agreement was 89.6%. High concordance between assays was confirmed by Lin's concordance coefficient (LCC=0.97). Patients with viable parenchymal NCC (LCC = 0.95) obtained the highest concordance between assays, followed by subarachnoid NCC (LCC = 0.93) and calcified NCC (LCC=0.92). Antigen detection was highly concordant between assays, suggesting that the TsW8/TsW5 Ag-ELISA can be used as a new alternative tool for this purpose. The reliability of antigen detection assays could contribute to clarify the diagnosis of NCC when neuroimaging is not conclusive or available.

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MULTIPLEX BEAD ASSAY (MBA) FOR THE ASSESSMENT OF ANTIBODY RESPONSES DURING CYSTICERCOSIS IN EXPERIMENTAL INFECTED PIGS

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Taenia solium is the cause of cysticercosis and results in a neurologic disease (Neurocysticercosis, NCC) when the central nervous system is infected. Pigs are the natural hosts and the preferred animal model for NCC. Antibody responses are usually assessed by the serological gold standard, the Lentil-lectin enzyme-linked immunoelectrotransfer blot (LLGP-EITB) assay, but this format is technically challenging, not quantitative and needs complex antigen purification process to obtain the seven diagnostic glycoproteins. Our group has characterized 6 recombinant antigens that represent the main protein families in LLGP-EITB diagnosis. LLGP-EITB antibody patterns in NCC types and stages have been identified, but the response of simultaneous recombinant proteins has not yet been quantified. We developed an immunoassay based on magnetic microspheres (MBA) coupled with all 6 diagnostic recombinant antigens that allows a simultaneous quantification of antibody levels. We evaluated 162 serum samples from 18 pigs who were experimentally oral infected at 1 (n=6), 3 (n=6) and 5 (n=6) months-old, and were bled at 9 time points post infection (PI) until day 90PI. Necropsy data from the original study demonstrated more efficacious infections and more viable cysts in younger pigs, and more degenerated cysts in older pigs. In our 6 antigens-MBA, the high-performance antigens (rGP50, rT24H and sTs14) showed differences in their ability to differentiate pigs with different cyst viability conditions. rT24H and rGP50 detected antibodies in pigs with viable or no viable cysts and during all the course of infection, while sTs14 has a stronger response in viable infections. In addition, there was a progressive increase in the antibody response of rGP50 from day 21PI and from day 28PI for all the other antibodies. Pigs infected at 3 and 5 months-old showed a marked decrease from day 57PI until necropsy. Therefore, our new 6 antigens-MBA was a valuable tool to quantify and compare the simultaneous presence of antibodies against T solium recombinant antigens during the progress of the cysticercosis infection.

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LATERAL FLOW TEST FOR NEUROCYSTICERCOSIS - PRELIMINARY EVALUATION

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Neurocysticercosis (NCC) is an infection of the central nervous system with the cystic form of the pork tapeworm, Taenia solium. NCC accounts for approximately one third of all cases of seizures worldwide and is the most important neurologic disease of parasitic origin according to the World Health Organization. NCC affects over 25 million individuals in endemic, and increasingly non-endemic, regions. In the U.S., it has been found in 2% of seizure patients presenting to hospital emergency departments. Thus, NCC, an officially designated "neglected disease", is an underrecognized but significant global cause of morbidity and mortality. Serological testing has been useful in diagnosing NCC, either to supplement imaging or where imaging is not available. However, the gold standard EITB (enzyme immunotransfer blot) test developed by CDC is of limited availability, and no point-of-care tests for NCC are commercially available. We have developed a prototype lateral flow test for NCC based on recombinant versions of selected glycoprotein antigens used in the CDC EITB. The NCC lateral flow test was evaluated on a panel of 59 sera from NCC patients comprising both parenchymal and extraparenchymal cases, confirmed by imaging and clinical history, 200 sera from healthy blood donors and 38 sera from patients with other disease conditions. The overall sensitivity of the NCC lateral flow test on confirmed NCC sera was 98.3% (58/59) when read with a reader device, or 96.6% when read visually; the single undetected sample was from a patient with a single cyst that was marginally detectable by ELISA. Overall specificity was 99.6% (237/238), with a single false positive blood donor serum detected. The lateral flow assay appears to be a promising candidate for point-of-care use in diagnosis of NCC, subject to further clinical testing, which is underway.

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LATE POST-TREATMENT INFLAMMATORY RESPONSE AND RESIDUAL CALCIFICATION IN NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is the leading cause of acquired epilepsy in developing countries. Cysts in the brain go from a viable resting state to complete resolution or calcification. Although it was previously believed that calcified lesions did not cause consequences, residual calcifications are associated with worse evolution of seizure disorders in NCC. We evaluated

the process of degeneration and calcification in the brain of pigs naturally infected with Taenia solium (n=15) and treated with 15 mg/kg albendazole and 25 mg/kg praziquantel orally. antiparasitic. The animals were divided into three groups of 5 animals each and the necropsy was performed at 4, 8 and 12 months post treatment. Inflammation and calcium deposits were evaluated by H&E, Masson's trichrome, Alizarin red, and Von Kossa stains, and immunomarkers such as GFAP, IBA, and neurofilament. The fifteen pigs showed 137 lesions, composed of 62 calcified cysts and 75 fibrotic lesions. The 4M group presented 13 calcified cysts, the 8M group had 35 calcified cysts, and the 12M group presented 14 calcified cysts. The 8M animals presented larger calcified lesions and greater intensity of calcium deposits compared to the other groups, as well as a greater amount of inflammatory cells that were distributed throughout the entire lesion. The 12M group has a greater number of fibrotic cells and has a greater area of fibrosis surrounding the lesion. This longitudinal study provides novel insight into the dynamics of inflammation and calcification and may contribute to the development of interventions aimed to reduce the likelihood of residual calcification.

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INFLUENCE OF EUKARYOTIC ENTERIC PATHOGENS ON THE GUT FUNGAL COMMUNITY IN MALIAN CHILDREN

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Eukaryotic enteric pathogens (EEP) pose a worrying public health issue in tropical countries. Yet, the interactions between EEP and the gut fungal community remain poorly understood. To evaluate the impact of EEP on fungal community, we carried a case control study in Malian children living in Bandiagara, Mali. Cases were defined as children with at least one EEP and control as children without EEP. Sample stools were collected from 296 Malian children to explore gut fungal by qPCR and metagenomics targeting, rRNA ITS1 and ITS2 regions metabarcoding. The 100 (33.8%) children in whom no EEP was detected were considered as controls, and they were compared to: a) 196 (66.2%) children who had at least one EEP; b) 91 (30.7%) children who had only Blastocystis; c) 35 (11.8%) children who had only Giardia intestinalis; and d) 12 (4.0%) children who had another (<1% each) EPP. The gut fungal community structure was homogenous in each of the children's group. Linear size effect discriminant analysis highlighted five species, including Fusarium longipes and Penicillium caseilulvum, which were relatively more abundant in children with at least one EEP whereas 28, including Aspergillus sydowii and Microdochium colombiense were more abundant in controls. Regarding Blastocystis infected children, the abundance of Fusarium, Pyxidiophora, and Stereum genera was higher in infected children whereas Ogataea, and Allocryptovalsa were more abundant in controls. Regarding Giardia intestinalis, Sordariales and Mortierellales abundance was higher in infected children, whereas Agaricales and Capnodiales abundance was higher in controls. Overall, EEP do not significantly impact the global gut fungal community structure, but further studies are warranted to confirm our finding that taxa of the gut mycobiota are associated with susceptibility or resistance to specific EEP.

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HELMINTH INFECTION DRIVES REDUCED SERUM COMPLEMENT AND COMPLEMENT REGULATORY PROTEIN ACTIVATION IN INDIVIDUALS WITH COINCIDENT TYPE 2 DIABETES

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Several clinical, epidemiological, and laboratory studies suggest that helminths could help mitigate the progression of Type 2 Diabetes Mellitus (T2DM) by modulating a host of pro-inflammatory pathways. Because complement hyperactivation has been observed in patients with T2DM and because the complement system can have unwanted consequences if not controlled appropriately (to prevent excessive activation), we sought to examine the effect of the helminth Strongyloides stercoralis (Ss) on the complement activation pathways in T2DM. We examined the circulating levels of the complement proteins C1q, C2, C3, C4, C4b, C5, C5a, and MBL and some of their regulatory components (Factor B, Factor D, Factor H, and factor I) in individuals with T2DM with (n=60; Ss+T2DM+) or without (n=58; Ss-T2DM+) concomitant Ss infection (n=58). Furthermore, we estimated the effect of anthelmintic therapy on complement pathway components 6 months after treatment. Complement levels of C1q (GM of 47.50 ng/ml in Ss+DM+ Vs 63.88 ng/ml in Ss-DM+; p=0.0065), C3 (GM of 125.5 ng/ml in Ss+DM+ Vs 150.1 ng/ml in Ss-DM+; p=0.0003), C4b (GM of 394.9 ng/ml in Ss+DM+ Vs 525.6 ng/ml in Ss-DM+; p=0.0024), C5a (GM of 1876 ng/ml in Ss+DM+ Vs 2319 ng/ml in Ss-DM+; p=0.0191), MBL (GM of 46.41 ng/ml in Ss+DM+ Vs 62.35 ng/ml in Ss-DM+; p=0.0016), Factor B (GM of 41.71 ng/ml in Ss+DM+ Vs 57.93 ng/ml in Ss-DM+; p=0.0010), and Factor D (GM of 38.40 ng/ml in Ss+DM+ Vs 56.11 ng/ml in Ss-DM+; p=0.0002) were significantly lower in Ss+DM+ compared to Ss-DM+ individuals. Following anthelmintic treatment the levels of C1q (an increase of 15%; p=0.0012), C4b (an increase of 11%; p<0.0001), and MBL (an increase of 11%; p=0.0201) were increased in T2DM+Ss+ individuals. Our data imply that Ss infection restricts complement activation and related pathological inflammatory process in T2DM individuals.

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DESCRIPTIVE AND PREDICTIVE ANALYSIS OF SOIL-TRANSMITTED HELMINTHIASIS IN SCHOOLCHILDREN OF TIERRALTA, CORDOBA, COLOMBIA

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Soil-transmitted helminths (STH) infect more than two billion people worldwide, especially in developing countries located in tropical and subtropical regions. The department of Cordoba, Colombia is located in a region with a high prevalence of this parasitic infection. Given the great burden that STH represent in our community, their impact on the normal development of childhood, and the scarce studies with an integrative approach in our country, a descriptive and predictive study was carried out for the evaluation of STH. We sampled 70 children aged 4 to 17 years old from Santa Fe de Ralito School in the municipality of Tierralta, Cordoba. Epidemiological information was collected through surveys and the parasitological diagnosis was performed by Kato-Katz in stool samples. Blood samples were collected to measure hemoglobin and blood cells. A set of inflammatory, anti-inflammatory, and regulatory cytokines were measured by flow cytometry. The prevalence of STH infection was 55.7%. Trichuris trichiura was the most frequent parasite, being present in 92% of infected participants, either as mono-infection or co-infecting with Ascaris lumbricoides or hookworms. The hematological and immunological parameters showed suppression of the anti-inflammatory response with

a predominance of the regulatory cytokine Transforming growth factor-beta. The Monocyte chemoattractant protein-1 had higher levels in the infected participants. Interferon-ɣ-inducible protein-10 was higher in the ones co-infected with two or more parasites. These findings suggest an attenuated immune response against STH, with effectors mechanisms to protect the host's tissues but failing in expelling the parasites. Finally, using the epidemiological data, a statistical predictive model of STH infection was designed with good performance (accuracy: 0.714) as a pilot tool for the prevention of these pathologies at the community and rural levels.

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TRICHURIS TRICHIURA INFECTION ASSOCIATED WITH AN INCREASED RISK OF PLASMODIUM FALCIPARUM INFECTION AMONG POPULATION LIVING IN BATA DISTRICT, EQUATORIAL GUINEA

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Sub-Saharan Africa is known to be endemic for Plasmodium and Soil-Transmitted helminth (STH) infections, where both diseases very often occur in the same host. In the case of co-infection, studies report either a worse or a beneficial effect of STH species on plasmodium infection. The objective of the present analysis was to evaluate the effect of STH infection on malaria in the continental region of Equatorial Guinea, a central African country where such data are lacking. We performed a cross-sectional study between October 2020 and January 2021 in Bata district. Venous blood was collected for Plasmodium infection testing, using mRDTs while stool samples were collected for the diagnostic of Ascaris lumbricoides, Trichuris trichiura, and hookworm infections using Kato-Katz technique. A general linear model was used to assess the association between Plasmodium and STH infections. A total of 340 participants were included in the study with a mean (SD) age of 24.5 (23.7) and 1.22 female-to-male sex-ratio. The prevalence of Plasmodium infection was 52% (95%CI: 46 - 58) while the prevalence of any STH was 60% (95%CI: 55 - 65). The prevalence of Plasmodium and STH parasites co-infection was 37% (95%CI: 31 - 42). Assessing the association with Plasmodium infection, a statistically significant association was found at bivariable analysis for A. lumbricoides (cOR=1.71; 95%CI: 1.11 - 2.66, p-value=0.01) and T. trichiura (cOR=2.64; 95%CI: 1.69 - 4.16; p-value<0.001). After multivariable analysis adjusting for age, sex, and STH species, the association with Plasmodium infection remained statistically significative only for T. trichiura infection (aOR=2.03; 95%CI: 1.23 - 4.16; p-value=0.006). Our results reveal a high prevalence of Plasmodium and STH parasites co-infection in the district of Bata, Equatorial Guinea, where both diseases are highly prevalent and where T. trichiura infection increases the risk of Plasmodium infection. This result calls for more investigation of STH and malaria comorbidity, and more attention on the overlapping of both infections for tailored control programs of those two infections in the country.

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INTESTINAL PARASITIC INFECTIONS AND ASSOCIATED RISK FACTORS, KNOWLEDGE, ATTITUDE AND PRACTICES IN CALABAR, CROSS-RIVERS STATE, NIGERIA

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The prevalence of intestinal parasitic infections, associated risk factors, knowledge, attitude and practices among residents of two LGAs in Calabar, Cross-Rivers State, Nigena was determined. A total of 600 persons who gave their consent to be part of the study made up of 356 females 59.33% and 244 males 40.67% within different age-groups had their faecal samples examined using the formol-ether concentration technique. Structured questionnaires which sought information on socio-demographic data of respondents, risk factors and KAPs regarding IPIs were administered. The results revealed that 321 persons 53.5% were infected with one or more parasites. Ascaris lumbricoides. Entamoeba coli, Entamoeba histolytica, Taenia spp, Hookworm and Trichuris trichiura were the parasites observed. Mixed infections occured 5.83%. More females.53.6% than males 53.2% were infected. Infection was highest in the age group 50-59-years 58.11%, the unemployed 78.8%, persons with no formal education 64.8%, the widows 67.0%, those who did not wash their hands after toileting 94.19%. The highest infection rate occured among the Nsidung community. In terms of risk factors and KAPs, those who used stream 76.6% and rivers 74.3% recorded high prevalences of infection. Those who used the bush and streams as toilets recorded high infection rates of 76.6% and 73.4% respectively. Many knew about IPIs 81.17%. Mode of transmission was attributed to ingesting improperly cooked food 48.33%, infected water 10.33%, Skin penetration 8.33%. Many went to the hospital/ clinic for treatment 49.0%, while some resorted to self-medication 24.5% and use of herbs 10.34%. The Government should show political will by acting now and invest in NTDs. Health education becomes paramount. There is need to progress toward reduction of infection through the implementation of Water, Sanitation and Hygiene (WASH) intervention policy. All should act together to bring an end to these IPIs ravaging our communities in various nations.

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MOLECULAR CHARACTERIZATION OF A NOVEL GHANA STRAIN OF NECATOR AMERICANUS HOOKWORMS

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Laboratory passage of an African strain of Necator americanus hookworms has been sustained through 9 passages in outbred hamsters using larvae (L3) cultivated from human study subjects in Beposo, Ghana. Initial cutaneous infections of 2-day old hamsters were conducted in parallel with subcutaneous (SQ) infections of 21-day old weanlings, with animals provided ad libitum water containing dexamethasone. Subsequent passages were sustained in weanling hamsters by SQ infection. Fecal egg excretion was detected as early as 45 days post infection (PI) and continued beyond 150 days PI. Amplification of β tubulin genomic DNA sequences spanning resistance associated SNPs revealed wild type loci with intronic heterogeneity in 20 adult worms recovered from the initial (F0) hamster passage. Egg hatch assays revealed that the field strain showed comparable benzimidazole sensitivity to an established laboratory strain of Ancylostoma ceylanicum. In silico analysis of an N. americanus reference genome was used to develop methods for amplification of di, tri and tetranucleotide microsatellite repeats of 100, 200, 300 and 400 base pair fragment sizes. Of the 40 loci evaluated using 20 (F0) adult worms, 21 loci showed reliable amplification of the expected size, while 15/21 loci deviated from Hardy-Weinberg equilibrium (p< 0.05). PCR-amplification of COX1

mitochondrial DNA sequences from 20 (F0) adult worms revealed that the Ghana strain is distinct from previously characterized isolates from China and Brazil. A full mitochondrial genome was reconstructed from a single adult worm using long-read sequencing on the Oxford Nanopore MinION. A maximum-likelihood phylogenetic analysis using full mitochondrial genomes further demonstrated the Ghana strain is distinct from N. americanus samples from China and Togo. These data provide the first in vivo, in vitro and genomic analysis of a Ghana strain of N. americanus successfully adapted from humans to an animal model. Use of these methods and the resulting reagents will accelerate the development of geographically targeted therapeutics, vaccines and advanced diagnostics for use in West Africa.

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ASSOCIATED SOCIOECONOMIC AND DEMOGRAPHIC FACTORS WITH SOIL-TRANSMITTED HELMINTHIASIS IN FIVE PROVINCES IN GABON

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Soil-transmitted helminthiases are Neglected Tropical Diseases endemic in Central Africa including Gabon. Populations living in remote areas had a lack of water supply and live in poor hygienic conditions. These populations are not access to anthelminthic drug due to isolation caused by the absence of passable roads. In the aim to help the Parasitic Diseases National Control Programme in Gabon to reach the objective to control Soil-transmitted Helminthiasis until 2030, an epidemiological study was performed in five provinces according to the urbanization level to identifying risk factors. A cross-sectional study was conducted in five provinces in Gabon according to the urbanization between December 18th, 2018 to July 10th, 2019. Socioeconomic and demographic data were recorded in a standardized case report form. After explanations of the fecal collection to participants, samples were analyzed using Merthiolate-Iodine-Formaldehyde coloration and concentration techniques. Data were analyzed by descriptive statistics and Chi squared test. In total, 201 volunteers were included in the study with a sex ratio of 0.71 and a median age of 24.0 [6.0 - 51.5] years. Nearly 60.0% of them lived in rural areas (59.7%; n = 108/181). The proportion of helminth carriage was 11.9% (24/201) with Ascaris lumbricoides, Trichuris trichiura and Necator americanus detected respectively in 7.5 (15/201), 6.5 (13/201) and 1.0% (2/201) of samples. The only association Ascaris lumbricoides + Trichuris trichiura was found in 6/201 participants (3.0%). The factors presenting an association with the infestation by soil-transmitted helminths were the residence in a rural environment (p=0.0012), the level of primary education (p=0.001), the consumption of drinking water (p=0.02), use of toilets outside the main residence (p = 0.05) and use of modern toilets (p=0.04). In conclusion, soil-Transmitted Helminthiases are found in more than one tenth of the study population. Sensitization of the populations and Water, sanitation and Hygiene must to be implemented in rural area where the prevalence was higher.

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THERAPEUTIC EFFICACY OF MEBENDAZOLE AGAINST HOOKWORM INFECTION AMONG SCHOOL CHILDREN IN BAHIR DAR ZURIA DISTRICT, NORTHWEST ETHIOPIA

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Soil-transmitted Helminths (STHs) are widely distributed in tropics and subtropics. Although MDA programs remain the cornerstone for controlling STHs, constant monitoring of benzimidazole resistance in areas where albendazole or mebendazole are periodically given is warranted to detect early rising of resistance in human STHs, prompting interventions to control this emergence in an early stage before genotypic and phenotypic resistance is widespread. This study was conducted to evaluate the efficacy of single-dose mebendazole against hookworm infection in school children. An open-label, single-arm trial was conducted in 4 primary schools from Bahir Dar Zuria district, Northwest Ethiopia from February, 2021 to March, 2022. Stool samples were collected and screened using double slide Kato Katz smear microscopy from 499 participants. A total of 132 hookworm-positive participants were treated with single-dose mebendazole (500 mg). Follow-up was done 21 days after treatment on 115 participants. Statistical analysis was performed by SPSS version 23 and R software version 4.2.1. P-values < 0.05 were considered statistically significant. Out of 132 participants, 50.8% participants were females. The mean age of the participants was 9.98 ±1.8. The mean egg counts per gram stool at baseline and after treatment (95% CI) were 180 (120, 251) and 68 (49, 91) respectively. The cure rate and egg reduction rate (95% CI) were 36.5% (28.3, 45.6) and 62.1% (59.2, 63.7) respectively. None of the variables considered for predicting cure were found statistically significant. The therapeutic efficacy of single-dose mebendazole against hookworm infection is below the WHO recommendation. Therefore; single-dose mebendazole should not be given as preventive chemotherapy against hookworm infection and another treatment regimen should be considered.

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DEVELOPMENT AND EFFICACY OF VARIOUS PAN-HOOKWORM VACCINE TARGETS

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Over 500 million people worldwide suffer from hookworm infections and disease. Despite years of concerted effort at deworming campaigns, hookworm infections remain prevalent due to imperfect anthelmintic efficacies and ease of reinfection. Development of a pan-hookworm vaccine would significantly impact hookworm disease by limiting primary infection and mitigating reinfections. Here we describe the identification and testing of potential targets suitable for vaccine development using two distinct approaches. First, we are using proteomics, transcriptomics (tissue-specific), immunomodulation, comparative bioinformatics, and immunoinformatics to identify >30 hookworm vaccine targets. To date, in addition to our previously published CP1, we have identified at least one other vaccine antigen that shows provides some level of reproducible protection against hookworm infection. Studies are on-going with additional antigens. Second, we are using hookworm extracts of various sorts and stages and have identified two specific conditions that provide a very high level of infection. Current efforts are focused on identification of protective antigens in these mixtures. Here we will present an update on all of these efforts that are making excellent progress towards a protective hookworm vaccine.

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NEW CURE FOR SOIL-TRANSMITTED HELMINTH INFECTIONS

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Gastrointestinal nematodes (GINs; alternatively soil-transmitted helminths or STHs), most notably, hookworms, whipworms, and Ascaris, are nematodes that infect more than 1.5 billion of the poorest people and are amongst the leading causes of morbidity worldwide. For decades, infections by STHs have been treated with small-molecule anthelmintic drugs, the heavy use of which has often selected for drug-resistance or recalcitrance. Bacillus thuringiensis crystal (Cry) proteins are the most widely used biological insecticides in the world and are nontoxic to vertebrates. We have shown that Cry proteins, in particular Cry5B, are highly effective against a broad range of free-living and parasitic nematodes that infect plants and animals. Here, we discuss several new Cry proteins, CryH18, CryH1, and CryH13. CryH18 is highly active against C. elegans and is able to kill C.elegans resistant to Cry5B. We cloned CryH18 into our IBaCC (Inactivated Bacterium with Cytosolic Crystal) expression system. IBaCC takes advantage of dead bacteria to safely deliver recombinant Cry proteins. Here, we report Cry18H IBaCC is toxic in vivo against A. suum, Ancylostoma ceylanicum hookworms, and Heligmosomoides polygyrus bakeri infections. We are also expanding studies on CryH1 and CryH13, both of which have been shown to be highly active against A. ceylanicum infections in vivo. We hypothesize that we might be able to control GINs using Cry18H at a single dose or in combination with different cry proteins to combat GIN resistance and increase clinical efficacy.

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EFFECT OF SOIL-TRANSMITTED HELMINTH INFECTIONS ON THE CYTOKINE BALANCE IN CHILDREN FROM AN ENDEMIC AREA IN MONTERÍA - CÓRDOBA - COLOMBIA

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Helminth infections can result in a strong immunoregulatory activity that affect the capacity of the host, mainly children population to develop co-infections, as well as being a risk factor in events such as asthma and atopy. The effect of these infections on the balance of pro- and anti-inflammatory cytokines in children from an endemic area in Córdoba - Colombia was measured. An analytical observational study was carried out, where seventy (70) school children were selected and studied and grouped into two groups (infected and control) and an epidemiological survey was carried out. Stool samples were processed by the Kato Katz method for identification and quantification of soil-transmitted helminths and blood plasma was used for flow cytometric quantification of cytokines and chemokines. The prevalence of STH was 56% (44.3-67.6); 77% (63.7-90.2) of the infections were mono infections and the remaining percentage were poly infections with at least two STH species. The intensity in most cases was moderate. When comparing cytokines and chemokines between the groups, TNF-α (P=0.0431) and IFN-γ (P=0.0484) had significant differences in both groups, for the chemokine MCP-1, the median values of the control group were significantly higher than that of the infected group (P=0.001). The anti-inflammatory profile cytokine TGF-β1 in the infected group had higher plasma concentrations than in the control group (P=0.0005). For IL4 and IL10, plasma concentrations were slightly higher in the control group than in the infected group, but there were no statistically significant differences between them; as was the case for TGF-β1, where the infected group had higher plasma concentrations than the control group. These data suggest that the STH infections presented by children in this endemic area have a behavior of chronic asymptomatic infections, established with a pattern of overdispersion and with a predominance of immune response with an anti-inflammatory and regulatory profile, apparently generated by TGF-β1.

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INTESTINAL PARASITE INFECTION AND RISK OF CONCOMITANT CERVICO-VAGINAL INFECTIONS IN THE PERUVIAN AMAZON

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Intestinal parasite infections, including helminths and protozoa, remain an important public health concern in tropical low- and middle-income countries, such as Peru, where cervico-vaginal (CV) infection rates are also high. As they establish chronic infection in the human gut, intestinal parasites must regulate the host's immune system to ensure their long-term survival, potentially impacting the host's defense against other pathogens. This cross-sectional study explored the relationship between intestinal parasite and CV co-infections, specifically bacterial vaginosis (BV) and Trichomonas vaginalis (TV) in 30–50-year-old Peruvian women. We enrolled 120 women undergoing routine cervical cancer screening in Iquitos, Peru, between August 2022 and February 2023. Participants provided demographic, clinical, and risk factor information, underwent testing for HPV, HIV, syphilis, chlamydia, BV (via Nugent score), and TV (via wet mount), and submitted specimens for stool ova and parasite microscopy. We used logistic regression to evaluate whether parasite infection was associated with BV or TV co-infection. Of 108 participants, 54.6% had intestinal parasite infection (9.1% (9/108) helminth [88.9% (8/9) Ascaris and 11.1% (1/9) hookworm] and 50.9% (55/108) protozoa [98.2% (54/55) Giardia and 1.8% (1/55) Entamoeba histolytica]). CV infections were: HPV 18.6% (19/102), HIV 0.9% (1/108), syphilis 0.9% (1/113), chlamydia 0% (0/50), BV 36.1% (39/108), and TV 6.5% (7/108). Whereas intestinal parasite infection overall was not associated with TV (p=0.89), participants with Ascaris lumbricoides were 12.84 times more likely to have TV (95% CI: 2.37, 69.52, p=0.0068). Intestinal parasite infection was positively associated with BV (adjusted OR 3.67, 95% CI: 1.02, 13.21, p=0.0466). Sexual and sanitation variables did not differ among women with and without parasite infection. These preliminary findings suggest that certain intestinal parasite infections may increase risk of CV co-infections like TV and BV. Thus, public health measures to reduce community intestinal parasite burden could reduce morbidity from CV infections.

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SUCCESSFUL TREATMENT OF CUTANEOUS LEISHMANIASIS WITH INTRAMUSCULAR INJECTION OF SODIUM STIBOGLUCONATE IN AN 18 MONTH OLD CHILD

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Cutaneous leishmaniasis is endemic in Ethiopia. It is one of the neglected tropical disease for which few treatments with variable success rate are available. Treatment varies depending on the site, size and number of the lesion, the leishmania species type, age of the patient etc. There are few reports available regarding the use of intramuscular sodium stibogluconate use for treatment of cutaneous leishmaniasis in children less than two years of age. In addition most guidelines do not clearly put the use of intravenous or intramuscular use of sodium stibogluconate in children less than two years. Here we present an 18month old male child treated with intramuscular injection of sodium stibogluconate for cutaneous

lesishmaniasis. The child presented with lesion over the face since four month which is asymptomatic. On physical examination there is 3cm x1.5cm erythematous indurated plaque just below the right lower eye lid and close to bridge of the nose with overlying hyperpigmented crust. On skin slit smear examination there is leishmania parasites (leishman Donovan bodies) seen. He was admitted and treated with daily intramuscular injection of 200mg of sodium stibogluconate. He was followed with weekly laboratory investigations which includes complete blood count, liver function test, renal function test, lipase, amylase and electrocardiograph. On the fourth week, 23rd day, he developed hepatotoxicty with more than five times elevation of liver enzymes and the drug was discontinued. At this moment the healing was adequate in which flattening of the lesion and reepithelization reached 80%. After a week the liver function test was normalizing and topical 15% parmomycin (approximately 3gm) was given and he applied it only for 6 days. After 2 months the child has complete flattening and reepithelization of the lesion. In conclusion, sodium stibogluconate can be used in children at least 18 month and older.

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A NOVEL TREATMENT FOR SCABIES

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Scabies is a highly contagious skin disease caused by Sarcoptes scabiei var hominis. It is associated with serious life-threatening secondary bacterial infections caused by Group A Streptococcus and Staphylococcus aureus. There is no vaccine and the most commonly used therapeutics, oral ivermectin and topical permethrin mainly target the parasite nervous system, killing only the motile stages. Therefore, they have sub-optimal efficacies and require repeat treatments. Prolonged use of current drugs and patient incompliance to repeat treatments have led to emerging parasitic resistance. This highlights the importance of a single dose treatment that targets all the stages of the S. scabiei life cycle. We tested two novel scabicides (ADF and FDF) in in vitro bio-assays and pre-clinical, using the porcine scabies model. In vitro results shows excellent miticidal and ovicidal effects of compounds ADF and FDF. When used in combination, the efficacy was significantly raised. The lethal time (LT100) to kill all mites and young eggs was 2h, and for late-stage eggs 8h. Four groups of 8 scabetic pigs were used in pre-clinical evaluation. Single topical application of the combined formulation on scabetic pigs for 4h or 8h resulted in complete cure of the infection by day 5 post-treatment and remained mite-free. The results were significantly better than two doses of ivermectin group and the un-treated control group remained infected. Pharmacokinetics of the compounds are being assessed by mass-spectrometry. In addition, combination treatment showed excellent anti-bacterial effects against scabies associated pathogens with significantly lower minimum bactericidal concentration (MBC) than the scabicidal concentration in vitro. We propose that our novel treatment is a promising next generation scabicide which only require a single application and likely prevents scabies associated secondary bacterial infections.

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KINETICS OF CARDIOVASCULAR AND INFLAMMATORY BIOMARKERS IN CHILDREN WITH DENGUE SHOCK SYNDROME

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Vascular leak is the hallmark of dengue infections which in some patients can lead to the potentially fatal dengue shock syndrome (DSS). Early identification and quantification of leak remains challenging, yet crucial to optimise fluid therapy. Endothelial glycocalyx layer (EGL) disruption and inflammation are implicated in the pathogenesis of vascular leak, however little is known about their association with intravascular volume and clinical outcomes. We investigated the association of EGL and inflammatory biomarkers and their kinetics during fluid resuscitation in DSS patients admitted to ICU. Paediatric patients were enrolled on admission to ICU at shock onset. Three daily blood samples were taken during ICU stay and one at 1-month follow-up visit (FU), for measurements of plasma levels of syndecan-1 (SDC1), hyaluronic acid (HA), suppression of tumorigenicity 2 (ST2), ferritin, and N-terminal pro-B-type natriuretic peptides (NT-proBNP), and atrial natriuretic peptides (ANP). The primary outcome was intravascular volume defined by a percentage haematocrit (HCT) change (values taken at shock onset and baseline at FU). Secondary outcomes were the development of recurrent shock and respiratory distress. 90 patients were enrolled; the median age was 12 years. Recurrent shock occurred in 16 patients and 10 had respiratory distress. Ferritin and ST2 were highest at enrolment (ICU admission), whilst HA and SDC1 peaked 24-hours after admission. These biomarkers decreased over ICU stay and returned to normal at FU. The natriuretic peptides had different trajectories, with increasing trends from ICU stay to FU. HA had a positive correlation with %HCT change ($rho = 0.37$, $p = .02$). None of the biomarkers at admission associated with recurrent shock or respiratory distress. Ferritin had a positive correlation with HA ($rho = .59$, $p < .001$) and SDC1 ($rho = .60$, $p < .001$) at all timepoints. In summary, we have shown the host inflammatory response is associated with EGL breakdown and HA could be a useful surrogate marker of leak severity in patients with DSS.

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THE IMPACTS OF COVID-19 ON THE RESURGENCE OF LASSA FEVER IN NIGERIA

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The Coronavirus (COVID-19) pandemic is one of the worst pandemics in history. Lassa fever is a viral hemorrhagic fever endemic in Nigeria and some other West African countries. This study aims to identify the relationship between the incidence/reporting of COVID-19 and Lassa fever, factors affecting the trends of both illnesses in Nigeria, and how public health agencies can be better prepared for the effects of future pandemics on the incidence/reporting of other diseases. Data was extracted from the Nigeria Centre for Disease Control disease situation reports. Lassa fever reports for [24th to 31st Dec. 2018], [23rd to 29th Dec. 2019], [27th Dec. 2020 to 2nd Jan. 2021] and [26th Dec. 2022 to 1st Jan. 2023], as well as COVID-19 reports for [21st to 27th Dec. 2020], [20th to 26th Dec. 2021], and [5th to 18th Dec. 2022] were obtained. A systematic search was done on PubMed to include the keywords [COVID-19], [Lassa fever], [Nigeria] for the years [2020 to 2022]. The total number of confirmed cases of Lassa fever in Nigeria was 633 in 2018, 833 in 2019, 1,181 in 2020 and 511 in 2021; a 56.7% decrease in 2021. However, the total number of confirmed cases increased by 109% to 1,067 in 2022. As of 27th December 2020, a total of 88,414 COVID-19 cases had been recorded. On 26th December 2021, the figure rose by 168.7% to 237,561 and on 18th December 2022, the number of confirmed cases rose by only 12% to 266,415. While COVID-19 was prevalent, Lassa fever reportage declined. A few reasons that may account for this disparity in the incidence of both diseases, as obtained from the review of literature, include: similarities in clinical manifestations, insufficient modulator laboratories (only 8) for Lassa fever testing in Nigeria, and the similarities in the laboratory and management facilities of both diseases. The 'seasonal' timing and symptoms of Lassa fever and COVID-19 surge are similar. Hence, public health agencies in countries that have such occurrences must be better prepared to adequately test, manage or co-manage multiple disease conditions in the same facility. Such agencies must also increase public awareness of such related diseases occurring concurrently.

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SCRUB TYPHUS AND Q FEVER AMONG HOSPITALIZED PATIENTS WITH ACUTE FEBRILE ILLNESS IN BANGLADESH

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Infection by Orientia tsutsugamushi (scrub typhus) or Coxiella burnetii (Q fever) have previously been reported in Southeast Asia, including Bangladesh, but remains underdiagnosed due to lack of diagnostic capacity and clinician awareness. From September 2021 to February 2023, we randomly enrolled 1,544 hospitalized AFI patients from five tertiary care hospitals across different geographical regions of Bangladesh; 778 were adults and 766 were infants and children (2 months-12 years). AFI was defined as a measured or history of fever (≥ 100.4°F) within the past 14 days. We detected 24 (1.5%) cases of scrub typhus and 7 (0.5%) cases of Q fever from blood samples by real-time PCR assay. Among the detected scrub typhus cases, 50% were male, and 19 (79%) were adult (25-75 years). Ceftriaxone (71%) was predominantly prescribed and doxycycline, the recommended drug, was only used in one patient. The average duration of hospital stay was five days. Of 24 patients, 10 (42%) were discharged with improved status, 13 (54%) left voluntarily before improving, and one died on the 11th day following admission. On follow-up in the 4th week, 54% of the cases reported improvement, 12% reported full recovery, 33% were lost to follow-up, and one additional death occurred.All seven Q fever positive cases were male and adult (20-55 years) and six were from Rangpur Division. Two of the cases reported contact with domestic cows and goats. All cases were treated with ceftriaxone. Only two patients reported improvement at discharge, and after 4 weeks, six reported full recovery.Scrub typhus and Q fever are not commonly detected in clinical settings in Bangladesh. Detection of hospitalized cases of scrub typhus and Q fever suggest that clinicians should consider these diseases as a differential diagnosis of severe AFI in Bangladesh. To support differential diagnosis and better management of these diseases, low-cost appropriate diagnostic tools along with education and knowledge of these diseases should be made accessible to clinicians at the point and time of care.

6293

TIMELY RETURN OF TEST RESULTS FOR MEASLES AND YELLOW FEVER: A SURVEY OF CARE PROVIDERS IN GHANA

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Laboratory tests are ordered to diagnose and manage patients, but also are critical to outbreak detection. Timely return of results for clinical decisions and surveillance depends largely on the prompt reporting of laboratory results. This study surveyed health care providers for their assessment of the timely return of test results for two epidemic-prone diseases (Yellow fever and Measles) in Ghana.A survey of healthcare providers was carried out in 53 randomly selected health facilities from the three ecological zones in Ghana, stratified by remoteness and population density. Data were collected from providers in hospitals and subdistrict facilities from February 2021 to July 2022. Descriptive analysis characterized providers' assessment of the duration of time between patient onset of symptoms and presentation to health facilities as well as the return of test results for patient management.Providers estimated 9.1 days (95%CI 7.47-10.72) for patients with symptoms of non-severe YF to present for care, compared to 6.4 days (95%CI 4.7-8.02) for severe cases of YF. Patients with non-severe measles were estimated to present in 5.2 days (95%CI 4.08-6.34) and with severe measles in 6.8 days (95%CI 5.98-7.54). All testing was reported to occur by send-out. Both yellow fever and measles testing was estimated to return in a median of 30 days (IQR 14-90 days). The median percentage of yellow fever results estimated to occur in a timely manner for patient management was 0% (IQR 0-40%) and for measles was also 0% (IQR 0-30%). Return of test results for Measles and Yellow fever was delayed, hence the need to strengthen the laboratory network since the potential for the transmission of epidemic-prone disease depended on both the time between infection onset until presentation to health facilities, as well as the time to receive testing results.

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CEREBROSPINAL FLUID CHLORIDE IN THE DIAGNOSIS OF TUBERCULAR MENINGITIS- A PROSPECTIVE STUDY FROM JODHPUR, INDIA

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Tubercular meningitis presents a diagnostic challenge as uniform criteria are lacking, and no single test can definitively rule it out. We explored cerebrospinal fluid chloride and cerebrospinal fluid-serum chloride ratio as diagnostic tools for tubercular meningitis. Adults with clinical suspicion of meningitis were enrolled prospectively from March 2021-September 2022 after informed consent and ethical approval. Tubercular meningitis was diagnosed using a combination of clinical findings, CNS imaging, cerebrospinal fluid analysis and nucleic acid amplification tests. Sensitivity, specificity, and area under the curve for receiver-operating curve were calculated for cerebrospinal fluid chloride and cerebrospinal fluid-serum chloride ratio to diagnose tubercular meningitis. Of 209 included, 56 were diagnosed with tubercular and 61 with viral meningitis, rest were pyogenic and others. The mean cerebrospinal fluid chloride was low in tubercular meningitis (115.4±10.6 mmol/L), as compared to viral meningoencephalitis (127.0±7.5mmol/L, p <0.0001). The mean ratio of cerebrospinal fluid-serum chloride (1.18±0.09) was also significantly lower in patients with tubercular meningitis in comparison to patients with viral meningoencephalitis (1.24±0.06, p =0.04). Area under the curve of cerebrospinal fluid chloride levels for the diagnosis of tubercular meningitis was 0.76 (p <0.0001, 95% CI 0.68-0.84) and cerebrospinal fluid-serum chloride ratio was 0.67 (p <0.0001, 95% CI 0.58-0.75). Cerebrospinal fluid chloride <121 mmol/L had a sensitivity and specificity of 70.5% and the cerebrospinal fluid-serum chloride ratio had a sensitivity and specificity of 65% for diagnosis of tubercular meningitis. Our study showed that absolute cerebrospinal fluid chloride and cerebrospinal fluid-serum chloride ratio are sensitive diagnostic markers for diagnosis of tubercular meningitis and specially to differentiate it from viral meningoencephalitis in the initial course of illness.

6295

A CASE OF MONKEYPOX VIRUS REINFECTION

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We present the case of a healthy man in his early 30's who presented with monkeypox virus infection six months after having completely recovered from a previous one. He identifies as a man having sex with men and is taking pre-exposure prophylaxis for HIV. The first episode was mild with a few umbilicated lesions on the penis. Cutaneous and pharyngeal swabs

were positive by real-time orthopoxvirus PCR. Within two weeks skin lesions resolved without complications. Six months later the patient was seen by his general practitioner for persistent anal pain. The pain had started after his return from Brazil where he had engaged in unprotected sexual intercourses including anal receptive intercourses with multiple partners. The last intercourse was reported two weeks before symptoms onset. He did not develop any skin lesions nor systemic symptoms. The anal swab came back positive for monkeypox virus by real-time orthopoxvirus PCR with a cycle threshold of 27, a repeated swab two week later was negative. Sexually transmitted disease (STD) screening was positive for Chlamydia trachomatis (non LGV) and negative for HIV and syphilis. A colonoscopy revealed an anal fissure but no typical mpox lesions. He was never vaccinated against mpox. Symptoms might have been due to mpox or to the concomitant presence of an anal fissure or Chlamydia trachomatis infection. It is therefore impossible to distinguish between a symptomatic or asymptomatic mpox reinfection. This case, although still anecdotal, suggests that certain individuals might not develop sufficient neutralizing immunity after natural infection and become reinfected when re-exposed to monkeypox virus. From a public health perspective, if reinfection become more prominent, it raises the questions of repeated testing of highly exposed symptomatic individuals regardless of prior infection or vaccination and of extending vaccination to individuals after an infection.

6296

IMPACT OF DIFFERENTIAL AND SYSTEMATIC DIAGNOSIS OF DENGUE, CHIKUNGUNYA AND MALARIA ON PATIENT MANAGEMENT AND ANTIBIOTIC USE IN BURKINA FASO AND IVORY COAST

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Over the last several decades, dengue and chikungunya have become more geographically dispersed with common clinical outbreaks. They are responsible for high morbidity and mortality in endemic areas, such as West Africa where there is limited data. The health systems in these countries therefore face major challenges. This study aims to assess the impact of differential diagnosis of these two arboviruses on febrile patients clinical management, prevention of complications, antibiotic and antimalarial misuses. Differential diagnosis of dengue and chikungunya will be performed using the VIDAS® Diagnostic Tests for the detection of Dengue Virus NS1 Antigen, Anti-Dengue Virus IgM and IgG and VIDAS® anti-CHIKV IgM and IgG (technology developed at the US NIAID, Vaccine Research Center), whereas malaria will be diagnosed by RDTs. 800 subjects with acute undifferentiated febrile illness will be enrolled in a prospective cohort study carried out in two West African countries with respectively one interventional and one control sites per country. In interventional sites, all subjects will be tested for dengue and chikungunya (VIDAS®) in addition to malaria (RTDs). Clinicians' final diagnosis will consider the patients' clinical symptoms and diagnostic tests results. In control sites, on-site routine diagnosis will be used. In parallel, all the biological samples will be tested for dengue and chikungunya (VIDAS®) to obtain the real rate of positive subjects. Clinical outcomes are i) the comparison using a Chi-2 test of antibiotic use in control and interventional sites, ii) the healthcare resource utilization and productivity losses, iii) the subject quality of life using EQ-5D questionnaire. The enrollment is expected to start in April 2023 for a 5 months duration. Intermediate analysis will be performed on 400 subjects and presented in the poster. These findings should highlight the relevance of differential diagnosis in febrile subjects' clinical management, generate seroprevalence data and demonstrate the potential for avoiding antibiotic misuse which amplify the emergence of antibiotic resistance and lead to greater mortality.

6297

INTESTINAL IMMUNOHISTOCHEMISTRY AND HISTOLOGY RELATIONSHIPS WITH FECAL ENTERIC PATHOGENS IN A PEDIATRIC POSTMORTEM STUDY

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Postmortem (PM) intestinal minimally invasive tissue sampling (MITS) has previously been demonstrated feasible and histologically informative despite autolysis concerns. We aimed to determine the informative value of immunohistochemistry (IHC) and pathogen analysis on PM intestinal samples. PM duodenal and rectal biopsies from children with acute illness and/or undernutrition who died as inpatients (MITS in Malawi, n=23), and duodenal biopsies from live children with environmental enteric dysfunction (EED) (Zambia, n=59) or no pathologic abnormality (NPA) (U.S., n=25) were endoscopically biopsied and stained for both hematoxylin and eosin (H&E) and a 14-marker IHC panel. Pathologists semi-quantitatively scored H&E images using a validated EED histology index. IHC images were digitally quantified and normalized to account for tissue size. Enteric pathogens were sought by qPCR on MITS stool, duodenal, and rectal samples. We used multivariable linear regression to (1) compare duodenal IHC readouts from MITS to EED and NPA samples and (2) test associations between fecal pathogens with IHC readouts and histology scores in MITS samples. MITS IHC stain quantification were similar to those of EED and NPA cohorts, but B lymphocyte, intraepithelial lymphocyte (IEL), brush border, and leukocyte proliferation marker readouts were significantly lower in MITS samples while granzyme B signal was higher. At least one pathogen was found per MITS participant, although detection was much more frequent in stool samples and fecal pathogens did not clearly correspond in intestinal samples. Fecal enteropathogenic E. coli was inversely associated with rectal histology summative index score (-0.18; 95% CI: -0.32, -0.05). Stool pathogen-IHC associations included enteroaggregative E coli with duodenal intraepithelial CD3 (-0.06; 95% CI: -0.09, -0.03) and rectal MUC2 (-1.98; 95% CI: -2.59, -1.37), and norovirus with rectal defensin 5 (0.33; 95% CI: 0.21, 0.45) and MUC2 (1.27; 95% CI: 0.01, 2.52). These novel data support the use of IHC along with H&E for histopathologic assessment in PM intestinal samples to improve knowledge of host pathobiology.

6298

TRAVEL HEALTH NEEDS OF CHILDREN IN US MILITARY FAMILIES STATIONED ABROAD

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The Military Health System (MHS) provides care to 9.6 million beneficiaries including uniformed service members, military retirees, and their family members with the mission to provide a medically ready force both at home and abroad. The US Department of Defense requires certain preventative health measures for service members serving abroad; however, many of these service members are living with spouses and children who have their own preventative health needs. We characterize the MHS pediatric population living outside of the United States and the recommended travel health specific preventive services. We assessed the registered country of residence of Active Duty Service Members (ADSM) and their families based on the Defense Enrollment Eligibility Reporting System to quantify the children of ADSM, under the age of 18, living abroad. Data were sorted by age group and region, excluding those living in the continental United States, Alaska, and Hawaii, as well as Canada. Data from Reservists and Retirees were excluded; although also MHS beneficiaries, their location is less likely to be service-related. There are 63,443 children of ADSM living abroad and rotating on a 2-3 year cycle. Of those children, 26,269

are aged five or younger with 37,174 children 6 to 17 years old. The largest populations are in Asia (26,172) and Europe (31,243), reflecting long standing bases in Japan and Korea as well as Germany, the United Kingdom, and Italy, with a sizable population also in Oceania (3,676) due to the US military presence in Guam. Thousands of military children live in countries without permanent military bases and MHS medical assets in these regions and those in Mexico/Central America/the Caribbean (1,658), Africa (397), and South America (297). We map recommended travel specific interventions across this population distribution. The children of military families serving abroad are a unique population in need of a range of preventative health services that differ from their counterparts in the United States. Utilization of preventive services and health outcomes associated with living abroad have not been studied in this population.

6299

VALIDATION OF AN NS1 AND IGM RAPID TEST IN THE EARLY DIAGNOSIS OF DENGUE IN A PRIMARY HEALTH CARE CENTRE IN BUCARAMANGA, COLOMBIA DURING THE YEARS 2018-2020

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Dengue has a broad spectrum of manifestations that difficult the clinical confirmation in regions where the acute syndrome febrile is multi-aetiology. The laboratory diagnostic requires specific and sensitive tests with the good advantage of cost, time, and easier manipulation. The rapid tests to detect NS1, play an important role in the early diagnosis of dengue however the implementation in primary health care is not the rule and the routinary IgM detection may not be useful during the acute phase. This study aimed to validate the use of the NS1 and IgM rapid test in primary healthcare facilities in the early detection of dengue cases during an outbreak in Colombia. From 2018 to 2020, a system was established in the healthcare of public networks in Bucaramanga, Colombia. After the blood counts and using the remaining sample, a commercial rapid test was run for antigen NS1 and IgM. One RT-PCR was performed for the detection of Zika, chikungunya, and dengue viruses. The quick test and the RT-PCR were performed independently and in a specific order: first, the rapid test and second the RT-PCR were done blinding. We estimated sensitivity, specificity, and positive and negative predictive values (SE, SP, PPV and NPV, respectively) for NS1 and IgM against PCR stratifying by disease's duration, considering a range of prevalence between 10-50%. We evaluated 566 patients with complete clinical and diagnostic data (32% were PCR positive). Overall, SE and SP were 81% and 72% for NS1 and 38% and 62% for IgM, respectively. SE increased with the disease's duration from 33.3-54.0% for IgM but remained stable around 80.0% for NS1, whereas SP was similar for both tests and showed a decreasing trend at larger disease duration. PPV and NPV ranged from 52.9-74.2% and 73.6-100.0% for IgM, and from 58.7-95.9% and 98.7-100.0% for NS1 at the disease's onset, respectively. According to our results, testing for NS1 is not only feasible in the context of primary care but also a highly accurate approach to diagnose tools for dengue in endemic areas where the acute syndrome febrile is multi-aetiology, allowing an early and suitable diagnosis to reduce complications due to the disease.

6300

THE EFFECTS OF L-CARNITINE SUPPLEMENTATION ON RATE OF WEIGHT GAIN AND BIOMARKERS OF ENVIRONMENTAL ENTERIC DYSFUNCTION IN SEVERELY MALNOURISHED CHILDREN: A DOUBLE-BLINDED RANDOMIZED CLINICAL TRIAL

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Severe Acute Malnutrition (SAM) and an asymptomatic small intestinal illness, Environmental Enteric Dysfunction (EED), are highly prevalent among children in resource-limited countries like Bangladesh. To best of our knowledge, limited trials have been conducted on malnourished children to evaluate the effects of carnitine, a vital micronutrient for ß-oxidation. Therefore, we sought to explore the role of L-carnitine on the rate of weight gain and EED biomarkers in SAM children. A prospective, double-blinded, placebo-controlled, randomized clinical trial (ClinicalTrials.gov# NCT05083637) was conducted at Dhaka Hospital of icddr,b. Participants were 9-24 months-old severely malnourished children who were randomly assigned to receive commercial L-carnitine syrup (100mg/kg/day) or a placebo for 15 days in addition to the protocolized treatment of SAM at the Nutritional Rehabilitation Unit (NRU). A total of 98 children with a weight-for-length z-score (WLZ) <-3 SD were enrolled between October 2021 and September 2022. All analyses were based on an intention-to-treat basis. The primary outcome variable, mean weight gain (g/kg/day), was comparable between the intervention and placebo groups [2.18 vs. 2.11; ß: 0.06, 95% CI: (-0.95, 1.07), p: 0.902], respectively. After the intervention, the mean difference between baseline and end line values of EED biomarkers were also comparable; for instances- Myeloperoxidase-ng/ml [-1129.99 vs. -152.93; ß: -977.06, 95% CI: (-8837.77, 6883.65), p: 0.806], Neopterin-nmol/L [166.67 vs. 342.44; ß: -175.78, 95% CI: (-719.78, 368.22), p: 0.523], Alpha-1 Antitrypsin-mg/ml [0.39 vs. 0.30; ß: 0.09, 95% CI: (-0.09, 0.27), p: 0.321], respectively, in L-carnitine and placebo groups. Our clinical trial results provided the best available information and laid the groundwork to show the effects of L-carnitine supplementation on the rate of weight gain and EED biomarkers in participants with severe acute malnutrition. A scaling-up of this intervention with high doses in contexts with limited resources should be considered.

6301

BRAINSTEM ENCEPHALITIS AND EXTRAPYRAMIDAL SYNDROME AFTER ZIKA VIRUS INFECTION IN SALVADOR, BRAZIL

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Zika virus (ZIKV) is an emerging flavivirus that caused a widespread outbreak in Brazil in years 2015-2016. In addition, shortly after its introduction in 2015, a cluster of cases with Guillain-Barré syndrome and other neurologic syndromes were described in Brazil. Herein, we present a case of a brainstem encephalitis with extrapyramidal syndrome in a patient in Salvador, Brazil. A 21-year-old Brazilian woman presented with fever, maculopapular rash, pruritus, arthralgia, headache, and edema of hands and feet. She was admitted to the hospital seven days after the onset of viral symptoms when neurological symptoms began: confusion, somnolence, inability to walk, and impairment of speech. After a generalized seizure she was admitted to the intensive care unit (ICU). She was lethargic, had dysphonia and dysarthria, right facial nerve palsy, impaired palate elevation, and severe dysphagia. She had normal muscle strength and brisk deep tendon reflexes. Cerebrospinal Fluid (CSF) was collected seven

days after the onset of viral symptoms, and a serum sample 12 days after the onset of those symptoms. CSF revealed two cells/mm3 (lymphocytes), 43mg/dL (protein), and 64mg/dL (glucose). RT-PCR for ZIKV, CHIKV, and DENV were negative in serum samples. ELISA Anti-ZIKV IgM and IgG antibodies were detected, as well as the ZIKV PRNT. She recovered over the following 34 days. This case report highlights a rapid and severe evolution of symptoms, requiring hospitalization in the ICU, with long-term treatment. Brainstem encephalitis is a rare disease. Herein,it was clinically diagnosed through the presence of cerebellar disorders, altered level of consciousness, and hyperreflexia. ZIKV should be considered a potential etiological agent of encephalitis in endemic regions. Healthcare workers must be aware of the potential severe neurological syndromes associated with ZIKV infection and be prepared to provide prompt diagnosis and supportive care.

6302

EFFECT OF PRIOR DENGUE INFECTION AND SINGLE-DOSE DENGUE VACCINATION ON THE RISK OF SUBSEQUENT VIROLOGICALLY CONFIRMED DENGUE: A FIVE-YEAR PROSPECTIVE COHORT STUDY IN CEBU, PHILIPPINES

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Dengue is a mosquito-borne viral illness causing significant morbidity and mortality. In 2015, a three-dose dengue vaccine (CYD-TDV,Dengvaxia) was licensed for those 9 years and older in dengue-endemic areas. In 2016, the World Health Organization (WHO) recommended that countries consider introduction of CYD-TDV in settings with at least 70% seroprevalence. The Philippines Department of Health (DOH) implemented a three-dose dengue vaccination program in high dengue burden regions targeting children aged 9 to 14 years old. In June 2017, the program was expanded to Cebu province. After a follow-up analysis of the CYD-TDV Phase 3 trials showed that vaccination conferred protection among dengue-seropositive but increased risk for severe dengue among dengue-seronegative participants, the dengue vaccination program was halted with children in Cebu offered only one dose. We conducted a prospective community-based cohort study in Cebu to evaluate the effect of baseline dengue serostatus and a single dose of CYD-TDV on the subsequent risk of virologically-confirmed dengue (VCD). We enrolled 2,996 healthy children 9 to 14 years of age in May 2017. Baseline sera were collected and batch tested by indirect IgG ELISA and focus reduction neutralization test (FRNT). From June to August 2017, 1,790/2,996 (59.7%) children received a single dose of CYD-TDV. Active surveillance for an acute febrile illness (AFI) in the cohort was conducted from November 2017 to October 2023 (5 years). Those who developed AFI were identified, epidemiological and clinical data were collected, and blood drawn for confirmation of dengue by RT-PCR. Incidence was 11 VCD cases/1,000 population/year. Crude (unadjusted) analyses showed that seronegative children at baseline who received one dose of CYD-TDV were more likely to develop VCD (RR 2.12, 95% CI 1.45-3.09), while those who were seropositive at baseline and received one dose of CYD-TDV were less likely to develop VCD (RR 0.47, 95% CI 0.32-0.69). Our findings support the 2018 revised WHO recommendation of pre-vaccination screening prior to administration of CYD-TDV.

6303

MOLECULAR SURVEILLANCE AND EPIDEMIOLOGY OF LEPTOSPIROSIS AND SCRUB TYPHUS FROM PATIENTS WITH FEVER OF UNKNOWN ORIGIN IN URBAN BANGALORE, INDIA

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Acute Febrile illnesses, usually accompanied by fever, malaise, and rashes could be associated with many infectious diseases transmitted by viruses, parasites, bacteria, or fungi in tropical countries. Leptospirosis and scrub typhus are neglected and re-emerging tropical infectious diseases, transmitted by gram-negative bacterium belonging to the Leptospiraceae family. and via the bites of infected chigger mites, spread through a bacterium Orientia tsutsugamushi belonging to the family Rickettsiaceae respectively. Sporadic outbreaks of both these infections have been concerning and over a million cases per annum, reported from South-Asian countries. Early detection and diagnosis of Leptospirosis and scrub typhus are challenging and rely usually on non-confirmatory detection tests such as ELISA respectively in both diseases, leading to underestimation of the actual disease burden. We conducted a molecular surveillance study screening 977 clinical samples across a metro city, Bangalore in South India, in collaboration with local municipal corporation-Bruhat Bengaluru Mahanagar Palike (BBMP). We aimed to understand the seroprevalence of Leptospirosis, Scrub typhus, and coinfections by ELISA and an inhouse designed multiplex TaqMan Probe-based RTPCR from the patient samples. We observed, 69/977 (7.06%) samples, tested positive for Leptospirosis, 134/ 977 (13.72%) for Scrub typhus and 21/977 (2.15%) had coinfection of both. Prevalence of both Leptospirosis and scrub typhus exhibited a significant decreasing trend from July to December ($\chi 2$= 123.44, df =3; P<0.001). The disease prevalence was compared across ELISA and q RT-PCR for both infections ($\chi 2$= 6.262, df =1). The study showcases a unique collaboration with local municipal corporation, contributing to public health surveillance. The study findings shall aid in understanding the actual disease incidence and prevalence using two different detection methods Further, this shall help in creating guidelines and detection protocols for, neglected infectious diseases from patient samples having febrile illnesses in low-resource settings.

6304

A CASE OF TYPE 1 LEPROSY REACTION WITH NASAL SEPTUM PERFORATION

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Leprosy reactions are caused by immune responses against M. leprae antigens. They are divided into Type 1 or reversal reaction (T1R), and Type 2 or ENL (T2R). Type 1 reaction can occur in up to 30% of patients usually after the start of treatment. The majority of the reactional episodes occur in borderline forms. It starts as a sudden worsening of skin lesions and nerve function impairment. Besides pre-reactional lesions presenting with more infiltration and desquamation, previous and newly developing lesions may be bright red, hot, and sensitive to the touch, sometimes ulcerated. We present the case of a 28-year-old male patient who presented to ALERT hospital Dermatology clinic with lesions on the face buttock and leg of 4 months duration. Nose lesion is associated with bleeding and stuffiness. On Physical examination, he had well-demarcated edematous erythematous plaque on the face involving the upper lip and nose with areas of hypopigmentation. The nasal septum is deviated and perforated (.5cm by 1cm). There is a hypo-pigmented erythematous anesthetic plaque of 10cm by 12 cm over the left buttock with ulcerations at the border and ulceration on the right malleolus. He had a hypopigmented patch with fine scales on the right dorsum of the hand. Sensory testing shows that there is loss of sensation on the hand and buttock lesions and the right foot over half of the plantar area. On Investigations slit skin smear is negative. Histopathology showed multiple well-formed granulomatous and giant cells along with mixed inflammatory cells composed of plasma cells and eosinophils. With

the diagnosis of Borderline tuberculoid leprosy with Type 1 reaction he started MDT ((Multi Drug Therapy) and prednisolone 1mg/kg. This case report highlights that new leprosy cases can present with reactions and reactions can occur before starting MDT treatment. Even though nasal involvement is common in the lepromatous leprosy type, it can occur as post-reaction tissue damage in T1R.

6305

PREDICTORS OF VIRAL UNSUPPRESSION AMONG ADOLESCENTS AGED 10 TO 19 ON ANTIRETROVIRAL THERAPY IN THE CITE VERTE HEALTH DISTRICT

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Globally, 37.7 million people were living with HIV in 2020. Adolescents living with HIV is on a steady rise from 1.65 million in 2018 to 1.8 million in 2021 yet very little evidence exists to comprehensively estimate adolescent viral suppression after initiation on antiretroviral therapy (ART). The National AIDS Control Committee 2020 report reveal a 29% viral suppression (<1000copies/ml) against a 93% target set for 2019. This greatly affects most HIV intervention programs as adolescents continue to lag behind in the HIV response with viral unsuppression thereby leading to increased drug resistance, transmission of HIV as well as increased morbididty and motality. This study therefore aims to identify Sociodemographic, Clinical and Behavioral predictors associated to viral unsuppression among adolescents aged 10 to 19. From a quantitative analytical study and using random probabilistic sampling, we collected data from 488 adolescents after informed consent and assent were obtained. Quantitative analysis revealed that59.2% were females, the mean age of adolescents was 15.19 years and median were 15.00 years. 16.4% of adolescent who participated still had an unsuppressed most recent viral load result. Age [(AOR = 1.10, 95% CI 0.51-0.88, P-value=0.017)], level of education [(AOR=1.46 95% CI: 0.84-2.55, P-value=0.007)] , religion [(AOR=0.25, 95% CI: 0.09-0.66)], caregiver type [(AOR=1.40, 95% CI: 0.78-0.99, P-value=0.025)], recieving care from a non-pediatric health facility {(AOR=0.51, 95% CI: 0.28-0.91, P-value=0.025)], treatment line [(AOR=3.81, 95% CI:1.88-7.74, P-vaalue<0.0001)], duration on treatment [(AOR=0.59, 95% CI, 0.34-0.81, P-value=0.044)] and poor adherence [(AOR=19.85, 95%CI, 9.53-41.36, P-value<0.0001)] were found to be predictors associated to viral unsuppression among adolescent. Hence, there is a great need to strengthen the health systems, intensify peer lead Differencial Service Deliver model, Enhanced Adherence Counselling, support groups, and therapeutic education amongs adolescents while promoting psychosocial suppor to both adolelescents and care gives.

6306

INTEGRATION OF FEMALE GENITAL SCHISTOSOMIASIS INTO HIV/SEXUAL AND REPRODUCTIVE HEALTH AND RIGHTS AND NEGLECTED TROPICAL DISEASES PROGRAMS AND SERVICES: A SCOPING REVIEW WITH A SYSTEMATIC SEARCH

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Female genital schistosomiasis (FGS) affects approximately 56 million women and girls across sub-Saharan Africa, and is associated with up to a threefold increased prevalence of HIV. Integrating FGS with HIV programmes as part of comprehensive sexual and reproductive health (SRH) services may be one of the most significant missed opportunities for preventing HIV incidence among girls and women. A search of studies published until October 2021 via Scopus and ProQuest was conducted using PRISMA guidelines to assess how FGS can be integrated into HIV/SRH and neglected tropical diseases (NTDs) programs and services. Data extraction included studies that integrated interventions and described the opportunities and challenges. A total of 334 studies were identified, with 22 eligible for analysis and summarised conducting a descriptive numerical analysis and qualitative review. We adapted a framework for integrated implementation of FGS, HIV and HPV/cervical cancer to thematically organize the results, classifying them into five themes: awareness and community engagement, diagnosis, treatment, burden assessment, and socio-economic evaluation. Most activities pertained to awareness and community engagement (n=9), diagnosis (n=9) and were primarily connected to HIV/AIDS (n=8) and school-based services and programming (n=8). The studies mainly described the opportunities and challenges for integration, rather than presenting results from implemented integration interventions, highlighting an evidence gap on FGS integration into HIV/SRHR and NTD programmes. Investments and will are needed to realise the potential of FGS integration to address the burden of this neglected disease and improve HIV and SRH outcomes for millions of women and girls at risk.

6307

DIAGNOSING A WOMAN PRESENTING WITH FOCAL WEAKNESS AND FACIAL PALSY IN MONROVIA, LIBERIA WITH PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY: A CASE REPORT

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A 45-year-old Liberian female with recently diagnosed HIV-1, stroke, and diabetes mellitus presented to the hospital in Monrovia, Liberia with reported generalized weakness for 2 weeks. On exam, she was hemodynamically stable. She had left lower lung crackles. She had facial asymmetry with cranial nerve VII palsy and left-sided facial paralysis. Right lower extremity strength was 1/5 and left lower extremity strength was 3/5. Right upper extremity strength was 3/5 and left upper extremity strength was 4/5. Admission complete blood count and complete metabolic panel were unremarkable. A CD4 count lateral flow assay showed CD4 <200 cells/μL. HIV viral load was pending. CT head demonstrated non-enhancing white matter hypodensity in bilateral parietal lobes with extension into right anterior limb of internal capsule and right external capsule. Per radiology, there was non-enhancing white matter hypodensity with signals of mild gliosis in aforementioned areas most likely due to progressive multifocal leukoencephalopathy (PML). Brain MRI was recommended. Given cerebrospinal JC virus PCR testing was unavailable, lumbar puncture was not performed. She was re-initiated on an antiretroviral (ARV) regimen of tenofovir disoproxil fumarate/lamivudine/dolutegravir for HIV/AIDS to reconstitute the immune system, which is the mainstay of treatment for PML, and trimethoprim/sulfamethoxazole prophylaxis. She received a course of azithromycin for pneumonia. She clinically improved over her several weeks of hospitalization with increased strength, particularly in the right side of her body. Her caretaker noted her improved functional strength. In summary, clinical and radiologic findings are important tools to diagnose PML. Particularly in limited resource healthcare settings, when diagnostics such as JC virus cerebrospinal fluid testing are not readily available, a clinical syndrome must be recognized. Supportive diagnostics include immunocompromised host factors, clinical symptoms and exam findings of focal neurologic deficits, and congruent radiologic brain imaging findings which can include white matter lesions.

6308

BONE MARROW CRYPTOCOCCOSIS: A RARE PRESENTATION OF A COMMON INFECTION IN AN IMMUNOSUPPRESSED PATIENT

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A 43-year-old man with AIDS (CD4 <40 cells/microliter and viral load 309,000 copies/mL) presented with right sided weakness with associated

6 months of general malaise with recent weight loss of 8kg. On exam, he was afebrile, but tachycardic up to 120. He was cachectic with marked hepatosplenomegaly but no adenopathy. His speech was dysarthric, had right facial paralysis, right hemiparesis with clonus. Labs revealed pancytopenia (Hb of 3.8 g/dL, platelets 31 and WBCs 1.66). CT scan of the chest, A/P and head were unrevealing, but MRI brain revealed a small acute infarct in the left globus pallidus and posterior limb of the internal capsule. CSF studies showed a Cryptococcus titer of 1:1997. Patient was subsequently started on amphotericin and flucytosine for induction therapy. Despite adequate coverage for Crypto, his pancytopenia persisted. This led to a bone marrow biopsy being obtained, which demonstrated Cryptococcus on mucicarmine, PAS fungus, and GMS stains. Due to concerns for bone marrow toxicity, flucytosine was held and ampho was continued. After a hiatus from flucytosine, his blood counts started to recover and normalize. After completing ampho induction, he was stabilized and discharged on fluconazole for maintenance therapy. Although Cryptococcus infection commonly presents with CNS, pulmonary, or skin involvement in patients with CD4 counts <100, bone marrow involvement has been previously described which can present with nonspecific symptoms such as fever, anorexia, weight loss, and fatigue. Bone marrow involvement will have certain implications on treatment as in this case. A known side effect of flucytosine is its bone marrow toxicity. It is important to recognize potential bone marrow involvement, as this makes flucytosine a relative contraindication. Continuing flucytosine in these cases will only worsen the pancytopenia which could cause other adverse outcomes (bleeding, worsening infection, etc.), but the goal should be to continue Ampho for induction therapy which also reaches good bone marrow concentrations and then transition to Fluconazole for consolidation and maintenance therapies respectively.

6309

TUBERCULOSIS CASE NOTIFICATIONS, TB/HIV CO-MORBIDITIES AND TREATMENT OUTCOMES IN AMHARA REGION, ETHIOPIA: A RETROSPECTIVE LONGITUDINAL PROGRAM BASED STUDY

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Globally, TB still remains as one of the major public health problems. Poor treatment outcomes, low TB case detections and its high co-morbidities are the main challenges for the success of TB program in Ethiopia. Therefore, we assessed the effectiveness of national TB control strategies on TB case notifications, treatment outcomes, and its co-morbidities between 2009 and 2018 in Amhara Region, Ethiopia. We conducted retrospective longitudinal program based study to determine the trends of TB/HIV case notifications, treatment outcomes and to identify associated factors from the reports of DOTS (Directly Observed Treatment Short-course) implementing health facilities. We extracted data from the regional TB/HIV program databases using a modified WHO (World Health Organization) reporting formats. Data were entered, cleaned and analysed using R-programming R x64 3.6.1 packages. The Case Detection Rate (CDR) of all forms of TB had increased from 55% in 2009 (95% Confidence Interval (CI) = 54.5% - 55.4%) to 73% in 2018 (95% CI = 72.2% - 73.2%). Over the same period, TB/HIV co-morbidity rate had been reduced from 32.6% (95% CI =30.7% - 34.5%) to 8.4% (95% CI = 8.04% - 8.8%). The odds of being co-morbid with HIV was higher for those TB cases who were diagnosed as extra-pulmonary TB cases [Crude Odds Ratio (COR) [95% CI] =1.26(1.07, 1.47)] compared to other forms of TB. Apart from this, being co-morbid with HIV [COR (95% CI) = 5.91 (5.52, 6.33)] and being diagnosed as extra-pulmonary TB cases [COR (95% CI) = 1.40 (1.35, 1.45)] were important predictors to be significantly associated with unsuccessful treatment outcomes. In conclusion, a huge proportion of all forms of TB cases (36%) remained undetected. Therefore, access to quality of diagnostic services such as fluorescence microscopy and GeneXpert needs to be improved through designing targeted TB case finding strategies for risky groups to TB infection. Additionally, designing of early linkage and treatment follow-up strategies need to be tailored for those groups of TB cases who are at risk to unsuccessful treatment outcomes.

6310

CLINICAL SIGNS AND IMMUNE RESPONSE CHANGES DURING PLASMODIUM FRAGILE CO-INFECTION OF ART-TREATED SIV+ RHESUS MACAQUES

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Plasmodium co-infection in untreated people with HIV (PWH) results in increased viral load (VL), decreased CD4+ T cell counts, and greater incidence of clinical malaria and malaria-related mortality. However, the impact of Plasmodium co-infection in antiretroviral therapy (ART) treated PWH has not been well described. We hypothesized that P. fragile co-infection of ART-treated, SIV+ rhesus macaques (RMs) would result in elevated VL, decreased CD4+ T-cell counts, and neutrophil disruptions. Male RMs (n=4) were intravenously (i.v.) inoculated with SIVmac239 (TCID50=50); initiated daily antiretrovirals (ART) at Week (W) 8 post-SIV infection; i.v. inoculated with P. fragile (20x10^6 infected erythrocytes [iRBCs]) at W12 post-SIV; and received anti-malarial treatment at W14 post-SIV. Peripheral parasitemia, anemia, plasma VL, and CD4 and neutrophil dynamics were monitored via quantification of iRBCs in Giemsa-stained thin blood smears, plasma hematocrit levels, SIV qPCR, and flow cytometry, respectively. Peak VL (median=9.92x10^06 RNA copies/ul) occurred at W3 post-SIV and decreased after ART, with 2/4 RMs becoming undetectable. P. fragile parasitemia occurred at W14 post-SIV (median %parasitemia=25.5% iRBCs) and all animals became anemic (median=19.8% hematocrit). At W13 post-SIV, RMs exhibited detectable VLs, sustained until W17 post-SIV (median=9.34x10^02 RNA copies/ul). Compared to baseline (median=306.905 cells/ul), CD4+ T-cell counts declined by W8 post-SIV (median=140.5 cells/ul), increased after ART (median=193.5 cells/ul), followed by a sustained decline (median=173.59 cells/ul) after P. fragile. Compared to baseline (median=53.58%), neutrophil frequencies increased at W14 post-SIV (median=73.25%), then stabilized to baseline levels after anti-malarial treatment. Our data indicates that P. fragile co-infection lowered ART efficacy and resulted in increased peripheral neutrophil frequencies coinciding with peak parasitemia. Additional studies are underway to characterize the mechanisms by which this cell subset may contribute to disease pathogenesis during SIV/P. fragile co-infection.

6311

EPIDEMIOLOGY OF CO-INFECTIONS IN PREGNANT WOMEN LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS 1 IN RURAL GABON: A CROSS SECTIONAL STUDY

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There is a lack of recent epidemiological data on HIV infection during pregnancy in Gabon. Moreover, it is unclear if HIV-positive pregnant women are more prone to suffer from other common co-infections. Thus, an HIV-prevalence-study was conducted among pregnant women, followed

by a cross-sectional case-control study in which the prevalence of various co-infections was compared between HIV-positive and HIV-negative pregnant women. Data for the HIV prevalence survey were collected retrospectively using routinely collected diagnostic data from 21 antenatal care centres (ANCs). For the cross-sectional co-infection study, all HIV-positive pregnant women and a comparator sub-sample of HIV-negative pregnant women were recruited at the ANC in Lambaréné. Co-infection status of vector-borne (VBI) and sexually transmitted infections (STI) was assessed. HIV positivity was 3.93% (646/16,417) among pregnant women, and 185 pregnant women were recruited.Overall, 63% of HIV-positive and 75% of HIV-negative pregnant women were diagnosed with at least one co-infection. HIV-negative women were more often co-infected with STIs than HIV-positive women (Mean [SD] STIs: 2.59 [1.04] vs 2.16 [1.35], respectively; p=0.056). The crude odds for a concomitant STI was lower in HIV-positive than in HIV-negative women. The change of magnitude from the crude to adjusted OR indicates a differential sexual risk factor profile among HIV-positive and HIV-negative women in this population. This might potentially be explained by the availability of sexual health care counselling for HIV-positive women within the framework of the national HIV control programme, while no such similar overall service exists for HIV-negative women. In conclusion, e found a high prevalence of STIs among pregnant women, an important finding for national policymakers and STI control programmes.

6312

A DECADE IN CHANGING TRENDS IN HIV PREVALENCE AND INCIDENCE IN PREGNANT WOMEN IN SOUTHERN MOZAMBIQUE

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Monitoring HIV rates at the antenatal care (ANC) clinic is needed for evaluating and targeting HIV preventive interventions in this vulnerable group. This study describes the prevalence and incidence trends of HIV over 10 years in pregnant women attending the ANC clinic in southern Mozambique. We analysed data from three studies carried out in HIV-infected pregnant women attending the ANC clinic between 2010 and 2021. HIV incidence was estimated between prevalence points using two validated methods. Method one was based on mortality rates and method two was based on survival information after HIV infection. The trend over time was obtained by fitting a log-regression model. Changes in the prevalence of anemia and rates of HIV vertical transmission during same period were also analyzed. Overall, 10392 pregnant women attending their first ANC visit were included in the analysis. There was a decrease of the HIV prevalence to 21.4% (95% CI: 19.6-23.2%) in 2021, after a peak of 35.3% (95% CI: 30.1-40.8%) in 2016. The peak of HIV tended to increase with age group from 2010 to 2021. The prevalence was the highest in women aged 20-25 in 2010 and then became the highest in those aged 35-40 in 2021. The overall incidence significantly increased from 3.7 per 100 person-years during 2010-2016 to 10.1 per 100 person-years in 2018-2019 but then subsequently decreased to 6.2 per 100 person-years in 2020-2021. In the last decade, HIV burden in pregnant women has declined in this area of southern Mozambique. However, HIV prevalence remains unacceptably high in this particularly vulnerable group, calling for a need to strengthen HIV preventive strategies to ending HIV/AIDs in the country.

6313

DRUG RESISTANCE MUTATIONS DETECTED IN HIV-1 PROTEASE GENES ISOLATED FROM HIV-1 INFECTED PERSONS FROM EASTERN REGION OF GHANA

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Human immunodeficiency virus (HIV) is an important public health concern with about 70% of the global burden in Africa. Since the introduction of antiretroviral therapy, a major problem is the emergence of drug resistance. HIV-1 protease (PR) is a retroviral aspartyl protease, an enzyme involved with peptide bond hydrolysis in retroviruses. Without effective HIV protease, HIV virions remain non-infectious. Protease inhibitors are mostly used as part of the 2nd line regimen following treatment failure. We therefore sought to determine the prevalence of drug resistance mutations in the HIV PR gene in the most endemic region in Ghana (Eastern Region) (2.8%) prevalence. We used purposive sampling to collect blood from 30 consented patients, confirmed as HIV-1 infections by serology. Twenty-one (21) of them were on triple combinations of five first line regimen (Zidovudine, Lamivudine, Nevirapine, Tenofovir, Efavirenz) and 9 were treatment naive. Ribonucleic acid was extracted using High Pure Viral RNA Kit from plasma, amplified via a nested RT-PCR assay and sequenced using gene-specific primers. The protease genes were analyzed for subtype and drug resistance mutations using the Stanford HIV Database. Five out of 30 samples were successfully amplified. The overall mean CD4 for the 30 samples collected was 473.4 and mean viral load was 31,226.17cps/ml. No trend was found between viral load and its implication on sequencing. Three (3) samples out of 5 were successfully sequenced. Two of these were recombinant subtype CRF02_AG and one was subtype G. HIV-1 unusual drug resistance mutations (N88K, K43T, I54N) were identified per patient. The mutations found had no PI drug resistance in the protease gene of the 3 sequenced samples. They did not carry resistant forms of HIV-1. Further investigations are needed on the unusual mutations at the known drug resistant positions. Continuous monitoring of drug resistance among HIV-1 infected patients is essential to improve their clinical management.

6314

CLOSING THE KNOWLEDGE GAP IN HUMAN IMMUNODEFICIENCY VIRUS PREVENTION AMONG ADOLESCENTS IN RURAL SETTINGS, BURKINA FASO

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In sub-Saharan Africa (SSA), HIV continues to pose a significant public health problem despite a 32% reduction in new infections in 2021. Adolescents in SSA account for nearly four out of five HIV infections. There is a lack of knowledge about HIV prevention methods and testing rates remain low among adolescents in Burkina Faso. This study assessed adolescents' knowledge of HIV prevention and testing as well as sexual risk behaviors in Nouna, Burkina Faso.We conducted a cross-sectional survey using a community-based sampling frame with 1,202 adolescents aged 10-19 years via a standardized questionnaire in the Nouna Health and Demographic Surveillance System in Burkina Faso from March to April 2022. We present descriptive results regarding adolescents' knowledge of and behavior related to HIV.The average age of the participants enrolled in the study was 14.1 (95% CI: 13.9-14.3) years old, 43.5% were female, and 59.4 % were students. About 41.9% had never heard of HIV. The

main sources of HIV information were schools (53.6%) and friends (26.7%). Among participants who have heard about HIV, only 4.3% have been tested. Additionally, 15.8% of participants had sexual intercourse in the past and 47.1% of them used condoms. The mean age at sexual intercourse was 16.0 years (95% CI: 15.8-16.2).In rural areas of Burkina Faso, adolescents are poorly informed about HIV and do not use HIV prevention measures. Adolescents need better access to HIV prevention information through innovative interventions. Adolescent reproductive health and HIV prevention awareness will contribute to reaching the 2030 target of ending the HIV/AIDS epidemic. Key words: Adolescents, HIV prevention

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KNOWLEDGE AND PERCEPTIONS OF PRIMARY HEALTHCARE PROVIDERS TOWARDS INTEGRATION OF ANTIRETROVIRAL THERAPY SERVICES AT DEPARTMENTAL LEVELS AT SELECTED HEALTH FACILITIES LIRA DISTRICT, UGANDA

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Investigations conducted among healthcare providers to assess their knowledge and perceptions towards the integration of anti-retroviral therapy related services in Sub-Saharan Africa are limited. This study explored the knowledge and perceptions of primary healthcare providers towards the integration of ART management services at departmental levels in health facilities in Lira district. We conducted a descriptive cross-sectional survey that employed qualitative methods of data collection in four selected health facilities in Lira district between January and February 2022. The study involved in-depth interviews with key informants and focus group discussions. The study population consisted exclusively of primary healthcare providers; however, those who were not full-time employees of the participating health facilities were excluded. We used thematic content analysis. A significant proportion of staff especially those who are not directly involved in ART still lack full knowledge of ART services integration. There was generally a positive perception, with some suggesting ART integration can minimize stigma and discrimination. The potential barriers to integration included limited knowledge and skills for providing comprehensive ART services, insufficient staffing and space, funding gaps, and inadequate drug supplies, coupled with increased workload due to enlarged clientele. Whereas healthcare workers are generally knowledgeable about ART integration, but their knowledge was limited to partial integration. The participants had a basic understanding of ART services being provided by different health facilities. Furthermore, participants viewed integration as critical, but it should be implemented in conjunction with ART management training. Given that respondents reported a lack of infrastructure, increased workload, and understaffing, additional investments in staff recruitment, motivation through training and incentives, and other means are needed if ART integration is to be implemented.

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PREGNANCY OUTCOMES IN WOMEN WITH INFECTIOUS AND CHRONIC COMORBIDITY IN WESTERN KENYA

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Antiretroviral therapy (ART) protects maternal health and prevents HIV transmission during pregnancy. However, there is evidence that ART started pre-pregnancy compared to during pregnancy increases the risk of other poor pregnancy outcomes. No studies have reported on the risk of poor pregnancy outcomes by timing of ART initiation, while accounting for comorbid infectious and chronic diseases. Here we present results from a large cohort of pregnant women in Western Kenya living without and with HIV (WLHA). Samples and data were collected to identify infectious and non-communicable diseases. Multivariable logistic regression was conducted to assess the effect of HIV on adverse maternal or infant outcomes. Sensitivity analysis further examined timing of ART initiation on poor outcomes. One in four of 1753 women experienced poor pregnancy outcomes. Anemia (57.7% vs 39.1%), malaria (15.2% vs. 11.7%) and COVID-19 (11.8% vs. 9.3%) in pregnancy were more common in WLHA, while obesity and hypertension were higher in women without HIV. By ART timing, malaria (19.0% vs. 12.1%) and hypertension (10.1% vs. 8.0%) were higher in women starting ART during pregnancy than before pregnancy, while obesity (24.1% vs. 30.3%) and diabetes (2.5% vs. 6.1%) were lower in those starting ART during pregnancy than before pregnancy. In multivariable logistic regression neither HIV nor ART timing had significant effect on maternal outcomes. However, women who started ART pre-pregnancy had increased risk of poor infant outcomes compared to women without HIV (aOR1.54 [95%CI 0.94-2.52], p=0.05). Our finding that WLHA on ART are at no significantly increased risk of poor maternal outcomes than HIV-uninfected women demonstrates the remarkable impact of PMTCT programming since the implementation of Option B+'s 'test-and-treat' approach nearly a decade ago. The benefits of ART to maternal health and the infant HIV-free survival are well-documented, and now that PMTCT coverage exceeds 90% in many high-burden settings, more research is needed on quantifying and mitigating other infectious and chronic disease effects on pregnancy outcomes.

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SOCIAL MOBILIZATION FOR ENHANCED MICROPLANNING IN DEWORMING PROGRAMS

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The goal was to design, operationalize and evaluate a Social Mobilization (SM) package specifically tailored to improve the quality of community-based treatment/ mass drug administration (MDA) for Soil Transmitted Helminthiasis (STH) and Schistosomiasis (SCH) as a pilot in Vihiga County. Tailoring SM messages and materials for the specific population groups at highest risk or with lower likelihood of participating in MDA and using the right channels of communication drives treatment coverage higher. This study was undertaken to (i) Assess the social contexts for community-based STH and SCH treatment; (ii) Identify potential population segments for tailored messaging; (iii) Development of a tailored social mobilization package in Vihiga county, Kenya; (iv) Produce user-friendly guides/standard operating procedure that other countries or implementing partners could readily adapt to their own contexts; and (v) To track progress and rigorously evaluate learnings. Conducting a formative and summative assessments using mixed methods; and developing and operationalizing a tailored social mobilization package. There was an increase in reach of the messages and materials from (29.9%, n=400) initially to (81%, n=402) during the summative assessment. Data indicated that the community had correct knowledge - transmission/spread of STH i.e., drinking / walking on water contaminated with faeces increased from 19.7% to 47.2% (by 28%) and ingestion of the worm's egg increased by 1% and on SCH, transmission/ spread of SCH i.e., penetration of the worm larvae through the skin and drinking or using contaminated water improved by 35.9% and 8.9%, respectively; the number of people treated in this county was STH (103%, 597,236) and SCH (94.91%28,858 94.91%). However, the community had limited knowledge about SCH. Findings from the pilot in Vihiga County informed scale-up of the SM process to include Bungoma, Kakamega and Trans Nzoia in the western region of the country.

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ENGAGING YOUNG PEOPLE AS AGENTS OF CHANGE: A PRIMARY SCHOOL EDUCATIONAL INTERVENTION TO DECREASE ARBOVIRAL AND PROTOZOAL RISK IN GRENADA

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School-based educational programs are effective in mitigating environmental health risks. In this ongoing randomized control study, we use a school-based educational intervention to improve knowledge, attitudes, and practices regarding arboviral and feco-orally transmitted protozoal diseases among 4th-grade students in Grenada. 27 case and 26 control schools were randomly assigned. Students completed pre- and post-intervention questionnaires at baseline and 3 months later. Case schools received a presentation, a video clip on mosquitos and demonstrations. School vector data was collected. Students at 10 case schools used the Our Voice Discovery Tool app to collect geotagged photographic and narrative data on aspects of their environment that make it easy or hard for mosquitoes to transmit diseases. Students have recorded 374 photos (135 good and 194 bad for environment) and 309 narrations. The intervention group reported significant improvements in arboviral and protozoal disease knowledge (53.3% increase), attitudes (15.1% increase), and practices (16.3% increase) at 3-month follow-up ($p<0.01$). In contrast, the control group only reported significant improvements in knowledge (20.9% increase, $p<0.01$), but not in attitudes (0.1% decrease, $p=0.96$) and behaviors (2.5% decrease, $p=0.28$). The intervention schools showed a more significant increase in knowledge (0.83 vs 0.36), attitudes (0.99 vs 0.02), and behaviors (0.55 vs -0.08) compared to the control schools ($p<0.01$). Among case schools, vector data show 26% and 100% reduction in total egg counts and total larvae counts, respectively, at follow-up ($p<0.01$). Among control schools, more indoor egg counts were recorded at follow-up, though they also showed a non-significant 11% reduction in total egg counts. Of 7 Parishes in Grenada, we found Aedes mosquitoes in all 7 regions and Culex in 6 but no Anopheles mosquitoes. 6-month follow-up will be completed by June 2023. Our intervention effectively improves knowledge, attitudes, and practices regarding arboviral and protozoal diseases among 4th-grade students in Grenada at follow-up and reduces vector abundance in schools.

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IMPROVING ACCESS TO MOBILITY MANAGEMENT AND DISABILITY PREVENTION MANAGEMENT OF LYMPHATIC FILARIASIS COMPLICATIONS TOWARDS THE WORLD HEALTH ORGANIZATION 2030 LYMPHATIC FILARIASIS ELIMINATION GOAL: A PILOT STUDY CONDUCTED IN LIBERIA 2022 TO CLOSE THE GAPS IN CASE MANAGEMENT NTDS CARE—LYMPHATIC FILARIASIS

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Lymphatic Filariasis (LF) has high prevalence rate in sub-Saharan Africa with two major complications requiring case management: hydrocele and Lymphedema. In Liberia, LF is prevalent in 13 of the 15 counties survey conducted in 2012. The only strategy for prevention and control of LF has been Mass Drug Administration (MDA) and an evaluation of the intervention (Pre-transmission Assessment Survey and Transmission Assessment Survey (PRE-TAS and TAS). The case management aspect remains a challenge in achieving the elimination target for Lymphatic Filariasis, the WHO Road Map (2030). However, to manage the complications of LF, the Case Management Project of Liberia's Neglected Tropical Diseases Program with Lymphedema care in Liberia, (2016) by providing comprehensive Home-Based Self Care (HBSC) Kits to affected persons with basic training in managing their conditions. Furthermore, in November 2022, the Case Management Project, initiated an integrated campaign to scale up the Mobility Management and Disability Prevention (MMDP) Campaign Project supported by Sightsavers International. The Mobility Management and Disability Prevention (MMDP) Campaign started in late November 2022 in five (5) counties (Bomi, Bong, Lofa, Nimba, and Maryland) with a target to perform 300 hydrocelectomies and distribute additional 260 HBSC Kits to both old and new lymphedema clients. The results against the target are as follows: Bomi (21), Bong (44), Lofa (39), Nimba (54) and Maryland (23). A total of 181 (60.33%) Hydrocelectomies were performed in 11 hospitals with an unmet target of 119 (39.7%) hydrocele cases due to several factors. With resource constraints, the Neglected Tropical Diseases Program remains committed to accelerating the MMDP Project to the remaining 8 counties in Liberia while providing routine care for lymphedema clients. This abstract seeks to explore opportunities to close the service gaps for those affected by LF complications to have adequate access to NTDs services without experiencing any financial consequences.

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THE EFFECT OF AN INNOVATIVE COMMUNITY HEALTH EDUCATION ON TRACHOMA PREVENTION AND CONTROL IN NORTHERN NIGERIA

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Trachoma is a leading cause of infectious blindness worldwide and an endemic public health problem in Northern Nigeria. The currently recommended surgery for trichiasis/entropion, antibiotics for active disease, facial cleanliness, and environmental change to reduce transmission (SAFE) strategy targets all key elements believed to be necessary for a short- and long-term intervention program. This study investigated the effect of innovative community health education on trachoma prevention and control in northern Nigeria. This was quasi-experimental study among Internally Displaced Person in Northern Nigeria. Two IDP camps were selected purposively and simple random sampling were used to select final participants for the study. We used a quantitative method approach was using a semi-structured questionnaire developed using SAFE strategy among 294 participants. The SPSS software version 27 was used for all statistical analyses which descriptive and inferential statistics were done at 5% significance level. The mean age of the participants was 33.1±8.8 years, some (45.9%) were male which 17.0% had no formal education. There was increase in the awareness of trachoma from 28.6% to 100.0% after the educational intervention. However, at baseline, few believed that trachoma is caused by curse while no one mentioned that after the educational intervention and they all knew ways trachoma could be transmitted. There was a significant increase in the knowledge level among participants from 20.1% to 73.5% good knowledge ($p<0.001$, CI=5.735 - 4.891, $t=24.795$) as well as positive attitude to trachoma prevention and control from 15.3% to 77.2% after the intervention ($p<0.001$, CI=14.914 - 13.065, $t=29.784$). Also, there was improvement in the prevention and control practices from 56.1% to 94.2% ($p<0.001$, CI=1.114 - 0.648, $t=7.437$). In conclusion, this study revealed that educational intervention can greatly influence knowledge on trachoma as well as the prevention and control attitude and practice.

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GEOSPATIAL RISK PREDICTION OF SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHS FOLLOWING A SCHOOL PREVENTIVE CHEMOTHERAPY PROGRAM IN HUAMBO, UIGE AND ZAIRE PROVINCES, ANGOLA

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A school preventive chemotherapy (PC) program for soil-transmitted helminths (STHs) and schistosomiasis has operated in Huambo, Uige and Zaire provinces, Angola, since 2013 and 2014, respectively, with an impact assessment conducted in 2021. Conventional methods to assess prevalence at province or district level to inform PC programs do not account for the environmental context of disease prevalence. This analysis provides geospatial risk predictions to provide a more detailed understanding of schistosomiasis and STH distribution to inform control strategies. A two-stage cluster survey design was used to select schools and schoolchildren to detect schistosomiasis and STHs in 2021 via rapid diagnostic tests (RDTs) and microscopy, respectively. School-level georeferenced parasitological data was incorporated with climatic, altitude, vegetation, landcover and distance to water bodies data to develop spatial regression models. Best fit multivariate generalised linear models were then used to develop risk prediction maps for schistosomiasis and STHs and ascertain areas of co-endemicity. Spatial regression models and risk prediction maps are being developed for the baseline survey to better assess the impact of the school PC program on the spatial distribution of these diseases. The impact assessment involved 17,880 schoolchildren from 599 schools for the schistosomiasis survey and 6,461 schoolchildren from 214 schools for the STH survey. Best fit regression models demonstrated considerable areas of moderate to high schistosomiasis risk (≥30% prevalence by RDTs) across all three provinces. For STHs, there remains substantial areas of high risk (≥50% prevalence by microscopy) in Uige province, with more focal areas of high risk in Huambo and Zaire provinces. There are considerable co-endemic areas in Zaire, but not Huambo or Uige. Despite regular school delivery of PC over several years, there remains considerable regions of Huambo, Uige and Zaire provinces that remain moderate to high risk for schistosomiasis and STHs, with focal areas of co-endemicity.

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ENHANCING TIMELINESS OF REPORTING FOR TRACHOMA MASS DRUG ADMINISTRATION THROUGH ELECTRONIC DATA CAPTURE: A PILOT STUDY IN TWO DISTRICTS OF UGANDA

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In 2023, The Uganda Ministry of Health supported by USAID's Act to End NTDs | East piloted an electronic data capture (EDC) mass drug administration (MDA) tally sheet in two trachoma persistent and recrudescent districts (Moroto, Nabilatuk). Previous, after-action review meetings had highlighted substantial delays (e.g. four months) in reporting the MDA data using a paper-based system that involved compiling, cleaning, and summarizing data. In this process one district lost their data when the computer they were using crashed. These delays and losses coupled with data quality issues that included arithmetic errors and wrong entries prompted development of an EDC tool using Open Data Kit (ODK). The EDC tool was rigorously tested and further improved for its accuracy to the original form, validation checks, and user friendliness. Data entry by the field supervisors started 10 days after the MDA field activities in January 2023. The central-level supervisors checked the inputs for accuracy and provided direct feedback to subcounty supervisors through their WhatsApp group and phone calls. The MDA results were produced one month after end of MDA activities. This approach improved MDA reporting turnaround time and 100% of the village level data was captured with no data loss. Furthermore, it was easy for the subcounty supervisors to easily identify errors from the hardcopy forms and fix them while in the field. Of note, this EDC approach did include additional cost including airtime, allowances, and training. These results illustrate the value of timely reporting of MDA data for decision making using EDC tools. This EDC approach also strengthened data ownership by subcounty supervisors who entered their own data, jointly reviewed, and provided feedback to the district-level biostatistician and central-level team. Finally, there was improved quality of data because of the data quality checks and validations embedded in the EDC forms. Expansion of this approach in all trachoma endemic districts would be valuable to the program for timely and accurate MDA data.

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FROM PRIORITY TO PRACTICE: MAKING APPLICATION OF DIGITAL PLATFORMS FOR IMPROVING TRACHOMA MDA PERFORMANCE A REALITY TOWARDS ADDRESSING END GAME CHALLENGES IN LONGIDO TANZANIA

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In the past 2 decades Tanzania has made a significant stride towards trachoma elimination. However, there are nine districts are considered persistent and recrudescent. Longido district is one of the persistent districts whose status is attributable to inadequate MDA coverage, mobile and migrant populations, thus required special strategies to address both challenges during MDA. Our objective is to present a case study on application of digital platforms to address MDA and other end game challenges in Longido, Tanzania, as a template for nationwide. We examine electronic data capture (EDC) and digitalized Supervisor Coverage (SCT) tool development, from inception, team selection, training and pilot testing to tool revision and improvement. The Unstructured Supplementary Service Data (USSD) was developed, and special code was enabled to community drug distributors (CDDs mobile phone for reporting daily MDA coverage summary. This summary was sent to a central server where national supervisors could review data daily on a dashboard. The platform was set to provide an automated text messages back to the village leaders and ward level supervisors with the daily MDA summary. To facilitate the SCT, an ODK collect application was installed in the smart phone for the district and ward level supervisor. GPS codes were captured to ascertain distribution of both CDDs and supervisors across the districts. We found that transitioning from paper-based monitoring tools to electronic motoring was feasible and effective. Daily feedback to village leaders prompted ownership and immediate action to troubleshoot poor coverage. CDDs and supervisors found the tools easy and simplified reporting and tracking. Few challenges, including some errors in the CDD reporting server spotty cellular network were noted for future improvement. Upon MDA assessment, reported coverage increased from 87% in 2019 to 97.5% in 2022.The results suggest that digital platforms to address the trachoma endgame challenges can support improved monitoring and evaluation of MDA and other SAFE relate interventions in line with the WHO target to eliminate trachoma by 2030

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THE IMPACT OF TEN ROUNDS OF TWICE-PER-YEAR TREATMENT WITH IVERMECTIN ON ONCHOCERCIASIS TRANSMISSION IN HYPERENDEMIC AREAS OF JIMMA AND ILLUBABOR ZONES, SOUTHWEST ETHIOPIA

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Onchocerciasis is a disease caused by Onchocerca volvulus and transmitted by the bite of Simulium vectors. Control efforts began in Ethiopia in 2001 with annual mass drug administration (MDA) with ivermectin. MDA must be given for 10+ years to control disease transmission. The program shifted toward elimination of transmission in 2012, commencing semi-annual treatment and targeting MDA to all endemic districts. This decision followed refinement mapping studies done in 2011 that uncovered untreated hyperendemic areas with nodule prevalence >40%. We undertook baseline surveys to document the prevalence of skin microfilaria (mf) in first-line villages in 7 districts in Oromia region. After at least 10 rounds of semi-annual MDA with >80% reported coverage, impact assessments were conducted in these districts in 2016 and 2017. A convenience sample was used for skin snip testing in ≥50 adults per community aged ≥20 years who had lived in the area for ≥10 years. Dried blood spots (DBS) were also taken at this time from 300 children per district aged <10 years. All consented/assented individuals underwent skin snip examination and DBS collection for Ov16 antibody analysis using ELISA following standard methods. In Jimma, 4 districts (Goma, Sokoru, Sigmo, and Setema) showed decreases in mf prevalence. Mf prevalence in Goma declined from 45.2% at baseline (2012) to 5.3% in 2017 (p=0.0), Sokoru dropped from 2.4% to 0% (p=0.08), Sigmo from 6.3% to 1.3% (p=0.02), and Setema from 10.6% to 4.7% (p<0.05). Ov16 antibody prevalence ranged from 0% to 1.6% at the time of follow-up. Three districts were evaluated in Illubabor. Sale Nono had mf prevalence of 54.5% in 2012, with significant reduction to 4.9% at impact assessment in 2016 (p=0.0). Bure and Hallu likewise showed significant decreases in mf prevalence, 28.5% to 1.9% (p=0.0), and 34.9% to 0.5% (p=0.0), respectively in 2016. Ov16 antibody prevalence at the second timepoint ranged from 0.3% to 4%. Twice-per-year treatment with high coverage showed encouraging progress towards the elimination of onchocerciasis transmission in hyperendemic districts.

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ELIMINATING ONCHOCERCIASIS IN LOIASIS ENDEMIC AREAS: ADDED VALUE OF THE SLASH AND CLEAR STRATEGIES

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In areas where onchocerciasis and loiasis are co-endemic, the routine control strategy, community-directed treatment with ivermectin (CDTI) is prohibited as it can lead in potentially deadly serious adverse events (SAEs) in patients heavily infected with Loa loa. It appears compulsory to identify SAEs risk-free alternative or complementary interventions to guarantee complete elimination of onchocerciasis. For this purpose, we carried out our study to assess the efficacy of an environment-friendly vector control approach, so-called the Slash and Clear (S&C). Monthly (3 days per month) capture of blackflies carried out using human landing catching over a period of 12 months along the Kelle River for baseline data collection. The trailing vegetation constituting blackfly breeding sites were destroyed by trained community volunteers (Slash and Clear) every month of the second year (4-5 days/month), and the impact of this breeding site destruction on blackfly densities was assessed by harvesting flies following the same procedure as during the baseline entomological survey. A total of 11,142 flies were collected during the two years, 9,720 before S&C and 1,422 after S&C, for an overall reduction rate of 100% in the head. The average larval reduction rate was 74.5%. These results confirm the significant impact of Slash and Clear on the reduction of blackfly densities, and might help accelerating the elimination of onchocerciasis in areas where loiasis in endemic.

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STRENGTHENING OF THE LOCAL HEALTH CAPACITY FOR THE IMPLEMENTATION OF THE FRAMEWORK FOR ELIMINATION OF MOTHER-TO- CHILD TRANSMISSION OF HIV, SYPHILIS, CHAGAS DISEASE AND HEPATITIS B IN PAMPA DEL INDIO, CHACO, ARGENTINA

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Pampa del Indio is a small locality in the province of Chaco, Argentina, located in the Gran Chaco ecoregion, traditionally a hotspot for Chagas Disease (ChD) due to vector transmission. Continuous vector control and environmental/land changes have reduced this transmission route in the area and vertical transmission of ChD is gaining importance. Given the presence of Mundo Sano in this municipality since 2008, working on vector control in a public-private association with local authorities, activities have evolved to a focus on diagnosis and treatment of ChD and implementation of the Elimination of Mother-To- Child Transmission (EMTCT) Plus initiative recommended by the World Health Organization (WHO) to eliminate mother-to-child transmission (MTCT) of ChD together with HIV, syphilis, and Hepatitis B. The activities are centered on achieving and sustaining the EMTCT of the four infections and to promote comprehensive access for pregnant women to high-quality control of their pregnancy and post-partum, specially focused on ensuring access to health to pregnant women living in rural communities. This is possible due to bi-monthly visits by a local mobile specialized team that perform the controls using rapid tests and a mobile ultrasound (US). Since its implementation in April 2022 and up to December 2022, five visits were performed in the urban area and rural settlements of Pampa del Indio with a 92.0% coverage of pregnant women (450 out of 489 estimated annual pregnancies for the area). All 450 women were screened for the four infections, and they all had access to US controls with an average of 2.3 comprehensive controls per woman. Hepatitis B and HIV infections were not detected while the prevalence of ChD and syphilis was 4.2% (n = 19) and 2.4% (n = 11), respectively. The use of rapid tests assured immediate application of treatment protocols and the planning of epidemiological actions to test other family members.

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MONITORING TRACHOMA MASS ADMINISTRATION USING AN ELECTRONIC SUPERVISOR COVERAGE TOOL

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An electronic Supervisor Coverage Tool (SCT) was developed and deployed in trachoma endemic districts in Uganda during the mass drug administration (MDA) implemented in August 2022 (round one) and January 2023 (round two) with the aim of improving MDA coverage. The surveys were carried out in Moroto and Nabilatuk. The main aim of the SCT was to measure MDA coverage and take immediate corrective action related to low MDA coverage. The SCT uses lot quality assurance sampling to classify communities coverage. The levels of coverage for trachoma are good coverage (80% and above), cannot conclude that coverage is good (55% to less than 80%) and inadequate coverage (less than 55%). Communities (supervisory areas) with previously low MDA coverage were purposively sampled, 20 households randomly selected, and one respondent per household randomly selected to be surveyed. In each district, 21 communities were visited in round one while 89 were visited in round two. Data was collected with android phones using Open Data Kit. Central, district, and subcounty supervisors administered the SCT. Data was analyzed using real-time data monitoring within the data collection form followed by post survey analysis in Stata. The number of communities with good coverage increased from 17 (81%) in 2022 to 80 (90%) in 2023, while 2(9.5%) and 7(8%) had inadequate coverage, and 2 (9.5%) and 2 (2.2%) had bad coverage, respectively. In 2023, 98% of surveyed individuals had been offered medicines while in 2022 it was only 87%. The main reasons for not being offered medicines in both 2022 and 2023 were similar: not present at home, distributor not come to home, busy/occupied, and unaware of MDA. The main immediate action taken was mop-up by distributors targeting missed individuals. SCT results can be used to make changes or enhancements to MDA while in the field, identify low performing communities, proportion reached and those that swallowed the medicines. Additionally, use of electronic data collection allows for central display of real time results for all communities surveyed, timely follow-up with supervisors at different levels and immediate action taken as needed.

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THE ROLE OF MICROBIOTA AND CO-LOCALIZATION IN THE DISSEMINATION OF VECTOR TRANSMITTED PATHOGENS

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Insect vectors are important agents in the transmission of infectious diseases. Through a processcalled dissemination, many pathogens can enter the body of a host through the bite of an insectvector and then exit the skin to cause a systemic infection. The details about how and whendissemination occurs are still unclear and elucidating this is important for understanding diseasepathogenesis and the development of new therapies and vaccines. Leishmaniasis is a vector-bornedisease, and in its visceral form, Leishmania spp. parasites can disseminate from the skin to internalorgans. Various factors from the host, vector and parasite have been implicated in thedissemination process, including the microbiota derived from the from the insect vector gut.However, while vector microbiota is required for dissemination, it is not sufficient. The goal ofthis study is to determine whether the micro-colocalization of parasites, vector- and host-derivedfactors, including the microbiota that occurs following sand fly bite versus bolus injection is arequirement to induce the physiological conditions that facilitate dissemination. The resultsobtained will contribute to a better understanding of the pathophysiology of leishmaniasis. Wehypothesize that bacteria, co-localized with other host and vector factors, influence the physiologyof the skin and facilitate the dissemination of Leishmania spp. To evaluate this, we will first studydissemination in wild type mice and mice deficient in several innate TLR-related signallingpathways employing a novel model of Leishmania spp. infection, the skin prick, that co-localizedthese factors in the skin. We will then determine the requirement of bacteria and co-localization,using skin-prick, bolus, and sand fly models of infection in Germ-Free (GF) mice allied with thetechniques of flow cytometry and Live Cell Imaging.

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INFECTION OF MONOCYTES WITH LEISHMANIA INFANTUM CAUSES DIFFERENCES IN EXTRACELLULAR VESICLE MIRNA PROFILES

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Leishmania infantum is an obligate intracellular protozoan that is spread through the bite of a sand fly and causes visceral leishmaniasis. Both the parasite and infected macrophages release extracellular vesicles (EVs), including exosomes. EVs contain proteins, lipids, mRNAs, and microRNAs that can spread widely and have biological activities throughout a host. Our lab has previously shown that the protein content of EVs from MDMs infected with L. infantum differs from uninfected MDMs. We wanted to question whether the miRNA content of EVs would differ between uninfected and infected MDMs. miRNA are potent regulators of post-translational gene expression. Blood from 3 healthy human donors were obtained from the University of Iowa blood bank. Monocytes were infected with L. infantum, and after 48 hrs EVs enriched in exosomes were purified from extracellular medium and analyzed on the nanosight to investigate concentration and size. Small RNAs were extracted from EVs, and the abundance of known or putative human miRNAs was screened using a NanoString human miRNA panel. There was a trending increase in the overall production of Evs from infected MDMs compared to uninfected control but no difference in mean or mode size. hsa-miR-29a-3p and hsa-miR-575 were significantly upregulated in EVs of infected MDMs and hsa-miR-1305 and hsa-miR-1285 were downregulated compared to EVs of uninfected MDMs. Known functions of these miRNAs include the upregulation of genes contributing to the M2 phenotype and possible suppression of proinflammatory response. Infection with L. infantum shows a trending increase of exosomes released from human MDMs as well as a change in miRNA content. Evs from infected cells show an increase in miRNAs that might influence M2-type polarization and target proinflammatory genes. These data suggest that Ev miRNAs of MDMs infected with L. infantum might alter the surrounding environment to potentially dampen local inflammatory or curative immune responses.

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PEOPLE WITH DIFFERENT CLINICAL PRESENTATIONS OF LEISHMANIA DONOVANI INFECTION HAVE DIFFERENT MICRO-RNA PROFILES IN CIRCULATING PLASMA

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Visceral leishmaniasis (VL) is a tropical neglected disease caused by Leishmania donovani, results in significant mortality in the Indian subcontinent. Several microRNAs have been associated with either susceptibility or resistance to leishmaniasis, including miR-210 (Leishmania major), miR-122 and miR-146a (L. donovani), and miR-21 in (L. infantum). miRNAs are ~22 nt non-coding RNAs that can regulate many biological

and molecular functions at the post transcriptional level. Mainly they function by base pairing in the 3' or 5' UTR of target mRNAs and interfering with targeting the mRNA for degradation or modifying translation. Some miRNAs modify immune responses but the precise target of miRNAs implicated in leishmaniasis are unknown. There is a paucity of prior studies of miRNAs in primary human samples from subjects with VL. Most circulating miRNAs are packaged into micro vesicles called exosomes, which can circulate free of cells in the blood. Hence, we investigated the roles of miRNAs in circulating exosomes of patients from Bihar, India with different manifestations of L. donovani infection. We selected 6 candidate miRNAs to screen in human plasma: miR-21, miR-122, miR-155, miR-206, miR-146-a and miR-let-7c. Plasma from subjects with VL or post-kala azar dermal leishmaniasis (PKDL) were compared to healthy, endemic controls. We isolated plasma exosomes and confirmed isolation by transmission electron microscopy imaging and Nano particle tracking analysis. Small RNAs were extracted and differential expression of candidate miRNAs were evaluated by TaqMan miRNA assays. When compared to endemic control subjects, expression of miR-146a was increased plasma of both VL and PKDL patients compared to controls ($p<0.05$), whereas miR-206 was decreased in VL plasma compared to control samples. This is consistent with data from murine models and human monocyte derived macrophages indicating miR-146a skews infected macrophages from M1 to M2 phenotypes. miR-206 is reported to target FOXP-1 expression and influence macrophage function. We hypothesize these miRNAs may be critical determinants of immune response to L. donovani infection.

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PREVALENCE OF CUTANEOUS LEISHMANIASIS IN ENDEMIC COMMUNITIES OF THE VOLTA REGION, GHANA

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Leishmaniasis continues to affect countries in the tropics and subtropics with previously non-endemic areas experiencing infections. In Ghana, an outbreak of suspected cases occurred in 1999 which led to the discovery of cutaneous leishmaniasis (CL) after Leishmania major was identified. Since then, various studies have been conducted in endemic communities that have revealed multiple Leishmania parasites. This has raised much public health concern, especially regarding effective control and treatment strategies. The study reports the baseline prevalence of CL infection in three communities in the Ho district of the Volta Region of Ghana. A total of 535 subjects were screened using Leishmanin Skin Test (LST) for detecting Leishmania exposure and finger prick blood for anti-leishmania IgG antibody levels. There was no significant difference ($p=0.9313$) in LST positivity (LST+) in all three communities. However, the highest LST positives were recorded by the age group 41-65 (62.8%) whiles the lowest (25%) was from the age group 6-18. It was also observed that the median levels of IgG units between both males and females were significant ($p=0.0002$). LST positivity correlated to higher levels of antibodies, suggesting their potential as a risk marker for CL acquisition in Ghana.Current reports from the Health Services of Volta region suggest ongoing infections in communities, thus control efforts need to be implemented to reduce the disease burden.

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EXPRESSION OF ENDOPLASMIC RETICULUM STRESS RESPONSE MARKERS IN CUTANEOUS LEISHMANIASIS

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Cutaneous leishmaniasis (CL) is an intracellular parasitic infection that can cause loss of endoplasmic reticulum (ER) homeostasis by disrupting the protein folding process. This leads to the accumulation of unfolded proteins in the ER lumen and stimulates ER stress response to restore protein homeostasis in the ER. The present study aimed to immunohistochemically validate the endoplasmic reticulum stress response in CL by determining the expression of the Inositol Requiring Enzyme1 (IRE1), Protein Kinase RNA like ER kinase (PERK) and Activating Transcription Factor6 (ATF6) sensory proteins in lesion tissues. Sections (4 µm) of formalin-fixed paraffin-embedded tissue samples from thirty leishmaniasis-confirmed patients and thirty control participants were mounted on positively charged slides. The tissue sections were deparaffinization in xylene and rehydrated with graded alcohol. Antigen retrieval was conducted by microwave-boiling of the slides in 10mM Sodium citrate buffer (pH 6.0) for IRE1 and ATF6, and EDTA buffer (pH 9.0) for PERK. Endogenous peroxidase was blocked by incubating in 3% hydrogen peroxide for 10 minutes followed by washing in deionized water. The tissue sections were incubated overnight at 4°C with rabbit polyclonal antibodies against IRE1 (ab37073), PERK (ab79483), and ATF6 (ab203119). The antigen-antibody complex was detected with the labeled streptavidin-biotin (LSAB) method. Visualization was done by reacting with 3,3′-Diaminobenzidine (DAB) and counterstained with hematoxylin. Staining was observed by a histopathologist, and data were analyzed using SPSS (version 25.0). Staining was observed in the patient samples in contrast to the control samples which showed minimal staining. A significant difference ($p<0.05$) was observed between gender and expression of IRE1, PERK, and ATF6 markers and the histological grading of CL tissue and ER stress marker expression. In conclusion, this study demonstrates a significant difference in the expression of ER stress markers with regard to gender and histological grading of infected tissue.

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IMPACT OF DECLINING DISEASE TRANSMISSION ON MAINTENANCE OF IMMUNOLOGICAL MEMORY IN SUBJECTS WITH PAST HISTORY OF VISCERAL LEISHMANIASIS

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Visceral leishmaniasis (VL) is a visceralizing form of leishmaniasis caused by L. donovani and its cure is associated with IFNγ dominant Th1 immune response. Infection induced immunological memory and its maintenance is crucial for resistance to re-infection. A loss of recurrent antigenic exposer in areas with no transmission may lead to loss of memory T cells responsible for this resistance and may increase the possibility of disease re-emergence. Although India is marching towards achieving the goal of elimination and current transmission may be very low to absent, the risk of VL re-emergence and future outbreaks cannot be neglected. The present study aims to identify soluble leishmanial antigen (SLA) specific cytokine responses and reactive T central memory (Tcm) and effector memory (Tem) cells profile with effector and proliferative potential in subjects with past history of VL from area of no transmission (NT; areas with no reported cases in last five years), continuous transmission (CT; areas with continuous

reported cases) and outbreak (OB; areas with reappearance of cases after a brief period of absence). Th1, Th2 and Th17 cytokines production was determined in supernatants of SLA stimulated whole blood using cytometric bead array (CBA). Also, peripheral blood mononuclear cell (PBMC) treated with SLA was assessed for the frequency of Tcm and Tem cells expressing activation and proliferation markers using flowcytometry. A significant increase in pro-inflammatory cytokines like IFNγ, IL-6 and IL-2 along with anti-inflammatory IL-10 was observed in the SLA stimulated whole blood of NT and OB groups. In addition to this increased activation of Tcm and Tem cells of both CD4+ and CD8+ types were observed in response to the antigenic stimulation. Only CD4+ Tcm of OB group exhibited proliferative potential. Overall, our current findings are suggestive of a mixed cytokine profile in OB and NT groups which indicates the persistence of possible immune regulatory mechanisms, similar to the active disease and the proliferative response of CD4+ Tcm may be an implication of recent antigenic exposer due to ongoing transmission in OB group.

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MULTIMODAL THERAPEUTIC TREATMENT FOR CHRONIC CHAGAS DISEASE

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Chagas disease is a neglected tropical disease that is caused by the parasite Trypanosoma cruzi, which is spread by a triatomine bug, also known as the “kissing” bug. The acute stage of this infection can result in flu-like symptoms and can be treated by killing the parasite with anti-parasitic treatments. Treatments such as Benznidazole and Nifurtimox are effective in the acute stage, though they may cause severe side effects. However, most infected patients will not present signs and symptoms until they have reached the chronic stage, which often leads to cardiomyopathy and enlargement of other internal organs. Unfortunately, antiparasitics have poor efficacy during chronic disease. Studies have shown that an appropriate immune response to the parasite, with a balanced TH1/TH2/TH17 cytokine response, correlates with better cardiac health.Our overall goal is to develop a multimodal therapeutic treatment strategy to improve treatment efficacy. Here we tested combination treatments using the small-molecule STAT3 inhibitor, TTI-101, as well as a recombinant protein vaccine containing the Tc24-C4 antigen and different doses of benznidazole. We infected female BALB/c mice with 5000 blood form bioluminescent H1 strain trypomastigotes and started treating these mice 70 days post infection (dpi). Vaccinations were given subcutaneously twice, three weeks apart. Benznidazole (100mg/kg and 25mg/kg) and TTI-101 (50 mg/kg) were administered orally once daily for 20 days. Mice were given one, two or three treatments sequentially. Mice were euthanized at 234 dpi, then blood and tissues were collected to evaluate cytokine responses. Our results show that combining our Tc24-C4 vaccine with a low dose of benznidazole and TTI-101 induced an antigen specific TH1/TH2/TH17 cytokine response with increased levels of IFNγ, IL-6, IL-2, IL-4, IL-10, IL-22 and IL-17A. This suggests that multimodal treatment induces a balanced cytokine response that could lead to reduced tissue pathology and improved cardiac health.

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INTESTINAL MICROBIOTA MEDIATE PROTECTION AGAINST GIARDIA INFECTION INDEPENDENT OF HOST ADAPTIVE IMMUNITY

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Giardia lamblia (Giardia) is a nearly universal gut pathogen in undernourished children. In these children, Giardia frequently persists for long durations, however, the specific mechanisms underlying this susceptibility to persistent infections are poorly understood. Experimental murine models indicate that intestinal microbiota may contribute to Giardia clearance. Whether microbiota protect against Giardia colonization by enhancing host immunity and/or by non-immune mediated pathways is unknown. Using gnotobiotic techniques, we challenged germ-free (GF) wild-type (WT) or immunodeficient (Rag2-/-) mice with axenic Giardia cysts either alone or together with a standardized murine cecal intestinal microbiota transfer (cIMT). In all GF mice, small intestinal Giardia colonization persisted at high burdens (≥ 106/4 cm) and for at least 21 days after challenge, regardless of diet. In contrast, all mice conventionalized with IMT were protected against Giardia colonization. Immune responses to Giardia extracts in splenocyte recall assays were similar between cIMT-conventionalized and mono-associated WT mice. In addition, the standardized cIMT was equally protective against Giardia colonization in Rag2-/- mice, despite absence of T/B cells in these immunodeficient hosts. In contrast, a fecal IMT (fIMT) from a different mouse colony permitted high-burden and persistent colonization. 16S rDNA amplicon profiles demonstrated differences in Clostridium spp. among other sequence variants differentiating cIMT-conventionalized Rag2-/- mice that were protected against Giardia colonization and fIMT-conventionalized Rag2-/- mice that were not. Our models indicate a crucial role for intestinal microbiota-mediated protection against Giardia colonization that occur through pathways independent from host-dependent adaptive immunity. These findings warrant further studies to determine how specific intestinal bacteria may alter susceptibility to Giardia infection, and whether similar interactions occur in undernourished children who also demonstrate impaired immunity and disruptions in intestinal microbiota.

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COMPARISON OF DERMAL AND SYSTEMIC IMMUNE RESPONSES IN PROGRESSIVE STAGES OF CANINE LEISHMANIOSIS

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Canine leishmaniosis (CanL), caused by the zoonotic obligate intracellular protozoan parasite Leishmania infantum, is a significant public health concern for humans and domestic dogs, the primary reservoir. In endemic areas, vector transmission by sandflies predominates, while vertical transmission has been found as an alternate important means of transmission. Leishmania spp. has significant dermal tropism. However, in xenodiagnoses studies, the most severe CanL cases had less transmission to naïve sandflies than mild to moderate CanL cases, despite dermal parasite burden increasing as disease progressed. These results indicate that additional host-parasite factors influence transmissibility. The interplay between parasites and systemic host immune cells linked disease progression to immune exhaustion and a shift in the systemic immune response from pro-inflammatory to regulatory. Due to continuous environmental antigen exposure, the cutaneous immune environment is more immunotolerant, potentially influencing its responses during CanL progression and altering transmission. Cutaneous immune cells/parasite interactions, which affect transmissibility to competent vectors, have not been evaluated. RNAscope, a sensitive immunofluorescence technique, was used to assess how the cutaneous immune environment correlates

with parasite presence and burden across clinical stages, determined by the LeishVet staging guidelines. An amastin probe identified amastigotes, and dermal macrophages were marked with a CD14 probe. Parasite and macrophage counts, along with spatial relationships between amastigotes, dermal macrophages, and cutaneous structures were evaluated and correlated with H&E-stained slides. Future work will investigate lymphocyte responses in the dermal immune environment and integrate spatial transcriptomics data to further characterize the cutaneous immune environment across CanL clinical stages. This is essential for understanding the host-parasite interactions that influence transmission of Leishmania from canines to sandflies.

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EVALUATION OF BLT2 RECEPTO IMMUNOREACTIVITY IN CARDIAC TISSUE FROM RATS INFECTED WITH TRYPANOSOMA CRUZI AT DIFFERENT POST-INFECTION STAGES

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Chagas disease is a public health problem caused by Trypanosoma cruzi. In the chronic stage of the disease, the leukotriene receptor type 2 (BLT2) pathway is linked to inflammatory mechanisms. BLT2 increases the mobilization of Ca2+, leading to a greater production of nitric oxide (NO). The released NO could interact with superoxide to form peroxynitrite, followed by nitration and dysfunction of cardiac cells with important pathological consequences, thus an exacerbated proinflammatory environment at the myocardial level could be involved in an increase in fibrosis at the cardiac level. In the present study, the immunoreactivity of the BLT2 receptor and its relationship with fibrosis were evaluated in a Chagas model using Holtzman rats infected with 2x104 trypomastigotes of Y strain, via the intraperitoneal route, thus having 7 groups, each group with 6 rats and the control groups. (uninfected rats). Sacrifices were made at 7, 15, 30, 3, 90, 6, 270, and 365 days post infection (DPI). Evaluation used immunohistochemistry, Masson's trichrome staining, and hematoxylin and eosin. Amastigotes were observed in cardiac tissue at 7 and 15 DPI. However, at 7 DPI it is possible to observe few mononuclear cells and an increase of these at 15 DPI. No nests of amastigotes were observed after 30 DPI; however, inflammatory foci were observed at the tissue level. Likewise, from 90 DPI, a slight increase in significant interstitial fibrosis/scarring is observed without mononuclear cells; on the other hand, it was found that the immunoreactivity of the leukotriene B4 type 2 receptor is higher in the acute phase and decreases after three months. To corroborate this, the analysis of BLT2 immunoreactivity was performed in infected rats and compared with controls, finding that this receptor is more expressed at 7 ($p<0.001$), 15 ($p<0.01$) and 30 DPI ($p<0.01$). Therefore, it is concluded that in the acute phase of the disease there is a correlation between inflammation and expression of the BLT2 receptor ($p<0.05$). This could be because LTB4 is a chemotactic eicosanoid. However, no relationship was found between increased fibrosis and expression of this receptor ($p>0.05$).

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PEPTIDE SELECTION VIA PHAGE DISPLAY TO INHIBIT LEISHMANIA-MACROPHAGE INTERACTIONS

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Leishmaniasis represents a complex of diseases caused by protozoan parasites from the Leishmania genus that causes life-threatening manifestations depending on the species responsible for the infection. Given the high toxicity and cost of the current therapies, leishmaniasis is a public health problem. New interventions to hinder the interaction of the parasite with phagocytic cells are urgently needed to accelerate the development of new treatments or vaccines. Here, we used a phage display library to identify peptides targeting interaction of metacyclic promastigotes of L. amazonensis (causative agent for cutaneous leishmaniasis) and L. infantum (causative agent for cutaneous and visceral leishmaniasis) with phagocytic host cells. We identified one L. amazonensis binding peptide (La1), and two L. infantum binding peptides (Li1 and Li2). Importantly, peptide binding to the parasite surface impairs parasite internalization into THP-1 macrophages. The La1 peptide inhibits L. amazonensis only. However, Li1 and Li2 inhibit both L. amazonensis and L. infantum. Li1 and Li2 show promise for multi-species vaccine development, while La1 is an alternative option for species-specific vaccine development.

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IN VITRO INTERACTION OF MACROPHAGE U937 WITH LEISHMANIA (VIANNIA) ISOLATES INFECTED WITH LEISHMANIA VIRUS IN PANAMA, CENTRAL AMERICA

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The presence of the RNA virus (LRV) in parasites of the genus Leishmania and its association with increased pathology and treatment failure in individuals with skin infections have been described. Categorized as LRV-2 in the Old World and LRV-1 in the New World, this virus was detected in Leishmania isolates in American countries such as Brazil, French Guyana, Colombia, Peru, Ecuador, and Costa Rica. However, in Panama it is unknown whether the presence of LRV in the Leishmania parasite influences the pathology and therapeutic response of cutaneous leishmaniasis (CL). It is hypothesized that LRV-1+ isolates are more infective, and therefore cause more severe pathologies. In this regard, in this study the in vitro behavior of LRV-1 positive and negative Leishmania isolates were studied, evaluating the differences in infectivity in U937 human macrophages at 24, 48 and 72 hours post infection. Ten fields were counted for each slide, obtaining a total of 100 cells per slide. This was done in triplicate for each isolate for the different infection times. To calculate the infection index, the percentage of infected macrophages was multiplied by the ratio of amastigotes/macrophages. Fourteen isolates were used, 7 LRV+ and 7 LRV-, including species of L. (Viannia) guyanensis, L. (V.) panamensis and L. Viannia sp. from the ICGES biobank. Additionally, 3 reference strains of L. (V.) guyanensisLRV+, L. (V.) panamensis LRV- and L. (V.) braziliensis LRV- were evaluated as controls. The presence of LRV was detected by the RT-PCR methodology with the primers LVR ORF-1/2 (850bp) and LVR-1F/1R (240bp) and confirmed by Sanger sequencing as LRV-1. Comparison analysis of infection index showed increased infectivity of Leishmania ViannaLRV+ compared to LRV- isolates. These results showed that Leishmania Viannia LRV+ isolates may be more infective than

LRV- for U937 human macrophages. Future studies are recommended to evaluate the anti and pro-inflammatory cytokine profile induced during in vitro infections with Leishmania LRV+ isolates.

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DETECTION OF LEISHMANIAVIRUS IN ISOLATES OF LEISHMANIA VIANNIA IN PANAMA, CENTRAL AMERICA

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Leishmaniasis is a vector disease caused by protozoa of the genus Leishmania that affect humans producing a wide spectrum of clinical forms. Recently, the association of some Leishmania species with the presence of an endosymbiont double-stranded ribonucleic acid virus from the Totiviridae family called leishmaniavirus (LRV) have been described, showing increased pathology and treatment failures in individuals with cutaneous and mucocutaneous forms of the disease. Two types of LRV have been describes, type 1 circulates in the Americas while type 2 in the Old World. In America, the presence of LRV has been reported in Leishmania isolates from French Guiana, Brazil, Peru, Colombia, Ecuador, and Costa Rica. In a recent pilot study in Panama, 10 L. (V.) panamensis LRV-1+ isolates were detected by RT-PCR. In Panama, it is unknown if there are other species of Leishmania Viannia (L. (V.) guyanensis and L. (V.) braziliensis) associated with the presence of LRV-1. Therefore, the aim of this study was to detect LRV-1 in 100 Leishmania Viannia isolates from different leishmaniasis-endemic areas in Panama cryopreserved at ICGES biobank. Samples were collected between 2015 and 2022. Two molecular methodologies were used based on a RT-PCR that amplify the RNA of the ORF1 and ORF2 regions of the viral capsid. The results show that, it was possible to detect seven L. Viannia LRV+ (7/100: 7%), characterized as LRV-1 by Sanger sequencing analysis. With the LRV ORF-1/2 primers (850bp), one isolate of L. (V.) guyanensis LRV+ was found, and seven with the LVR-1F/1R primers (240bp), including species of L. (V.) guyanensis, L. (V.) panamensis and L. Viannia sp. These results demonstrate the circulation of LRV-1 in leishmaniasis endemic areas of Panama, and in different Leishmania (Viannia) species.

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CELL-BASED CARDIOMYOPATHY MODELS FOR CHAGAS DISEASE BIOMARKER DISCOVERY

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Chagas heart disease (CHD), the malignant cardiomyopathy triggered by Trypanosoma cruzi infection, is among the most prevalent neglected tropical diseases. Lacking relevant in vitro models, biomarker development for CHD prognostication and precision care has lagged.Methods; Murine and human cardiomyocytes were infected with trypanosomes to model CHD in vitro (CHD-CMs). Trypanosomes from variable genetic strains were assessed of cytopathogenicity (RTCA eSight). Motion vectors (SI8000 Imaging System) and calcium handling (FDSS/µCELL) analyses characterized CHD-CM excitation/contraction features. Transcriptomic analysis, in bulk and in single-cell resolution, and secretory phenotyping of CHD-CMs were applied for elucidating the host response signatures and its pseudotime trajectories.Results; 'Tc I/II' genetic strain Trypanosomes evoked evident cytopathogenic effects in vitro ($p < 0.05$). CHD-CMs recapitulated the excitation/contraction abnormalities in CHD and the extent of phenotypic deterioration was associated with tissue tropism per trypanosome genotype. Trypanosome infection led to differential expression of chemokine/cytokine activation-, heart beta-oxidation-, and oxidative stress-related genes. Along with known CCL/CXCL (MCP-1 and IP-10), an emerging signaling peptide GDF-15, was identified to be upregulated upon infection ($p < 0.001$). Co-culture experiments of CHD-CMs with other cardiac cell types (e.g. fibroblasts etc) indicated humoral factor-specific pathogenic roles in intra-cardiac cellular communication.Conclusions; Cardiomyocytes act as the upstream sentinels of pathogen encounter. Signatures of the CHD-CM response against trypanosome invasion constitute candidate CHD biomarkers.

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GENETIC TAXONOMIC ANALYSIS OF CHILOMASTIX GENUS

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There are many species named Chilomastix, such as C. caulleryi, C. cuspidata, C. wenrichi, C. cuniculi, C. bettencourti, C. caprae, C. gallinarum, C. equi, C. sulcatus, C. motellae Alexeieff. These species have been named based on morphology, with varying naming conventions such as author names or local host vocabulary, and generally lack gene-based evidence. To address the molecular taxonomy of Chilomastix species appropriately, the 18S small subunit of ribosomal RNA (18SrRNA) gene locus of Chilomastix spp. detected from 356 stool samples isolated from humans and 380 stool samples isolated from animals which were collected in Wainyapu Village, Sumba Island, Indonesia were analyzed. From 100 18SrRNA partial positive sequences, 52 unique genotypes (1,425-1,986 bp) were confirmed and phylogenetically analyzed with the references of GenBank. Based on estimated posterior probability values, we clustered the DNA haplotypes of Chilomastix spp. into Subgroup1 and Subgroup2. Subgroup 1-A (human-specific, containing C. mesnili reference sequences), Subgroup 1-B (pig/human/buffalo/dog specific), and Subgroup 1-C (chicken specific, which we consider C. gallinarum). Subgroup 2 is mainly Rodent-hosted. But divide into two separate subtypes Subgroup 2-A (rodent-single host) and Subgroup 2-B (Rodent-Duck-buffalo hybrid, which includes a C. caulleryi reference sequence). In conclusion, the Chilomastix species that infect each host have a certain degree of specificity, and although the number of examined samples was limited, we could address a wide variety of genetic diversity of this species. The accuracy of the molecular epidemiology of Chilomastix can be improved by further registering reference sequences.

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MOLECULAR STUDY OF THE NUCLEOLAR METHYLTRANSFERASE FIBRILLARIN OF THE HUMAN PATHOGEN LEISHMANIA MAJOR

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Fibrillarin is the enzymatic component of box C/D small nucleolar ribonucleoparticles (snoRNPs) involved in early processing and modification of ribosomal RNA (rRNA) primary transcript, and ribosome subunits assembly. Despite its importance, little is known about the functions

that Fibrillarin performs in the ancestral protozoan parasites of the genus Leishmania, microorganisms that cause different debilitating to fatal diseases. In this work, we initiated the molecular characterization of the Fibrillarin orthologue of L. major (ID:LmjF.36.3070; LmFib). Our in silico results showed that LmFib possesses the typical and conserved GAR region and methyltransferase domain. In addition, the predicted three-dimensional structure of LmFib is similar to the one reported in Saccharomyces cerevisiae. Furthermore, we generated transgenic L. major parasites that express a PTP-tagged version of LmFib to identify proteins that interact with it. By tandem affinity purifications, mass spectrometry and bioinformatic analyses, we found several activities (RNA helicases, GTPases, methyltransferases, among others) reported in yeast and human to interact with Fibrillarin, as well as approximately 65 structural ribosomal proteins. Notably, we also purified several interesting nucleolar proteins whose function has not been described. We are currently identifying the snoRNAs to which LmFib binds and analyzing if LmFib interacts with rRNA genes. PAPIIT IA200623

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ESTABLISHMENT OF AN IN VITRO CULTURE MODEL OF TOXOPLASMA GONDII BRADYZOITE CYSTS

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Toxoplasma gondii is an apicomplexa with a prevalence of 30% worldwide. The presentwork focuses on the chronic stage of the disease that is produced by the bradyzoite tissue cyst, as it tends to be drug resistant and is of high risk in immunosuppressed patients, so the study of its biology is of great importance. In the present study, we developed an in vitro model of bradyzoite cysts using LLCMK2 cells as host, with the aim of obtaining the highest number of cysts, the cells were cultured in 6-well plates containing cover slips where we infected the monolayers with the RH strain in a 1:1, 1:5 and 1:10. The initial phase of infection was performed in RPMI medium with 2% FBS at pH 7.2, at 37°C in the presence of CO2 for 24 hours for the correct establishment of the parasite. After this time, the medium was changed to RPMI 2% FBS, pH 8.5, at 37°C and in the absence of CO2. Four times were analyzed after the change of culture conditions: 72, 96, 120 and 144 hours post-change (h.p.c.). To identify bradyzoite cysts, cover slips were fixed with methanol:acetone, then stained with Giemsa and another group was fluorescence assayed using biotinylated Dolichus biflorus agglutinin (DBA) as primary marker and Alexa 594 streptavidin as secondary marker, together with DAPI. It was observed under a confocal microscope and then bradyzoite cysts and tachyzoite were counted in 50 fields using epifluorescence microscopy. As a result, at 120 h.p.c there was a better yield of bradyzoites/tachyzoites in relation to the other 3 times, however, being still low (10%) and showing high loss of the monolayer due to the high amount of extracellular tachyzoites. It is expected that with the 1:5 and 1:10 concentration the yield will increase and the monolayer and monolayer will remain intact. The next strain to be tested will be ME49, known to be highly cystogenic. It is expected that the results from this strain will have a better yield and number of cysts. Once standardized, these bradyzoites will be used to generate specific chronic phase antigens and thus implement a chronic phase diagnosis.

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DRUG REPURPOSING AND SCREENING OF LIBRARIES OF CHEMICAL COMPOUNDS TO IDENTIFY NEW ANTI-PARASITIC AGENTS

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The Trypanosoma and Toxoplasma spp, are etiological agents of diseases capable of causing significant morbidity, mortality, and economic burden, predominantly in developing countries. Currently, there are no effective vaccines for the diseases caused by these parasites; therefore, therapy relies heavily on antiprotozoal drugs. Non-biased screening of libraries of chemical compounds including the repurposing of well-characterized compounds is emerging as viable approach in identifying lead candidates for early drug development against parasitic diseases. As a proof-of-principle screen to identify effective anti-parasitic agents, we evaluated libraries of natural product (503), FDA-approved (640) compounds as well as imidazole derivatives (26) for potential to inhibit T. gondii growth. We identified 39 new compounds that potently and selectively restrict the growth of T. gondii. Furthermore, we evaluated some these compounds for activity against Trypanosoma growth both in vitro and in animal models. Findings revealed eight (8) imidazole derivatives active against Trypanosoma growth. Together, the findings are new and promising, and do not only strengthens the prospects of drug repurposing and the screening of wide range of chemical compounds as a viable approach in drug discovery toward effective anti-parasite therapy but also support imidazole-based compounds as alternative source of effective anti-parasitic agents.

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DEEP LEARNING APPROACH SUCCESSFULLY IDENTIFIES FDA APPROVED MOLECULES TO PRESENT ANTI-LEISHMANIA EFFECT AT THE PROMASTIGOTE STAGE

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Drug repositioning, a cost-effective approach in drug discovery, identifies new therapeutic applications for existing 'drugs' against NTDs, including Leishmaniases. An example of a successfully repurposed molecule is the anticancer treatment, Miltefosine, the first oral drug licensed for the treatment of leishmaniases. In this context, we have conducted a computer-aided drug repositioning approach based on the deepDR pipeline, an artificial intelligence (AI) tool. Then, we evaluated their activities in vitro against the promastigotes of three strains belonging to L. infantum (2) and L. major (1) species, using an MTT assay with the standard anti-Leishmania drugs Amphotericin B and Miltefosine as positive controls. We have selected, in silico, 14 FDA approved drugs to be potentially effective against leishmaniases, out of which 6 were previously described as anti-Leishmania agents and 2 tested on human and/or in vivo. We could confirm the anti-Leishmania effects for 2 out of the 8 molecules previously described, Posaconazole and Ketoconazole. Their IC50 values ranged from 5 to 35 µg/mL on our strains, out of the most published range. As these molecules are azoles, known to interfere with the sterol biosynthesis, we investigated the effect of Fetal Bovine Serum (FBS) as an exogen source of cholesterol on their activities. The experimental conditions "in absence of FBS" improved the IC50s values of ketoconazole, and led to the identification of two active compounds belonging to another class of molecules. One of these compounds, never described for its anti-Leishmania effect, presented an IC50 < 5µg/mL on our strains in the absence of FBS suggesting that it may target the sterol pathway or be sensitive to FBS content. To conclude computer-aided repositioning of FDA approved molecules as anti-leishmanial agents identified azoles, already known as antileishmanial molecules that we reconfirmed as effective on additional Leishmania sp promastigotes, and another class of molecules among which one is highly promising and calls for further investigations on intracellular forms of the parasites and its mechanisms of action.

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IN VITRO ANTITRYPANOSOMAL, ANTIOXIDANT AND CYTOTOXICITY ACTIVITIES, LC-MS ANALYSIS AND MOLECULAR DOCKING ANALYSIS OF BIOACTIVE COMPOUNDS FROM ANOPYXIS KLAINEANA AGAINST TRYPANOSOMA BRUCEI'S UDP-GALACTOSE 4`-EPIMERASE (TBGALE)

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African Trypanosomiasis is a major public health concern worldwide, especially in developing countries. Current chemotherapies are highly toxic, resistant and ineffective. Hence, novel effective and potent trypanocides are needed. Medicinal plants have been documented to be a potential source for the development of antitrypanosomal compounds. Anopyxis klaineana is an ethnomedicinal plant used in west Africa to treat many ailments including protozoan diseases. In this study, we investigated the in-vitro effects of crude methanol extracts and fractions of A. klaineana for their antitrypanosomal activities against Trypanosoma brucei using Alamar blue assay. Additionally, the crude extract's antioxidant and cytotoxicity activities were also determined. The phytochemical profiling of the crude extract was determined using LC-ESI-QTOF-MS to identify major bioactive compounds present. A. klaineana crude extracts and fractions (hexane, chloroform and ethyl acetate) exhibited potential anti-trypanosomal activities with IC50values of 21.25,4.35,2.57and 22.92ug/ml respectively. Moreover, the crude extracts showed moderate cytotoxicity against HepG2 and PNT2 cells, with IC50 values of 68.0±2.05 and 78.7±2.63ug/ml respectively. Antioxidant potential was observed in the crude extracts of A. klaineana. LC-MS analysis revealed the presence of 24 bioactive compounds. Furthermore, the bioactive compounds identified were subjected to molecular docking studies to identify novel compounds against Trypanosoma brucei's UDP-Galactose 4`-Epimerase (TbGalE). Three potential leads CID 5078, CID 4615 and CID 10347880 with binding energies -10.8, -9.9 and -9.6 kcal/mol respectively were identified. Molecular Dynamics simulation and Molecular Mechanics-Poisson Boltzmann Surface Area calculation were performed to elucidate the stability and the binding free energy of the potential leads' complexes. These compounds will further be investigated experimentally to determine their potential efficacy and could serve as candidates for the design of novel anti-trypanosomal therapeutics.

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HIGH LEVEL OF 'NEVER TREATMENT' IN MASS DRUG ADMINISTRATION AGAINST NEGLECTED TROPICAL DISEASES IN KENYA, NIGERIA, DEMOCRATIC REPUBLIC OF CONGO AND CAMEROON

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Mass Drug Administration (MDA) to eliminate Neglected Tropical Diseases (NTDs) has been ongoing for many years. Recently, there has been interest to measure the magnitude and impact of 'never treatment (NT)', understand the associated factors and how to address them within programmatic setup. 'Never treatment' refers to people in endemic areas (receiving MDA) who have never taken any MDA treatment. Sightsavers has been conducting coverage evaluation surveys (CES) in evaluation units in supported countries. We focus here on NT measurement nested within CES in the following EUs: four Local Government Areas for onchocerciasis and Lymphatic Filariasis MDA in Nigeria; one Sub-County in Kenya for trachoma following a failed impact survey; 12 Health Districts in Cameroon and four in Democratic Republic of Congo (DRC) for routine MDA programme evaluation for schistosomiasis and soil-transmitted helminthiasis (Shisto/STH). Within the selected EU, a two-stage cluster sampling with the village segment as the primary sampling unit and household the secondary sampling unit was employed to select participants. Sample size and selection were guided by the WHO coverage sample builder. At EU level: in Nigeria, NT varies from 15.4-69.9% among people ≥ 10 years of age; in DRC and Cameroon, from 1.7- 8.3% and from 0-25.5% among school aged children (10-14 years), respectively; and 29.6% in Kenya among ≥5 years. There was marked variation and more pronounced NT level among clusters within each EU - with some reaching 100% NT. Of those NT, a vast majority were not treated in the last round of MDA as a result of them not being offered the drug mostly due drug distributors failing to visit. Study is needed in districts/clusters with high NT levels to clarify drivers of low coverage, the transmission potential of these NT and highlight mitigating actions ensuring they are reached in future campaigns. Programmes should consider NT as a key indicator for programme performance for NTD elimination and as a potential proxy to failed impact survey and vice-visa.

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OPHTHALMOLOGICAL COMPLICATIONS IN VISCERAL LEISHMANIASIS AND POST KALA-AZAR DERMAL LEISHMANIASIS

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Recent reports of ocular complications in post kala-azar dermal leishmaniasis (PKDL) patients have propelled ocular safety as a research priority in Leishmaniasis. A systematic review of all published studies was carried out to collate ophthalmological events reported in patients with Visceral Leishmaniasis (VL) or PKDL. A total of 1821 records were identified of which 1683 were excluded at title/abstract screening and 85 excluded at full-text stage leading to 53 unique records included (1924-2022). From 37 records in VL, 120 ocular events were reported of which 32 occurred at baseline, 61 following a treatment and the time of occurrence was unclear in 27. The following events were reported at baseline: uveitis (n=13), retinal haemorrhage (n=8), papillary alteration (n=2), ocular motor dysfunction (n=1), endophthalmitis (n=1), retinitis (n=1), foveal haemorrhage (n=1), conjunctival involvement (n=2), blindness (n=1), chorioretinitis (n=1), and roth spots (n=1). The following were reported following a treatment: night blindness (n=39), uveitis (n=6), conjunctivitis (n=7), retinal haemorrhage (n=3), eye movement disorder (n=2), blindness (n=2), keratitis (n=1), macular haemorrhage (n=1). The following had unclear occurrence time: retinal/foveal haemorrhage (n=12), cotton wool spots (n=2), retinal involvement/detachment (n=6), uveitis (n=5), conjunctivitis (n=1), and blindness (n=1). From 17 unique records in PKDL, 38 complications were reported of which 1 occurred at baseline (conjunctival involvement), 33 occurred after a treatment, and the time was unclear in 4. The following were reported after treatment: keratitis (n=10), uveitis (n=8), keratopathy (n=4), scleritis (n=4), blindness (n=2), Moreen's ulcer (n=2), corneal involvement (n=1), retinal involvement (n=1), and conjunctival oedema (n=1). The following reports had unclear time: conjunctivitis (n=1), blindness (n=1), uveitis (n=2). This preliminary research suggests that ophthalmological outcomes should be actively solicited in clinical studies and in surveillance programme. Further work is ongoing to collate the events by treatment regimens.

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HOST, PARASITE AND DRUG DETERMINANTS OF TREATMENT OUTCOMES IN VISCERAL LEISHMANIASIS: AN INDIVIDUAL PATIENT DATA META-ANALYSIS USING THE INFECTIOUS DISEASES DATA OBSERVATORY DATA PLATFORM

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There is a geographical variation in the efficacy of the current first line therapies in use against Visceral Leishmaniasis (VL). An individual patient data meta-analysis (IPD-MA) was undertaken to explore the determinants of therapeutic outcomes using the Infectious Diseases Data Observatory (IDDO) VL data platform. Hierarchical logistic regression models were fitted in one-stage IPD-MA to identify risk factors associated with relapse; between study clustering was considered using random intercepts for study sites. Thirty-four studies (31 published; 3 unpublished; 2000-2019) from the IDDO VL data platform were included in the IPD meta-analysis. Of the 9,207 patients enrolled in these studies, 5,778 (62.8%) were from the Indian sub-continent (ISC), 2929 (31.8%) were from Eastern Africa (EA), 377 (4.1%) from Brazil and 123 (1.3%) were from Greece. Of the enrolled, 664 (7.2%) were <5 years old, 3,402 (37.0%) were 5-15 years old, 5,129 (55.7%) were aged 15 or older and age was missing in 12 (0.1%). Miltefosine was administered in 2,109 (22.9%), pentavalent antimony (PA) in 1,912 (20.8%) patients, amphotericin B (non-liposomal) in 1,213 (27.3%), liposomal amphotericin B (L-Amb) in 485 (5.3%), paromomycin in 900 (9.8%), combination of one or more drugs in 1,283 (13.9%), and placental extract in 5 (0.1%) patients. In univariable analysis, the following variables were associated with an increased risk of relapse: male sex and treatment with a monotherapy drug. Multivariable analysis was undertaken by including the following predictors: age, sex, geographical region, drug regimen, calendar year, and baseline haemoglobin measurement of which male sex and geographical region remained significantly associated with the increased risk of relapse. Males were at 1.61 [95% confidence interval (CI): 1.25-2.07] increased odds of relapse compared to females and patients from the ISC region were at 3.17 [95% CI: 1.24-8.07] increased odds of relapse compared to those from EA. Further analysis is ongoing to delineate the relationship between different host, parasite and drug related characteristics on initial cure, definitive cure, and mortality.

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SAROCLADIUM STRICTUM SECONDARY METABOLITES BLOCK PLASMODIUM FALCIPARUM TRANSMISSION TO MOSQUITOES

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Malaria is a deadly disease caused by mosquito-transmitted protozoan Plasmodium parasites. There are more than 200 million malaria cases every year worldwide. Fungal secondary metabolites provide a great resource to discover malaria transmission-blocking drugs because of their structural and active diversity. We screened our Global Fungal Extract Library (GFEL) and found the 10 µg/ml Sarocladium strictum ethyl acetate extract could completely block the transmission from Plasmodium falciparum to Anopheles gambiae by using standard membrane feeding assays (SMFA). The fractionation of the extract was conducted by using column chromatography, thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC), followed by the antimalarial activity-guided method. We found four fractions that significantly reduced the number of oocysts in mosquitoes compared to the control at 1 µg/ml. Two bioactive pure compounds are being isolated and identified from these activity fractions. The active fungal secondary metabolites are potent leads to stopping malaria transmission.

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VACCINE-LINKED CHEMOTHERAPY AS A NOVEL STRATEGY FOR CHAGAS DISEASE

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Chagas disease, caused by infection with the protozoal parasite Trypanosoma cruzi, affects almost 7 million people globally. Parasite persistence causes chronic myocarditis and progressive fibrosis, which can manifest clinically as chronic Chagasic cardiomyopathy (CCC). Current antiparasitic treatments with either Benznidazole (BNZ) or Nifurtimox have limited efficacy beyond early disease and do not address the underlying host pathology. We developed a candidate therapeutic vaccine based on a mutated version of the T. cruzi calcium-binding flagellar protein, Tc24, designated Tc24-C4 that contains recombinant Tc24-C4 protein and a TLR4 agonist adjuvant. In mouse models of acute infection, the vaccine induces a balanced TH1/TH2/TH17 immune response, reduces tissue parasite burdens, and reduces cardiac inflammation and fibrosis. More recently we have demonstrated that vaccine-linked chemotherapy, combining a low dose of BNZ with therapeutic vaccination with the Tc24-C4 vaccine, leads to reduced cardiac inflammation and fibrosis in mouse models of acute T. cruzi infection and improved cardiac remodeling and function in a mouse model of chronic T. cruzi infection. In the current study, we evaluated a new vaccine-linked chemotherapy strategy in our mouse model of chronic infection that combined Tc24-C4 vaccine and BNZ with TTI-101, a small-molecule STAT3 inhibitor shown to reduce tissue fibrosis in non-infectious mouse models of lung and liver fibrosis. Female BALB/c mice were inoculated with bioluminescent T. cruzi H1 strain trypomastigotes. At 70 days, mice were administered the Tc24-C4 vaccine, BNZ, or TTI-101 alone or sequentially in combination. Vaccination was given subcutaneously twice, three weeks apart; BNZ and TTI-101 were administered orally once daily for 20 days. Cardiac structure and function were evaluated by echocardiography and electrocardiograms approximately once monthly, then endpoint cardiac fibrosis was evaluated by microscopy at approximately 8 months of infection. The impact of TTI-101 on further reducing cardiac fibrosis and improving cardiac structure and function over time will be discussed.

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SURVEILLANCE OF ENTERIC VIRUSES AND SARS-COV-2 IN SELECTED LEAFY VEGETABLES AND FARMERS IN THE OFORIKROM DISTRICT, KUMASI, GHANA

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The emergence and spread of enteric viruses and SARS-CoV-2 have increased concerns over food safety and the potential for foodborne

transmission. Green leafy vegetables such as cabbage, lettuce, and green onions are commonly consumed raw and have been implicated in outbreaks of enteric virus infections. Also, the recent pandemic has raised the question of whether the virus can be spread through the fecal-oral route or contaminated food. Farmers who work with these crops may also be at risk of infection. This suggests that there may be a high prevalence of enteric viruses and SARS-CoV-2 in green leafy vegetables and farmers may not be aware of the potential transmission of these viruses through the vegetables they cultivate. Therefore, this study sought to determine the burden of enteric viruses and SARS-CoV-2 in farmers and the green leafy vegetables they grow and identify potential sources of contamination. The study involved the collection of cabbage, lettuce, and green onions, oral swabs, and stool samples from 10 different farm sources followed by laboratory methods of detecting viral RNA by RT-PCR. The current results of the study for SARS-CoV-2 detection in vegetables and farmers are negative implying that they did not have an active infection with the virus at the time the samples were collected or the viruses were inactivated due to exposure time and some environmental factors. However, testing the samples for the other viruses is yet to be done. This study will highlight potential sources of contamination, reduce the risk of foodborne transmission and create awareness of the possible transmission of viruses through food.

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HOUSING STRUCTURES AND VISCERAL LEISHMANIASIS TRANSMISSION IN BARINGO COUNTY, KENYA

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Visceral leishmaniasis (VL) is endemic in Baringo County, Kenya, and contributes significantly to the burden of disease in the region. Housing structures and other environmental risk factors contribute to transmission dynamics, but these have not been widely studied in Baringo. Drought, famine, and insecurity in the region have changed the disease landscape in recent years. This study aims to examine environmental risk factors in relation to VL transmission in Tiaty East and West sub-counties. Data collection began in February 2023 and will continue through May 2023 at Chemolingot Sub-County Hospital and patients' homesteads. Data collection is being performed via questionnaires of primary VL patients being treated and VL follow-up patients that still reside in the same house as when infection occurred. Factors being assessed are housing materials, distance to termite towers, proximity to animals and animal sheds, sleeping behavior, use and access to insecticides, and previous health education. 18 household interviews were performed in March 2023 where heads of households were asked in-depth questions about housing structure choices, behavior, and access to VL prevention materials. 3 key informant interviews were performed in March 2023 with community health volunteers (CHVs) regarding VL awareness and environmental challenges in the communities. A baseline assessment of housing types through direct observation including materials, distance to water sources, distance to vector sites, and overall homestead condition is ongoing. Preliminary data indicates that the majority of VL patients reside in stick and mud houses and within proximity to animals. Most patients do not take any actions to prevent sandfly bites or sandflies from entering their home. Preliminary data from household interviews indicate that some individuals would prefer to build their house out of iron sheet because it is more permanent but lack the finances to do so. Current household building materials do not allow for adequate protection from VL, and other environmental factors likely exacerbate this risk. Strategic environmental interventions are imperative.

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A PREDICTIVE MODEL ACCOUNTING FOR DEFORESTATION ACROSS TEMPORAL AND SPATIAL SCALES IDENTIFYING ANNUAL SHIFTS IN THE ODDS OF EBOLAVIRUS ZOONOTIC SPILLOVER

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Outbreaks of filoviruses, such as ebolaviruses, typically result from zoonotic transmission from infected animals, and most recent outbreaks have resulted from zoonotic spillover. Past analyses of ebolavirus emergence have found relationships between ebolavirus spillover and forest loss (FL), however, FL data has not ever been incorporated into predictive analyses of ebolavirus emergence. We developed a novel predictive model of ebolavirus zoonotic spillover incorporating FL, vegetation, population, and meteorological data from 2001-2021 using model ensembles fit with boosted regression trees. FL was measured across multiple spatial and temporal scales, as it is unknown whether spillover is driven by FL on local or regional scales, and whether a temporal lag exists between FL and ebolavirus emergence. Models were fit for all ebolavirus species (All-species analysis) and Zaire virus only (Zaire-only analysis), as Zaire virus has a unique ecology compared to other ebolavirus species, and annual predictions of the relative odds of spillover were generated. Model fit was slightly better in the Zaire-only analysis (AUC: 0.91) compared to the All-species analysis (AUC: 0.87). Resulting predictions identified specific areas throughout equatorial Africa with elevated relative odds of spillover as high as 30 times the baseline odds, which shifted annually based on recent forest loss. Predictions which accounted for FL were distinct from previous models that ignored FL data, leading to identification of new locations where elevated spillover odds were driven by FL. Relative importance of FL variables in predicting spillover was higher in the Zaire-only model than in the All-species model, suggesting that FL may play a more important role in Zaire virus ecology compared to Sudan and Bundibugyo viruses. Spillover events from 2022-2023 in DRC and Uganda both occurred in locations predicted to have a relative odds ratio >5. FL variables improved the predictive ability of models, suggesting the importance of habitat disruption in ebolavirus ecology, and its value in prioritizing ebolavirus surveillance and prevention efforts.

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INTEGRATING ECOLOGY AND EPIDEMIOLOGY TO EMPOWER ONE HEALTH: A STUDY OF RIFT VALLEY FEVER

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Emerging zoonoses, such as Rift Valley fever (RVF), require a One Health (OH) approach to predict, mitigate and prevent outbreaks. An arbovirus, RVF virus (RVFV) causes periodic, yet widespread outbreaks with high rates of abortion and death in ruminant livestock. People often have mild influenza-like symptoms with rare but serious complications: hemorrhagic fever, hepatitis, retinitis, and meningitis. Outbreaks have been linked to complex climatic events (El Niño/La Niña) that drive favorable environmental conditions for large populations of mosquito vectors. The integration of human, livestock, wildlife, and environmental health data requires multidisciplinary methods, integrating ecological and epidemiological

approaches. We conducted a OH study of RVFV seroprevalence in livestock and people in South Africa. Here we provide an example of an approach for the collection and analysis of OH zoonotic disease data. We used a systematic grid of geographic points to achieve a probability proportional to size sampling framework for each species (human, cattle, goats, and sheep). We demonstrate how joint models can be used to determine risk factors for RVFV seroprevalence in people, cattle, sheep and goats with demographic variables, risk behaviors, husbandry characteristics and environmental variables. This method improves the ability to identify and compare risk factors across species, is explicitly designed to account for correlation amongst species, reduces multiple testing and the need for p-value correction. Examples of multiple testing include using the same predictors for multiple outcomes (e.g. seroprevalence of RVFV and Sindbis virus), siloed analyses evaluating the results in people separate from those in animals and/or environmental data or variable selection resulting in higher false positive rates, requiring p-value correction (Bonferroni) and loss of statistical power. Joint estimation is suited for reducing multiple tests without the resultant loss of power. As OH study design becomes increasingly integrated, it is important to develop adequate analysis methods that can harness the power of a OH study design.

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EVIDENCE AND GAP MAP FOR MULTI-SECTOR AND ONE HEALTH RESEARCH IN ZOONOTIC NEGLECTED TROPICAL DISEASES

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Directly referenced in the WHO's 2030 road map for the Neglected Tropical Diseases is the need for a "One Health" approach in addressing diseases possessing zoonotic components. This report aims to map where the current research evidence lies across the human, animal, and environmental health sectors and multisector (human-animal, human-environment, animal-environment, One Health) regarding the transmission, surveillance, and control of the zoonotic Neglected Tropical Diseases (zNTDs) by presenting the information in simple, accessible Evidence and Gap Maps. These Maps may serve as interactive tools for users while providing a structured framework that serves to highlight current research gaps in the field. A comprehensive search strategy was implemented across MEDLINE, EMBASE, and GLOBAL HEALTH databases. Overall, 6920 records were screened by titles, abstracts, and keywords from articles published between 1990 and 2020. A total of 2269 articles were excluded for not being a journal article, not focusing on a zNTD, and not discussing transmission, surveillance, or control in some capacity, leaving 4732 records which met the inclusion criteria. These articles were subsequently coded using a standardized tool according to their relevant zNTD, health sectors, and areas of evidence (transmission, surveillance, control). Three evidence and gap maps were generated. In general, across all zNTDs, individual health sectors were disproportionately represented in the evidence, with multisector and One Health approaches lacking across the zNTDs. Despite the cross-sectoral aspects of zNTD transmission, surveillance and control, there is a clear segregation of the evidence into single-sector research. Visual presentation of the existing literature in the form of Evidence and Gap Maps should serve as a powerful tool for researchers, policymakers, and academics implementing and advocating for cross-cutting approaches to achieve the zNTD control targets set in the WHO's 2030 road map.

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PREVALENCE, DISTRIBUTION AND DIVERSITY OF BARTONELLA IN SMALL MAMMAL AND BAT COMMUNITIES ACROSS CAMBODIA

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Bartonella species are Gram-negative, facultative intracellular bacteria that represent the only genus in the family Bartonellaceae. Small mammals and bats are natural reservoirs of many Bartonella species. We investigated Bartonella presence, distribution and diversity in small mammals and bats across 249 locations in 23 provinces across different habitat types in Cambodia from 2016 to 2020. A total of 3,515 small mammal and bat blood and lung spleen kidney (LSK) samples were screened with pan-bartonella PCR primers targeting the beta subunit of bacterial RNA polymerase (rpoB) gene. Bartonella DNA was detected in 19.32% (337/1,744) of bats and 8.3% (147/1771) of small mammals collected during this project including 26 small mammal species and 61 bat species. Highest prevalence was detected in Rattus complex from deciduous forest (34%) and Rhinolophus acuminatus from evergreen forest (38.89%). Phylogenetic analyses of 203 rpoB gene sequences showing the Bartonella genotypes circulating in the small mammal (58) and bat (145) populations across Cambodia are presented.

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EPIDEMIOLOGY OF ANIMAL BITES AND POST-EXPOSURE PROPHYLAXIS (PEP) OF RABIES IN RUPANDEHI, NEPAL

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Animal bites remain an important public health problem in Rupandehi District, Nepal. The secondary data from Jan to Dec, 2022 were obtained from Anti-rabies vaccination record of Bhim hospital, Bhairahawa. The data were entered into MS Excel and later analyzed by SPSS for descriptive statistics. The objective of the study was to estimate the burden of animal bite victims and the requirement of anti-rabies vaccines in Rupandehi District, Nepal. Out of total 3,617 cases of animal-bites reported, 65.00% (2,369) were males, 26.10% (944) were children of 0-10 years age group and 50.00% (1,823) victims hailed from urban areas. Dogs (93.22%, 3,372) were responsible for a majority of bites. The maximum number of bites were reported from January to April and in December of 2022. Leg (59.71%) was the commonest site of bite followed by hand, trunk and head. The majority of bites belong to Category II of the WHO classification (98.41%). Among the total bite victims, 94.91% (3,433) were found to complete the full course of vaccination. 13.98% of the victims received their first dose of PEP on the same day of exposure while 67.68% of the victims received it after 1 day of exposure. 90.36% and 89.23% of the bite victims received their 2nd and 3rd doses respectively on time. A well-planned vaccination program should be implemented to ensure the compliance with anti-rabies PEP schedule after animal bites. All age groups from both rural and urban areas should be prioritized for awareness and education programs to improve their treatment and PEP seeking behavior.

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DETECTION AND MOLECULAR CHARACTERIZATION OF MULTI-RESISTANT ENTEROBACTERIACEAE CARRIED BY HOUSEFLIES IN THE CITY OF BOBO-DIOULASSO, BURKINA FASO

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Houseflies (Musca domestica) are synanthropic insects that are vectors of a wide range of pathogens (multidrug resistant) responsible for infectious diseases. This study aimed to detect and characterize multidrug-resistant Enterobacteriaceae carried by houseflies in the city of Bobo dioulasso. A total of 500 houseflies were captured in 25 hospital and non-hospital environments in the city of Bobo-Dioulasso. They were divided into 125 batches of 5 flies for bacteriological analysis. Multidrug-resistant bacteria, isolated on MacConkey agar supplemented with cefotaxime 4µg/ml, were identified on the basis of biochemical characteristics. Antibiotic susceptibility profiles were determined by the agar diffusion method. Detection of blaCTX-M resistance genes, quinolone resistance genes (PMQR) and determination of E. coli phylogroup were done by conventional PCR. Among 115 bacterial strains obtained, 26 were extended-spectrum beta-lactamase (ESBL)-producing enterobacteria: E. coli (15), Klebsiella pneumoniae (6), Enterobacter cloacae (4), Morganella morganii (1). This carriage was statistically more important in hospitals (9/30, p=0.03). No carbapenem-resistant strains were observed. ESBL resistance genes (CTX-M group 1) (25/26) and quinolone resistance genes (QnrS) (6/26) were found. Houseflies in the city of Bobo-Dioulasso are vectors of transmission of multidrug-resistant enterobacteria. Surveillance of the associated risks to public health is necessary.

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HIGH PREVALENCE OF TETRACYCLINE RESISTANT ESCHERICHIA COLI ISOLATES IN AMERICAN CROCODILE CROCODYLUS ACUTUS LIKE BIOINDICATOR IN CAÑAS GUANACASTE COSTA RICA

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In recent years bacteria have acquired resistance genes causing "antibiotic resistance". The agricultural, animal, and aquaculture industries are one of the main causes, of the excessive use of antibiotics that are released into the environment. The American crocodile found in this type of ecosystem becomes a bioindicator. The aim of the research is to characterize antibiotic resistant bacterial isolates of Escherichia coli obtained from the American crocodile sewer in a tilapia production system. The study was in collaboration with the company AquaCorporación in Cañas and the samples were of 53 crocodiles captured in the tilapia ponds. Each of the captured animals made a swab of the cloaca and it is introduced to a nutritious broth and transported to the laboratory at a cool temperature. The swabs were inoculated on selective agars until obtaining pure isolates of E. coli were. Then an antibiotic sensitivity profile was performed with the Vitek 2 equipment on the isolates. Those for veterinary use were evaluated in dishes with antibiotics and the Minimum Inhibitory Concentration (MIC). Resistance isolates were sequenced from the entire genome by MicrobesNG on the Illumina HiSeq platform with a 250 bp end protocol. The results obtained from the resistant isolates were for florfenicol (11.8%), Ampicillin (16.4%), Ampicillin Sulbactam (7.3), Nalidixic Acid (3.6%), Trimethoprim/ Sulfamethoxazole (3.6), and a high prevalence of tetracycline (75%), with a MIC 50 of 32 µg/ml and MIC 90 of 128 µg/ml. Complete genome sequencing can visualize a variety of types of MLST and the transport of known mobile genes that encode resistance against antibiotics and, various plasmid sequences were detected. This work concludes that the information obtained in this research is important because resistance detected in wild animals is also associated with a production system and that in the future may become a risk to public health and the environment. Finally, it is important to assess in the future the role of dispersion of the resistance mechanisms detected and possible changes that may occur in the natural structure of ecosystems

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WHOLE GENOME SEQUENCING TO ELUCIDATE THE ZOONOTIC TRANSMISSION OF STRONGYLOIDES STERCORALIS AND ANCYLOSTOMA CEYLANICUM BETWEEN DOGS AND SCHOOL AGED CHILDREN LIVING IN THE SAME COMMUNITIES

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Strongyloides stercoralis and Ancylostoma ceylanicum are parasitic soil-transmitted helminths that impact on the health of humans and dogs in the tropics. Both parasites are categorised as agent of neglected tropical diseases by the World Health Organization. The ability of these parasites to transmit between humans and dogs living in closed proximity via contaminated environments is of particular concern in areas characterised by poor sanitation . Despite this, there is a lack of understanding about the extent to which these parasitic nematodes are transmitted between different host species, particularly humans and community dogs. To quantify the zoonotic potential and transmission of S. stercoralis and A. ceylanicum, we isolated single eggs of A. ceylanicum from faecal samples of 14 children and 25 dogs and single larvae of S. stercoralis from 20 children and 35 dogs living in the same communities in Cambodia. Whole genome amplification was performed on extracted DNA to increase concentration for whole genome sequencing. By analysing genetic variation within and among parasites, the intra- and interspecies transmission and dispersal between communities of these parasites can be traced, with the ultimate goal of identifying genetic markers associated with specific human/animal host species. This information will help elucidate the risk of transmission from domestic animals to humans and inform the parameterisation of multi-host transmission dynamics models. These findings will be essential to the development of effective elimination strategies for these zoonotic parasites of major public health and socio-economic importance.

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DETECTION OF BRUCELLA IN HUMANS AT TEKNAF, COX'S BAZAR IN BANGLADESH

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Human brucellosis is a serious infectious disease caused by a gram-negative bacteria of the genus Brucella. Brucellosis in humans is considered as a neglected and underreported disease. From February 12, 2022 to July 31, 2022, a routine examination was conducted to detect brucellosis in patients who presented with fever using a triple antigen test along with Salmonella and Rickettsia at Severe Acute Respiratory Infection, Isolation and Treatment Centre (SARI, ITC), icddr,b, Teknaf, Cox's Bazar, Bangladesh. From SARI, ITC, 120 patients were enrolled for the test. Based on the findings, we investigated the positive patients from August 03-05, 2022. Among 7 patients, we could trace 5 during this investigation. After taking verbal consent, we interviewed the patients and collected blood specimens for further investigation and laboratory confirmation by the TaqMan real-time PCR test at icddr,b Biosafety level 2 laboratory. Further, we conducted a small survey at the same hospital from October 4, 2022, to December 14, 2022. We enrolled the patients who were admitted to the hospital with ≥ 7 days of fever, muscle ache, headache and joint pain coming from different villages in the host population and from the refugee camps of Forcibly

Displaced Myanmar Nationals as well. We collected blood samples from 33 patients. We also collected demographic information and the history of exposure to livestock and livestock products of the patients to identify the source of infection. Among the patients tested by triple antigen, 7 were positive for Brucella spp (5.8%). Among them, 5 patients we could trace during the investigation, 1 confirmed positive by PCR. During the survey, out of 33 patients, 1 was found to be positive both by triple antigen test and PCR (3%). The positive patients, their families, and their neighbors had a history of raw milk consumption and exposure to livestock. Among the patients, enrolled for the survey, 21% reported consuming raw milk by them or their families. Consumption of raw milk might be considered as one of the important causes of Brucellosis in this area. Therefore, intervention should be carried out in this area to avoid raw milk consumption.

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MAPPING HOUSEHOLD-SCALE LIVESTOCK HUSBANDRY IN LOW- AND MIDDLE-INCOME COUNTRIES BY ANIMAL TAXON: A BAYESIAN PREDICTION MODEL OF A KEY INFECTIOUS DISEASES RISK FACTOR

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Around 70% of the world's 880 million rural poor depend on traditional animal husbandry systems for their livelihoods which, while having numerous economic and health benefits, can be a significant source of infections through exposure to fecal contamination and respiratory pathogens. It is estimated that over 60% of human pathogens are zoonotic, and we are living in the age of pandemics resulting from the spillover of a zoonotic pathogen, such as Ebola, SARS-CoV2 and Mpox yet there have been few attempts to estimate the interphase of human and domestic animal interaction at a global scale. This represents a barrier to the improved understanding of the dynamics of both endemic and emerging infectious diseases. This analysis aimed to map the distribution of household-scale livestock husbandry in LMICs by animal taxon. Data on animal ownership were compiled from around 300 nationally representative, population-based household surveys, and species were classified into ruminants, monogastrics and poultry. A novel georeferencing methodology was implemented and a suite of time-static environmental and demographic spatial covariates were compiled based on their hypothesized associations with the outcome variables. Variable values were extracted at the georeferenced cluster locations and a Bayesian Multi-level based logistic regression approach was used to model associations and generate predictions for all LMICs at a 6km resolution. A Markov Random Field (MRF) smooth algorithm was employed to improve spatial correlation and continuity of the prediction maps. Model evaluation statistics were mixed, but weighted average recall was 0.89 for monogastric, 0.78 for ruminant and 0.74 for poultry ownership. High prevalence of poultry ownership was predicted across the Tibetan Plateau and in pockets in the Andes, Ethiopia, and Kenya, while ruminant ownership rates were high in parts of Amazonia, Syria and Yemen. The resulting prediction maps can be used by policymakers and program planners to generate disease burden estimates, target outbreak prevention interventions geographically and identify hotspots of risk for zoonotic spillover.

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ISONIAZID URINE COLORIMETRY FOR EVALUATION OF TUBERCULOSIS PHARMACOKINETICS IN ADULTS AND CHILDREN

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Treatment failure and emergence of drug-resistance in tuberculosis (TB) can be caused by suboptimal pharmacokinetics. Dose adjustment can be personalized by measurement of peak serum concentrations; however, the process involves cold-chain serum preservation and sophisticated laboratory procedures unavailable in many high-burden TB settings. Isoniazid is an important drug in many TB treatment regimens. Urine colorimetry provides a low-cost alternative with simple sampling and quantification methods. We enrolled 56 adults and 89 pediatric patients in a prospective, observational study of patients taking first-line anti-TB medications that was conducted in Tanzania (children) and the United States (adults). Serum was collected pre-dose and 1, 2, 4, 6, and 8 hours post dose for measurement of isoniazid concentrations using validated LC-MS/MS methods. Urine was collected between 0-4, 4-8, and 8-24 hour intervals post dose, and pooling was done to determine concentrations at 0-8 and 0-24 hours, with urine concentrations measured using colorimetric methods. The average peak serum concentrations were 4.8 mg/L and 6.4 mg/L for adults and pediatric patients, respectively. The average total serum exposure over 24 hours was 16.4 mg*h/L for adults and 26 mg*h/L for pediatric patients. Correlation between serum parameters and urine values was highest at the 0-4 hour collection interval for adults (r=0.7) with area under receiver operator characteristic curve (AUC of ROC) of 0.9 (CI: 0.7-1) for urine values predicting subtherapeutic serum concentration for dose adjustment. Unexpectedly in children, correlation was lower than that observed in adults and occurred for urine at the 8-24 hour (r=0.5). Isoniazid urine absorbance correlated with serum concentrations at different urine collection intervals in adults and pediatric patients. Colorimetric methods may improve feasibility of personalized dosing in high-burden TB regions but requires further study of dose adjustment based on urine thresholds in adults, and exploration of urine trough measurements in children.

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PERFORMANCE OF SARS COV-2 IGG ANTI-N AS AN INDEPENDENT MARKER OF EXPOSURE TO SARS COV-2 IN AN UNVACCINATED WEST-AFRICAN POPULATION

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The determination of previous SARS-COV-2 infection is hampered by the absence of an accurately sensitive standardised test. The most relevant marker used to assess previous exposure is IgG antibody to the nucleocapsid (IgG anti-N), although it is known to wane quickly from peripheral blood. The sensitivity and specificity of seven antibody tests either singly or in combination namely, virus neutralization test, IgG anti-N, IgG anti-S, IgG anti-RBD, IgG anti-N + anti-RBD, IgG anti-N + anti-S and IgG anti-S + anti-RBD were evaluated on 502 cryopreserved serum samples collected pre-vaccination rollout in 2021 in Kumasi, Ghana. Accuracy of each index test was measured using a composite reference standard based on a combination of type neutralization and IgG anti-N

antibody tests. According to the composite reference, the most sensitive test was virus neutralization test that yielded 95.4% sensitivity (95% CI: 93.6-97.3), followed by 79.8% for IgG anti-N + anti-S (95% CI: 76.3-83.3) and a ROC value of 0.98. The most specific tests were virus neutralization and IgG anti-N, both with specificity 100% (95% CI: 100-100). Arbitrarily, viral neutralization and IgG anti-N + anti-S were the overall most accurate tests with specificity/sensitivity of 100/95.2% and 79.0/92.1% respectively. In conclusion, our findings indicate that IgG anti-N alone is an inadequate marker of prior exposure to SARS COV-2 in an unvaccinated population. Virus neutralization assay appears to be the most accurate assay in discerning prior infection. A combination of IgG anti-N and IgG anti-S is also highly sensitive and specific, and suited to low resource settings in the assessment of SARS COV-2 exposure prior to vaccination.

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FEASIBILITY OF CASH TRANSFERS TO FACILITATE TUBERCULOSIS SCREENING AMONG HOUSEHOLD CONTACTS OF TUBERCULOSIS PATIENTS IN TANZANIA

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Tanzanian tuberculosis (TB) guidelines recommends facility-based TB screening for household contacts (HHCs) of TB patients who are symptomatic or under the age of 5 years. However, many households are unable to complete HHC screening due to cost barriers. Here, we evaluate the feasibility of unconditional cash transfers to facilitate completion of HHC screening and explore factors that impact screening completion in a rural setting with high TB prevalence. In this prospective cohort study, we consecutively enrolled index TB patients within 8 weeks of TB treatment initiation from the TB clinic at Haydom Lutheran Hospital and surrounding dispensaries in Haydom, Tanzania. The study provided a cash transfer of up to 40,000 Tanzanian Shillings ($17.09) to affected households to facilitate HHCs TB screening and covered medical cost incurred from screening activities. In addition, telephone reminders occurred every 2 weeks for 2 months to follow up on screening progress. We collected data on demographics, TB diagnoses, and socioeconomic/household characteristics, as well as feedback on the utility of cash transfers and additional interventions. The study enrolled 120 index TB patients and their households from July 13th through December 21st, 2022 with total 397 HHCs. Median age for index patients 35 years, 63% males. 69 (58%) of participating households completed the recommended screening for all HHCs. Only 48 households (40%) were able to fully cover the cost of HHC screening. In a logistic regression model, households that were able to fully cover the cost of HHCs and households that received sputum collection containers through a separate program were significantly more likely to complete HHC screening for all members (aOR 3.46 and 3.98 respectively, $p<0.01$). The use of cash transfer is feasible and positively impacts the completion of HHC screening in Haydom, Tanzania. Exploring additional support to households impacted by TB including cash transfers to cover TB screening cost, telephone reminders, and sputum collection containers can further improve completion of HHC TB screening.

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THE EFFECT OF THE COVID-19 PANDEMIC ON HEALTHCARE SEEKING IN AN INFORMAL URBAN SETTLEMENT IN NAIROBI AND A RURAL SETTING IN WESTERN KENYA, JANUARY 2016 TO AUGUST 2022

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The COVID-19 pandemic caused widespread disruptions to healthcare seeking. There are limited studies on the effect of the COVID-19 pandemic on healthcare-seeking patterns in low-and middle-income countries (LMICs), especially in rural settings and informal urban settlements with limited access to healthcare. We investigated the effect of the COVID-19 pandemic on reported healthcare seeking at health facilities and pharmacies using household morbidity data among study participants in a well-established longitudinal disease surveillance platform located in two diverse sites in Kenya: Asembo, a rural setting in western Kenya, and Kibera, an urban informal settlement in Nairobi. We described healthcare seeking before (1st January 2016 to 12th March 2020) and during the pandemic (13th March 2020 to 31st August 2022) using frequencies and percentages. We used a generalized estimating equation with an exchangeable working correlation structure to assess the effect of the pandemic on healthcare seeking in the two sites. Overall, there was a 15% (adjusted odds ratio, aOR: 0.85; 95% CI: 0.82 -0.88) reduction in health facility-based healthcare seeking in Asembo during the pandemic, and 23% (aOR: 0.77; 95% CI: 0.74 -0.81) reduction in Kibera. The pandemic resulted in increased care seeking at pharmacies in the two surveillance sites (aOR: 1.25; 95% CI: 1.21-1.28 in the Asembo site, and aOR: 1.42; 95% CI: 1.36 -1.48 in the Kibera site). We observed higher odds of healthcare seeking among ill participants who reported respiratory syndromes (e.g., in Asembo, aOR (95% CI) for Acute Febrile Illness was 2.80 (2.69-2.92), Acute Respiratory Illness was 1.40 (1.30-1.51, and for Severe Acute Respiratory Illness was 3.75 (3.58-3.93)). However, there was a decrease in healthcare seeking at pharmacies among ill participants who reported severe acute respiratory illness. This study highlights interruptions to healthcare facility utilization in resource-limited settings due to the COVID-19 pandemic. Strategies are needed to optimize healthcare provision and utilization at health facilities during pandemics.

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HEPATITIS B AND INFLUENZA VACCINE COVERAGE AMONG HEALTHCARE WORKERS IN SELECTED HEALTH FACILITIES IN BANGLADESH

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Healthcare workers (HCWs) carry a higher risk of both hepatitis B and influenza virus infection due to occupational exposures. Despite the availability of a safe and effective vaccine, routine adult immunization programs against these infectious pathogens among HCWs are overlooked in low-middle-income countries like Bangladesh. This study aims to investigate the extent of hepatitis B and influenza vaccine coverage among HCWs. From July 2021 to March 2023 we recruited a cohort of healthcare workers from 13 primary, 2 secondary, and 5 tertiary care hospitals of four administrative divisions across Bangladesh. Field staff interviewed the HCWs to collect demographic information and records of hepatitis B, and influenza vaccination using a structured questionnaire. We summarized the data using descriptive statistics. We enrolled 3684 HCWs: 22% (810) physicians, 48% (1763) nurses, and 30% (1111) support staff. Of 3684,

70% (2583) were recruited from tertiary, 22% (793) from primary, and 8% (308) from secondary-level healthcare facilities. The median age of the HCWs was 35, (IQR= 29-44) years and 67% were female. In the cohort, 8% (289) of HCWs reported to receive the influenza vaccine for the current influenza season and 53% (1968) reported to complete three doses of the hepatitis B vaccine. Overall, 8% of physicians, 10% of nurses, and 6% of support staff reported to receive the seasonal influenza vaccine. Hepatitis B vaccine uptake was highest among physicians (81%), followed by nurses (56%), and support staff (28%). Seasonal influenza vaccine uptake was highest in tertiary-level facilities (10%) followed by secondary (5%) and primary-level facilities (3%). In contrast, hepatitis B vaccine uptake was highest in primary-level facilities (60%) followed by tertiary (54%) and secondary-level facilities (34%). Both hepatitis B and influenza vaccine coverage were low among HCWs in Bangladesh, especially among support staff. Educational interventions to build awareness and subsidized vaccination policies for HCWs may improve vaccine uptake among this high-risk group.

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ASSOCIATION OF ALTERED BASELINE HEMATOLOGICAL PARAMETERS WITH ADVERSE TUBERCULOSIS TREATMENT OUTCOMES

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Tuberculosis (TB) treatment monitoring is an essential tool for effective TB treatment management. Identifying parameters that predict adverse TB treatment outcomes (failure, recurrence and death) could significantly improve clinical management. The association of hematological parameters with poor TB treatment outcomes is not well defined. To study the relationship of hematological parameters with TB treatment outcomes, we examined data from pulmonary tuberculosis (PTB) patients with successful and unsuccessful treatment outcomes. We enrolled 68 cases (poor treatment outcomes) and 133 controls (good treatment outcomes) through a nested 1:2 case; control study, matching for age, sex, body mass index, diabetes status, alcohol and smoking. Median age of the study population is 45 years and it ranges from 36 to 52 years. Hematological profiling showed significant differences in the absolute counts of white blood cells (WBC), lymphocytes, neutrophils and monocytes between cases and controls. In addition, increased neutrophil to lymphocyte (NL) ratio and monocyte to lymphocyte (ML) ratio were present in cases in comparison to controls. Similarly, decreased hematocrit and red blood cell counts were detected in cases when compared with controls. Univariate and multivariate analysis demonstrated a significant association of absolute counts of WBC, neutrophils, monocytes NL and ML ratios with poor treatment outcomes. Altered baseline hematological parameters are clearly associated with poor TB treatment outcomes, showing potential for clinical prediction to enhance the management of at-risk cases.

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SARS-COV-2 OMICRON VARIANT DETECTION WITH BINAXNOW, PANBIO, AND ID NOW RAPID TESTS

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The SARS-CoV-2 pandemic has seen multiple variants of concern arise and spread around the world. Throughout 2022 the omicron variant has diversified and spread, with dozens of subvariants in multiple waves. With each new variant, it is important to evaluate whether currently available diagnostic assays continue to accurately detect the virus. Here, we sequenced SARS-CoV-2 omicron variant lineages from patient nasal swabs collected over 12 months and tested them with Alinity m SARS-CoV-2, BinaxNOW COVID-19 Antigen Self Test, Panbio COVID-19 Ag Rapid Test Device, and ID NOW COVID-19 diagnostic tests. Patient nasal swabs in VTM from confirmed SARS-CoV-2 infections were collected between December 2021-November 2022 from South Carolina, Wisconsin, and New York. Viral load was measured on a quantitative research use only m2000 assay to determine genome equivalents per milliliter (GE/ml) and genomes were sequenced from xGen-enriched metagenomic libraries on Illumina platforms followed by classification with Pangolin and Nextclade tools. Sufficient genome coverage was achieved for classification of n=635 VTM samples. In parallel with viral load testing, VTM samples were tested on BinaxNOW (LOD; Log 4.5 GE/test) and Panbio (LOD; Log 5 GE/test) assays without specimen inactivation. Selected variants with sufficient volume were tested on ID NOW (LOD; Log 2.5 GE/test) and Alinity m (LOD; Log 10 copies/mL) assays after inactivation at 65oC for 30 minutes. Samples collected between January and November of 2022 spanned the full diversity of omicron, including BA.1, BA.2, BA.3, BA.4, and BA.5 variant waves and more than 70 subvariant lineages. All tested SARS-CoV-2 omicron variants were successfully detected by BinaxNOW, Panbio, Alinity m and ID NOW at levels consistent with expected assay limits of detection for freshly collected specimens. All four assays robustly detect circulating omicron variants, confirming that current rapid diagnostic tests are effective at detecting SARS-CoV-2 omicron infections at expected levels of sensitivity compared to previous variants of concern.

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ANALYTICAL PERFORMANCE OF 17 COMMERCIALLY AVAILABLE POINT-OF-CARE TESTS FOR C-REACTIVE PROTEIN TO SUPPORT PATIENT MANAGEMENT AT LOWER LEVELS OF THE HEALTH SYSTEM

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C-reactive protein (CRP) is an acute phase biomarker. A glycoprotein produced by the liver and released into the blood stream within a few hours of tissue injury; occurring, at the start of an infection, or due to other sources of inflammation. CRP levels are typically below 3 mg/L in healthy patients, ranging from 10 to 100 mg/L during a mild infection, reaching as high as 500 mg/L in patients experiencing severe inflammatory responses. Point-of-care (POC) tests for CRP are increasingly used in primary care to assist general practitioners (GPs) in the case management of various health complaints, including acute cough and abdominal pain, and to differentiate between mild and severe respiratory tract infections. To support health care providers in the clinical management of patients, it is crucial that the CRP tests used are accurate, precise and reliable. In this study, we compared the performance of 17 commercially available POC CRP tests. Eight quantitative and nine semi-quantitative tests were evaluated using stored samples (n=660) which had previously been tested for CRP using the Cobas 8000 Modular analyzer (Roche Diagnostics International AG, Rotkreuz, Switzerland), which represented the reference standard for evaluation. CRP values fell within the clinically relevant range (10-100 mg/L) and were grouped into four categories (<10 mg/L, 10-40 mg/L or 10-30 mg/L, 40-80 mg/L or 30-80 mg/L, and > 80mg/L) for majority of the semi-quantitative tests. Of the eight quantitative POC tests evaluated, the QuikRead go and Spinit exhibited a higher level of agreement with the reference method, (slope =0.963 and 0.921, respectively). The semi-quantitative tests showed a poor percentage agreement for the intermediate categories and higher percentage agreement for the lower and upper limit categories. More generally, analytical performance varied

considerably for the semi-quantitative tests. Our findings suggest that the quantitative tests might represent the best choice for a variety of use cases, as they can be used across a broad range of CRP categories.

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EVALUATION OF TUBERCULOSIS TREATMENT OUTCOME AND THEIR PREDICTORS IN PUBLIC AND PRIVATE HEALTH INSTITUTIONS, SOUTHEAST, NIGERIA; AN IMPLICATION FOR POLICY IMPLEMENTATION, CLIENT CENTERED EDUCATION AND TREATMENT FOLLOW-UP

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Although Tuberculosis (Tb) treatment centres exist in Nigeria, information on treatment outcomes and their predictors especially in private hospitals are poorly documented. Identification of predictors of poor treatment outcomes may enable understanding and development of interventions to improve outcome. This study therefore evaluated tuberculosis treatment outcomes and their predictors in public and private hospitals in Abakaliki, Nigeria. A retrospective study of clients managed in the two hospitals over a five year period (Jan 2018 to Dec 2022). All clients who have completed treatment over the study period were enrolled. Relevant information from the case register was retrieved and entered into proforma and study forms. Treatment outcomes were evaluated according to WHO and National Tuberculosis Control Program guidelines. A total of 522 and 732 clients were enrolled in AE-FUTHA and M-4H with mean ages 45.3±7.2 years and 46.1±3.8 years respectively. Majority (84%) were new cases with treatment success rate of 82.6% in both facilities. Treatment outcome showed that relapse, treatment failure and death were 1.5%, 1.0% and 4.6% respectively in AE-FUTHA, 1.4%, 1.2% and 6.4% respectively in M-4H with default averaging 10% in both facilities. Age (15-29), far distance to health facility (>5km) and Tb category (re-treatment) were predictors of poor treatment outcome in AE-FUTHA while area of residence (rural), far distance to health facility (>5km) and Tb category (re-treatment) were predictors of poor treatment outcome in M-4H. Clients were mostly males with twice (1.6%) DRTb than females. Although treatment success rate was close to the 85% WHO bench mark, there were still large pockets of default with similar predictors of poor treatment outcomes in both facilities. Young people on treatment need close monitoring for improved treatment outcome. Defaulter rate can be reduced by patient-centered education and counseling, follow-up reminder system, effective contact tracing, and referral to support group. Decentralization of treatment centres to rural areas would further reduce defaulter rate.

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ISONIAZID MONORESISTANT TUBERCULOSIS (HR-TB) IN ODISHA, INDIA, DURING 2019

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We conducted this study to determine the prevalence of Hr-TB (rifampicin-susceptible, isoniazid-resistant), and mutations in katG and inhA genes in Odisha, India, during 2019. The retrospective data analysis from January-December, 2019, was performed at the National Reference Laboratory (NRL), at ICMR-Regional Medical Research Centre Bhubaneswar, Odisha. NRL Bhubaneswar offers diagnostics services to 10 districts of Odisha under the National Tuberculosis Elimination Programme. The line probe assay (LPA) was performed using GenoType MTBDR plus assay version 2, (Hain Life Sciences, Germany). A total of 3282 Mycobacterium tuberculosis (MTB) positive samples from 8 districts of Odisha, for which LPA results were available, were analyzed. Of the 3282 samples, 90.2% (2961/3282) samples were smear positive, and LPA was performed directly from samples. For 9.8% (321/3282) samples which were smear negative, automated liquid culture using Mycobacteria Growth Indicator Tube (BACTEC MGIT 960 system, United States) was performed, followed by LPA assay from the positive liquid culture samples. Resistance patterns were observed in 60 isolates, of which 10 (16.7%, 10/60) had resistance to both RIF and INH, and 50 (83.3%, 50/60) had Hr-TB (INH resistance only). The prevalence of Hr-TB during the study period was 1.53% (50/3272) with a range of 0 to 3.4% in the 8 districts. Among the 50 Hr-TB strains, katG mutation and inhA mutations were seen in 74% (37/50) and 26% (13/50) strains respectively. In conclusion, compared to other Indian studies, the lower prevalence of Hr-TB in Odisha could be due to the success of Directly Observed Treatment Short-course (DOTS) leading to effective treatment of drug-susceptible TB cases in the state and decreased transmission from primary DR TB cases.

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INFLUENZA, RSV, AND SARS-COV2 SURVEILLANCE IN MACHA, ZAMBIA IN 2022

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Respiratory infections are a major cause of morbidity and mortality worldwide but are relatively understudied in sub-Saharan Africa. In December 2018, surveillance for influenza-like illness (ILI), influenza virus, respiratory syncytial virus (RSV), and later SARS-CoV2, was established at Macha hospital, which is located in a rural part of southern Zambia, and is ongoing. Here, we report on the burden of ILI, influenza A/B virus, RSV, and SARS-CoV-2 among outpatients in 2022 and compare to prior years before (2019) and during the COVID-19 pandemic (2020-2021). All outpatients were screened for ILI and an age-stratified sample of outpatients with ILI were enrolled. A nasopharyngeal swab was collected for testing for influenza A/B virus, RSV, and SARS-CoV-2 using the GeneXpert platform. Testing of samples from 2022 is ongoing and will be completed by July 2023. The annual and monthly pathogen prevalence among outpatients with ILI will be estimated. From January 1 to December 31, 2022, 21,630 outpatients were screened for ILI and 1693 (7.8%) participants had ILI. The proportion with ILI in 2022 was comparable to 2021 (6.9%) and 2020 (9.7%) and lower than 2019 (16.9%) prior to the COVID-19 pandemic. In 2022, 502 outpatients with ILI were enrolled. In January and February 2022, 7 participants to date tested positive for influenza A virus and 12 for SARS-CoV-2. No participants tested positive for influenza B virus or RSV. Through this surveillance platform, we continue to document the burden of respiratory viruses in this underrepresented region and provide important information in this changing context to inform prevention and control efforts.

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IMPORTANCE OF SEROLOGY DIAGNOSTICS FOR CHRONIC PULMONARY ASPERGILLOSIS IN POSSIBLE TUBERCULOSIS PATIENTS IN COTE D'IVOIRE

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Some patients with apparent pulmonary TB don't have TB but chronic pulmonary aspergillosis or CPA. However, the lack of diagnostic capacity for fungal infections and low index of suspicion for fungal respiratory infections among clinicians has been a challenge to CPA diagnosis and management in resource-limited settings. The most sensitive laboratory test for CPA is

Aspergillus IgG (doi: 10.3201/eid2408.171312) The study aimed to provide serological evidence of persistent Aspergillus infection among PTB patients in Cote d'Ivoire.This was a pilot cross-sectional laboratory-based study conducted in the last trimester of 2022. The study population was 39 adult patients with persistent clinical symptoms of pulmonary TB despite anti-TB treatment. Sputum samples were subjected to microscopy and standard fungal culture. Serological detection of Aspergillus fumigatus IgG was done using an enzyme-linked immunosorbent assay (BIO-RAD®). The procedures and results were done and interpreted according to the manufacturer's protocol. The cut-off value is 10 UA/mL for positive results and borderline when concentrations are between 5 and 10 AU/ml.Preliminary data showed that serological evidence of CPA or fungal sensitization was positive in 8 Xpert TB negative patients (20.5%); 5 (12.8%) positive and 3 (7.7%) borderline positive. The most common clinical features of the patients positive for Aspergillus IgG were productive cough and fever; 2 (25%) presented with hemoptysis. The most fungal isolates from positive sputum were Aspergillus fumigatus 4(50%).Our findings suggest that CPA is common in GeneXpert MTB/RIF® negative patients and could be the cause of persistent clinical symptoms in PTB patients in our setting, as described by others in West Africa. We recommend the validation of these findings in a larger cohort study. This will be important to contribute to efforts in the expansion of the TB program to include CPA as an integral component of care.

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SEX DIFFERENCES IN PLASMA CYTOKINE PROFILES BETWEEN TUBERCULOSIS PATIENTS BEFORE AND DURING TREATMENT

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Tuberculosis (TB) remains a global public health threat, with men bearing a higher disease burden than women. Men's higher burden is associated with more significant socio-economic and cultural risk factors. Host biological factors may also account for this difference, yet there is little information on sex differences in host immunity to Mycobacterium tuberculosis (Mtb). This study, therefore, aimed to explore sex-specific differences in cytokines and inflammatory mediators in plasma supernatants before and during TB treatment to understand the sex bias in TB disease. Supernatants from whole blood of HIV-negative female (n=19) and male (n=21) adults with active pulmonary TB were collected at TB diagnosis, two and six months of treatment. Supernatants were then analyzed using Luminex Multiplex assay to quantify seventeen different cytokines and inflammatory mediators of importance in the pathogenesis of Mtb: MMP-1, MMP-2, MMP-8, MMP-9, Myeloperoxidase/MPO, S100A8, S100A9, TNF-alpha, IFN-gamma, IL-1 beta/IL-1F2, IL-8/CXCL8, IL-12/IL-23 p40, IL-10, IL-13, NCAM-1/CD56, CD40 Ligand/TNFSF5, GM-CSF. A similar proportion of men and women had moderate to far advanced TB disease at diagnosis (54.1% vs. 45.9%, p=0.7850), while more men had worse severity six months after treatment (88.2% vs. 11.4%, p<0.0001). Sixteen of the seventeen cytokines and inflammatory mediators in unstimulated samples were elevated at the time of TB diagnosis and significantly declined at two- and six months following treatment. The decline was observed in both men and women. Higher median levels of MMP1 and MMP8 were detected in men compared to women at baseline (MMP1: 3754 vs. 1507, p=0.0012; MMP8: 31623 vs. 16346, p<0.0001) at two months (MMP1: 1404 vs. 680.9, p=0.0028; MMP8:10405 vs. 6830, p=0.0204) and at six months post-treatment (MMP1: 1084 vs. 517.3, p=0.0230; MMP8: 7498 vs. 4910, p=0.1042). MMP1 and MMP8 levels are higher in men before and after treatment. Further understanding of the observed differences in the context of clinical disease outcomes may advance our understanding of sex biases in TB.

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BURDEN OF TUBERCULOSIS AMONG CHILDREN UNDER FIVE HOSPITALIZED IN THE RESPIRATORY UNIT OF THE LARGEST DIARRHEAL DISEASE HOSPITAL IN BANGLADESH: A PROSPECTIVE CROSS-SECTIONAL STUDY

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Detection of tuberculosis (TB) in children remains challenging even in high-risk populations. We sought to determine the burden of TB among hospitalized under-five children at risk of TB. In this prospective cross-sectional study we stratified three high-risk groups of 0 to 59 months children to screen them for TB disease between December 2020 and Dec 2021. Group I had conventional presumptive criteria of TB, group II had severe malnutrition with pneumonia, and group III was severely malnourished children unresponsive to nutritional rehabilitation. Here severe malnutrition included severe wasting z score weight for length less than -3 of the WHO median or nutritional edema or severe underweight z score weight for age less than -4 of the WHO median. Children unresponsive to nutritional rehabilitation were defined as failure to gain weight at least 5 gm/kg/day for 3 successive days during rehabilitation or the presence of edema by day 10 after admission. In addition to symptom-based history and clinical examination, we performed a tuberculin skin test, chest radiography, and Xpert Ultra of induced sputum and stool for diagnosing TB. During the study period, the burden of TB among 272 enrolled children was 22% (59/272). Our study confirmed tuberculosis by microbiological detection in 14.33% (39/272) of children, of whom 25 by Xpert Ultra in sputum, and 24 by Xpert Ultra in stool, and among them, ten children were confirmed in both sputum and stool samples. Twenty (7.35%, 20/272) children had been clinically diagnosed with tuberculosis. Our study affirms that the burden of childhood TB is as high as 14.3% among high-risk populations which underscores the importance of the introduction of routine screening of TB in such children in resource-limited settings.

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HYPOXAEMIA PREVALENCE, MANAGEMENT AND OUTCOME AMONG CHILDREN PRESENTING TO LOW-LEVEL HEALTH FACILITIES IN TANZANIA AND RWANDA

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Hypoxemia is a known predictor of death in acute respiratory infections. In primary care settings in low- and middle-income countries, oxygen is often not accessible. The Integrated Management of Childhood Illness (IMCI) chartbook recommends using pulse oximetry (POX) when available, to identify severely hypoxemic children (oxygen saturation <90%) for classification as severe pneumonia and referral to the hospital. Evidence on the impact of this approach is scarce. ePOCT+ is a digital clinical decision support algorithm that guides primary care clinicians in managing

acutely sick children aged 1 day to 14 years in Rwanda and Tanzania. The algorithm recommends POX for all young infants and older children with IMCI pneumonia. We conducted a post-hoc analysis of ePOCT+ data to assess the prevalence of severe hypoxemia among paediatric outpatients attending participating health facilities. We further analysed the overlap with IMCI danger signs, the referral status, and the 7-day outcome of severely hypoxemic children. Our analysis included 28'294 consultations from 36 health facilities conducted between December 2021 and October 2022. 4% of children were <2 months, 77% 2-59 months, and 19% 5-14 years. 4'003/28'294 (14%) children met the criteria for POX measurement, which was performed in 86% of these cases. 68/4'003 (1.7%) children had severe hypoxemia, including 8 aberrant results. The prevalence was lower in dispensaries than in health centres (1.3% and 2.0%, respectively). 14/68 (21%) children had at least one other IMCI danger sign warranting referral. Of the 54 children requiring referral based on the POX results alone, health workers referred only 14 children, and 6 were actually hospitalized. None of the severely hypoxemic children died. Our results show that prevalence of severe hypoxemia was low, and POX changed the actual management in only 0.05% of all children. Further studies are needed to assess the impact of POX on morbidity and mortality in low-level health facilities in resource-constrained settings. Training of health workers is essential to improve the quality of POX measurement and compliance with referral guidelines.

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FACTORS CONTRIBUTING TO DISPARITIES IN RESPIRATORY CARE AT ADAMA HOSPITAL MEDICAL COLLEGE, ETHIOPIA

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Prior research suggests disparities exist in respiratory care in low- and middle-income countries. We assessed 1) the structure and processes in place for respiratory care, including mechanical ventilation (MV) management, at Adama Hospital Medical College (AHMC) in Ethiopia and 2) reported barriers faced by staff when caring for respiratory patients. We conducted a single-center cross-sectional study of healthcare workers (HCWs) and hospital leadership involved in respiratory care at AHMC between January and February 2023. We administered paper surveys, which included qualitative and quantitative items to assess the current care practices, educational background, the self-reported confidence level in the provision of respiratory care (including MV use), barriers encountered, and perceived impact on patient outcomes. Participants (n=90) mainly included 39 nurses, 35 nurse practitioners, and four physicians. Five are in hospital leadership. Most worked in the intensive care unit (ICU) (n=44) or emergency department (n=17). Among the HCWs who manage patients with MV, 62% provided daily care. However, most (82%) lacked specific training in managing MV, with 23.2% feeling uncomfortable and 24.4% feeling somewhat comfortable in managing MV. The most significant barriers to effective care were lack of training in MV management, difficulty troubleshooting malfunctioning ventilators, and lack of necessary diagnostic tests. The five leaders reported similar barriers to quality respiratory care, including a lack of trained staff in MV management, poor staff-to-patient ratios, limited equipment, diagnostic tests, and ICU beds. Nearly half (40%) of participants felt preventable MV-related complications increased ventilator days, while 60% believed these complications prolonged hospital stays, increasing healthcare costs and mortality. Lack of training and resources for healthcare workers managing respiratory illnesses and MV creates health disparities for patients at AHMC. This study highlights the need for targeted interventions, such as training programs to ensure equitable respiratory care for all patients at AHMC.

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THE EFFECT OF SOAP USE CONDITIONS ON SCHISTOSOME CERCARIAE IN WATER

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To move towards eliminating schistosomiasis as a public health problem, a comprehensive control strategy which incorporates water, sanitation and hygiene (WASH) interventions is needed. Since the successful penetration of schistosome cercariae during water contact (e.g., washing clothes, bathing) is the key component in disease transmission, the use of soap, as part of good hygiene, might play a critical role in schistosomiasis prevention by reducing human exposure to cercariae. According to our recent systematic review, soap has the potential to reduce Schistosoma infection risk and there are two potential protective aspects of soap: (1) soap has direct adverse effects on cercariae (i.e. in terms of mortality, motility, morphology, infectivity, viability); (2) soap on the skin prevents cercariae from penetrating into skin, developing into adult worms and producing eggs in the human body. For the first protective aspect, laboratory experiments have been carried out to quantify the effect of different soaps on cercarial mortality, using two powder and two bar soaps which are commonly used in Tanzania. S. mansoni cercariae were exposed to different concentrations of soap from a few minutes up to one hour. All four soaps were able to kill cercariae, with their effectiveness related to the soap concentration and exposure time. We will also report on other protective mechanisms of soap (e.g. rendering cercariae incapable of finding a host's skin or penetrating skin) which will form the basis of comprehensive guidance for soap use in endemic regions to prevent schistosomiasis.

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COST-EFFICIENT SURVEY DESIGNS FOR MONITORING AND EVALUATION OF SOIL-TRANSMITTED HELMINTHS CONTROL PROGRAMS

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To monitor and evaluate soil-transmitted helminth (STH) control programs, the World Health Organization (WHO) recommends screening stools from 250 children across 5 schools, deploying Kato-Katz thick smear (KK). However, it remains unclear whether these recommendations are sufficient to make adequate decisions about stopping preventive chemotherapy (PC) (prevalence of infection <2%) or declaring elimination of STH as a public health problem (prevalence of moderate-to-heavy intensity (MHI) infections <2%). We developed a simulation framework to determine the effectiveness and cost of survey designs for decision-making in STH control programs, capturing the operational resources to perform surveys, the variation in egg counts across STH species, across schools, between and within individuals, and between repeated smears. Using this framework and a lot quality assurance sampling approach, we determined the most cost-efficient survey designs (number of schools, subjects, stool samples per subject, and smears per stool sample) for decision-making. For all species, employing duplicate KK (sampling 4 to 6 schools and 64 to 70 subjects per school) was the most cost-efficient survey design to assess whether prevalence of any infection intensity was above or under 2%. For prevalence of MHI infections, single KK was the most cost-efficient (sampling 11 to 25 schools and 52 to 84 children per school). KK is valuable for monitoring and evaluation of STH control programs, though we recommend to deploy a duplicate KK on a single stool sample to stop PC, and a single KK to declare the elimination of STH as a public health problem.

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ASSOCIATION OF FEMALE UROGENITAL SCHISTOSOMIASIS WITH HIGH-RISK HUMAN PAPILLOMAVIRUS AMONG WOMEN IN ZAMBIA: BASELINE RESULTS OF A LONGITUDINAL COHORT STUDY (THE ZIPIME WEKA SCHISTA STUDY)

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Female genital schistosomiasis (FGS), caused by Schistosoma haematobium (Sh) egg-deposition in the female genital tract, is highly prevalent in sub-Saharan Africa (SSA). Women in SSA also face the highest cervical cancer incidence and mortality rates globally, caused by high-risk (HR-) human papillomavirus (HPV) infection. FGS and HR-HPV infection share socio-demographical and behavioural risk factors related to disease exposure. Cross-sectional studies previously found an increased risk of HR-HPV infection in women co-infected with Sh compared to those without. Yet, the interplay of these infections is unknown. We explored the association between Sh and HR-HPV co-infection in two communities in Zambia from an ongoing longitudinal community-based study, the Zipime Weka Schista! Study. Women were recruited by community health workers at home. A urine sample, two cervicovaginal self-swabs, HIV and Trichomonas self-tests were obtained and a questionnaire completed. Clinic follow up was done by a midwife who performed point-of-care colposcopy and obtained genital samples. Urine microscopy was used for Sh-egg detection and cervicovaginal self-swabs were tested by GeneXpert and PCR for HR-HPV and Sh DNA detection respectively. A total of 2,511 women aged 15-50 years old have been recruited to date (median age 28 years, [IQR] 22-36). Preliminary results from 2,488 urine samples and 1,547 cervicovaginal self-swabs revealed a prevalence of egg-patent Sh and HR-HPV infection of 5.3% (131/2,488) and 27.4% (424/1,1547), respectively. Multivariable logistic regression adjusted for age and Trichomoniasis status, revealed women with egg-patent Sh were significantly more likely to be HR-HPV positive compared to those without (OR=1.9, p=0.03). Women aged 15-25 had 1.6 higher odds of having HR-HPV compared to women aged 26+ (OR=1.6, p<0.01). Further analysis exploring the association of HR-HPV infection and cervical precancer with FGS status by PCR and colposcopy is ongoing. These findings will inform possible points for integration of FGS and cervical cancer screening strategies.

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INVESTIGATING THE GENETIC DIVERSITY OF THE SCHISTOSOMA MANSONI TRANSIENT RECEPTOR POTENTIAL MELASTATIN (SMTRPMPZQ) CHANNEL IN RESPONSE TO PRAZIQUANTEL TREATMENT IN NATURAL UGANDAN S. MANSONI POPULATIONS

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Schistosomiasis is a neglected tropical disease (NTD) caused by parasitic trematodes (Schistosoma genus), with the highest burden in sub-Saharan Africa. The disease is treated with praziquantel (PZQ) which is typically delivered annually through large scale mass drug administration programs in endemic countries. These programs have been successful in reducing the prevalence and intensity of infection but their impact on the evolution of drug resistance is unknown. As control efforts to eliminate schistosomiasis intensify to reach the WHO NTD roadmap targets, there is a need to detect and track PZQ resistant Schistosoma isolates. The transient receptor potential melastatin praziquantel channel (SmTRPMPZQ) is now recognised to be involved in the mode of action of PZQ with mutations in this target resulting in drug resistance. However, this was conducted in a single Brazilian S. mansoni laboratory-selected resistant strain; it is unclear if this mechanism will be conserved in African S. mansoni populations, in which little is known about the extent of genetic variation of SmTRPMPZQ in natural Schistosoma populations. This project aims to analyse natural Ugandan S. mansoni populations (pre- and post-PZQ treatment) to identify polymorphisms associated with drug resistance. We sequenced the whole genomes of single S. mansoni miracidia from a clinical trial in Lake Albert, Uganda. We developed a high throughput amplicon deep sequencing method to screen genomic regions encoding the PZQ binding site to identify PZQ resistance polymorphisms. Overall, our preliminary baseline (pre-treatment) data suggests that there is limited genetic diversity within the PZQ binding site in SmTRPMPZQ. Our data will provide valuable insights into the genetic variation SmTRPMPZQ in field collected schistosome populations and suggest how this may affect treatment efficacy. Monitoring for changes in the frequency of PZQ resistance mutations will reveal how natural S. mansoni populations are evolving in response to PZQ treatment.

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LIVESTOCK CATTLE AS PREDICTOR OF TRANSMISSION OF SCHISTOSOMIASIS IN NIGERIA

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Schistosomiasis, a neglected tropical disease, remains a parasitic disease of public health concern, especially in sub-Saharan African countries where reported cases are predominant. The focus of this study is to examine the relationship between prevalence of schistosomiasis and livestock cattle index in Nigeria. The study's data came from three sources: the demographic and health survey, the malaria indicators survey, and the expanded special project for the eradication of neglected tropical diseases. Analysis of variance, correlation, and logistic regression were used to investigate the mean difference in schistosomiasis prevalence across geopolitical zones, the association between schistosomiasis prevalence and livestock cattle, and the risk of schistosomiasis in each geopolitical zone when the cattle index was known, respectively. According to disaggregated and combined data for 2018 and 2021, the prevalence of schistosomiasis and livestock cattle index are highest in the country's North Central, North East, and North West geopolitical zones (P <0.05). The association between the prevalence of schistosomiasis and livestock cattle was found to be positive and statistically significant (r =0.029, P<0.05). The likelihood of schistosomiasis decreases in the North-Central, North-East, and South-South as livestock increases, while the chance increases in the North West, South East, and South West as livestock increases. The estimated risk difference of the disease from one geopolitical zone to the next is marginal; however, it is highest in the South East and North West zones and least in the South West. The possibility that livestock cattle are a predictor of transmission of schistosomiasis cannot be disparaged; hence, policies that will curtail this mode of transmission should be developed and implemented in the risk regions identified in this study.

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HUMAN SCHISTOSOMIASIS RISK AND SNAIL ABUNDANCE HAVE A UNIMODAL RELATIONSHIP IN THE NATURAL ENVIRONMENT

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Non-linear relationships in host-parasite interactions can complicate the prediction and control of human infectious diseases, including

schistosomiasis. Schistosomiasis affects 200 million people in 52 countries and is caused by parasites released by freshwater snails. A dynamic energy budget (DEB) model predicts that parasite production by snails should be low both when snail densities are low and also, paradoxically, when they are high (as there is less energy per capita for parasite production). To test whether such a unimodal relationship between parasite and snail densities occurs in nature, we estimated snail densities, environmental food availability for snails, and per capita parasite production every other week for a year at four water bodies in West Africa. Consistent with DEB theory, we show that unimodal patterns exist between snail host densities and per-capita parasite production for both Schistosoma haematobium and S. mansoni. The interaction between snail densities and food resources was significant and non-linear for total parasite production (human risk), likely because at high snail densities there is greater competition for food resources. These patterns may explain why field snail densities are often not associated positively with human schistosomiasis prevalence and suggest that the greatest risk to humans may not coincide with peak snail densities at sites. Further, epidemiologic models for schistosomiasis based on non-linear relationships between snails and parasites may improve predictions of risk to humans.

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RISK FACTORS AND PREVALENCE OF SCHISTOSOMIASIS AND INTESTINAL PARASITES INFECTIONS IN VILLAGES IMPACTED BY AGRICULTURAL ACTIVITIES IN THE NORTH AND SOUTH OF GABON

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The installation of the Olam group in the North and South of Gabon has encouraged a migratory flow of populations from urban areas to rural areas and the creation of favorable conditions for the transmission of intestinal parasites and schistosomiasis. The aim of this study was to assess the prevalence and risk factors of schistosomiasis and intestinal parasitosis infections (IPIs) in Olam villages and surrounding villages. A cross-sectional study was conducted in the North (in Bitam and Minvoul) and in the South (in Mouila) of Gabon among school-age children and adults > 60 years old between August 2019 and January 2020. Each participant presenting eligibility criteria for inclusion and having given his consent by his guardian was included. A total of 419 participants were approached and 326 gave their consent to participate in the study. The median age of the participants was 11 [10-12] years old. Five cases of schistosomiasis were found mainly in Olam villages of Mouila. The IPIs were found in 65.7% (175/266) of cases. Among them, protozoa and nematodes were diagnosed in 36.4% (99/226) and 42.1% (122/226) participants respectively. The proportion of IPIs was similar between the villages of Olam (69.2%; 63/91) and the surrounding villages (66.2%; 116/175) (p = 0.9). On the other hand, it was significantly higher in Bitam (82.0%; 114/139) compared to Minvoul (52.8%; 28/53) and Mouila (44.5%; 33/74) (p=0 ,03). Living in Mouila (p=0.01), being between 11-16 years old (p=0.04), living in a Earthen house (p=0.02), the use of latrines (p=0.01) and medicinal plants (p=0.01) was risk factors associated with IPIs. Median parasite density of participants infected with T. trichiura was more higher in Olam villages compared in surrounding villages (p<0.001). This work revealed a predominance of schistosomiasis in Olam village of Mouila. IPIs were more frequent in Bitam and the intensity of the transmission of ascariasis and higher trichocephalosis in Mouila and Minvoul would make it possible to orient the interventions of the program.

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COMBINING GENOMICS DATA WITH SOCIAL AND ENVIRONMENTAL CONNECTIVITY MEASURES TO IDENTIFY PATHWAYS OF SCHISTOSOMA JAPONICUM IMPORT IN RURAL CHINA

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Persistent transmission hotspots remain for several high burden parasitic diseases despite control efforts. One hypothesis is that infectious parasites are moving along social and environmental gradients, by human or animal movement, or along hydrological channels. In this study, we investigate how import has contributed to infections in a region where schistosomiasis transmission has persisted in spite of aggressive control programs. We also evaluate whether import is linked to social and hydrological connectivity pathways. This study leverages data collected in 2007 from 53 rural farming villages located in Sichuan, China with recent schistosomiasis reemergence. Within each of our sampled villages, all household members over the age of five and all bovines were invited to participate in schistosomiasis infection surveys. Participant demographics, household GPS coordinates, and household- and village-level mobility were assessed via head of household and village leader surveys. Survey data was paired with open-source environmental data to generate metrics that describe each village's potential to attract migrant parasites along social and hydrological gradients, taking into account road networks, drainage patterns and attractive resources within villages (e.g., schools, commerce). Individual Schistosoma japonicum samples, collected from infected human and bovine hosts, were whole genome sequenced to estimate the genetic relatedness and historical migration patterns among villages. Multivariable regression models will be used to model the association between the inferred connectivity between villages using genetic data and our social and hydrological connectivity metrics. As a result of this analysis, we expect to obtain insight into the geographic scale, pathways of import, and overall importance of parasite migration events to residual infection hotspots. Additionally, our study allows us to evaluate the utility of pairing social, environmental and genomics data to identify likely sinks and sources of persistent infections for use in targeted end-stage parasite elimination programs.

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PROTEOMICS OF ADULT PARAGONIMUS KELLICOTTI EXTRACELLULAR VESICLES RELEASED IN VITRO OR PRESENT IN LUNG CYSTS

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Paragonimiasis is an important zoonotic, food-borne trematode infection that affects some 21 million people (mostly in Asia). Trematode parasites release extracellular vesicles (EV) in vivo that contain parasite proteins and RNA cargo that may interact with other parasites and with the host. Here we detail the composition of Paragonimus kellicotti EVs purified from both adult worm excretion/secretion products in vitro (EV ESP) and from lung cyst fluid of infected gerbils (EV CFP). Electron microscopy showed that most of the EVs were 30-50 nm in diameter, but small (10-20 nm) and large (90-120 nm) subpopulations of vesicles were also present. We identified 548 P. kellicotti-derived proteins in EV ESP by mass spectrometry. The three most highly represented GO terms in the molecular function category were ATP hydrolysis activity, ATP-dependent activity and ribonucleoside triphosphate phosphatase activity. We detected 8 proteins in the EV CFP of which 7 were also present in EV ESP. A cysteine protease (MK050848,

CP-6, previously reported as useful for serology) was the most abundant protein found in EV CFP in all technical and biological replicates. Immunolocalization of CP-6 showed no staining in lung tissue of uninfected gerbils. However, strong labeling for CP-6 was observed in the tegument of adult P. kellicotti and in the diseased lung cyst tissue that contained worm eggs. These results suggest that CP-6 is released within EVs by adult worms in vivo. This study has provided new insights regarding interactions between Paragonimus worms and their mammalian hosts.

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EFFECT OF INTENSIVE TREATMENT FOR SCHISTOSOMIASIS ON VACCINE SPECIFIC RESPONSES AMONG UGANDAN ISLAND ADOLESCENTS: THE POPVAC A TRIAL

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Helminths have long been proposed as modulators of vaccine-specific responses. We hypothesised that Schistosoma mansoni (Sm) infection suppresses responses to unrelated vaccines, and that this effect can be reversed, at least in part, by intensive praziquantel treatment intervention. We conducted a randomised-controlled trial of intensive versus standard intervention against Sm among school children in Koome islands, Uganda. Participants in the intensive arm received three doses of praziquantel (40mg/kg) each two weeks apart (the last of these 2-4 weeks before the first immunisation, BCG, at week 0), followed by quarterly during follow up. Participants in the standard arm were not treated until the week 8 primary endpoint. Participants received five vaccines: BCG [week 0], Yellow Fever, oral typhoid, HPV prime [week 4], HPV booster, tetanus/diphtheria [week 28]. Data were collected at baseline and at each follow up visit; primary outcome was vaccine responses at week 8, and for tetanus/diphtheria, at week 52. Sm infection status was determined retrospectively through plasma measurement of circulating anodic antigen (CAA). We enrolled 478 participants, 239 in each arm. Among the Sm positive at baseline, preliminary data (intention to treat) indicates that intensive Sm treatment significantly reduced infection intensity by week 0 (median [IQR] CAA concentration, pg/ml, 29[7;226] vs 1527[317;9105] in the standard arm), and significantly improved the week 8 BCG-specific IFN-γ response as assessed by ELISpot: geometric mean ratio SFU/106 PBMC 1.30 (95%CI 1.03-1.64). There was no effect on the yellow fever-, oral typhoid- and tetanus/diphtheria-specific antibody response. Data analysis on HPV-specific IgG responses is underway. Our preliminary data support the hypothesis that current helminth infection reduces the BCG-specific response, and may have different impact on cellular versus humoral vaccine-specific responses. Our data contribute to the debate on whether effective control of Sm infection improves vaccine responses (and by extension efficacy) in endemic settings.

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TRANSFORMING GROWTH BETA LEVELS IN INDIVIDUALS WITH SCHISTOSOMIASIS IN FEDERAL CAPITAL TERRITORY, NIGERIA

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Schistosomiasis is a public health concern, globally and specifically in Nigeria that has one of the highest burden. Morbidities occur with genito-urinary and gastrointestinal presentations such as haematuria, chronic anaemia, stunted growth, abdominal distention affecting multiple organs, female genital schistosomiasis etc and could lead to several complications. Transforming growth factor-β (TGF-β) signaling has been found to play vital role in pathogenesis of Schistosomiasis-associated complications. This study evaluated the profile of TGF-β in persons with Schistosomiasis. A descriptive, cross-sectional study design was conducted on eighty (80) individuals of different age groups with symptoms suggestive of schistosomaisis. Stool, urine and venous blood samples were collected from the individuals, screened for Schistosomiasis and TGF-β in plasma samples were quantified using Enzyme linked immune sorbent assay (ELISA).The prevalence of schistosomiasis in the study area was 58.8%, 46 (57.5%) females and 34 (42.5%) males participated in the study, their age ranged from 5-15 years and with mean age of 16.5±10.2 years. The geometric mean of TGF-β was 2194.1 (range of 49.0 - 48,780.3). The geometric mean TGF-β of female participants, 2220.6 was higher than that of male participants, 2007.1, though not significant (P=0.677). There was no association between TGF-β and age of the participants (P=0.080) although the geometric mean TGF-β decreased as age of participants increased from <10 years, 2875.7 to 16-20 years, 925.7 but increased to 2298.6 in those above 20 years. This study has demonstrated increased serum levels of TGF-β in patients with Schistosomiasis compared with uninfected patients. There was a negative correlation (γ = -0.097) between TGF-β level and density of eggs from the samples collected but not significant (P-value = 0.448). The level of TGF-β in individuals infected with schistosomes did not differ with the infecting schistosome specie. Increased serum levels of TGF-β in patients with Schistosomiasis suggests that this growth factor may contribute to pathophysiologic remodeling in the disease.

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MEASURING WATER QUANTITY USED FOR PERSONAL AND DOMESTIC HYGIENE IN A LOW-INCOME URBAN COMMUNITY IN BANGLADESH

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There is a paucity of recent research on direct water quantity measurement for personal and domestic hygiene. We aimed to measure the water quantity used for personal and domestic hygiene and to explore the reasons and determinants for variation of water usage. We conducted this study from September 2014 to June 2016 in a low-income urban community in Dhaka. In 12 households, the team conducted a day-long bimonthly ethnographic observation for one year to measure the volume of water used per activity per person. They conducted 28 in-depth interviews to explore the reasons for changes of water usage. Participants used a median of 75 L (61–100) of water per capita per day (LCPD) and of this 75 LCPD they used a median of 39 LCPD (26–58) for personal hygiene. Women used less water than men. Individual and social norms, beliefs, and weather determinants determined personal hygiene. Water availability determined domestic hygiene (e.g., washing dishes, toilets and bathrooms). This study helps to elucidate a range of determinants of water usage of the participants from the participants' perspective. The quantity of water used for domestic and personal hygiene and its relationship to fecal-oral transmitted disease can be explored in future research.

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SUPPORTIVE SUPERVISION IS ASSOCIATED WITH AVAILABILITY OF WORLD HEALTH ORGANIZATION INFECTION PREVENTION AND CONTROL CORE COMPONENTS IN HEALTH FACILITIES IN SOUTHWESTERN UGANDA

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Core components for infection prevention and control (IPC) support recommended IPC practices, which can reduce nosocomial infections and antimicrobial resistance. Quality improvement, including supportive supervision, promotes adherence to IPC, which can be challenging in resource-limited settings. We assessed the ability of supportive supervision to improve the availability of the World Health Organization (WHO) core components for IPC at health facilities in southwestern Uganda. We employed a before and after study design that included a baseline assessment of the availability of the WHO IPC core components followed by supportive supervision activities for targeted areas for improvement. We conducted a second assessment and determined differences in the availability of the core components between assessments. A score less than 70% was inadequate, a score between 70 and 85% was intermediate, and a score greater than 85% was adequate. Re-assessment occurred at 23 (21%) of 111 health facilities. The number of facilities that were <70% for each core component stayed the same or decreased at each facility type, but there was an increase from five to six health center III facilities scoring <70% for personal protective equipment (PPE). Conversely, the number of facilities that scored >85% for each core component stayed the same or was increased at each facility type, but there was a decrease from 4 to 2 health center III facilities scoring >85% for instrument processing. There was an increase in the median (interquartile range [IQR]) overall score from baseline to follow-up assessment for all facilities (65 [54-72] vs 75 [68-73], p=0.0001). Supportive supervision activities were associated with improved availability of the core components of IPC at health facilities in southwestern Uganda. PPE availability remained inadequate across visits and should be prioritized in health care facilities in the study area.

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A SEMI-AUTOMATED SCOPING REVIEW OF MICROPLASTIC CONTAMINATION IN FOOD AND WATER BANGLADESH PERSPECTIVE

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Microplastic are fragments of plastic debris that are less than five millimetres usually generated from the breakdown of consumer products and industrial waste. Everyday millions of metric tons of industrial waste are disposed in the environment. The health impact of microplastic in food and water is yet to be fully understood. Plastic trash accounts for 60-80% of all marine litter and is one of the fastest-growing segments of urban garbage. The microplastic pollution is higher in LMICs. Bangladesh is recognized as a nation with a plastic pollution crisis. The objective was to explore the existing knowledge by analysing scientific abstracts relating to the research on microplastic pollution and its effect on human health. We conducted a literature search in the indexed databases using the keywords “Microplastic AND (food OR water) AND Bangladesh”. We then processed the text of abstracts and converted these into a data where a row contained an abstract and each column a unique word across all abstracts. The frequency of words is recorded. Fitted a Latent Dirichlet Allocation (LDA) model to find common sub-themes across the abstracts. We found 121 abstracts based on the search. The first abstract was dated back to 2014 and it could be an indicator that research in microplastic is emerging recently. After initial processing we found 1262 unique words across all abstracts. Using LDA we found ten sub-themes. During the COVID-19 pandemic the amount of plastic pollution increased and it can be seen that one of the themes is concentrated, with the keywords, mask, pandemic, PPE etc. The marine and urban settings are the most affected areas. Fish and freshwater pollution is a key research domain. None of the themes showed any evidence of research relating to interventions in reducing plastic pollution or the assessment of the health impact of microplastics in food and water. The findings shows that there is a lack of research on the effect of the presence of microplastics in food and water on human health in Bangladesh. A rigorous research study is required to identify the level of knowledge, attitude and practices on the use of plastic products to develop interventions.

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TOILET FUNCTIONALITY AND CLEANLINESS STATUS IN HEALTHCARE FACILITIES IN DHAKA, BANGLADESH

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Lack of access to functional and clean toilets is a major public health concern in LMICs, including healthcare facilities (HCF), contributing to the spread of infectious diseases. Most recent sanitation assessments were conducted in sub-district level hospitals rather than larger hospitals in major cities. We conducted research in 10 government and 2 private hospitals to understand the availability, functionality, cleanliness, and toilet-user ratios in Dhaka. From Aug-Dec 2022, we conducted infrastructure assessments and collected information on toilet numbers and users from hospital daily registers. Given the heterogeneity of user numbers and structural complexity of different departments (inpatients vs. outpatient), we observed all toilets in selected hospitals. The number of toilet users was categorized into patients and their caregivers and hospital staff (doctor/nurse/cleaner). Cleanliness of the toilets was assessed using two parameters (clean/unclean) and associated criteria, and functionality was defined according to the WHO/UNICEF Joint Monitoring Programme definition for HCF. Amongst 2611 toilets, 2243 (86%) were directly observed, and more than 85% of toilets were functional. In government hospitals, 15% of toilets were not functional, and in private hospitals, 6% were nonfunctional. The main reasons for non-functionality were broken doors or locks (14%). Additionally, 84% (2200) of toilets were found clean in all hospitals. However, 16% of toilets were not clean in government hospitals, and 6% were not in private hospitals. An unacceptably high toilet:user ratio was observed with an average ratio of 1:51, whereas the national standard notes 1:6. The toilet:user ratio was higher in government hospitals (1:52) than in private hospitals (1:21), and the highest ratio was 1:395 for patients and 1:30 for staff. Overall, the study suggests that interventions are required to ensure adequate toilet facilities, maintenance, and cleanliness in hospital settings in Dhaka, which will require relevant leadership and resources to be allocated, including a significant augmentation of the number of toilets relative to users.

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ASSESSING FAECAL CONTAMINATION IN SOILS OF INFORMAL SETTLEMENTS- A COMPARATIVE STUDY OF TRADITIONAL SOIL TESTING AND INNOVATIVE BOOTSOCK TECHNIQUE

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Diarrhoeal transmission is commonly attributed to water, food, and sanitation (WaSH). However, recent research suggests that WaSH interventions must holistically consider the different pathways of the F-diagram. Soil transmission of diarrhoea, including through ingestion,

has been largely understudied despite evidence of high levels of microbes in soil environments. Gold standard soil sampling methods are unable to collect spatially representative data across community scales; requiring instead, the implementation of composite methods to increase our knowledge of direct soil transmission. Bootsock sampling, previously used for assessing diarrhoeal pathogens in poultry houses, was laboratory- and field-tested to collect surface soils within informal settlements for measuring E. coli concentrations. In the laboratory, a 5x1 m soil box was spiked with E. coli across the length of the walkway. E. coli was detected in 87% (n=24) of bootsock samples and 55% (n=20) of grab samples from the same uniformly inoculated transect. Paired bootsock and grab samples were also collected from 11 informal settlements in Suva, Fiji. In the field, 73% (n=33) of bootsock and 75% (n=79) of grab samples had detectable concentrations of E. coli. Bootsock estimations of E. coli levels were consistently higher than paired grabs. These findings demonstrated that bootsock results were comparable to those of the gold standard methods in measuring bacteria. Furthermore, a post-hoc power analysis also showed that a lower number of bootsock samples were needed to measure the same mean E. coli transect loads as grab samples. In this study, we demonstrated that alternative composite sampling methods, such as bootsock sampling, was able to consistently measure higher and more spatially representative levels of E. coli across the same transect. The successful optimisation and application of this method will increase the accuracy of faecal pollution and exposure assessment in contaminated settings. This would, in turn, add more information to our collective knowledge of soil transmission and risk, and thus, result in the development of better mitigation strategies.

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PREVALENCE OF PATHOGENIC MDR ESCHERICHIA COLI IN FAECAL SLUDGE TREATMENT PLANTS AND ADJACENT HOUSEHOLD DRINKING WATER OF ROHINGYA CAMPS, BANGLADESH

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Extended-spectrum β-lactamase (ESBL) producing pathogenic E. coli are responsible for high rates of community acquired infections and are linked to high mortality rates, increased healthcare costs and longer hospital stays. The contamination of drinking water is one of the primary routes of ESBL E. coli transmission in the community. This study aimed to investigate the prevalence, characterization of major ESBL and pathogenic genes, antibiotic susceptibility patterns and biofilm formation capability of ESBL producing E. coli in treated and untreated faecal sludge and adjacent household drinking water samples of Rohingya camps, Cox's Bazar, Bangladesh. A total of 127 ESBL E. coli isolates were obtained of which 87 from faecal sludge and 40 from adjacent household drinking water samples. In regards to ESBL gene presence, blaCTX-M was the most prevalent, being present in 44.5% of the isolates, followed by blaTEM and blaSHV in 18.6% and 2.3% isolates respectively. The genes blaTEM and blaSHV were detected only among faecal sludge isolates, which also harbored a higher percentage of blaCTX-M. With respect to pathogenicity, a total of 9.3% and 9.9% were found to be ETEC and EAEC, which are pathotypes of diarrheagenic E. coli. Both ETEC and EAEC were found among fecal sludge samples, whereas only EAEC was present in only drinking water. In the case of extra-intestinal pathogenic genes, a total of 3.2% of the isolates were found to be ExPEC. In regards to antibiotic susceptibility patterns, 99.2% of the isolates were found to be multi-drug resistant. Strong biofilm formation was observed at 25°C and 37°C for 33.9% and 3.9% of isolates respectively. Contaminated household drinking water can be an important mode of transmission of ESBL E. coli, and the prevalence of ESBL E. coli in faecal sludge might be a point of origin for spreading in the community. The continued exposure of the Rohingya individuals to these organisms may explain the high rates of diarrheagenic diseases within the region.

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ASSESSING THE IMPLEMENTATION OF WASH INTERVENTIONS IN A COASTAL DISTRICT WITH HIGH DIARRHOEA BURDEN, GHANA, 2022

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WASH interventions have significantly reduced diarrhoeal diseases globally. However, marginal declines have been recorded in some coastal settlements in Ghana where WASH interventions Were initiated over 20 years ago. As communities vulnerable to climate change consequences, there was the need to identify implementation challenges to build resilience and improve WASH. We assessed the WASH implementation gaps in Anloga, a coastal district in Ghana.We conducted a process evaluation of WASH interventions implementations (provision of water, and sanitary facilities) in the district. We used the USCDC 4-level socio-ecological model assessing the problem from intrapersonal, interpersonal, community, and societal levels. We conducted 30 household interviews, four community focus group discussions, 10 in-depth interviews with community leaders and four key informant interviews with district staff. We observed newest structures for accessibility. We transcribed and identified gaps using thematic analysis.Most individuals (18/30) had no knowledge of the history of WASH structures around them and had not received education on its use. Community members reported being only engaged for labour during construction. Both community leaders and members confirmed receiving a one-time education at commissioning of interventions. Most community leaders(7/10) said implementation engagements were done with selected leaders. Leaders(8/10) reported community's main role in implementation as labour provision. All district staff (4/4) mentioned that community leaders were the main people engaged throughout the process and implementation of interventions were subject to availability of district funds. We found that inadequate education on intervention, poor information flow, and lack of extensive engagement led to poor utilisation. We recommend the district adapts an all-inclusive implementation approach to ensure community ownership and appropriate use. Also, periodic supervision of interventions by the district with short educational talks would remind community members of relevance of interventions available to them.

6401

DETECTION OF SARS-COV-2 AND ENTERIC PATHOGENS IN MEGACITY DHAKA WASTEWATER: FINDINGS FROM AN ENVIRONMENTAL SURVEILLANCE PLATFORM

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Environmental surveillance has proved to be a valuable tool to monitor trends of infections with SARS-CoV-2 and enteric pathogens in the population. Dhaka city, the capital of Bangladesh, faces considerable challenges with unimproved sanitation and poor fecal sludge management. In this city, 80% of areas are not connected to centralized sewers, and household toilets are directly connected with open drains. We conducted wastewater surveillance from October 2022 to February 2023 on open drains/canals of seven zones of Dhaka North (non-sewer area) and four sewage pumping stations of Dhaka South to monitor temporal and spatial trends in vaccine-preventable enteric (Group A Rotavirus, Salmonella typhi, and Vibrio cholerae) and respiratory (SARS-CoV2) infections. 180 wastewater samples (119 from open drains/canals and 61 from pumping stations) were collected and quantified through multiplex qPCR. High proportions of wastewater samples tested positive for Rotavirus (96%), V. cholerae (56%), SARS-CoV-2 (54%), and S.typhi (43%). A higher proportion of samples from open drains/canals were positive for S.typhi, V.cholerae, and SARS-CoV-2 (58%, 61%, and 69% correspondingly) compared to samples from pumping stations (13%, 41%, and 31% correspondingly). The median log10 concentration of Rotavirus gene copies/Liter was 8.7 (range=4.7-10.4), V. cholarae was 6.2 (range=4.5-7.8), SARS-CoV-2 was 4.8 (range=3.9-6.5), and S.typhi was 5.8 (range=4.3-7.6). V.cholerae (50% to 65%) showed an increasing temporal trend in positivity from October 2022 to January 2023, while the detection of the other three pathogens had no obvious temporal patterns. Environmental surveillance is a useful tool for monitoring temporal and spatial trends of existing and emerging infectious diseases and supports evidence-based public health measures. Historical evidence for SARS-CoV-2 suggests a strong correlation between clinical cases and the presence of pathogens in wastewater. Findings also suggest that wastewater surveillance could play a crucial role where clinical case detection and reporting are not optimal due to scarce resources.

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FINDINGS OF ENVIRONMENTAL SURVEILLANCE FOR SARS-COV-2 AND ENTERIC PATHOGENS TRIGGER FUTURE PATH: LEARNING FROM A MEGACITY AND HUMANITARIAN SETTINGS IN BANGLADESH

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Environmental surveillance data have been recognized as a valuable supplement to epidemiological case data, especially in understanding the burden associated with enteric diseases. In low-income countries like Bangladesh, environmental surveillance can detect and quantify selected pathogens from wastewater and can be a useful and low-cost public health tool when limited epidemiological data are available. icddr,b conducted environmental surveillance in Dhaka city and Cox's Bazar (refugee camps and the municipality) with technical support from the Institute of Epidemiology Disease Control and Research. Wastewater samples were collected from open drains and sewage pumping stations that captured nearly one million people across 32 square kilometers. Transect walks, scoping visits, and GIS tools were used in 28 locations of Dhaka city, and finally, 11 sites were selected. In contrast, transect walks, stakeholder meetings, STRAVA mapping were used in 18 locations of Cox's Bazar, and 12 were finalized for wastewater sampling. Laboratory method optimization was completed with the development of the standard operating procedures for the detection of the Rotavirus, Salmonella typhi, Vibrio cholera, and SARS CoV-2 genetic markers by multiplex qPCR. Weekly samples across 23 sampling sides over 17 weeks provided insights on the presence/absence of the pathogens, as well as total viral concentration, enabling analysis of spatiotemporal trends. Multisectoral collaboration between the research team, government, and multinational stakeholders was established from the project onset. It will enable data-sharing health authorities to empower a more targeted and rapid public health response during outbreaks and infectious disease spikes. Environmental surveillance data will be compared to clinical data and analyzed in the context of climate variability to validate findings, explore changing patterns over time, and identify intervention points.

6403

HOUSEHOLD COPING STRATEGIES DUE TO WATER INTERMITTENCY: A MIXED-METHODS STUDY IN NORTHWESTERN ECUADOR

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While global access to improved water systems has increased, access to reliable piped water remains a concern. Intermittent water supply (IWS) systems are characterized by services being unavailable for hours or days at a time. How households cope with these two types of IWS are not well known. We collected data on household water supply and coping strategies (2019 – 2021) in response to IWS among three communities of different sizes and diverse access in northwestern Ecuador. We classified piped water service frequency (days/week) as low (<3), medium (3-5) and high (>5), and water service duration (hours/day) as low (<4), medium (4-8) and high (>8). We assessed the association between frequency and duration of piped water and household coping strategies using logistic models and complemented this analysis with in-depth qualitative interviews of residents. Intermittency patterns differed by community. Most households in the town of Borbon received a medium frequency and duration of water, the intermediate town of Maldonado received a high frequency but low duration of water, while the village of Timbire received a high frequency and high duration of water. Accordingly, communities responded differently to water intermittency. Compared to Timbire, households in Borbon and Maldonado were more likely to purchase bottled water, treat their domestic water, and store water. Compared with Borbon, households in Maldonado were more likely to purchase bottled water and treat their domestic water. Regardless of the community, households that received ≥5 days of water service had lower odds of purchasing bottled water for drinking and treating domestic water, but higher odds of using multiple drinking water sources. Households that received ≥8 hours of water service had lower odds of treating their domestic water source. Although being discontent with the water service was a recurrent theme during interviews, community members preferred the predictability of a high frequency, low duration water service. Household coping strategies depended on water supply characteristics, but all coping strategies incurred substantial financial and labor costs.

6404

DENGUE SEROEPIDEMIOLOGY RELATED TO DEFORESTATION RATES IN RURAL VILLAGES OF THE PERUVIAN AMAZON COMMUNITIES

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Dengue fever, the most common arboviral disease in humans, has increased globally due to climate change and human activities. In Peru, more than half of its population is at risk of dengue infection, and its aggressive and precary urban expansion in the Amazon region could exacerbate dengue incidence. In this study we explore the relationship between deforestation, as a proxy of urban expansion, and dengue seropositivity in Peruvian Amazon communities. We conducted a cross-sectional analytical study in 19 communities of Indiana and Belen districts in Loreto, Peru. Socioeconomic and human behavior questionnaires were applied to individuals in each randomly selected household, which was geo-referenced. Dried blood spots were collected for serological analysis. Deforested area data was extracted in a buffer of 5 km of each community using the Hansen Global Forest Change collection from 2000 to 2021. Seropositivity was stratified by age groups. Finally, a population weighted linear regression model adjusted by age groups was used to explore the relationship between deforestation rates and seropositivity in each community. A total of 1114 individuals were analyzed across both districts. Our findings showed a total seropositivity of 59.1% (range from 41.4% to 85.7%). The mean annual forest lost area rate (km2/year) was 0.46 (SD= 0.15). Seropositivity in age groups between 0 to 5, 6 to 10, 11 to 15, 16 to 20, and 21 or more years old were 26.5%, 37.4%, 49.4%, 56.4%, and 78.0%, respectively. The weighted regression model reveals that the annual forest lost rate (km2/year) is positively associated (β= 0.33; 95% CI= 0.16 - 0.51) with an increase in seropositivity at community level after adjusting for age trends. The results of this study highlights that, even in rural communities, higher dengue seropositivity levels were found. Finally, this study provides evidence that higher rates of annual deforestation rates, controlled by age (time of exposure), were correlated with an increase in dengue seropositivity at community level, highlighting the impact of rural communities' growth speed on dengue seropositivity.

6405

SPATIOTEMPORAL MODELLING TO INVESTIGATE THE IMPACT OF CLIMATE AND EXTREME WEATHER EVENTS ON ARBOVIRUS TRANSMISSION IN BRAZIL

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Brazil experiences large-scale annual outbreaks of dengue, chikungunya and zika virus infections, which are transmitted to humans by Aedes mosquitoes. The transmission of these three arboviruses is highly seasonal and their distribution is heterogeneous in space and time. There is evidence that dengue is expanding into previously protected regions in the north and south of Brazil, and previous analyses have demonstrated that transmission is associated with population demography, environmental temperatures and precipitation, with long-term hydrometeorological events such as drought and extreme wet periods also influencing the relative risk of dengue in Brazil. A key limitation of previous analyses is that they are often performed at coarse spatiotemporal resolution, for example using monthly dengue incidence data at the state or microregion level, or at the local level but for sub-national analyses. In this work, we aim to generate new evidence of the relative importance of demographic, socioeconomic, climatic and hydrometeorological factors in driving the observed seasonal transmission dynamics measured by dengue, chikungunya and zika virus incidence across Brazil at fine-scale temporal and spatial resolution. We analyse weekly case notification timeseries of chikungunya (between 2015-2020), zika (2015-2020) and dengue virus (2012-2020) at the municipality level (n = 5572) using spatiotemporal mixed-effects regression models, with climate predictors such as the range, average, and extremes of daily environmental humidity, temperature, and precipitation across different time periods, and long-term hydrometeorological events. We also explore the importance of socioeconomic factors, demography, land-use, human mobility and importation risk, and El Niño-Southern Oscillation (ENSO). Our results suggest that minimum humidity, long-term periods of extreme wetness and ENSO anomalies are important factors associated with increased human infections of all three arboviruses, thus highlighting the health impact of extreme weather conditions driven by changing climate on arbovirus transmission in Brazil.

6406

PRIOR ZIKA VIRUS INFECTION INCREASES RISK OF SUBSEQUENT SYMPTOMATIC INFECTION BY DENGUE VIRUS SEROTYPES 2 AND 4 BUT NOT SEROTYPES 1 AND 3

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The 4 dengue virus serotypes (DENV1-4) and the related Zika virus (ZIKV) are major concerns worldwide. We have shown that primary (1°) ZIKV infection increases risk of symptomatic and severe disease caused by DENV2 in our long-standing Nicaraguan pediatric cohort. Further, we found prior DENV immunity differentially modulates secondary disease: enhancement of DENV2, protection vs DENV1, and protection and enhancement of DENV3, depending on antibody level and disease outcome. We hypothesized that prior ZIKV infection may have similar associations with secondary dengue by serotype. In 2022, DENV4 circulated for the first time, along with DENV1-3, enabling us to test these hypotheses for all 4 serotypes. We used ZIKV and DENV inhibition ELISAs, ZIKV NS1 BOB assay, and clinically confirmed case data to define prior infection histories. All analyses used linear mixed models adjusted for age and sex. Compared to naïve individuals, 1° ZIKV infection significantly increased probability of symptomatic dengue and Dengue with Warning Signs/Severe Dengue. Stratifying by serotype, 1° ZIKV infection increased disease risk with DENV4 (probability = 3.74% [2.5, 5.59] vs Naïve, prob = 1.31% [0.82, 2.08]) but not DENV1. Children with one prior DENV infection before ZIKV and vice versa (ZIKV-DENV) were also at increased risk of subsequent disease caused by DENV4 but not DENV1. We re-ran models across 18 years of cohort data and found flavivirus (FV)-immune individuals had a significantly higher risk of dengue disease overall, compared to naïve

individuals. By serotype, this effect was significant for DENV2 and DENV4, but not DENV3, while FV-immune individuals were at lower risk of DENV1. Pre-existing anti-DENV antibodies increased risk of dengue caused by DENV2 across all titers and DENV3 and DENV4 at low titers. Conversely, low titers showed no association with DENV1 disease, while high titers were protective vs DENV1 and DENV3. In sum, we show prior ZIKV infection, like prior DENV infection, increases disease caused by certain DENV serotypes. Considering serotype-specific effects is essential when assessing the safety and efficacy of ZIKV and DENV vaccines.

6407

INVESTIGATING THE POTENTIAL OF DENGUE AND ZIKA VIRUS TO ESTABLISH A SYLVATIC TRANSMISSION CYCLE IN THE NEOTROPICS THROUGH A MODELING LENS

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Dengue (DENV) and Zika (ZIKV) virus are maintained in sylvatic cycles between non-human primate (NHP) hosts and arboreal mosquitoes in Africa and Asia. DENV was introduced to the Americas centuries ago, while ZIKV was introduced within the last decade. Despite its long residence in the neotropics, there is no evidence that DENV has established a sylvatic cycle there, but whether ZIKV will do so is an open and urgent question. Key determinants of sustained transmission in a novel environment are the replication of a virus within novel hosts and its transmission to vectors. We aimed to analyze parameters of DENV and ZIKV sylvatic transmission dynamics through statistical and mathematical modeling approaches. Recently, we used Aedes albopictus to infect novel hosts (squirrel monkeys, Saimiri boliviensis boliviensis) with sylvatic strains of DENV and ZIKV. We monitored host viremia and transmission to mosquitoes over the course of infection. Individuals infected with DENV showed low levels of virus replication, but we were able to fit a mechanistic within-host compartmental model to ZIKV viral dynamics in squirrel monkeys. We estimated the within-host basic reproduction number R0 to be 3.7 (median, 95% highest density interval [2.3 ; 5.1]), consistent with previous estimates in rhesus macaques using needle delivery of the virus. Lastly, we coupled viral dynamics with dose-response relationships within-vector, and estimated the probability to produce a saliva-positive Ae. albopictus upon bite on a ZIKV-infected squirrel monkey to be above 50% between days 3 and 5 post-infection. Transmission could be further enhanced if vectors are more likely to feed on infected than uninfected hosts. We therefore assessed the effect of host sex, temperature, weight, and viral load, as well as virus species, mosquito infection status, and time of feeding, on the proportion of mosquitoes taking a blood meal. None of these were significantly associated with Ae. albopictus feeding behaviour, in contradiction with recent results in mice. Nonetheless, our results suggest that a neotropical ZIKV sylvatic cycle may be imminent.

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INVESTIGATING THE VECTOR COMPETENCE OF A SCOPE OF MOSQUITO SPECIES IN THE TRANSMISSION OF GETAH VIRUS

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Getah virus (GETV) is an important Alphavirus of the Togaviridae family. Its genome is made up of a single-stranded positive sense RNA and it is transmitted by mosquitoes. Although no known clinical symptoms in people, GETV has been linked to epidemics in animals. Serological proof of GETV exposure and the threat of zoonotic transmission, however, makes GETV an important arbovirus in the field of veterinary medicine. With inadequate investigations into the vector transmission of GETV, there is very little information on the variables influencing the spread and the sporadic outbreaks of GETV infections. As a result, we assessed the GETV's host range in both in vitro and in vivo models. Cell lines derived from selected species of mosquitoes with medical importance were assessed by plaque assay to determine their susceptibility and replication under in vitro laboratory conditions. Conversely, quantitative Real Time Polymerase Chain Reaction and a plaque assay was carried out to evaluate the susceptibility and transmission potential of mosquito species to GETV infection in vivo. All examined mosquito-derived cell lines were GETV-susceptible with detectable cytopathic effects. The highest replication titres of GETV were recorded in C6/36 and NIID-CTR cell lines derived from Aedes albopictus and Culex tritaeniorhynchus mosquitoes, respectively. Comparisons of the infection, dissemination and transmission rates across species varied significantly with Cx. tritaeniorhynchus colony being the most effective species in GETV vector competency. This study is also the first account of An. stephensi and Ae. albopictus capability to transmit GETV under laboratory conditions, highlighting the potential risks of GETV transmission in nature, especially in unidentified potential vectors of GETV transmission in endemic regions where these vectors are prevalent.

6409

EXPOSURE TO WEST NILE VIRUS AND STRAIN-SPECIFIC DIFFERENCES SHAPE TRANSMISSION BY CULEX PIPIENS UNDER CLIMATE CHANGE

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Arthropod-borne viruses are associated with over 140 human diseases. The most widespread arboviruses belong to the flavivirus family, which includes West Nile virus (WNV), Zika virus, dengue virus, and several others. Across the globe, temperature is increasing and such increases influence the distribution and prevalence of vector-borne disease transmission. Life history traits of both the mosquito and pathogen have been utilized in modeling vector-borne diseases, thus far, models for WNV have identified species and vector population-specific differences. Previous studies have demonstrated that exposure and infection with WNV can influence mosquito longevity, fecundity, and blood-feeding behavior, yet trait-based R0 models have historically been generated using data from unexposed mosquitoes. The purpose of this study is to determine the interactions among temperature, infection status, viral strain, and WNV transmission in order to create more accurate predictive models of WNV transmission under climate change. Culex pipiens were fed a blood meal containing genetically distinct strains (WN02 or NY10) or a noninfectious blood meal. Following feeding, lifespan, biting rate, ovipositing, vector competence, and pathogen development rate were recorded at constant temperatures ranging from 10°C to 33°C and a mean cycling around 25°C. Bodies and legs of dead females were harvested to determine infection and dissemination rates of exposed mosquitos and qPCR was used to quantitate viral load. These data were used to generate thermal performance curves in conjunction with previously published life-history data, which were then used to inform R0 models. Our results demonstrate that WNV infection significantly influences the relationship between temperature and Cx. pipiens life-history traits, and that these relationships are strain-specific. Consideration of infection status and viral genetics, therefore, is necessary to improve models of WNV transmission under climate change. These results have broader implications for understanding the role of heterogeneity in vector-borne disease modeling.

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IDENTIFICATION OF ZIKA VIRUS GENES INVOLVED IN MOSQUITO TRANSMISSIBILITY

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Zika virus (ZIKV) is a flavivirus mainly transmitted by Aedes aegypti mosquitoes that recently emerged across the Pacific region and Latin America, causing large human outbreaks associated with birth defects and neurological disorders. Phylogenetic analyses show that ZIKV genetic diversity can be divided into an African lineage and an Asian lineage. Although to date, human outbreaks have exclusively been associated with strains from the Asian lineage, a growing body of evidence points towards higher transmissibility of ZIKV strains from the African lineage. To elucidate the viral genetic determinants underlying differential transmissibility between African and Asian ZIKV strains, we used a combination of viral reverse genetics and mosquito transmission assays in vivo. We constructed a set of six chimeric ZIKV strains from two parental strains with different levels of transmissibility by swapping the genome fragments encoding structural proteins, non-structural proteins or untranslated regions. We compared the in vivo transmissibility of the chimeric viruses in mosquitoes experimentally exposed to an artificial infectious blood meal. We detected viral genomes in mosquito head and infectious viruses in saliva and calculated transmission prevalence as the proportion of virus-positive head with a virus-positive saliva. We found that replacing the genome region encoding structural proteins of the low-transmissibility Asian strain with the same region from the high-transmissibility African strain significantly increased transmission prevalence. The reciprocal replacement resulted in the opposite pattern. Swapping the genome fragments encoding the structural proteins also resulted in significant changes in viral growth kinetics in mosquito cells in vitro. We concluded that the difference in mosquito transmissibility between African and Asian ZIKV strains is due to genetic variation in the viral structural proteins. Future work will provide mechanistic insights into these data using a mathematical model of within-mosquito infection dynamics and extend the results in a mouse-to-mosquito ZIKV transmission assay.

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CRYPTOSPORIDIUM PARVUM: THIOREDOXIN REDUCTASE ACTS AS THE PRIMARY REGULATOR OF GLUTATHIONE AND THIOREDOXIN REDOX PATHWAYS AND IS A TARGET FOR DRUG DISCOVERY FOR CRYPTOSPORIDIOSIS

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Cryptosporidium parvum (Crypto) is a protozoan parasite that causes cryptosporidiosis, a highly contagious disease with nearly 30% of the global population potentially exposed to the parasite. The options for treatment are severely limited; only a single drug (Nitazoxanide) is currently approved by the FDA and it is not fully effective in the young, elderly, or immunocompromised patients. Auranofin, which is clinically used for rheumatoid arthritis and in clinical trials for cancer and other infectious diseases, was shown to be active against Crypto in vitro. Auranofin is thought to function, in part, through inhibition of thioredoxin reductase (TrxR). While TrxR has numerous functions, some of its most important are regulating cellular redox balance and preventing damage caused by reactive oxygen species generated by the host immune response. In humans, TrxR and glutathione reductase (GR) are responsible for regulating thioredoxin (Trx) and glutathione (GSH) dependent pathways, respectively. No GR is present in the Crypto genome. We hypothesize that TrxR is the primary regulator of both Trx and GSH in Crypto and that its inhibition would disrupt both pathways and be lethal. To test this hypothesis, C. parvum (Cp)TrxR and CpTrx proteins were expressed and characterized. CpTrxR was found to have Trx reducing activity, but no GR activity. However, the combination of CpTrxR and CpTrx had high levels of GR activity. An IC50 was determined to be 2.4 nM for auranofin against CpTrxR. These results indicate that CpTrxR is an essential protein for both TrxR and GR activities, meaning that this protein acts at the primary regulator for both Trx and, subsequently, GSH pathways. We have identified crystallization conditions and successfully determined the structure of CpTrxR in complex with auranofin. These findings are significant in providing a foundation for future structure-guided drug development studies and redox biochemistry for improved cryptosporidiosis treatment.

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PROGRESS IN DEVELOPING METHIONYL-TRNA SYNTHETASE INHIBITORS FOR CHAGAS DISEASE

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The protozoan parasite, Trypanosoma cruzi, infects 6-8 million people primarily in Latin America. Antiparasitic drugs for chronic T. cruzi infection (Chagas disease) are inadequate due to bad side-effects and poor efficacy. T. cruzi has a single methionyl-tRNA synthetase (MetRS) which is essential for protein synthesis. We are developing inhibitors of the T. cruzi MetRS as therapeutics for CD. The MetRS inhibitors were initially developed against the T. brucei MetRS guided by crystal structure of that enzyme bound to inhibitors. Over 550 MetRS inhibitors synthesized by our group have been screened against mammalian-stage T. cruzi cultures establishing structure activity relationships. Nearly 150 compounds have been identified with EC50 values <10 nM. Most compounds are highly selective with cytotoxicity (CC50) values on mammalian cells of greater than 20,000 nM. An exemplary compound was tested in an in vitro washout assay (16-day exposure at 25X the EC50) and shown to have trypanocidal activity (with no outgrowth in the 60 day observation period) comparable to the clinical drug, benznidazole. Work has focused on two areas for lead development: 1) optimizing pharmacological properties to maximize exposure of free compound in mammalian models, and 2) maximizing the therapeutic window to avoid potential toxicity to mammalian cell mitochondrial function. A subset of lead compounds is being tested in the murine chronic T. cruzi infection model with results to be presented. MetRS inhibitors represent a promising class of compounds for treating Chagas disease.

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METABOLOMIC ANALYSIS REVEALS A NOVEL IMMUNOMODULATORY ROLE OF LYSOPHOSPHATIDYLCHOLINES IN IMMUNIZATION WITH A GENETICALLY MODIFIED LIVE ATTENUATED PARASITIC VACCINE

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Leishmaniasis is a spectrum of diseases caused by the blood borne protozoan parasites belonging to several different Leishmania species. Currently, there are no FDA-licensed vaccines against human leishmaniasis. Centrin-deleted Leishmania major (LmCen-/-) parasites were developed as a vaccine candidate for leishmaniasis using CRISPR/Cas9 gene-editing technology. Preclinical research has demonstrated the safety of LmCen-/- parasites in animal models and significant efficacy against sand fly-mediated infections with parasites causing either cutaneous or visceral disease. Substantial variations between the LmCen-/- and LmWT infections were seen in the immunological properties of the innate and adaptive responses. Since neutrophils are the first innate cells to arrive at the site of infection, it is hypothesized that metabolic reprogramming occurring in these cells could mediate the immune mechanisms of the protection using LmCen-/- and LmWT parasite strains. C57Bl/6 mice were intradermally infected with LmWTmCherry or LmCen-/-mCherry parasites. At 48h post-infection, 2.5-3x106 parasitized and non-parasitized neutrophils were sorted by flow cytometry and quenched immediately. Untargeted

metabolomic analyses were performed on the neutrophil populations using mass spectrometry. Three analytical runs per sample were performed. Mass spectrometric analyses showed that neutrophil populations isolated from ear draining lymph nodes of mice infected with LmCen-/-contained higher levels of lysophospatidylcholines (LPC), a class of metabolites that are derived from phosphatidylcholines, compared to neutrophils isolated from naïve or LmWT infected mice. The role of LPCs in immune regulation of neutrophils are further being explored using a LPC receptor antagonist in in vitro and in vivo studies. These investigations will shed light on immune defense processes and aid in the discovery of novel biomarkers for vaccine-induced immunity.

6414

NEW TRYPANOSOME GENOMES DEMONSTRATE THE CO-EVOLUTIONARY RELATIONSHIP BETWEEN ENERGY SOURCE AND SURVIVAL STRATEGY

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African (Salivarian) trypanosomes persist in the host bloodstream where they are exposed to the full force of the mammalian immune system. However, Trypanosoma cruzi (Stercoria) can invade host blood cells and tissues allowing the parasite to hide from the immune response. Fundamentally, these environments differ greatly in terms of the metabolic stress experienced by the parasite. The intracellular environment is rich in triacylglycerides, a frequently targeted energy source by pathogenic microbes, and extracellular parasites have access to soluble sugars, amino-acids and lipids. We predict that by assessing the metabolic capabilities between groups of trypanosomes it may be possible to link these traits with survival strategy. Further, it may be possible to predict the survival strategy of novel or understudied parasites based on this information. In this study we present three novel trypanosome genomes and one reassembled genome that allow us to investigate the genomic basis for differences in metabolic capability between trypanosomes with different survival strategies. We show that loss of genes in fatty acid metabolism pathways may have facilitated the switch to an extracellular lifestyle in the Salivaria. We also demonstrate that metabolic information, along with other genomic information, can allow us to make predictions about the survival strategy of understudied trypanosome species and give insight into the evolutionary history of these important pathogens of humans and livestock.

6415

FACING ADVERSITY: CHAGAS DISEASE TREATMENT TOLERABILITY AND ADVERSE EVENTS AT AN ACADEMIC SAFETY-NET HOSPITAL IN NEW ENGLAND

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Anti-trypanosomal therapy is generally recommended for individuals under age 50 with the indeterminate form of Chagas disease to prevent progression to cardiac or gastrointestinal (GI) disease. However, benznidazole (BNZ) and nifurtimox (NTX) carry a substantial risk of adverse drug reactions. We performed a cross-sectional retrospective chart review of treatment tolerability among patients with confirmed Chagas disease referred to Boston Medical Center from June 2017 to June 2021. Ninety patients with confirmed Chagas disease were evaluated, of whom 17 (18.9%) had contraindications to treatment. Fifty-eight patients started on therapy, with dosing and monitoring co-managed by an infectious diseases physician and pharmacist. Following initiation of BNZ as first-line therapy, 53 patients (91.4%) had at least one adverse event, of which GI side effects (27/58, 46.6%), rash (26/58, 44.8%), and symptoms of potential peripheral neuropathy (16/58, 27.6%) were most common. Rashes led to treatment discontinuation in 14 patients (24.1%) and met criteria for grade 3 severity in 9 patients (15.5%). Adjunctive therapies for rash included topical and systemic steroids and systemic antihistamines. Concern for peripheral neuropathy led to treatment cessation for 8 patients (13.8%). GI side effects occurred in 27 patients (46.6%), were relatively mild, and commonly managed with famotidine. Adverse events necessitated cessation of BNZ for 18 patients (31.0%), of whom 12 went on to receive NTX. NTX was associated more frequently with GI side effects (10 patients or 83.3%). Ultimately, a total of 53 patients (91.4%) received at least one month and 42 patients (72.4%) completed at least 60 days of either BNZ or NTX. Multiple strategies were used to prevent and alleviate adverse events; co-management with a multi-disciplinary team was essential to assist patients in tolerating therapy. Even so, most patients experienced some adverse events, of which rash and peripheral neuropathy were most concerning. These findings underscore the grave need for expanded safe and effective treatment options for patients living with Chagas disease today.

6416

INTRA-SPECIES GENETIC CLASSIFICATION OF ENTEROMONAS SP. DETECTED FROM HUMAN AND ANIMAL HOSTS IN INDONESIA

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Due to its non-pathogenic characteristic, Enteromonas sp. has been rarely studied, despite its widespread prevalence in both human and animal hosts, especially in low-hygiene tropical areas. As a result of such neglect, only a few genetic references of Enteromonas sp. are available in the GenBank, and the intra-species genetic diversity remains unrevealed. In this study, we aimed to address the genetic classification of Enteromonas sp. among humans and animals through a molecular epidemiological study conducted in Wainyapu village, where humans and animals live closely, in Sumba Island, Indonesia. Stool samples were collected from 2013 to 2016. The total DNA was extracted from the stools for the Polymerase Chain Reaction (PCR) screening of the 18S small subunit ribosomal RNA (18S rRNA) gene locus Enteromonas species. All the PCR amplicons confirmed approximately 1,400 base pairs of DNA sequences. The prevalences of Enteromonas sp. were 33.9% (73/215) in humans and 25.2% (68/270) in animals, including unique DNA haplotypes of 61 in humans and 90 in animals. On the reconstructed phylogenetic tree, we observed at least four clusters among the intra-species genetic diversity of Enteromonas species. Haplotypes from goats, rodents, and buffalos were clustered separately from other clusters indicating the presence of animal-specific groups. The human-derived haplotypes were grouped into another cluster at the same Operational Taxonomic Unit (OTU) level as the animal-specific ones. Among the human-derived haplotypes, three sub-clusters were also observed. The molecular taxonomy of minor intestinal protozoans, especially commensal types like Enteromonas sp., is essential to investigate and understand human gut microbiota dynamics. The classification proposed in this study will pave the way for investigating the roles of Enteromonas sp. in host gut homeostasis.

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CHEMICAL AND GENETIC INVESTIGATIONS ON LEISHMANIA DEXD/H-BOX PROTEINS AS POTENTIAL DRUG TARGETS AGAINST LEISHMANIASIS

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Leishmaniases, ill controlled and neglected diseases, constitute major public health problems. Besides the limited repertoire of obsolete 'drugs', current challenges also include high costs, toxicity, adverse effects, and emergence of drug resistance. Thus, identification of novel drugs constitutes a global research priority. Our objective is to validate members of the Leishmania DExD/H-box protein family, particularly DEAD-box proteins, also known as a rich source of drug targets in humans, as potential Leishmania drug targets, using chemical and genetic validation approaches. First, biochemical and genetic expression in yeast of the Leishmania infantum initiation factor 4A (LieIF) have shown its potential as a drug target. Then, we identified, through in silico modelling and virtual screens of small molecules, different ligands, which were screened on the ATPase activity of this protein. This allowed the selection of 6-aminocholestanol as LieIF inhibitor; this molecule presented an anti-Leishmania activity against promastigotes and intracellular amastigotes, which confirmed 6-aminocholestanol as a selective inhibitor and confirmed the chemical validation of LieIF as a drug target. Thus, we expanded our interest to other members of the DExD/H- box protein family. Our second target was encoded by L. infantum LINF_080005700 (LINF08), which has been identified as a close member to the Ded1/DDX3 protein by phylogeny and in silico search of conserved sequence motifs within sequence alignments of a large collection of DEAD-box proteins from various organisms. We interestingly demonstrated peculiar enzymatic characteristics of the recombinant protein so far not described for DExD box proteins; we have also demonstrated using CRISPR technology its nuclear localization both in promastigotes and axenic amastigotes. We are currently investigating its essentiality, which would genetically validate it as a drug target. To conclude, this study delivers two promising drug targets against leishmaniases that deserve further investigation for the development of novel therapeutic drugs.

6418

EFFICACY OF MOXIDECTIN VS. IVERMECTIN COMBINATION TREATMENTS FOR BANCROFTIAN FILARIASIS IN COTE D'IVOIRE: PRELIMINARY 24 MONTH RESULTS

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Lymphatic filariasis (LF) remains endemic in much of Africa despite many years of annual mass drug administration with ivermectin (IVM) and albendazole (ALB). Moxidectin (Mox) is a macrocyclic lactone that is superior to IVM for long-term clearance of onchocerciasis microfiladermia. To determine whether Mox combination therapy might also be superior for LF, we are conducting a phase III, open label, randomized trial in Côte d'Ivoire to compare the standard mass drug administration regimen of annual IVM+ALB (IA) vs. a single dose of Mox+ALB (MoxA) and Mox+DEC+ALB (MoxDA) vs. IVM+DEC+ALB (IDA) in persons with Bancroftian filariasis. The primary study endpoints are Mf clearance at 12 (IA vs. MoxA) or 24 (IDA vs. MoxDA) months post-treatment, as assessed by 1ml filtration of night blood. Secondary endpoints include decrease in circulating filarial antigen (CFA) (based on semiquantitative reading of filarial test strips, FTS) and clearance of adult worms nests in men as assessed by scrotal ultrasound. Enrolment for the study began in August 2020, and to date we have 24-month efficacy data for 66 of 121 (54%) participants infected with >40 Mf/mL of blood at baseline. At 24 months 9 of 19 (47%) participants in the IA arm (after two annual doses) had undetectable Mf compared to 13 of 14 (93%) participants in the single dose MoxA arm (p=0.006). There was no difference in Mf clearance between single dose IDA and MoxDA (81% vs 88% respectively, p=0.576). Adult worm nests were cleared in 2 of 11 (18%) men after IA and 7/8 (88%) of men after MoxA. Sixty percent of men (3 of 5) cleared their worm nests after IDA compared to 100% (9/9) after MoxDA (p=0.171). There was no difference in reduction of CFA between IA and MoxA (11% vs 36%, p=0.08) at 24 months, however more people in MoxDA compared to IDA (53% vs 19%, p=0.041) had reduction in CFA. These preliminary data strongly suggest that MoxA is superior to IA and comparable to IDA and MoxDA for clearance of W. bancrofti microfilaremia and inactivation of adult worm nests at 24-months. Additional 24-month data will be available after August 2023. Additional studies are needed to determine whether MDA with MoxA can accelerate LF in Africa.

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EFFICACY AND SAFETY OF ALBENDAZOLE 400 AND 800 MG ON HYPERMICROFILAREMIC LOIASIS: PRELIMINARY RESULTS OF A PHASE IIB, RANDOMIZED, SINGLE-BLIND CLINICAL TRIAL IN NORTHERN GABON

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Albendazole (ALB) is used safely for the reduction of Loa (L.) loa microfilaremia. However, there is no official recommendation. This molecule could be used routinely in onchocerciasis outbreaks in case of coendemicity with loiasis, in order to make hypermicrofilaremia carriers eligible for mass treatment with ivermectin. The purpose of this study is to compare the efficacy and safety of two ALB treatment regimens in the management of hypermicrofilaremic loiasis. The study was conducted in the Woleu-Ntem region of northern Gabon. Socioeconomic, demographic and clinical data as well as parasitological results were collected on a standardized form. Patients were to be divided into 3 groups: 2 groups of hypermicrofilaremia (≥8000 mf/mL) treated with 400 mg and 800 mg for 30 days and a control group consisting of patients with low microfilaremia (<8000 mf/mL) treated with ALB 400 mg for 30 days. Microfilaremia and adverse events were investigated and monitored weekly until day 30. Of 1363 individuals screened for loiasis, 72 were included and followed for 30 days on daily ALB administration. The control group consisted of 38 patients with microfilaremia less than 8000 who received ALB 400 mg. Of the remaining 34 patients with microfilaraemia greater than 8000 mf/mL, 16 received ALB 400 mg and 18 received 800 mg. L. loa microfilaremia and eosinophilia were measured at day (D) 0, 2, 7, 14, and D30. Clinical data were monitored daily before each ALB dose administration. Microfilaremia decreased at D30 in 82.3% of hypermicrofilaremic subjects to below 8000 mf/mL. No serious adverse events were recorded; 30.0% had clinical manifestations after ALB, and for 20.0%, the main adverse event recorded was pruritus. No difference between the two groups of hypermicrofilaremic patients was observed in the reduction of microfilaremia and the occurrence of clinical manifestations. In conclusion, treatment of hypermicrofilaremic loiasis with ALB dosed 400 mg and 800 mg for 30 days, significantly reduces microfilaremia and can be used for eligibility of microfilariae carriers for mass treatment with ivermectin.

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DEVELOPMENT OF AN ELISA TO DETECT ANTIBODY TO ONCHOCERCA VOLVULUS INFECTION USING A MAMMALIAN EXPRESSED RECOMBINANT ANTIGEN OV16

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The World Health Organization (WHO) recommends serological assessments to document onchocerciasis elimination. National onchocerciasis programs are hindered by the lack of diagnostic tests that meet WHO target product profile (TPP) criteria. One of the tests used by onchocerciasis programs, an ELISA based on the Ov16 antigen expressed in bacteria, has had several challenges when performed in endemic country laboratories. Ov16 produced in bacterial expression systems may have different conformation than the native antigen, may lack posttranslational modifications like glycosylation, and infected individuals may have antibodies to bacterial proteins that are difficult to remove in the Ov16 purification process; any of which could result in decreased assay performance. In addition to the issues related to bacterially expressed protein, the current ELISA takes 7 hours to complete, lacks standardized quality controls and is not available as a commercial kit. We sought to overcome the challenges of the current assay with a new ELISA utilizing a mammalian-expressed protein and decreased time to final result. We engaged a commercial company to express Ov16 in a Chinese Hamster Ovary mammalian expression system and purified the antigen using GST-tag and sizing column chromatography. The resulting 47-kDa purified protein, Ov16m, was used to optimize the ELISA. Using pre-coated and blocked plates, the total assay time was 1.5 hours. We also added a standard curve using a humanized IgG4 monoclonal anti-Ov16 antibody to improve assay comparability. Both sera and dried blood spots (DBS) were used to test the performance of the assay in receiver operating characteristic analysis. The sensitivity and specificity of the assay using 94 negative and cross-reactor sera and 134 Onchocerca volvulus positive sera, confirmed by skin snip microscopy or PCR, were 92% and 100%, respectively. In addition, 39 confirmed positive and 170 confirmed negative DBS were tested, yielding 100% sensitivity and 100% specificity. This Ov16m ELISA satisfies WHO TPP requirements and may be useful for informing programmatic decisions for onchocerciasis elimination.

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LABORATORY EVALUATION OF ONCHOCERCIASIS RAPID DIAGNOSTIC TESTS (RDTS)

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Reliable diagnostic tests are needed to support onchocerciasis programs, especially in low prevalence settings. Recently two target product profiles (TPPs), one for disease mapping and one for stopping mass drug administration (MDA) were developed. The TPPs outline performance characteristics required for new tests, including clinical sensitivity (F60% for mapping and ≥89% for stopping) and specificity (≥99.8% for both). Two antibody detection rapid diagnostic tests (RDTs) developed by DDTD were independently evaluated at CDC. Test A, previously described in 2022, contained Ov16 in one band. Test B included four antigens in two bands: Ov16 and Ov33.3 (band 1) and OvOC10469 and OvOC3261 (band 2); both bands must be visible for a positive result. Tests were performed according to manufacturer instructions using two independent readers. A panel of serum samples (n=146) from persons who were skin snip positive for Onchocerca volvulus by microscopy or PCR was used to evaluate sensitivity. A specificity panel included subpanels of Mansonella perstans and/or Loa loa (n=26), Wuchereria bancrofti (n=50), Plasmodium falciparum and/or P. vivax (n=16), Schistosoma mansoni (n=40), Strongyloides stercoralis (n=9), Rheumatoid factor/Type 1 diabetes (n=20) and North Americans with no history of international travel (n=50). Sensitivity and specificity of Test B were 90.4% and 94.3%, respectively. The two tests were then directly compared on a subset of 20 positive and 150 negative samples, Test A was 90% sensitive and 97% specific, and Test B was 85% sensitive and 92% specific. Both tests met the TPP sensitivity requirements for mapping or stopping MDA but not the specificity requirements. While the specificity issues may arise in part from the choice of biomarkers, it should be noted that nearly all problematic samples were M. perstans+/O. volvulus– but from an O. volvulus endemic country. Based on these data, development of an improved version of Test B is underway. In addition, the results show that to validate any new test for onchocerciasis, there is a need for M. perstans and L. loa samples from areas where O. volvulus exposure can be rigorously ruled out.

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WB5, A NOVEL BIOMARKER FOR MONITORING EFFICACY AND SUCCESS OF MASS DRUG ADMINISTRATION PROGRAMS FOR WUCHERERIA BANCROFTI ELIMINATION

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The success of mass drug administration (MDA) at reducing the prevalence of lymphatic filariasis (LF) in endemic countries has led to an increased need for diagnostic targets designed to monitor for recrudescence and ongoing transmission. While diagnostic targets exist for detecting Wuchereria bancrofti [Wb] and Brugia malayi [Bm] infections, additional targets may increase the sensitivity of these tests. For Wb at least, new biomarkers (in conjunction with Wb123) may be needed to supersede the current WHO recommendations which fail to reflect microfilariae (mf) clearance. Hence, diagnostic tools that reflect the presence/clearance of mf or early infection could be instrumental for not only MDA stopping decisions but also for monitoring. To this end, bioinformatic analyses coupled with stage-specific expression data for Wb and/or Bm resulted in the identification of 12 targets that were: 1) present in Wb and/or Bm; 2) have very little to no homology with proteins from other filariae; and 3) were enriched in the mf or L3 stages. Screening of these 12 antigens by a Luciferase Immunoprecipitation System (LIPS) assay for IgG with serum from Wb-infected (n=170) and uninfected individuals (n=60) identified a single antigen, termed Wb5, that was specific for Wb infections only. Recombinant Wb5 proteins were generated in multiple expression systems for use in a variety of IgG4-based immunoassays. Preliminary screening indicated a very high degree of correlation ($p<0.0001$) between the data derived from LIPS and those determined by more standard immunoassays. To assess if Wb5 could provide additional sensitivity to assays already using IgG4 antibodies to Wb123, head-to-head comparisons were performed using serum from 381 samples (231 Wb-infected; 150 controls). Using IgG4 based immunoassays at 100% specificity, Wb5 and Wb123 had individual sensitivities of 60.2% and 75.3%, respectively, while a combination resulted in 81.0% sensitivity. Moreover, kinetic studies of patients that were treated and followed up longitudinally demonstrated a sharper decline in Wb5 titers compared to Wb123, thus paving the way for Wb5 as a complementary tool to Wb123.

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PROTEIN INVENTORY OF ONCHOCERCA VOLVULUS NEOPLASMS IDENTIFIED BY DEEP VISUAL PROTEOMICS

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The nematode Onchocerca volvulus is the agent of river blindness and targeted by WHO for elimination. The main strategy for elimination is mass administration of ivermectin to endemic populations. The drug is microfilaricidal, but weak macrofilaricidal effects have been reported after many rounds of treatment. A small fraction of adult O. volvulus contain pleomorphic neoplasms, and their development is more common after

ivermectin. We analyzed 428 female worms by histological evaluation of paraffin embedded nodule sections as part of a trial of ivermectin combination treatments. Neoplasms were present in 5.6% of these worms. The purpose of this study was to compile protein inventories of adult worm tissues to identify protein profiles associated with neoplasms. We used digital image analysis of histological sections, laser capture microscopy and highly sensitive mass spectrometry analysis (ThermoScientific, Eclipse). Neoplasm tissue from three female worms was analyzed, and compared with normal tissues from the body wall, uteri and intestine of these worms and also tissues from a healthy female without neoplasm. Unlike healthy females, females with neoplasms did not show any signs of embryogenesis. A protein was called present, if supported by 2 peptides and found in at least 2 of the 3 biological replicates. In worms with neoplasms, we detected 151 proteins in the body wall, 215 proteins in the intestine, 47 proteins in the uterus and 1577 proteins in the neoplasms. The uterus of the healthy female with intact embryogenesis had a high number (1710) of proteins detected that was similar to that of neoplasms. A majority of the 20 most abundant proteins detected in neoplasms was highly conserved, and only two proteins were nematode specific. Proteins that were found in neoplasms but not in the other analyzed tissues included peroxiredoxins, proteases, and proteins related to signal transduction, and ribosomal or proteasome activity. In conclusion, we have successfully used deep visual proteomics to analyze the proteome of individual O. volvulus tissues in nodule sections and identified proteins that are overexpressed in neoplasms.

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ASSOCIATION BETWEEN ALTERED COGNITION AND LOAISIS: FIRST EVIDENCE FROM A CROSS-SECTIONAL STUDY IN A RURAL AREA OF THE REPUBLIC OF CONGO

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Individuals with high Loa loa microfilarial densities are at risk of developing severe encephalopathy after administration of antiparasitic drugs. Recent epidemiological data suggest an increased mortality and morbidity in L. loa infected individuals and a systematic review of atypical cases of Loa loa revealed that many organs appear to be affected by the parasite, including the brain. Apart from these findings, loiasis is still considered benign and studies are mandatory to evaluate the possible neurological morbidity associated with loiasis. We conducted a cross-sectional study to assess cognitive alteration in a population living in a rural area endemic for loiasis in the Republic of Congo. Fifty individuals with high L. loa microfilarial densities (MFD) were matched on sex, age and residency with 50 individuals with low MFD and 50 with no MFD. MoCA (Montreal Cognitive Assessment) tests and neurological ultrasounds were performed for all participants. For the main analysis, individuals with MoCA scores below 23/30 were considered to have altered cognition. Altered cognition was analyzed by L. loa MFD, sociodemographic characteristics and neurological ultrasound results. Mean MoCA score was 15.6/30 (range : 3/30 -28/30). Individuals with more than 15,000 microfilariae per milliliter of blood (mean predicted score:14.0/30) are more than twenty times more likely to have an altered cognition, compared to individuals with no microfilaremia (mean predicted score: 16.3/30). Duration of schooling were strongly associated with better MoCA results. Extracranial and intracranial atheroma were not associated with L. loa MFD with respectively 7 (14.9%) and 13 (13.7%) individuals with atheroma in microfilaremic and amicrofilaremic individuals. Loaisis microfilaremia is probably involved in cognitive impairment, especially when the MFD are high. These results add to the evidence that the burden of loaisis is highly underestimated and highlight the urgent need to better understand loaisis-induced neurological morbidity.

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DEVELOPING NOVEL FLATWORM ION CHANNEL LIGANDS TO TREAT NEGLECTED TROPICAL DISEASES

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Praziquantel (PZQ) is the mainstay for treatment of parasitic flatworm infections. After ~40 years of clinical usage, a putative target for PZQ was identified: a transient receptor potential ion channel in the melastatin subfamily (TRPMPZQ). This channel is conserved across all profiled parasitic flatworm species, and in vitro potency at each ortholog mirrors the known clinical sensitivity of each parasite. Notably, Fasciola spp. are insensitive to PZQ mirroring the lack of activation of Fasciola spp. TRPMPZQ in vitro. It was discovered that there are residues in the binding pocket of TRPMPZQ responsible for the observed differential sensitivity, and this knowledge prompted the development of molecules that could tolerate this variation. Given the increasing resistance of Fasciola spp. to triclabendazole, the discovery of new fasciolicidal targets is timely. Therefore, for proof-of-principle the decision was made to interrogate the druggability of F. hepatica TRPMPZQ (Fh.TRPMPZQ). Employing a target-based screen of >600,000 small molecules against both Sm.TRPMPZQ and then Fh.TRPMPZQ, a series of chemotypes that activate both channels were identified, and the pharmacophore shown to be most potent at Fh.TRPMPZQ was selected for further development. A library of molecules was synthesized to interrogate structure-activity relationships around the core of this molecule resulting in S55, a new molecule with submicromolar potency at both channels. When applied ex vivo to Schistosoma mansoni, S55 produced rapid contraction of the flatworm with concomitant tegument damage, phenocopying PZQ. Likewise, S55 produced an identical phenotype on freshly excised triclabendazole-sensitive and triclabendazole-resistant F. hepatica. S55 was non-toxic in HepG2 assays and is active and well-tolerated in vivo. Given these results, the data show that there is differential druggability among flatworm TRPMPZQ orthologs and demonstrate that Fh.TRPMPZQ is a druggable target that warrants further exploration.

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NOVEL INHIBITORS OF THIOREDOXIN GLUTATHIONE REDUCTASE WITH SCHISTOSOMICIDAL ACTIVITY

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Over 200 million people are infected with schistosomiasis resulting in more than 200,000 deaths annually. Schistosomiasis control strategies rely almost exclusively on mass drug administration (MDA) using praziquantel (PZQ) monotherapy, which is ineffective against juvenile worms. There are currently no available alternatives to PZQ, and few drugs or vaccines are in the clinical pipeline. Of immediate concern are results from MDA campaigns finding that PZQ cure rates are often less than 50%, and the possibility of emergence of PZQ resistant parasites is inevitable. Our aim is to develop new compounds that are effective against different developmental stages and species of the schistosome parasite. We have shown that S. mansoni thioredoxin glutathione reductase (TGR) is essential for worm survival in the mammalian host and druggable. Compounds targeting TGR identified to date are irreversible and/or covalent inhibitors with unacceptable side effects. To identify TGR inhibitors for clinical use, small molecule fragments obtained by X-ray crystallography screening were ligated and partially optimized as first-in-class non-covalent inhibitors of TGR. A first cryo-EM structure of TGR demonstrated that these inhibitors bind at a secondary

site adjacent to the NADPH binding site, blocking enzyme function. All compounds are found to be reversible via jump dilution experiments. These compounds display schistosomicidal activity against cultured worms equal to or better than praziquantel and superior to thresholds set by the WHO. Most importantly, several novel TGR inhibitors demonstrated efficacy against schistosome infections in mice, including treatment targeting juvenile worms, significantly outperforming praziquantel. These findings open a new avenue for the design of non-covalent inhibitors of TGR for the treatment of schistosomiasis.

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HIGH SENSITIVITY BUT LOW SPECIFICITY OF FEMALE GENITAL SCHISTOSOMIASIS SYMPTOMS AND RISK FACTORS DIAGNOSTIC TOOL ON GENITAL LESIONS ASSOCIATED WITH FEMALE GENITAL SCHISTOSOMIASIS IN ADOLESCENT GIRLS AND WOMEN IN MASWA DISTRICT, TANZANIA

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Female Genital Schistosomiasis (FGS) is a clinical feature of urogenital schistosomiasis caused by S. haematobium. Chronic FGS affect the women's reproductive system and even cause irreversible changes. The Liberia Ministry of Health developed the symptoms and risk factors checklist to help healthcare workers at primary healthcare facilities in endemic areas to identify and manage FGS. However, the sensitivity and specificity of the tool were not known. In that view, we hypothesized that the FGS checklist would have high sensitivity and specificity for diagnosis of FGS in women compared to colposcope and hence would improve early diagnosis of FGS among women in Tanzania. A community-based cross-sectional study was conducted among sexually active women at Maswa District. Women with informed consent, who produced 10mls of urine for urine filtration test were recruited and underwent thorough speculum examination by trained gynaecologists using a portable digital colposcopy to capture images of the cervix and vagina. A total of 347 adolescent girls and women aged 18-45 years were screened between October and November 2022. The mean age of women was 30 years (±0.414). Majority of women were aged 25-34, 153/347(44.09%), 186/347(54.07%) contacted fresh water bodies and 313/347 (90.20%) of the women had never used praziquantel. Among the 177 women who underwent a thorough colposcopy examination, the overall prevalence of genital schistosomiasis was 15.82% (28/177). Common FGS features detected were 14/28 (50%) homogenous yellow sandy patches, and 7/28(25%) abnormal blood vessels. The prevalence of urogenital schistosomiasis was 3.48% (13/345) among the study participants. The sensitivity, specificity, positive and negative predictive values of symptom and risk factor diagnostic tools were 85.71%, 8.72%, 15.00% and 76.47% among women who underwent gynaecological examination. Through this observational study, this diagnostic tool has shown high sensitivity but low specificity in diagnosing FGS. Studies with longer follow-ups and larger samples are needed to assess its validity in diagnosing FGS in endemic areas.

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OPTIMISATION OF THE DNA DIPSTICK AS A RAPID EXTRACTION METHOD FOR SCHISTOSOMA JAPONICUM IN INFECTED MICE SAMPLES AND SPIKED HUMAN CLINICAL SAMPLES

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Schistosomiasis remains a public health issue and the need for accurate and affordable diagnostics is crucial in the elimination of the disease. While molecular diagnostics is highly effective, it is expensive, with the main costs been associated with DNA extraction. The DNA dipstick is a rapid, affordable and simple DNA purification method that allows DNA to be extracted from diagnostic samples within 30 seconds. We aimed to optimise the DNA dipstick method for samples from mice and egg-spiked human samples. Urine, blood and faeces were collected from mice exposed to Schistosoma japonicum infection at weekly intervals from Day 0 to Day 42. Urine and faecal samples were collected from volunteer, uninfected humans and spiked with S. japonicum eggs. All samples were subject to several optimisation procedures and DNA extracted with the DNA dipstick. Amplification of the target DNA was carried out using LAMP and visualised using agarose gel electrophoresis and flocculation. The DNA dipstick successfully identified S. japonicum from infected mice and human clinical samples spiked with cracked eggs or genomic DNA from S. japonicum. The DNA dipstick combined with LAMP has huge potential in providing cost-effective, simple and accurate detection of schistosomiasis infection in endemic regions.

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ACCEPTABILITY OF GENITAL SELF-SAMPLING FOR THE DIAGNOSIS OF FEMALE GENITAL SCHISTOSOMIASIS IN HARD-TO-REACH COMMUNITIES

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Female genital schistosomiasis (FGS), caused by the waterborne parasite Schistosoma haematobium, is a debilitating gynaecological disorder that is difficult to diagnose. The 2022 WHO guideline on the control and elimination of human schistosomiasis anticipates that a screen-and-treat approach will be a useful programmatic strategy in certain contexts. We investigated the acceptability of a home-based genital self-sampling strategy for screening in two districts in Ghana. From October 2021 to January 2022, 250 non-pregnant, sexually active women were recruited from the Tain and Yeji Districts after community engagement and documentation of voluntary consent. Women were recruited using lot quality assurance sampling and trained to provide self-sampled cervicovaginal swabs and urine specimens for parasitological analysis. Women were subsequently invited to the community health centre for repeat sampling after a week. The mean age was 26.3±7.6. The prevalence of S. Haematobium ova by urine microscopy was 9.6%. Most participants rated self-sampling to be "very easy" or "easy" (82.4%: n=206), and "painless" (70.4%: n=176) and were confident that the sample was collected as they had been directed (81.2%: n=203). In addition, most women were willing to take another sample for FGS screening in future (96.8%: n=242) and were willing to recommend self-sampling to a close friend or family member by sending a customized text message (89.6%: n=224). Preference for sampling strategy was based on concerns of convenience, privacy and the need for supervision. Key informant interviews uncovered negative partner sentiments regarding genital screening programmes at health facilities in study communities. The self-sampling strategy can be successfully implemented for women in hard-to-reach communities as a patient-centred diagnostic strategy for FGS to improve screening coverage and promote healthcare equity. Opportunities to integrate self-sampling strategies into community health and extension services exist and should be explored in order to accelerate action towards schistosomiasis elimination targets.

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EXPANDING FEMALE GENITAL SCHISTOSOMIASIS LEARNING AND APPLICATION THROUGH AN ONLINE TRAINING FOR MIXED CADRES OF HEALTH CARE WORKERS IN FRANCOPHONE AFRICA

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Female Genital Schistosomiasis (FGS), a tropical disease caused by a parasitic worm (Schistosoma haematobium), is estimated to affect up to 56 million women and girls. It is a leading neglected issue in sexual and reproductive health in sub-Saharan Africa. Women and girls with FGS suffer physiological and social consequences from the infection which is associated with a three-fold increase in the risk of HIV acquisition. Most research on FGS focuses on epidemiology and treatment options. However, little attention is given to effective methods for awareness and education on FGS in healthcare workers (HCWs) and communities. Addressing the FGS knowledge gap in endemic areas is imperative. HCWs are generally unfamiliar with the effects of parasitic diseases on women's reproductive and sexual health as it is not typically included in medical training. FGS is often misdiagnosed and left untreated as symptoms mimic sexually-transmitted infections. HCWs need the expertise and tools to identify and treat FGS. Exacerbating this knowledge gap in Francophone countries, the English language dominates scientific literature and training. Therefore, the scientific community in Francophone Africa is isolated from contributing to and using this knowledge, limiting the uptake of research for decision-making. To help address these gaps, we are implementing an interactive online training in French to increase health capacity for FGS in Francophone countries by (i) training HCWs on FGS and its manifestations and presentations, (ii) supporting HCWs to develop action plans to integrate FGS into their practice and establish a culture of awareness in their local context, and (iii) creating an independent network of HCWs across Francophone Africa, linking them with a broader FGS network across endemic countries. Building a grassroots strategy advances economic and social well-being as it supports opportunities for communities to overcome health and education barriers. This presentation will share lessons from this experience developing a new cadre of Francophone FGS subject matter experts and review the local solutions detailed in the action plans developed.

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THE STATUS OF SCHISTOSOMIASIS AFTER A DECADE OF MASS DRUG ADMINISTRATION IN SIERRA LEONE

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In 2008, schistosomiasis (SCH) was found to be endemic in 14 health districts (HDs) of Sierra Leone. Endemic HDs were classified as low (≥1 and <10%) in the five coastal HDs; moderate (≥10 and <50%) in five HDs; and high (≥50%) prevalence in four HDs. Schistosoma mansoni is present in all nine high/moderate endemic HDs and S. haematobium in three HDs. Annual MDA began in 2009 to target school aged children (SAC) in six high/moderate endemic HDs and was scaled up in 2010 to all SAC and at-risk adults in the nine high/moderate endemic HDs. In 2016, a SCH impact assessment was conducted in the nine HDs; results showed an overall reduction in prevalence from 42.2% to 20.2%. MDA was subsequently revised to a sub-district (chiefdom) level treatment strategy. In 2022, after five rounds of MDA with effective SAC coverage, another school-based impact assessment was conducted in the same nine HDs. The sampling was statistically powered to estimate chiefdom prevalence; a total of 201 sites were selected using probability proportional to estimated population size of the chiefdoms with special consideration for large towns and small chiefdoms. In each site, a total of 24 children aged 5-14 years were tested. Fresh stool samples were examined by Kato Katz. Urine samples were tested by Haemastix with haematuria positive urines only tested by filtration technique. A total of 4,736 (male: 51%, female: 49%) and 4,618 (male: 51%, female: 49%) children were examined for S. mansoni and S. haematobium, respectively. Overall prevalence for S. mansoni was 16.3% (95% CI: 15.3-17.4), for S. haematobium was 2.0% (95% CI: 1.6-2.4), and for any SCH was 17.7% (95% CI: 16.7-18.8). The arithmetic mean intensity for S. mansoni and S. haematobium was 30.0 epg (95% CI: 24.8-35.2 epg) and 4.0 eggs/10ml (95% CI: 3.9-4.1 eggs/10ml), respectively. Of the 201 sites surveyed, 11 (5.5%) had high prevalence of S. mansoni versus 23 of 60 sites (38%) at baseline and 5 of 40 sites (12.5%) in 2016. Although prevalence remains high in a limited number of communities, SCH prevalence in Sierra Leone has overall reduced significantly. A more focused and intensive strategy could help reach Sierra Leone reach SCH control.

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DISCORDANT CIRCULATING AND MUCOSAL ANTIBODY RESPONSES ELICITED BY SARS-COV-2 INFECTION AND VACCINATION IN A LONGITUDINAL COHORT FROM BRAZIL

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The contribution of mucosal antibody responses to protection from SARS-CoV-2 infection and pathogenicity in humans remains understudied. We examined the systemic and mucosal immune responses elicited by varying exposures to infection and/or vaccination among a community-based cohort of urban slum residents from Salvador, Brazil, followed before and during the pandemic. We collected serum, nasal and saliva samples over the course of two sequential surveys (Survey 1, November 2020 to February 2021; Survey 2, July to October 2021) among 1,570 participants. We selected a stratified sample of 137 participants and examined the relationships of antibody responses within and between the serum, nasal, and salivary compartments. Of the 137 participants, 19 individuals were seronegative, 53 were vaccinated and had no serologic evidence of infection, 30 had experienced one infection, 14 had experienced two infections, and 21 had experienced both infection and vaccination. We found that 10/19 (52.6%, 95% CI 29.5-74.8%) individuals who were unvaccinated and seronegative had detectable antibodies in the nasal compartment, and 12/19 (63.2%, 95% CI 38.6-82.8%) had detectable antibodies in the salivary compartment. Furthermore, mucosal IgA responses remained detectable 6 months after infection. An unsupervised hierarchical clustering analysis identified discordance of antibody responses between the serum, nasal, and salivary compartments. Individuals with high serum neutralization activity against the ancestral, Gamma, Delta and Omicron variants exhibited increased and coordinated antibody response in their mucosal compartments compared to individuals with poor serum neutralization activity. Our findings suggest that measurement of serum antibody responses may underestimate the true prevalence of SARS-CoV-2 exposures and the degree of functionally relevant immunity in previously exposed populations. Various sequences of exposure to infection and vaccination can induce effective mucosal antibody responses and confer protection from infection and severe disease.

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DIFFERENTIAL PROTEOME EXPRESSION IN A DIVERSE POPULATION OF HOSPITALIZED PATIENTS WITH COVID-19

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The role of differential proteome expression in the pathogenesis of COVID-19 remains largely undefined, particularly in diverse racial/ethnic groups of hospitalized patients. As such, proteomic profiling of plasma was performed upon the initial phase of hospitalization (≤ 3 days) in a subset of COVID-19 patients (n=40) admitted to the University of New Mexico Hospital, matched according to age, sex at birth, race/ethnicity, time from admission, duration of symptom onset, and time since first PCR-confirmed infection. Patients were stratified as either (a) severe (n=20): defined as admission to the ICU and/or death, or (b) non-severe (n=20): defined as non-ICU requirements and survival. Proteomic analysis was performed using an aptamer-based technology for which 6,628 circulating proteins were quantified. There were 339 differentially expressed proteins (DEPs) at P<0.05 between the groups: 302 were up-regulated and 37 were down-regulated with a log2 mean fold-change between 3.29 to -1.08. Enrichment analyses revealed that the top-ranked pathway maps were Vascular Endothelial Cell Damage (FDR-adj. P=1.136x10-4) and Blood Coagulation (FDR-adj. P=1.370x10-4). Consistent with this finding, Blood Coagulation emerged as a top process network (FDR-adj. P=4.765x10-3). Canonical network analyses revealed IL6-HSP70-IL18R1-BAFF(TNFSF13B)-CCL2 as a central regulatory interaction with TRAF6 as the convergence hub (14 edges) and NF-kB as the divergence hub (13 edges). Collectively, these proteomic results in diverse populations illustrate that endothelial cell damage and coagulopathy are central pathogenic features of severe COVID-19 in which aberrant intracellular responses to protein folding are a substantial component.

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EXTENSIVE TRANSMISSION OF SARS-COV-2 BQ.1 VARIANT IN A POPULATION WITH HIGH LEVELS OF HYBRID IMMUNITY

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The SARS-CoV-2 BQ.1* variant spread globally in late 2022, yet there is limited data available regarding the transmission and disease severity caused by this variant. This study aimed to determine the incidence and severity of BQ.1* infection in a population with high levels of hybrid immunity. As part of a long-term cohort study, we conducted a prevalence survey during the BQ.1* wave between Nov 16th and Dec 22nd, 2022 in Salvador, Brazil. We performed interviews and collected nasal samples for SARS-CoV-2 antigen and RT-PCR testing and whole genome sequencing. Cumulative incidence was estimated by using RT-PCR positivity and cycle threshold values, together with external data on RT-PCR positivity following infection, to estimate daily probability of infection. Of 535 cohort participants, 54% had a documented SARS-CoV-2 exposure and 74% received COVID-19 vaccination prior to the survey. Among these, 79 (14.3%) had a positive SARS-CoV-2 test with BQ.1* identified in 90.7% of positive samples. The prevalence was highest (32.1%) in the week of Nov 23 – 29th, 2022. The cumulative incidence was estimated to be 56% (95% CI, 36 – 88%). Of 79 positive participants, 38 (48.1%) had a symptomatic illness and a lower proportion had fever (37% vs. 51%, p=0.221) and fulfilled the WHO COVID-19 case definition (47% vs. 70%, p=0.023) than cases identified from the cohort in prior Omicron waves. No participants required medical attention. Early exposure to SARS-CoV-2 during the pandemic was associated with a lower risk of infection during the survey (multivariate OR= 0.50, 95% CI=0.25 – 0.97). By reconstructing transmission dynamics from PCR prevalence data, we found that the BQ.1* variant disseminated widely (attack rate of 56%) despite high population-level hybrid immunity. The lower disease severity associated with BQ.1*, as compared with prior Omicron variants, contributed to significant under-reporting of infection. As observed for BQ.1* in this study, hybrid immunity may provide weak protection against future SARS-CoV-2 variants and may not prevent widespread transmission after their introduction.

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PERFORMANCE OF A NOVEL REALTIME-TIME PCR DEVICE FOR DETECTION OF SARS-COV-2, RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA VIRUSES FROM AUGUST 2022 TO JANUARY, 2023

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Real-Time PCR (RT-PCR) is the gold standard for the detection of respiratory viruses. Despite high sensitivity and specificity, RT-PCR method is sophisticated, expensive, time-consuming, laboratory-based and unsuitable for point-of-care (POC) use in resource-limited settings. We evaluated the novel Lab-On-An-Array (LOAA) digital real-time PCR (dPCR) analyzer for the detection of SARS-CoV-2, Respiratory Syncytial Viruses (RSV) and influenza viruses type A and B.A cross-sectional multi-centre hospital-based study was conducted between August 2022 to January 2023 in Ashanti and Savannah Regions of Ghana. Oropharyngeal swabs from 356 patients were tested for respiratory viruses by LOAA and RT-PCR simultaneously. Nucleic acids were extracted using Qiagen Viral Mini kit (QIAGEN Diagnostics GmbH, Germany). LOAA tests were done using LOAA dPCR analyzer and GenoplexorTM COVID-19/Flu/RSV Detection Kit (Optolane Technologies Inc, South Korea) while RT-PCR tests were done using Bio-Rad CFX96 and FluoroType SARS-CoV-2/Flu/RSV kits (Hain lifesciences, Germany). Sensitivity, specificity, accuracy, kappa (κ), positive, and negative predictive values (PPV and NPV) were assessed for LOAA using RT-PCR as the gold standard. Overall positivity rate for respiratory viruses was 106 (29.8%) for LOAA and 116 (32.6%) for RT-PCR. The sensitivity of LOAA to detect RSV was 87.8% (95%CI: 84.1-90.9), SARS-CoV-2 87.5% (95%CI: 84.1- 90.9), influenza B 80.7% (95%CI: 76.5-84.8) and influenza A 75.0% (95% CI: 70.5-79.5). Specificity for LOAA was ≥98.0%. The accuracy of LOAA was 98.9% for SARS-CoV-2, 98.0% for both RSV and influenza A, and 97.8% for Influenza B. The PPV for RSV (97.7%), SARS-CoV-2 (95.5%), Influenza B (92.6%), and Influenza A (69.2%). The NPV was ≥98.0% for all respiratory viruses. There was very good agreement for RSV (κ=0.91), SARS-CoV-2 (κ=0.91), influenza

B (κ=0.85), and substantial for influenza A (κ=0.71).LOAA showed strong diagnostic agreement and comparable accuracy with RT-PCR for detecting SARS-CoV-2, RSV, and influenza B infections and moderate agreement for influenza A in low-resource clinical settings.

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PATHWAYS & MORTALITY OF UNDER 5 CHILDREN IDENTIFIED AS SEVERE CASES WITH ROUTINE PULSE OXIMETRY USED INTO THE INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS GUIDELINES AT PRIMARY HEALTH CENTERS IN WEST AFRICA, JUNE 2021 TO JUNE 2022

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The Integrated Management of Childhood Illness (IMCI) guidelines for children under5 is a symptom-based algorithm, adapted for resource-limited countries at primary health center (PHC) level. To improve the diagnosis & care-management of severe cases with hypoxemia, the AIRE project, UNITAID-funded, has implemented the routine Pulse Oximeter (PO) use into IMCI consultations at PHCs in Burkina Faso, Guinea, Mali & Niger. The purpose of this study was to describe the care pathway & mortality of children with serious illness. In 16 AIRE PHC research sites (4/country), all under5 children attending IMCI consultations with routine use of PO & classified as severe cases were enrolled in a prospective short cohort study with 14-Days of follow-up, with parental consent. From June 2021 to June 2022, 39,360 children attended IMCI consultations at the research PHCs. Among the 3,163 identified as severe cases, 1998 were followed of whom 463 (23.2%) were referred to district hospital (DH) while 1499 (75%) were treated at PHC & 36 (1.8%) were neither referred nor treated at PHC. The D14-mortality rate was at 4.7% (95/1998 - 95% CI: 3.9-5.8). It was significantly different among children managed at hospital level with 14.7% (68/463 - 95% CI: 11.5 -18.2) & those treated at PHC level with 1.3% (19/1499 - 95%CI: 0.8 -2.0). Among the 1998 followed, severe hypoxemia (SpO2<90%) was detected in 142 children of whom 117 (82.4%) were referred at DH vs 17 (12%) treated at PHC. Their D14-mortality rate was estimated at 26.1% (37/142; 95%CI: 19.1-34.1). In conclusion, unexpectedly, referral of severe case to hospital is not systematic even for hypoxemia for whom oxygen therapy was not available at PHC level. The D14-mortality rate remain high especially at hospital level. The proper management of severe case (transfer and oxygen therapy) remain challenges in West Africa.

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IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINES ON PENICILLIN RESISTANT STREPTOCOCCUS PNEUMONIAE

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The use of Pneumococcal Conjugate Vaccine (PCV) has effectively reduced antimicrobial resistance in pneumococci. This study assessed the prevalence of penicillin resistance in carriage pneumococci from children under 2 years old pre-PCV (2006-2008) and after PCV13 (2018-2019) introductions. In this study nasopharyngeal swabs were collected from healthy children <2yo in Lima, Peru before PCV (n=999) and after PCV13 (n=996). We whole-genome sequenced all pneumococcal isolates from the carriers on an Illumina MiSeq. In silico serotype and antimicrobial susceptibility were predicted from the genomes using CDC analysis pipeline. Changes were indicated by odds ratio (OR) and 95% confidence interval using logistic regression. Logistic regression models were adjusted for sex, age, hospital, previous hospitalization, attending daycare, and the number of children at home. The pneumococcal carriage rate was 25% (253/999) in pre-PCV and 19% (193/996) in post-PCV13 period. The prevalence of penicillin-non-susceptible isolate did not change between pre-PCV and post-PCV13 periods (12% vs. 14%, p-value>0.05). However, the odds ratio of penicillin-resistant pneumococcal carriers due to PCV13 vaccine serotypes decreased from 10% to 3% (adjusted OR= 0.29, 95% CI 0.19-0.45; p value <0.001). Conversely, the odds of penicillin-resistant pneumococcal carriers due to non-PCV13 vaccine serotypes increased from 3% to 10% (adjusted OR= 4.64, 95% CI 2.85-7.54, p value <0.001). The PCV has reduced overall penicillin resistance in pneumococci from healthy children in Peru. However, penicillin resistance was observed to increase in pneumococci that are not targeted by PCV13.

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MULTIPLEXED ANTIGEN SPECIFIC ANTIBODY FC PROFILING FOR POINT OF CARE DIAGNOSIS OF TUBERCULOSIS

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Tuberculosis (TB) is a leading cause of infectious disease related deaths despite the existence of effective treatments. Lack of accurate yet rapid and inexpensive diagnostics contributes to a significant proportion of TB deaths. Key challenges in TB diagnostics include the heterogenous spectrum of disease, ranging from latent TB infection (LTBI) to active TB (ATB), and difficulty in obtaining and processing sputum samples, especially from children. Antibody (Ab) titer-based serological tests, which are used as a simple means to detect many infections, have failed for TB. Recently, we and others have observed that the inflammatory state of Mtb-specific Abs, driven by changes in Fc-glycosylation, differs across LTBI and ATB. Here, we report the discovery of a M. tuberculosis (Mtb)-specific Ab Fc profile based biomarker for TB to distinguish ATB from LTBI and a method for its point-of-care (POC) detection using an inexpensive, multiplexed and high throughput optical biosensing method. First, highly multiplexed bead-based Ab biophysical profiling (both Fab and Fc) was applied to sera from a set of ATB and LTBI patients. Antigen-coated barcoded beads were incubated with serum and probed with fluorescently-labeled isotype and subclass probes, tetramerized Fc receptors and lectins. Machine-learning based methods (LASSO-SVM) applied to the resultant high-dimensional dataset, revealed a minimal Ab Fc profile biomarker. Next, a POC detection method was developed where multiple TB antigens (Ag85A, PPD, Esat6, HspX) immobilized on laser cut PDMS microwells, are incubated with drops (<10μL) of TB patient serum. Horseradish peroxidase labelled Fc and lectin probes are added, followed by silver substrates to produce a quantitative and sensitive enzymatic metallization based optical readout which can be read out using a cellphone camera. Application of this to two geographically distinct cohorts of TB patients (South Africa and Vietnam, n=40), achieved a high diagnostic accuracy (AuROC~0.9). Thus, a non-sputum based Ab Fc profile biomarker for TB and a method for its inexpensive yet accurate POC detection from a drop of serum was developed.

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THE IMPACT OF NEXT-GENERATION DUAL-ACTIVE INGREDIENT LONG-LASTING INSECTICIDAL NET DEPLOYMENT ON INSECTICIDE RESISTANCE IN MALARIA VECTORS DURING A THREE-YEAR CLUSTER-RANDOMIZED CONTROLLED TRIAL IN TANZANIA

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Insecticide resistance among malaria vector species is now a pervasive problem, which threatens to jeopardize global disease control efforts. Novel vector control tools, including long-lasting insecticidal nets (LLINs) incorporating new active ingredients (A.I.s), with different modes of action, are urgently needed to delay the evolution and spread of resistance.During a four-arm cluster-randomised controlled trial in Tanzania, evaluating the effectiveness of three dual-A.I. LLINs compared to pyrethroid-LLINs (PY-LLINs), we measured longitudinal phenotypic and genotypic insecticide resistance profiles among 47,258 female Anopheles mosquitoes collected over 36 months. In the PY-LLIN arm, a significant increase in alpha-cypermethrin and permethrin resistance intensity and concomitant decline in mortality, following exposure to the synergist PBO, was observed in An. funestus s.l. (the predominant vector species complex) over 24 months. A similar phenomenon was apparent in the pyriproxyfen-PY LLIN arm over three years, with the greatest escalation in resistance intensity evidenced in the PBO-PY LLIN arm. The chlorfenapyr-PY LLIN arm had no significant effect on pyrethroid resistance, supported by minimal reductions in chlorfenapyr susceptibility. By comparison, An. funestus s.l. populations displayed limited sterility following pyriproxyfen exposure. Highly over-expressed detoxification enzymes presented dynamic patterns of selection throughout the trial. Phenotypic data strengthened trial epidemiological findings; chlorfenapyr-PY LLINs provided superior protection from malaria across multiple transmission seasons, with little impact on insecticide resistance. Rapid fifty-fold pyrethroid resistance intensification in the PBO-PY LLIN arm and pre-existing tolerance of vector populations to pyriproxyfen in the trial site may explain the poorer performance of these two interventions on malaria outcomes. Ongoing work is elucidating potential mechanisms driving cross-resistance between pyrethroids and novel A.I.s, to better inform pragmatic design of resistance management schemes.

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WHOLE GENOME SEQUENCING AND RNASEQ IDENTIFIES POTENTIAL MOLECULAR MARKERS OF INSECTICIDE RESISTANCE WITHIN THE ANOPHELES GAMBIAE SPECIES COMPLEX

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The Anopheles gambiae species complex represents the major malaria vector species across the African continent. Insecticide-based vector control is the single most important tool in combating malaria, with insecticide treated bed nets being the most important intervention. All bed nets contain insecticides from the pyrethroid class leading to widespread insecticide resistance to these chemistries. Despite the importance of tracking the evolution and spread of new and described resistance mechanisms, the number of markers to track insecticide resistance in endemic settings are minimal. Here, we use whole genome sequencing on seven insecticide resistant colony populations from West Africa, a foci of intense insecticide resistance. Within this study 157 individual female mosquitoes from insecticide resistance An. coluzzii, An. gambiae and An. arabiensis were analysed. The results reveal evidence of shared haplotypes between An. arabiensis and An. coluzzii at loci putatively involved in insecticide resistance. Of particular note is evidence of the 'new' kdr mutation I1527T in An. arabiensis which was confirmed using TaqMan analysis. Further, a clear haplotype spanning the GSTE cluster was shared between An. arabiensis and several An. coluzzii populations, including four non-synonymous SNPs in GSTE1 and GSTE8. To determine the impact of these SNPs on pyrethroid resistance, two colonies were generated differing in this haplotype and changes to resistance scored. Finally, the availability of RNAseq data for these populations also allowed elucidation of potential eQTL markers linked with resistance loci.

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EFFICACY OF DUAL-ACTIVE INGREDIENT LONG-LASTING INSECTICIDAL NETS RELATIVE TO STANDARD NETS, AGAINST HIGHLY PYRETHROID-RESISTANT ANOPHELES MOSQUITOES IN TANZANIA: AN EXPERIMENTAL HUT TRIAL

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The global fight against malaria vectors has been threatened by widespread insecticide resistance across multiple chemical classes. There is a need for new vector control tools with different modes of action to combat the issue of resistance. This study aimed to evaluate the bio-efficacy of Olyset Plus (combining PBO and permethrin), Interceptor G2 (chlorfenapyr and alpha-cypermethrin), Royal Guard (pyriproxyfen and alpha-cypermethrin) long-lasting insecticidal nets (LLINs), compared to a standard pyrethroid-only net (Interceptor) across their operational lifespan in experimental hut trials. a total of thirty nets were withdrawn from the community at 12, 24 and 36 months, as part of a large-scale cluster-randomized controlled trial. Hole size and number were recorded. A Latin square design was used to rotate net type and sleepers between huts. The following morning mosquitoes were collected, and mortality monitored every day up to 72 hours. Live, blood fed female Anopheles at 72 hours, collected from the huts with Royal Guard, Interceptor and untreated nets were dissected to assess the effect of pyriproxyfen on egg development. Interceptor G2 LLIN induced significant superior 72-hour mortality compared to standard LLINs at 12 months (43% vs 13%); 24-hour mortality was also higher with Royal Guard LLINs compared to standard LLINs (21% vs 13%), and marginally higher also with Olyset Plus (19%). Seventy-two-hour mortality was still slightly higher at 24 months for Interceptor G2 LLINs compared to standard LLIN (24% vs 11%). None of the other nets showed higher mortality at 24 months. The effect of the second active ingredient or synergist was not observed at 36 months for any of the LLINs. The effect of pyriproxyfen on Anopheles mortality was not observed at any of the time point. All dual active ingredient (dual-A.I.) LLINs performed better than standard Interceptor nets up to 12 months of field use.

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EVIDENCE SUPPORTING DEPLOYMENT OF NEXT GENERATION INSECTICIDE TREATED NETS IN BURKINA FASO: BIOASSAYS WITH CHLORFENAPYR AND PIPERONYL BUTOXIDE INCREASE MORTALITY OF PYRETHROID-RESISTANT ANOPHELES GAMBIAE

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Before deploying alternative insecticide treated nets (ITNs) on a large scale, it is crucial to characterize the resistance profiles of primary malaria vector species for evidence-based decision making. Anopheles gambiae (s.l.) were collected in 2020 from 15 sites located throughout Burkina Faso for synergist and WHO bottle bioassays with chlorfenapyr at a dose of 100µg/bottle. An. gambiae s.l. were found resistant to all pyrethroid insecticides in all sites. The piperonyl butoxide synergist (PBO) pre-exposure followed by deltamethrin restored full susceptibility in one site. The PBO pre-exposure followed by permethrin partially restored susceptibility in 12 sites. There was no significant increase in permethrin mortality after PBO pre-exposure in 3 out of 15 sites; while in Seguenega, Orodara and Bobo-Dioulasso there was a significant increase in mortality. Susceptibility to chlorfenapyr was confirmed in 14 sites. Based on these results, PBO+deltamethrin ITNs would likely provide greater protection than pyrethroid only nets. Since susceptibility in bioassays was not restored in most sites following pre-exposure to PBO, chlorfenapyr ITNs may likely provide greater protection as susceptibility was recorded to chlorfenapyr in nearly all sites. This study provides evidence supporting the 2019 mass distribution of next generation ITNs, such as Interceptor G2 nets and PBO nets, rather than pyrethroid only ITNs

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PHENOTYPIC RESISTANCE TO PYRETHROID ASSOCIATED TO METABOLIC MECHANISM IN VGSC-L995F RESISTANT-ANOPHELES GAMBIAE MALARIA MOSQUITOES

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The indiscriminate use of insecticides in agriculture and public health lead to a selection of resistance mechanisms in malaria vectors compromising vector control tools and strategies. This study investigated the metabolic response in the Vgsc-L995F Anopheles gambiae Tiassalé resistance strain after long-term exposure of larvae and adults to deltamethrin insecticide. We exposed, over 20 generations, Vgsc-L995F An. gambiae Tiassalé strain larvae to deltamethrin (LS) and adults to PermaNet 2.0 (AS) and combining exposure at larvae and adult stages (LAS) and compared to unexposed (NS) group. All four groups were subjected to the standard World Health Organization (WHO) susceptibility tube tests using deltamethrin (0.05%), bendiocarb (0.1%) and malathion (5%). Vgsc-L995F/S knockdown-resistance (kdr) mutation frequency was screened using multiplex assays based on TaqMan real-time polymerase chain reaction (PCR) method. Additionally, expression levels of detoxification enzymes associated to pyrethroid resistance, including CYP4G16, CYP6M2, CYP6P1, CYP6P3, CYP6P4, CYP6Z1 and CYP9K1, and glutathione S-transferase GSTe2 were measured. Our results indicated that deltamethrin resistance was a response to insecticide selection pressure in LS, AS and LAS groups, while susceptibility was observed in NS group. The vectors showed varied mortality rates with bendiocarb and full susceptibility to malathion throughout the selection with LS, AS and LAS groups. Vgsc-L995F mutation stayed at high allelic frequency level in all groups with a frequency between 87% and 100%. Among the overexpressed genes, CYP6P4 gene was the most overexpressed in LS, AS and LAS groups. Long-term exposure of larvae and adults of Vgsc-L995F resistant-An. gambiae Tiassalé strain to deltamethrin and PermaNet 2.0 net induced resistance to deltamethrin under a significant effect of cytochromes P450 detoxification enzymes. These outcomes highlights the necessity of investigating metabolic resistance mechanisms in the target population and not solely kdr resistance mechanisms prior the implementation of vector control strategies for a better impact.

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RNASEQ-BASED GENE EXPRESSION PROFILING OF THE CHLORFENAPYR -RESISTANT ANOPHELES GAMBIAE FROM CAMEROON HIGHLIGHTS DOWN-REGULATION OF MAJOR PYRETHROID RESISTANCE GENES

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Chlorfenapyr (CFP) has shown great promise at controlling pyrethroid-resistant malaria vectors, but its sustained use can be threatened by the evolution of CFP resistance. An understanding of how CFP interacts with other insecticides used in vector control and the molecular basis of CFP resistance is needed to achieve successful malaria control. Here, we assessed the resistance status of the major malaria vectors to CFP across Africa and performed RNA-seq to detect the major genes conferring CFP resistance. Resistance to CFP (100µg/ml) was detected in Anopheles gambiae populations from DRC (Kinshasa) (mortality rate: 64.3 ± 7.1%), Ghana (Obuasi) (65.9 ± 7.4%), and Cameroon (Mangoum ;75.2±7.7% and Nkolondom; 86.1 ± 7.4) whereas all An. funestus populations were fully susceptible. After RNA-seq, commun metabolic genes ussually associated with pyrethroid resistance (e.g: CYPs, GSTs···) were down-regulated in CFP-resistant samples compared to the susceptible lab-strain Kisumu. Carboxylesterases and transcriptions factors were among the predominant over-expressed genes in CFP-resistant mosquitoes with fixed mutations detected and reduced susceptibility observed in the resistant strain. Also, a negative association was observed between the L1014F-kdr mutation and CFP resistance with a greater frequency of homozygote-resistant mosquitoes among the dead after exposure compared to alive (OR=0.5; P=0.02).This study reveals a greater risk of CFP resistance in An. gambiae populations than in An. funestus although most pyrethroid-resistant individuals were more vulnerable to this insecticide. Ongoing functional validation will help to establish the contribution of carboxylesterases and other transcription factors or P450/GST's suppressors to CFP resistance and to design a DNA-based diagnostic tool for the rapid detection and monitoring of the resistant markers in the field. This will help preserve the efficacy of chlorfenapyr-based control interventions such as Interceptor G2 which is currently largely distributed across Africa for malaria control.

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INSECTICIDE RESISTANCE AND WHOLE TRANSCRIPTOME PROFILES OF ANOPHELES FUNESTUS POPULATION IN WESTERN KENYA

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Anopheles funestus is an efficient vector of Plasmodium falciparum malaria in Africa. The resurgence of An. funestus in western Kenya was partly attributed to insecticide resistance. However, there is a limited body of evidence on the molecular basis of pyrethroid resistance in western Kenya. Indoor resting An. funestus mosquitoes were collected by aspiration in Bungoma, Teso, Siaya, Port Victoria and Kombewa in western Kenya. The F1 progenies were exposed to deltamethrin (0.05%), permethrin (0.75%), DDT (4%) and pirimiphos-methyl (0.25%) following WHO guidelines for insecticide susceptibility test. A synergist bioassay using Piperonyl butoxide (PBO) (4%) was conducted to determine cytochrome P450s role in pyrethroid resistance. Illumina RNA-seq was performed on a pool of specimens which were 1) Resistant, 2) susceptible and 3) unexposed to unveil the molecular mechanisms of pyrethroid resistance. Pyrethroid resistance was observed in all the sites with a mortality rate (MR) ranging from 11% to 87%). Port Victoria had the highest level of resistance to permethrin (MR=53%, n=217) and deltamethrin (MR=11%, n=100) pyrethroids. Teso had the lowest level of resistance to permethrin (MR=70%, n=100) and deltamethrin (MR=87%, n=100). Resistance to DDT was observed only in Kombewa (MR=89%, n=100) and Port Victoria (MR=85%, n=100). A full susceptibility to pirimiphos- methyl (0.25%) was observed in all the sites. PBO synergist assay revealed high susceptibility (>98%) to the pyrethroids in all the sites except for Port Victoria (MR=96%, n=100). Whole transcriptomic analysis revealed that the main enzyme families associated with pyrethroid resistance are cytochrome P450s, GSTs, COEs, cuticular proteins and salivary gland proteins. The highly upregulated genes include P450s (CYP4H18, CYP4H17, CYP9J3, CYP4G16, CYP6Y1, CYP18A1, AFUN008357, CYP4D17, AFUN019401 and CYP4C25), GSTs (GSTE2, GSTE1, GSTE5, GSTU2, GSTU3 and GSTD6), and others (AFUN002514, AFUN010203, AFUN016508, AFUN000373 and AFUN001273). This study unveils novel insights into the molecular mechanisms underlying the pyrethroid resistance of An. funestus in western Kenya.

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THE THREE-DIMENSIONAL APPROACHES BY MULTIPLE CORRESPONDENCE ANALYSIS CAN DIFFERENTIATE LEPROSY DISEASE STATES AND HOUSEHOLD CONTACTS WITH HIGH ACCURACY

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The development of clinical leprosy is multifactorial; however, there are still gaps in our knowledge about risk factors and predictors of disease. Multiple Correspondence Analysis (MCA) is a statistical tool that can characterize associations between immunologic and sociodemographic parameters and the presence/absence of M. leprae infection. MCA works based on the reduction of dimensionality and considers each variable as a dimension of space. We conducted MCA on data from 101 participants from Minas Gerais, Brazil: 14 paucibacillary leprosy [L(PB)], 14 multibacillary leprosy [L(MB)], 42 household contacts of PB disease HHC(PB), and 31 household contacts of MB disease HHC(MB). Blood was collected for cytokine measurement and interviews were done to obtain demographic data. The MCA allowed for the disposition and association of laboratory and sociodemographic variables in the Euclidean space with two Dimensions representing more than 40% of the total variability of parameters (Dimension 1 [DM1 = 28.73%, x axis] and Dimension 2 [DM2 = 15.36%, y axis]. Cytokines production from M.leprae-stimulated culture allowed for better discrimination of the study groups, by showing defined clusters according to the operational classification of each group. The cytokine IFN-γ was more associated with (Dim2), as was the L(PB) group (y-axis associated). On the other hand, cytokines IL-4 and IL-10 were more related to (Dim1), in the same way as the L(MB) group, the x-axis associated group. Using these associations, the mathematical model then classified the individuals with an accuracy of 0.8317. The sensitivity and specificity for L(PB) (0.7778, 1.00); L(MB) (0.8333, 0.9550); HHC(PB) (0.8409, 0.9123); and HHC(MB) (0.8519, 0.8919) were respectively, established. By incorporating immunological and demographic parameters in an advanced model, MCA allowed for the classification of leprosy cases and contacts with high sensitivity and specificity. Consequently, this approach holds promise for using these statistical models for predicting disease and complementing clinical diagnosis.

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LEPTOSPIROSIS SEROPREVALENCE AND RISK FACTORS AMONG SLAUGHTERHOUSE WORKERS IN BURKINA FASO

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Leptospirosis is an occupational disease affecting risk groups that are exposed to animal reservoirs. Given the general lack of awareness of the disease and difficulties in its diagnosis, the epidemiological status of human leptospirosis in Burkina Faso has not been well defined. The objective of this study was to determine the seroprevalence and risk factors of leptospirosis among slaughterhouse workers in Burkina Faso. We have performed a cross-sectional survey of slaughterhouse workers from Ouagadougou and Bobo Dioulasso between March and April 2021. Questionnaires were used to collect information from these workers on socio-demographic characteristics, work activities, knowledge of zoonotic diseases, and risk behaviors. Blood was collected by venipuncture and serum samples were tested for leptospirosis using Enzyme-Linked Immuno Assay (ELISA): “SERION ELISA classic Leptospira IgG and IgM”, and Microscopic Agglutination Test (MAT). Of the 172 subjects investigated, 28 (16.28%) were found positive for leptospirosis using ELISA or MAT. The main Leptospira infecting serogroups were: Mini, Autumnalis, Canicola, Copenhageni, L. mayottensis (ND), Icterohaemorrhagiae, Pyrogenes/ Tarassovi (cross reaction), Panama, and Ballum. Risk factors included: residence in Bobo Dioulasso (Odds Ratio ajusté: ORa=2.53; 95% CI: 1.11-15.00; p = 0.02), working at the bleeding station (ORa=5.51; 95% CI: 1.19-29.5; p = 0.03), contact with feces and urine (ORa=2.50; 95% CI: 0.97-6.65; p = 0.04), and the practice of agriculture outside the slaughterhouse (ORa=4.28; 95% CI: 0.79-20.80; p = 0.05). However, working at the stunning station (ORa=3.57; 95% CI: 0.79-15.00; p = 0.08) had a higher risk of Leptospira seropositivity without statistical significance. These findings indicate that a significant proportion of slaughterhouse workers is being exposed to pathogenic Leptospira. Public-health interventions against leptospirosis are needed to target this occupational group.

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LEPTOSPIROSIS OUTBREAK AFTER HURRICANE FIONA, PUERTO RICO, 2022

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Leptospirosis is a bacterial disease endemic to Puerto Rico, which reported 51% of all cases nationally during 2016-2019 and historically reported increased cases after hurricanes. On September 18, 2022, Hurricane Fiona hit Puerto Rico, leading to major flooding. In response, we investigated leptospirosis cases and characterized temporal and spatial patterns. The Puerto Rico Department of Health expanded leptospirosis laboratory testing, increased messaging to providers, and used existing surveillance to investigate cases reported with clinical suspicion for leptospirosis. Confirmed cases had a positive PCR result for pathogenic Leptospira, probable cases only had a positive IgM result, and suspected cases had negative or no laboratory results. We compared cases in the 37 weeks before Hurricane Fiona (January 2-September 17, 2022) and during the 11 weeks after Hurricane Fiona (September 18-December 3, 2022). Before Hurricane Fiona, 173 leptospirosis cases were reported including 16 (10%) confirmed, 90 (52%) probable, and 67 (38%) suspected cases. After Hurricane Fiona, 743 cases were reported, including 31 (4%) confirmed, 84 (12%) probable, and 628 (84%) suspected cases; median age was 41 (interquartile range: 25-59) years, 486 (65%) were male, 375 (50%) were hospitalized, and 6 (1%) died. After Hurricane Fiona, the mean weekly number of confirmed or probable cases was 10.5, 3.6 (95% CI: 2.5-5.3) times higher than before (2.9 cases). Confirmed and probable cases were identified in 42/78 (54%) municipalities before Hurricane Fiona versus 47/78 (60%) municipalities after; 32 municipalities reported cases in both periods. For both periods, the four municipalities with the highest attack rates were western inland municipalities. We identified an outbreak of leptospirosis that lasted >2 months after Hurricane Fiona, using existing surveillance built after previous hurricanes. In endemic areas, health departments should reinforce leptospirosis surveillance and increase clinician awareness, particularly during hurricane season.

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OCULAR CHLAMYDIA TRACHOMATIS INFECTION MONITORING WITHIN DISTRICT-LEVEL TRACHOMA IMPACT AND SURVEILLANCE SURVEYS: RESULTS AND LESSONS LEARNED 2018-2021

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A World Health Organization (WHO) report has recently recommended monitoring for ocular Chlamydia trachomatis (Ct) infection within districts experiencing persistent trachoma. The Trachoma Control Program in Amhara, Ethiopia, has monitored ocular Ct since 2011 to provide prevalence data at the zonal and regional levels. Beginning in 2018, the Program has focused on collecting Ct data to generate district level estimates with the aim of better understanding infection patterns within trachoma persistent districts. Trachoma impact surveys (TIS) and trachoma surveillance surveys (TSS) conducted in the Amhara Region of Ethiopia as part of this study were population-based, multi-stage cluster random surveys. Persistent districts were defined as having ≥2 trachoma impact surveys (TIS2) with a trachomatous inflammation-follicular (TF) ≥5%. Following a household questionnaire, certified graders assessed participants for trachoma signs using the WHO simplified grading system. After grading, children ages 1-5 years were swabbed for infection. All samples were pooled 5 samples to 1 pool and tested using the Abbott Real Time PCR at the Amhara Public Health Institute. Between 2018 and 2021, Ct monitoring was included in 35 TIS and 4 TSS. Among the TIS districts, 34/35 were considered persistent districts (16 TIS2, 17 TIS3, 1 TIS5). A total of 17,534 children ages 1-5 years were swabbed in 1170 communities. Among TIS districts, the TF ranged from 4.1% to 42.6%, and the trachomatous inflammation-intense (TI) ranged from 0.05% to 6.6%. The mean, standard deviation (SD) and range of Ct infection among TIS districts overall was 6.0% (6.8), 0-34.4%, while among districts with TF ≥30% it was 15.2% (10.2), 7.1-34.4%. Among the 4 TSS, 2 districts had Ct infection, 1 district with TF <5% (Ct=1.2%) and 1 district with TF ≥5% (Ct=2.2%). Across all 39 districts, the correlation between Ct and both TF (r=.67) and TI (r=.72) was high. Considerable Ct infection was present among trachoma persistent districts in Amhara. The experience from Amhara demonstrated that with the proper systems and processes in place, monitoring Ct infection at a programmatic scale is possible.

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PHOTOGRAPHIC GRADING OF TRACHOMATOUS SCARRING AMONG ADULTS IN TRACHOMA ENDEMIC AMHARA REGION OF ETHIOPIA

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Trachomatous scarring has been shown to progress regardless of active Chlamydia trachomatis infection, indicating that drivers may be unrelated to ongoing transmission. Scarring prevalence has been associated with older age, and women are more likely to develop signs of severe trachoma such as entropion and trichiasis. This study aimed to characterize the magnitude of scarring in a trachoma endemic setting using a validated 5-point severity scale and to elucidate contributing factors to different stages of scarring. This analysis used conjunctival photographs collected during trachoma impact surveys conducted in 2017 within Amhara, Ethiopia. Photographs of left and right upper tarsal conjunctiva of adults (ages >15 years) in 10 survey districts were collected by a trained photographer. Two graders, trained at Johns Hopkins Hospital and masked to each other's scores, examined each photograph for signs of scarring to record eye-level data based on a 5-point severity scale. Concordant grades were aggregated to the participant level. Discordant grades were adjudicated by another experienced grader. Scarring scores were generated for 729 individuals and 19 individuals were excluded due to poor photograph quality. The mean age of the sample was 38 years and 62.8% were female. Overall, most cases (19.9%) fell within the highest level of scarring category (S4), categorized as scarring comprising more than 90% of the upper tarsal conjunctiva, compared to the prevalence of S3a and b (11%), S2 (8%), and S1 (18.8%). Scarring at every stage was observed among the youngest age group (15-19 years old). Older participants, particularly those over age 60 years, experienced a greater burden of scarring than their younger counterparts, with an S4 prevalence reaching 32.6%. While early stages of scarring were more comparable between women and men, the prevalence of severe scarring (S4) among women was 1.74 times the prevalence observed among men (CI: 1.14-2.7, p<0.01). The prevalence of trachomatous scarring, and its potential for progression to trichiasis, may prove a considerable barrier to achieving the elimination of trachoma as a public health problem.

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IMPACT OF PARTNERS IN SCALING UP THE PREVENTION OF BLINDNESS FROM TRACHOMA IN SOUTH SUDAN

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South Sudan has one of the region's most significant burdens of Neglected Tropical Diseases (NTDs). Out of the 17 NTDs identified by the World Health Organization (WHO), South Sudan harbors 13. Trachoma, an infectious disease caused by Chlamydia trachomatis, is one of the causative agents of preventable, irreversible blindness worldwide. The Ministry of Health (MoH) engaged and collaborated with partners in trachoma surveys, mass drug administration, and trachomatous trichiasis (TT) surgeries to eradicate trachoma. One of the strategies to eliminate trachoma is developing a system that can identify and manage incident TT cases and have the financial resources to implement these strategies. To show the results of the collaborative efforts of the MoH with partners in reducing the backlog of TT in some of the endemic areas, we reviewed the data collected in areas where activities had been conducted by Christian Blind Mission (CBM) project in Unity State (UNS) in Mayom county and Ruweng Administrative Area (RAA) in Abiemnom county, and the Ophthalmological Association of South Sudan (OASS) in Jonglei State (JS) in Old Fangak, Ayod, Akobo, and Waat counties). Out of the 9,632 patients who attended the trachoma program services, 59.5% (5,728) were from JS, 31% (2,988) from RAA, and 9.5% (916) from UNS. TT cases were 21.7% (2,094) of the screened cases, in which the majority, 49.7% (291), were from JS, 36.4% (762) from RAA, and 13.9% (291) from UNS. In addition, a total of 54.3% (2,272) underwent trachoma lid correction surgery, with 53.6% (1,055) in JS, 25.3% (576) in RAA, and 21.1% (479) in UNS. The number of males and females who received eyelid surgery was 74.5% (1,713) and 25.5% (579), respectively. Through collaborative efforts with partners, the MoH has reached a milestone in increasing access to TT surgeries to prevent corneal scarring and irreversible blindness in the affected regions. Urgent scaling up of the program is needed in the endemic/hyper-endemic states with the involvement of different partners, using integrated approaches, capacity building, and community initiatives to reach the global elimination targets for trachoma in South Sudan.

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AN RNA VACCINE FOR PLAGUE

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Plague is a dangerous zoonotic disease which can present in two forms: bubonic and pneumonic. The death rate is 50 to 70 % for the bubonic form and can reach 100 % for the pneumonic form if not treated properly. Despite the threat that this disease poses, no approved vaccine is currently available for prevention. Self-amplifying RNA vaccine for F1 and V antigen of Yersinia pestis were prepared, formulated in 20 % v/v alhydrogel and tested on mice model. Groups of OF1 mice (8/group) were immunized by the intra-muscular route with the saRNA vaccine at 1 µg (group 1 and 4) and 5 µg (group 2 and 5) using 2 immunizations (at day 0, then boost dose at day 28). Results were then compared to a positive control those immunized with a reference vaccine (group 6) and the negative controls which consisted of the injection of equivalent doses of irrelevant RNA in LNP (group 3 and 7) or 20 % v/v alhydrogel (group 8). Immunized mice were challenged with Y. pestis at day 56 (28 days post-boost) at doses of 180 or 1800 cfu and monitored for 14 days. Spontaneous deaths not related to vaccine dose-level and to plague were observed in group 1, 2 , 4, 7 and 8 (1death/group). RNA vaccine protected 5 of 7 mice at either 1µg or 5µg for both of the challenge doses compared to just 1 survivor in the negative control groups (group 3, 7 and 8) and to the reference vaccine which protected 7 out of 8 mice for the challenge at 1800 cfu. Post-mortem culture of the survivor's spleen on CIN agar and BHI broth were negative for Y. pestis. SaRNA vaccine showed protective effect against plague in these preliminary results giving this approach a potential for further development.

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A SALIVA-BASED, DNA-EXTRACTION-FREE APPROACH FOR THE MOLECULAR DETECTION OF STREPTOCOCCUS PNEUMONIAE

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Streptococcus pneumoniae is a common cause of severe diseases including meningitis, pneumonia, and sepsis. Pneumococcal carriage is a prerequisite for pneumococcal disease and surveillance is crucial for evaluating the performance of current vaccines and informing new vaccination strategies. In recent years, molecular methods have improved the sensitivity of pneumococcal carriage detection as compared to the gold standard culture-based method. However, nucleic acid extraction from samples collected is resource-intensive, limiting scalability for extensive surveillance particularly in low-resource settings. We previously developed a saliva-based PCR test for SARS-CoV-2, having identified that nucleic acid extraction can be omitted and replaced with a simple enzymatic lysis or heat treatment step without compromising the accuracy and efficiency of testing. Here, we compared pneumococcus detection in saliva samples collected weekly from an observational longitudinal study in childcare centers in New Haven (CT, USA), using our standard protocol (culture-enrichment followed by DNA extraction) and a DNA extraction-free protocol (addition of proteinase K then incubation at 95°C for 5 min). The presence of pneumococcus was determined by qPCR detection of pneumococcal genes, piaB and lytA, when Ct values <40 for both targets. A total of 754 saliva samples were collected from 92 children (median age 3.65 years; IQR:2.46-4.78). Pneumococcus was detected in 356 (47.2%) samples by the extraction-free protocol and in 367 (48.7%) samples by the culture-enrichment protocol. There was a substantial agreement (Cohen's kappa: 0.62) and a high Ct-value correlation (r=0.92) between the two methods, though the extraction-free protocol reported lower bacterial loads (ΔCt -3.16, $p<0.05$). Our findings suggest that this DNA-extraction-free protocol offers a cost-effective alternative to the resource-intensive culture-enrichment method for pneumococcal carriage detection and offers a sustainable approach for pneumococcal carriage surveillance particularly in resource-limited settings.

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PNEUMOCOCCAL CARRIAGE IN THE SAHEL REGION OF BURKINA FASO BEFORE A 13 VALENT PNEUMOCOCCAL CONJUGATE VACCINATION CAMPAIGN

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Burkina Faso introduced 13-valent pneumococcal conjugate vaccine (PCV13) among infants in 2013 and subsequently achieved more than 90% three-dose coverage nationally. PCV13 coverage in the Sahel region has been substantially lower due to an ongoing security crisis, resulting in reduced access to health services and an increased number of internally displaced persons. In 2022, a PCV13 catch-up campaign was conducted among children aged 9-59 months in the Dori and Gorom-Gorom districts of the Sahel region. We conducted a cross-sectional, age-stratified

pneumococcal carriage study in Dori to describe vaccine-type (VT) carriage before the catch-up campaign. Healthy individuals were recruited into five age groups: 1 month to less than 1 year, 1 year, 2-4 years, 5-14 years, and more than 15 years. We collected nasopharyngeal swabs (participants of all ages) and oropharyngeal swabs (participants age more than 5 years). Each swab was immediately placed in a cryotube containing skim milk, tryptone, glucose, and glycerol, vortexed, and frozen at -80°C until laboratory analysis. Pneumococcal carriage was determined by culture and isolated pneumococci were serotyped by polymerase chain reaction. For this analysis, any serogroups containing PCV13 serotypes were considered VT strains. We evaluated preliminary overall and VT carriage and serotype distribution by age group. Among 1080 participants, overall pneumococcal carriage was 60%; carriage was highest among children 1 year of age (77%) and lowest among participants more than 15 years (32%). VT carriage ranged from 14% (31/217) to 17% (37/215) in the age groups less than 15 years and was 7% (14/213) in participants more than 15 years. Among 691 pneumococcal isolates from all ages, the most common VT were 6A/6B/6C/6D (9%) and 19F (4%); the most common non-VT were 11A/11D (6%) and 21 (6%). These results will serve as the baseline for assessing the impact of the catch-up campaign through future carriage studies and will help inform future strategies to reduce VT carriage in settings with low vaccine coverage and disrupted health services.

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PNEUMOCOCCAL CARRIAGE AND CHANGES IN SEROTYPE DISTRIBUTION AFTER A SWITCH FROM PCV10 TO PCV13 IN CHILDREN IN A RURAL SITE IN MATIARI, PAKISTAN

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In 2021, the 10-valent Pneumococcal conjugate vaccine (PCV10) was replaced with the 13-valent in Pakistan's Expanded Program on Immunization. We aim to study the effect of the switch from PCV10 to PCV13 on the nasopharyngeal carriage in the same population carriage in children under 2 years of age in Pakistan. Children< 2 years were randomly selected from a line listing in two rural union councils of Matiari, Sindh, Pakistan. Nasopharyngeal swabs were collected using standard WHO guidelines by trained staff and were processed at Infectious Disease Research Laboratory at The Aga Khan University, Karachi using culture on sheep blood agar. Whole genome sequencing (WGS) was performed on culture-positive isolates. Analysis was done using Pathogenwatch. The serotypes were then classified as either vaccine type (VT) or non-vaccine type (NVT). Of the 200 children enrolled, pneumococcal isolates were detected in 140 (70%). However, WGS could only be performed in 100 isolates. The proportion of children who had received all 3 doses of PCV13 was 55.0%. Overall carriage remained similar when compared to the pre-PCV13 data from 2018 (70% vs 72.8%). PCV13-specific serotype carriage decreased from 16.6% in 2017/18 to only 5% in the current survey. Thus, we saw a rapid decline in PCV13-specific serotype 18 months after switch to PCV13 from PCV10 with modest vaccine coverage. Most of this decline could be attributed to decrease in serotype 19A. Epidemiology of the prevalent serotypes in a population is extremely useful to guide vaccine introduction in a country.

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ANTIBIOTIC USE AMONG ADULT PATIENTS WITH SEVERE ACUTE RESPIRATORY INFECTION IN TERTIARY LEVEL HOSPITALS ACCORDING TO THE WHO ACCESS, WATCH, AND RESERVE (AWARE) CLASSIFICATION IN BANGLADESH

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Acute respiratory infections, often caused by viruses, are a leading cause of antibiotic use contributing the exponential growth of antimicrobial resistance. To promote rational antibiotic use, the world health organization (WHO) introduced Access, Watch, and Reserve (AWaRe) classification system. We investigated antibiotic use among adult patients with severe acute respiratory infection (SARI) according to the AWaRe classification in Bangladesh. We analyzed data for adult (≥18 years) SARI patients collected during January 2013-December 2022 from the hospital-based influenza surveillance platform at nine tertiary-level hospitals in Bangladesh. Surveillance physicians identified inpatients meeting the WHO-SARI case definition and recorded patient demographics, and antibiotics received during hospitalization. Surveillance tested nasopharyngeal swabs for influenza by rRT-PCR. We used descriptive statistics to summarize the data. We enrolled 17,358 adult SARI patients [median age: 45 years (IQR: 30-60); 64% male]. Of them, 3,045 (18%) had influenza. Of enrolled patients, 14,989 (86%) received at least one antibiotic and 22% received >1 different course of antibiotics. Around 2,547 (84%) patient with lab-confirmed influenza received antibiotics. Most of the antibiotics prescribed were from Watch group (12,149; 81%) followed by Access group (4,791; 32%) and none received Reserve group of antibiotics. The most frequently used antibiotics were ceftriaxone (7,427; 40%), followed by amoxicillin+clavulanic acid (3,823, 21%), azithromycin (2,757, 15%), clarithromycin (1,470, 8%) and cefuroxime (645, 4%). Among these frequently used antibiotics all were from Watch group except amoxicillin+clavulanic which is not recommended by WHO for clinical use. Over four of five adult SARI patients received antibiotics despite a confirmed viral etiology indicating irrational antibiotic use. Predominant use of Watch group antibiotics is also concerning. Strengthening hospital antimicrobial stewardship programs can reduce inappropriate antibiotic use and help mitigating antimicrobial resistance.

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PREVALENCE OF SOIL-TRANSMITTED HELMINTH CO-INFECTION AMONG PERSONS WITH TUBERCULOSIS

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Tuberculosis (TB) remains an enduring threat to human health. In 2021, 10.6 million individuals developed active TB and 1.6 million died of TB. When we map the global distribution of TB, the parts of the globe that light up are overwhelmingly in tropical and sub-tropical areas. Intestinal parasitic infections are also concentrated in these regions and the geographic overlap is striking. An estimated one billion people are infected with soil-transmitted helminths. As such, the probability of intestinal parasitic infections in persons with latent and active TB is high. Very few studies have described the prevalence of parasitic infections in persons with TB (PWTB). A key limitation of these studies is that they used stool microscopy which may have underestimated the prevalence of parasitic infections. The prevalence of intestinal parasitic infections among PWTB in India has not been well documented. The TB LEOPARD study was designed to assess the prevalence of parasitic infections among PWTB in Puducherry and rural areas of Tamil Nadu in India. This study is currently in the recruitment phase. We present preliminary data from this study. Fresh stool samples from 38 persons with TB were collected. After sonication of the stool

specimen, we extracted DNA and conducted multiplex polymerase chain reaction testing for Ascaris lumbricoides, Strongyloides stercoralis, Trichuris trichuria, Necator americanus, and Ancylostoma duodenale. We found that 14 (39.4%) participants tested positive for at least one helminth infection and 3 (7.8%) tested positive for 2 helminths. The most common parasite detected was Necator americanus which constituted 78.4% of the heminth infections. These preliminary data are intriguing as the prevalence of helminth infections considerably exceeds the expected rate of helminth infection (20-30%) for the general population. Future studies should assess the significance of asymptomatic carriage of helminths among PWTB given the potential impact of parasitic infections on the immune response to TB. Additionally, the value of systematic screening and treatment of helminths for PWTB in India should be assessed.

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ASSESSING PROGRESS TOWARDS THE WORLD HEALTH ORGANIZATION TARGET OF ZERO CATASTROPHIC COSTS DUE TO TUBERCULOSIS BY 2035

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When the total of household expenditures and lost income due to tuberculosis (TB) exceeds 20% of pre-illness annual household income these costs are termed 'catastrophic' because it is unlikely that it will allow treatment completion to be affordable. The World Health Organization End TB strategy prioritizes the target of zero catastrophic costs. Costs due to TB have been assessed by repeatedly surveying patients throughout treatment about their recent costs; or by asking patients once at the end of treatment to recall all costs due to TB over more than 6 months since their illness began. There is little evidence comparing these strategies. The optimal approach depends on how long patients with TB can reliably remember their costs. To address this important research question, 174 patients newly diagnosed with TB recalled their recent pre-diagnosis costs due to TB to have been USD$=437 (IQR=95-1450). Then, 6 months later, without being reminded of their previous answers, patients again recalled these pre-diagnosis costs to be median USD$=660 (IQR=100-1880). Between both assessments, the Spearman correlation coefficient was 0.68, ($p<0.001$). The costs due to TB during treatment were median USD$782 (IQR=210-3200). Pre-illness annual household income was median USD$=15,960 (IQR=10,200-24,000). Thus, if pre-diagnosis costs due to TB were assessed recently at the time of diagnosis then catastrophic costs due to TB affected 34% of households (95% confidence interval, CI=27-42, 60/174). This was not significantly different (P=0.5) if pre-diagnosis costs due to TB were assessed later at the time of treatment completion then catastrophic costs due to TB affected 38% of households (95% CI=31-45, 66/174). Thus, patients with TB can usually reliably recall costs due to TB for many months, and catastrophic costs due to TB can be reliably assessed with a questionnaire applied only once at the end of treatment.

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THE EPIDEMIOLOGICAL SHIFTS OF DRUG-RESISTANT TUBERCULOSIS IN SABAH, EAST MALAYSIA DURING THE COVID-19 PANDEMIC: A 6-YEAR REVIEW OF THE GAINS AND LOSSES FROM 2016 TO 2021

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As the world's oldest pandemic, TB has been the world's leading cause of death by a single infectious agent, usurped only by Covid-19 in 2020 and 2021. In 2019, TB incidence in Malaysia was at 92 per 100,000 people, with an "upper-moderate" categorization. These cases were not evenly distributed, with the eastern-most state of Malaysia, Sabah, reporting 135 cases per 100,000 in the same period, qualifying as an endemic region. There is an evidence gap on the burden of multidrug-resistant TB (MDR-TB) in Sabah, we aim to describe the epidemiology and clinical characteristics of MDR-TB to inform public health measures. All cases of TB between 2016 to 2021 from the state TB registry was reviewed, with a focus on MDR-TB. The impact of Covid-19 was evaluated by designating 2016-2019 as pre-Covid, and 2020-2021 as Covid years. Factors under investigation include age, citizenship, and other indicators. A descriptive analysis of characteristics and logistic regression of variables associated with poor MDR-TB treatment outcomes was done using R software. Sabah reported an average of 5027 TB cases annually pre-Covid, declining by 10.3% to 4508 per year during Covid. Within study period, there were 97 MDR-TB cases, with median age of 38 years, and 33% of these being non-citizens (n=32). The proportion of notified MDR-TB cases in Sabah was 0.27% of all TB cases pre-Covid, but rose to 0.47% of all TB cases reported during Covid years. A marked increase in MDR-TB cases means the actual burden remains unknown. The proportion of MDR-TB cases treated successfully decreased from 60% to 24% between pre-Covid and Covid periods (OR=3.45, $p<0.01$); in this time, proportion of non-citizens who successfully completed MDR-TB treatment decreased from 47.4% to 10.0% ($p>0.05$). Improving adherence to MDR-TB treatment and adequate management of side effects could reduce likelihood of poor outcomes. While the proportion of MDR-TB in Malaysia and the state of Sabah remains relatively low compared to endemic countries, vigilant surveillance is needed to detect, isolate, and treat new cases to prevent future outbreaks.

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MALARIA IN CAMEROON: A RETROSPECTIVE ANALYSIS

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The Cameroon National Malaria Control Programme (NMCP) sought to understand the epidemiological situation and to assess the impact of malaria control interventions deployed over the period 2015 to 2020. Using DHIS2 data and programmatic data from the NMCP, key malaria indicators - on incidence, mortality rate, case management and preventative interventions were analyzed at the regional and district level, disaggregated by demographic group. The impact of seasonal malaria chemoprevention (SMC) was also assessed using differences in differences analysis to compare districts receiving SMC to adjacent districts not receiving SMC. Malaria incidence had an upward trend with the Centre region seeing the greatest increase, with higher incidence in pregnant women across all regions compared to other groups. Mortality decreased over the study period at the national level, however some regions still had more than 100 deaths per 100,000 in the under 5's, namely the North, Extreme North and Adamoua. For case management there was a large improvement in testing rates in health facilities increasing to over 80% in most districts by 2020 with test positivity rate increasing to above 50% in most districts. Treatment of simple malaria with first-line ACT was over 50% nationwide by 2020, and the proportion of severe malaria cases receiving third-line treatment quinine increased, with second-line treatment artemether decreasing. In terms of the impact of SMC, the 2016 and 2017 campaigns had a statistically significant impact, decreasing under 5 incidence, however this effect was not seen in later campaigns. The results highlight the efforts of the NMCP to reduce the malaria burden across the country and the heterogeneous epidemiology of malaria across regions. Focus on protecting vulnerable groups such as pregnant women and children under 5 from malaria illness must continue. SMC has had a positive impact in reducing malaria illness in the under 5's and there should be more research to assess factors that could be limiting the effectiveness of SMC in later years as there could be scope to expand the geographical reach of the intervention or expand to the over 5's.

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QUANTIFYING THE IMPACT OF MALARIA IN PREGNANCY ON MATERNAL ANEMIA AND ITS ASSOCIATED BURDEN ACROSS AFRICA

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Plasmodium infection during pregnancy causes maternal anemia but quantitative estimates of the burden of malaria on maternal anemia are lacking, in part because the impact of untreated infections cannot be ethically measured. To address this gap, we used individual-level data on hemoglobin (Hb) concentrations and malaria PCR status at enrolment into 4 recent trials of alternative approaches to malaria prevention in pregnancy, involving 12,608 women in seven countries (Burkina Faso, The Gambia, Ghana, Kenya, Malawi, Mali, and Tanzania). We developed a Bayesian inferential framework to account for the various exclusion criteria of the trials, using data on gestational age at enrolment as a proxy measure for the length of time an infection was left untreated to capture Hb dynamics up to the end of the second trimester (T2). We estimate that among primigravid women, reductions in Hb associated with malaria infection increase throughout gestation, reaching a reduction of 1.24 [95% Credible Interval (CI) 1.13, 1.36] g/dL at the end of T2. Accounting for concomitant declines in Hb throughout gestation in non-infected women, we estimate that, in primigravidae with ongoing infection, the risk of malaria-associated severe anemia (Hb < 7 g/dL) increases from 2.2% [95% CI 1.1-3.5] to 14.3% [95% CI 10.8-17.9] between the ends of the first trimester (T1) and T2. The impact of malaria upon Hb in multigravid women varied by transmission intensity, with the impact similar to primigravidae in areas of lower prevalence but increasingly diminishing in areas of higher transmission, following well-understood patterns in acquisition of pregnancy-specific malaria immunity. Using modelling, we estimate that among women who have experienced infection in one previous pregnancy, the reduction in Hb concentration associated with ongoing infection at end of T2 is 0.38 [95% CI 0.21, 0.55] g/dL, and no reduction in Hb concentration in any subsequent pregnancies. Using this framework, we will extrapolate the associated burden across Africa using estimates of fertility and malaria endemicity collated by the Malaria Atlas Project and the World Health Organization.

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A GLOBAL MALARIA CASE-MANAGEMENT MODEL CASCADE WITH AN INTERACTIVE TOOL FOR POINT-OF-CARE CONSUMPTION ANALYSIS

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Quality malaria case management is essential for preventing severe disease and death, both from malaria and other severe illness. In preventative intervention mix planning, consensus has emerged that data-driven decision making - supported by models - is necessary for optimal allocation of resources. But limited evidence exists on the (relative) impact of each component of the post-infection care cascade on population-level outcomes. This work represents a step towards treating post-infection intervention policy planning with the same rigour as preventative interventions. Here we present an interactive online tool, using which policy-designers can easily explore the impact of case-management policy initiatives on coverage and consumption of malaria drugs and diagnostics. Retaining the ease of 'back of the envelope' calculations, our tool captures nuances including community-based positivity rates and the age structure of symptomatic malaria. For such scenario analysis to be worthwhile one must first estimate the status quo in absolute terms. We have developed a complete case-management modelling framework which produces estimates for each step in the logical flow through the health-system: an individual developing symptoms; seeking medical advice; receiving a diagnostic test; and, finally, being treated with an antimalarial. The natural conditionality here poses challenges to quantifying coverage - both routine and survey data suffer from increasingly small sample sizes, variations in interpretation, and recall biases. Our framework is statistical, leveraging multiple sources of data including cross-sectional surveys and a comprehensive literature review, and provides baseline estimates of point-of-care malaria commodity consumption across 75 malaria-endemic countries reflecting an estimated 448mil RDTs consumed in public-sector clinics in 2021, and 314mil ACTs, of which 75% were consumed in malaria-endemic Africa.

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MALARIA AS A RISK FACTOR FOR COVID-19 IN WESTERN KENYA AND BURKINA FASO (MALCOV)

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It is unknown whether malaria affects COVID-19 severity or duration. We conducted a cohort study in newly diagnosed COVID-19 patients of all ages in western Kenya and Burkina-Faso. Participants were screened for SARS-CoV-2 using rapid antigen tests. Patients co-infected with Plasmodium falciparum malaria were treated with 3-day artemether-lumefantrine or pyronaridine-artesunate. COVID-19 disease progression was assessed daily by Flu-Pro+ questionnaires until day 14 by mobile phone or at clinic visits. Nasal swabs and blood samples were taken on days 1, 3, 7, 14, and 28. SARS-CoV-2 and viral load were assessed by RT-PCR. All analyses were adjusted for enrolment age, disease severity, and viral load. From February 2021 to January 2022, 708 COVID-19 patients were enrolled; 139 (20%) had malaria. Malaria patients were younger: 43/139 (31%) were aged <15 yrs vs 31/569 (5%) without malaria (P<0.0001). SARS-CoV-2 clearance in the first week was slower among malaria patients (aHR=0.59 95% confidence interval 0.45-0.76, p<0.001). By day 7, 71/131 (54%) and 319/481 (66%) had cleared SARS-CoV-2 in the malaria and non-malaria group (adjusted RR=0.90, 0.78-1.04, p=0.2) and this was 118/132 (89%) and 418/468 (89%) by Day-14 (aRR=0.98, 0.79-1.21, p=0.90). There were no differences in viral load on Day-7. Patients with malaria were more likely to have moderate-to-severe disease at enrolment (all ages: 70% vs 60%, aRR=1.25, 1.09-1.41, p<0.001; <15 years: aRR=1.61, 0.97-2.95,

p=0.085; >=15 years: aRR=1.23, 1.06-1.39, p=0.002), but the time to clearance of moderate-to-severe symptoms (aHR= 1.04, 0.85-1.28, p=0.7) and duration of any symptoms were similar (aIRR=1.01, 0.89-1.16, p=0.8). Overall, 3 (2.0%) and 7 (1.2%) patients with and without malaria had to be hospitalised, and 2 (1.3%) and 3 (0.5%) died. Patients co-infected with SARS-CoV-2 and P. falciparum malaria were more likely to have moderate-to-severe disease at enrolment. SARS-CoV-2 clearance was slower in malaria patients, but malaria did not affect COVID-19 disease progression or the duration of illness after successful antimalarial treatment of malaria.

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PREVALENCE OF MALARIA INFECTION AND COVERAGE OF KEY CONTROL INTERVENTIONS AMONG SEASONAL MIGRANT WORKERS AT FARM SITES AND SURROUNDING RESIDENT POPULATIONS IN NORTHWEST AMHARA REGION, ETHIOPIA

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In many malaria-endemic countries, population mobility presents a key challenge to malaria elimination efforts due to the potential importation of infection. In Amhara Region, Ethiopia, the expansion of large-scale agricultural development in lowland areas attracts close to half a million seasonal migrant workers annually, mainly from highlands where malaria transmission is low. These groups are at a higher risk of malaria due to poor living conditions, and behavioral and occupational factors at farms. A cross-sectional study was conducted to estimate the prevalence of malaria infection and coverage of key interventions among seasonal migrant workers and the surrounding resident population in the Delello farm site, Metema District, northwest Amhara Region in October 2022 following the major rainy season. Through multistage cluster sampling, 1,900 seasonal migrant workers from 32 farms and 1,001 residents from 15 hamlets were randomly selected and tested for malaria using rapid diagnostic tests (RDTs). Dried blood spots (DBS) were collected for molecular analysis. Half (50.4%) of participants in the resident population were male, compared to 96.8% of the seasonal migrant workers. Malaria infection prevalence by RDT was 19.5% [95% CI: 17.8-21.4] in seasonal migrant workers, and 8.5% [95% CI: 6.9-10.4] in the resident population. Only 8.0% [95% CI: 6.9-9.3] of seasonal migrant workers and 74.2% [95% CI: 71.4-76.8] of the resident population owned mosquitoes net, and 6.5% of seasonal migrant workers and 68.4% [95% CI: 64.9-71.6] of the resident population slept under a net the previous night. The proportion of households covered with indoor residual spraying in the last 12 months was 76.1% [95% CI: 70.2-81.1] among the resident population, whereas seasonal migrant workers slept in un-sprayable structures or worked outdoors at night. These results indicate high malaria prevalence and low coverage of vector control interventions among seasonal migrant workers and suggest the need for targeted interventions to reduce the malaria burden in these populations and the potential importation of infection in low-transmission areas.

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MALARIA SEROEPIDEMIOLOGY IN VERY LOW TRANSMISSION SETTINGS IN THE PERUVIAN AMAZON

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Peru is on track to malaria elimination, due to control programs such as the Zero Malaria Plan (2017) and the National Malaria Elimination Plan (2022). However, measuring malaria exposure in low transmission areas remains essential to gain insight in these contexts and achieve elimination. This study aims to determine malaria exposure and associated risk factors according to distance to facility as a proxy for access to care in two very low transmission areas of Loreto. A cross-sectional analytical study was conducted in 38 communities in Indiana and Belen districts. Standardized questionnaires were applied to capture socio demographic and behavioural information, households were geo-referenced and blood samples were collected for serological and molecular analysis. Local Getis-Ord Gi* statistic was performed to identify clusters of households with high (hotspots) or low (coldspots) seroprevalence. A total of 4000 individuals were analyzed across both districts. Our findings show an overall malaria seropositivity of 9.3% (95%CI: 8.4%-10.2%). We also found a seropositivity level to any exposure (recent or historical) of 2.5% (95%CI: 2.0%-3.0%) and 7.8% (95%CI: 7.0%-8.7%) for P. falciparum and P. vivax, respectively. The seropositivity trend in P. Vivax changed in the [40-50) age group ($\beta 1 = 0.04$, $p = 0.003$), while in P. Falciparum occurred in the [50-60) age group ($\beta 1 = 0.004$, $p = 0.010$). Moreover, distant and extra distant villages were more exposed to any malaria (recent or historical) than those classified as proximate (DSCFdistant = 16.29, p<.001; DSCFextra distant = 18.86, p<.001) and moderate (DSCFdistant = 10.48, p<.001; DSCFextra distant = 12.53, p<.001). The spatial analysis showed that cold spots were located mostly in the center of Belen district, while hot spots were located on the border, and hot spots were located near the Amazon river in Indiana. Higher concentrations of malaria exposure were found in more distant communities. This information may be useful for the redesign of control strategies focused on distant subpopulations to improve malaria surveillance and continue on the path to elimination.

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CAUSES OF DEATH AMONG INFANTS AND CHILDREN ENROLLED THROUGH THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) NETWORK

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Globally, 2.8M deaths occur yearly among children aged 1-60 months (53% of all deaths in children <5 years). Detailed characterization of childhood deaths could inform interventions to improve child survival. The Child Health and Mortality Prevention Surveillance (CHAMPS) Network conducts childhood mortality surveillance in sub-Saharan Africa and South Asia using innovative postmortem minimally invasive tissue sampling (MITS). We describe the causes of child deaths across CHAMPS sites in 7 countries. From 2016 to 2020, 632 MITS (331 in 1-11 months; 301 in children 12-59 months) were completed on decedents. Expert panels determined locally the underlying, intermediate, and immediate conditions in the chain of events leading to death, based on histopathology, microbiological diagnostics, clinical data, and verbal autopsies. The six most common underlying causes of death were malnutrition (104; 16.5%), HIV (75, 11.9%), malaria (71, 11.2%), congenital birth defects (64, 10.1%), lower respiratory tract infections (LRTI; 53, 8.4%) and diarrheal diseases (46; 7.2%). Infection was present in the causal chain in 549/632 (87%) of deaths with Klebsiella pneumoniae (155/549, 28.2% of all infectious deaths; 82% considered nosocomial) Plasmodium falciparum (122/549; 22.2%) and Streptococcus pneumoniae (109/549; 19.9%) being the commonest pathogens contributing to infectious deaths. Cytomegalovirus (57; 10.4%) or Acinetobacter baumannii (39; 7.1%; 35/39 [89.7%] considered nosocomial), also played important roles. Expert panels considered 78% (494/632) of all deaths preventable and 4% (26/632) preventable under certain conditions. CHAMPS results show that, in high-mortality settings, infectious diseases continue to cause most deaths in infants and children, often in conjunction with malnutrition. Results highlight opportunities for action to prevent fatalities and reveal common interactions of various etiologies in the path towards death. The previously unrecognized significance of pathogens such as Klebsiella pneumoniae and cytomegalovirus highlights the need to focus on them to improve child survival.

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INFANT MORTALITY AND GROWTH FAILURE AFTER ORAL AZITHROMYCIN AMONG LOW BIRTHWEIGHT AND UNDERWEIGHT NEONATES

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Biannual mass azithromycin distribution has been shown to reduce all-cause child mortality, with the largest effects in children aged 1 to 11 months, who have the highest mortality rates. Low birthweight (birthweight <2500 grams, g) and underweight (weight-for-age Z-score, WAZ, < -2) infants have higher risk of poor outcomes compared to their well-nourished peers. Interventions to improve growth and reduce mortality must not interfere with breastfeeding. If effective, azithromycin could represent an easily implementable intervention for infants. We evaluated the role of azithromycin for reducing mortality and improving growth outcomes in low birthweight and/or underweight infants in Burkina Faso. Infants aged 8-27 days of age weighing ≥2500 g at enrollment in Burkina Faso were randomized 1:1 to a single, oral dose of azithromycin (20 mg/kg) or matching placebo. Birthweight measurements were extracted from each child's government-issued health card. We evaluated mortality and anthropometric outcomes in four subgroups: 1) both low birthweight and underweight at enrollment; 2) low birthweight-only; 3) underweight-only; 4) neither low birthweight nor underweight. Of 21,832 enrolled infants, 21,320 (98%) had birthweight measurements and included in this analysis. Of these, 747 (3%) were both low birthweight and underweight, 972 (5%) were low birthweight-only, 825 (4%) were underweight-only, and 18,776 (88%) were neither low birthweight nor underweight. Infants who were both low birthweight and underweight receiving azithromycin had lower odds of underweight at 6 months compared to placebo (OR 0.65, 95% CI 0.44 to 0.95), but the treatment group by subgroup interaction was not statistically significant (P=0.06). We did not find evidence of a difference between groups for other outcomes in any subgroup. In conclusion, azithromycin may have some growth-promoting benefits for the highest risk infants, but we were unable to demonstrate a difference in most outcomes in low birthweight and underweight infants. As a secondary analysis of a trial, this study was underpowered for rare outcomes such as mortality.

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EFFECT OF A SINGLE DOSE OF PROPHYLACTIC AZITHROMYCIN TO INFANTS ON FECAL CARRIAGE OF ENTEROPATHOGENS IN PAKISTANI INFANTS

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Azithromycin (AZ), a macrolide, is recommended by the World Health Organization (WHO) for mass drug administration (MDA) in low-middle-income countries (LMICs) for treatment of infections. MDA-AZ improves child survival and may have a role in improving infant growth outcomes. Concerns about antimicrobial resistance gene (ARG) carriage and enteropathogen burden remain even in antibiotic naïve infants. The study aimed to assess AZ impact on ARG carriage and enteropathogen burden in 8-week-old infants. Mumta study was a 1:1:1 randomized controlled trial of malnourished lactating women (LW) and their infants (n=957 dyads). Interventions were lactation counseling (LC) only, LC and balanced energy protein (BEP) sachet for the mother, and LC, BEP with one dose of AZ to the infant at day 42 of birth. Fifty infants from each arm were randomly selected for biomarker and microbiome analysis at day 56 of birth. Enteropathogen burden and ARG carriage were assessed using a customized TaqMan Array Card (TAC). There was no difference between enteropathogen burden in healthy infants who received AZ and those who did not. Enteropathogen count in infants was strongly associated with mothers (p<0.001) even at 8 weeks after birth, regardless of place, mode of delivery and exclusive breastfeeding. In our study of 150 infants, 91.3% of infants were positive for ARG CTX-M type extended-spectrum β-lactamases. The prevalence of fluoroquinolone resistance genes with the gyrA mutation was 66.7%, and the parC mutation was 45.3%. There was no difference between ARG carriage between infants who received AZ and those who did not. Factor analysis of TaqMan data showed three distinct factors: the Campylobacter family, E. coli family, and ARGs (CTX-M, gyrA, and parC types). Enteropathogen count was predicted by an increase in three infant EED biomarkers MPO, LCN-2 and CALPR, and CRP. In conclusion, we show early vertical transmission of enteropathogens in infants, with substantial antimicrobial carriage irrespective of AZ use. Our study lends insight into mechanistic pathways for AZ action in low-resource malnourished settings.

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EVALUATING THE ACCURACY OF INTERVA-5 AND INSILICOVA ALGORITHMS IN DETERMINING THE LEADING CAUSES OF MORTALITY IN INFANTS AND CHILDREN UNDER-5 IN WESTERN KENYA

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Verbal autopsy (VA) guides public health priorities in communities where physician certification of deaths is largely unavailable. VA has been frequently validated against physician coding of causes of death (CoD), but none have done so with CoDs rigorously determined from multiple data sources, including minimally invasive tissue sampling (MITS) and post-mortem laboratory and pathology testing. Child Health and Mortality Prevention Surveillance (CHAMPS) investigates causes of death in children under 5 using MITS, post-mortem laboratory and pathology testing, VA, and clinical and demographic data in seven countries. The CHAMPS Determination of Cause of Death (DeCoDe) expert panel analyses all available data, and ascertains the immediate, underlying and other antecedent causes of death. We compared results of the VA algorithms InterVA-5 and InSilicoVA to the CHAMPS-Kenya site DeCoDe CODs in children 1 to 59 months of age. InterVA and InsilicoVA had closer agreement with each other than with DeCoDe. The highest agreement across three systems was for malaria as a cause of death (Kappa=0.29 [CI:0.17-0.41]). Both VA systems indicated that gastroenteritis and 'other causes' were in the top five causes of death (24.3% and 15.3% respectively) but had low agreement on meningitis (15.8% and 5.0%), which wasn't detected by DeCoDe in any cases. DeCoDe indicated malnutrition was responsible for 26.6% of deaths, while the VA algorithms indicated this as causing 2.7% and 3.2% of deaths. Both InterVA-5 and InsilicoVA underestimated malnutrition, malaria, sepsis and HIV disease. InterVA-5 overestimated diarrheal diseases and InsilicoVA overestimated respiratory infections including pneumonia. The VA algorithms performed suboptimally in determining the leading causes of mortality, likely because they cannot accurately differentiate between conditions with similar symptoms and because recall bias may confuse results where no medical records exist. Our findings underscore the importance of maintaining gold standard surveillance systems in countries where VA is widely relied on and to use rigorous results to validate and refine VA algorithms.

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IDENTIFYING RISK FACTORS FOR MATERNAL NEAR MISS AMONG RURAL PREGNANT WOMEN ADMITTED TO A TERTIARY PUBLIC HOSPITAL IN BANGLADESH: A CASE-CONTROL STUDY

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Maternal near miss (MNM) refers to women who experienced complications during pregnancy, childbirth, or within 42 days of termination and narrowly escaped death. The Child Health and Mortality Prevention Surveillance (CHAMPS) network is conducting health and demographic surveillance in Baliakandi, a rural sub-district of Bangladesh and tracking each pregnancy and its outcome. We studied risk factors and pregnancy outcomes of MNM in women from Baliakandi admitted to Bangabandhu Sheikh Mujib Medical College Hospital (BSMMCH), a tertiary-level hospital. We conducted an unmatched case-control study using WHO clinical and laboratory criteria for MNM to identify cases and randomly selected women from Baliakandi who gave birth without experiencing significant morbidity at BSMMCH in 2022 as controls using a 1:1 ratio. We examined demographic, obstetric, and treatment-related characteristics using multivariate logistic regression controlling for age, education, and parity. HDSS 2022 data recorded 5930 pregnancy outcomes in Baliakandi; 219 got admitted to BSMMCH, 62 experienced MNM, and controls shared similar demographic profiles to cases. Hypertensive disorders (60%) and obstetric hemorrhage (32%) were common admission complaints of MNM cases compared to 2% hypertensive disorders and 5% obstetric hemorrhages in controls. No antenatal care (ANC) (adjusted odds ratio [aOR]: 3.23, 95% CI: 1.73 - 6.38) and >4 hours delay in seeking care from the onset of the complaints (aOR: 1.89, 95% CI: 1.10 - 3.37) was associated with a higher risk of MNM. No significant association with age and parity with MNM was found. Most (88%) MNM cases and half (58%) of controls were referred from other healthcare facilities. MNM was significantly associated with increased risk of stillbirth (aOR: 5.8, 95% CI: 2.27 - 16.95, p: <0.001) and cesarean delivery (aOR: 2.07, 95% CI: 1.01 - 4.30, p: 0.04). Implementing interventions that address reduction of first-step delay, improvement of quality antenatal care and establishment of effective referral systems in low-resource settings is crucial to decrease MNM events, improve maternal health, and increase child survival.

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ANTENATAL CARE SERVICES IN BENIN AND TANZANIA, 2021-2022: AN EQUITY ANALYSIS STUDY

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Antenatal care (ANC) improves maternal and neonatal outcomes, yet access to ANC and quality of care (QoC) may be inequitable due to sociocultural factors and monetary and time costs. Examining drivers of ANC disparities may identify those amenable to policy change. We conducted an ANC equity analysis of public facilities in Tanzania, where services are free, and in Benin, where there is cost-recovery. Using data from representative household surveys in the catchment of 40 clinics per country, we assessed total ANC visits in last pregnancy, QoC indicators (e.g., blood pressure (BP) and urinalysis), and wait times, disaggregated by education and wealth quintiles. We used indices of inequality, concentration indices, and Oaxaca-Blinder decompositions to determine the distribution, direction, and magnitude of inequalities and the contributing factors. We assessed out-of-pocket (OOP) expenses associated with ANC visits relative to income. Wealthier individuals had more ANC visits than poorer ones at every education level in both countries, with the wealthiest and most educated having two visits more than the poorest, least educated. In Benin, individuals who attend ANC receive similar care regardless

of socioeconomic status; BP was measured for 98% of women in the highest and lowest wealth quintiles. In contrast, in Tanzania, there are wide disparities in QoC received by education or wealth; 83% of the wealthiest women had BP measured versus 64% of poorest. In Tanzania, wealthier and more educated clients spent 27 fewer minutes at ANC. In Benin, OOP expenses are 2.7% of annual income for women in the lowest wealth quintile compared to 0.8% for the highest; cost recovery is the primary cost. In Tanzania, the values are 3.1% and 0.5%, respectively; transportation is the main cost. We identified inequities in total ANC visits, favoring wealthier, more educated individuals. In Benin, removal or reduction of cost-recovery could improve ANC access. In Tanzania, ensuring healthcare staff have necessary training and supplies will help ensure uniform and high-quality care, while community health services could address the transportation cost barrier.

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COSTING OF A COMBINATION INTERVENTION (KYATEREKERA) ADDRESSING SEXUAL RISK-TAKING BEHAVIORS AMONG VULNERABLE WOMEN IN SOUTHWESTERN UGANDA

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In Uganda, women engaged in sex work (WESW) have an HIV prevalence of 31.3% and account for 18% of all new HIV infections in the country. This marginalized population is at the intersection of multiple vulnerabilities. The Kyaterekera intervention is targeted at WESW in Rakai and the greater Masaka regions in Uganda and combines a traditional HIV risk reduction (HIVRR) approach with a savings-led economic empowerment intervention and financial literacy training (FLT).We estimated the economic costs of the Kyaterekera intervention from a program provider perspective using a prospective activity-based micro-costing method. All program activities and resources used were identified, measured, and valued across the two study arms: 1) control arm (7 clusters, 186 women) receiving a traditional HIVRR intervention; 2) treatment arm (12 clusters, 356 women) receiving a matched individual development savings account (IDA) and FLT on top HIVRR. Estimated costs were summed per each arm and divided by the participant numbers to calculate the per-participant cost by arm. All costs were adjusted for inflation, discounted at an annual rate of 3%, and presented in 2019 US dollars.The total per-participant cost of HIVRR and HIVRR+IDA+FLT arms was estimated at $323 and $1,435, respectively, using the treatment-on-the-treated (TOT) sample. When calculated based on the intent-to-treat (ITT) sample, the per-participant costs were reduced to $183 and $588, respectively. The key cost drivers were the capital invested in IDAs at opening and through matched contributions and the personnel and transportation costs for program operations, linked to WESW's higher mobility and the dispersed pattern of hot spot locations.This is the first study to estimate the costs of a combined HIVRR and economic empowerment intervention for WESW in Uganda. The findings contribute to a dearth of evidence on the economic costs of implementing a targeted intervention for this marginalized population in resource-constrained settings and sheds light on the scale of potential investment needed to better achieve the health equity goal of HIV prevention strategies.

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THE COLLABORATIVE CROSS REVEALS A SINGLE LOCUS REQUIRED FOR PROTECTIVE IMMUNITY AGAINST HIGHLY VIRULENT TOXOPLASMA GONDII STRAINS

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We employed an unbiased forward genetics screen to determine new requirements for immunity to Toxoplasma gondii against a highly virulent strain of T. gondii, the causative agent of human toxoplasmosis. To detect immunity QTLs generated by vaccination or natural infection with a low-virulent strain, we screened the available panel of 59 lines of the Collaborative Cross (CC), a highly diverse genetic panel of inbred mice captures ~90% of the genetic variation within the Mus musculus species. We challenged immunized mice with a highly virulent French Guyana strain, GUY-DOS, capable of evading immunological memory responses in some but not all founder CC lines. We found one highly significant Quantitative Trait Locus (QTL) in a small region on chr11 that correlated with survival to GUY-DOS secondary infections in vaccinated or naturally infected animals. The chr11 QTL accounts for 70% of the total phenotypic variance in the CC. The protective effects to GUY-DOS in the CC mice were related to PWK/PhJ (Mus m. musculus) and CAST/EiJ (M. m. castaneous) alleles but not those from common laboratory mice (M. m. domesticus) at this locus. The number of mutations and GO enrichment of genes in the chr11 QTL indicates that the most probable candidate in the region corresponds to Tcf7, a known regulator of CD4+ T follicular and CD8+ T central memory lymphocytes. A further evaluation revealed enhanced central memory CD8+ T cells and higher frequencies of TCF-1+ in CD8+CD44+ lymphocytes in resistant CAST/EiJ and PWK/PhJ compared to susceptible C57BL/6J mouse genetic backgrounds. To test the genetic effect of the chr11 QTL, we applied the same infection model to congenic B6.PWD-chr11.1 mice and observed complete protection against challenge with the highly-virulent strain VAND but partial protection to GUY-DOS, suggesting that chr11 7-60 Mb from the M. m. musculus genetic background promotes immunity to atypical strains in a strain-specific manner. Furthermore, we utilized a Tcf7 deficient mouse line (Tcf7 P45-/-), whereby TCF1 expression is reduced but not abrogated, and observed that vaccinated Tcf7 P45-/- mice succumbed to a challenge with the Type I RH T. gondii strain, typically non-lethal in vaccinated C56BL/6J mice. Together, these results show the contribution of Tcf7 in immunity to T. gondii and reinforce the importance of Tcf7/TCF-1 regulation in vaccination against T. gondii and other parasitic diseases.

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EXPLORING NATURALLY ACQUIRED IMMUNITY TO PLASMODIUM FALCIPARUM IN A GENOTYPIC ANALYSIS OF A LONGITUDINAL COHORT STUDY

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We genotypically profiled six thousand samples from a longitudinal cohort study in Kalifabougou, Mali to characterize malaria infection dynamics with unprecedented clarity. In this cohort which spanned May 2011 to January 2012, about half of the subjects were infected with Plasmodium falciparum at enrollment into the cohort, across all ages (3 months-25 years old). To better understand the distribution and prevalence of polyclonal infections, particularly as they relate to naturally acquired immunity (NAI) development, we generated Illumina amplicon sequencing data from 464 subjects in this cohort. We estimated complexity of infection (COI), the

number of genetically distinct clones within a sample and found that over 50% of the P. falciparum positive samples (1210 of 2315 samples) were polyclonal, regardless of subject age. This finding is consistent with previous findings from this cohort showing similar times to first PCR-detectable infection, regardless of age, suggesting that NAI does not reduce rates of infection or the clonality of infection. We also compared the time to the first new infection across multiple subject groups. We found that subjects who were already infected with parasites at study enrollment, before the transmission season, acquired a new infection more quickly during the transmission season itself than those who were uninfected at baseline, suggesting that ongoing blood-stage infections may not protect against superinfection. As this pattern was also unchanged with subject age, as well as with stratification by number of new infections, as a proxy for heterogeneity in exposure, the rate of superinfection establishment does not appear to be impacted by NAI. Future work will screen for elusive signs of immunity at a molecular level, including analyses of allelic exclusion, spontaneous infection resolution, and duration between infection onset and presentation of symptoms. This work highlights the utility of longitudinal amplicon sequencing data to provide a deeper look at molecular signatures, suggesting that both COI and rates of superinfection establishment are not molecular signs of naturally acquired immunity.

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INVESTIGATION OF THE RELATIONSHIP BETWEEN NATURALLY ACQUIRED ANTIMALARIAL ANTIBODIES AND THE DURATION AND CLEARANCE OF ULTRA-LOW DENSITY PLASMODIUM VIVAX INFECTIONS

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Subclinical Plasmodium spp. infection is attributed to the acquisition of non-sterilising antimalarial immunity, particularly antibodies. The spontaneous clearance of subclinical peripheral Plasmodium spp. parasitemia, including P.vivax, occurs frequently in low transmission settings. Subclinical Plasmodium spp. infections contribute significantly to ongoing malaria transmission, therefore understanding the role of antibody mediated immunity in the spontaneous clearance of parasitemia is essential to the broader understanding of the epidemiology and transmission potential of P.vivax. We sought to identify IgG responses associated with subclinical P.vivax infection and clearance of peripheral parasitemia. IgG to a suite of 30 P.vivax antigens was determined by Luminex assay in participants of a nested cohort study of subclinical Plasmodium spp. infection in Laos (n=202) and Cambodia (n=150). Participants were sampled monthly for 12 months (n=3041), and Plasmodium spp. infections detected by high-volume ultrasensitive qPCR. Mixed effects regression models were used to determine the association between antigen specific IgG levels and spontaneous clearance of peripheral P.vivax parasitemia. Over 12 months, a total 610 subclinical Plasmodium spp. infections were detected, including 293 P.vivax infections. Spontaneous clearance of peripheral P.vivax infection was observed in 79% and 67% of participants and the median time to clearance of peripheral P.vivax parasitemia was 93 and 68 days in Laos and Cambodia, respectively. Anti-P.vivax IgG responses were higher in participants with detectable P.vivax infection compared to those free of P.vivax during the study period, for all 30 antigens investigated. Individual antigen-specific IgG responses were not associated with clearance of peripheral P.vivax parasitemia. Future investigations will include analysis of multi-antigen responses and time to clearance of peripheral P.vivax parasitemia. These findings will further our understanding of acquired immunity in the maintenance, clearance and ultimately the transmission and epidemiology of P.vivax infections.

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NEW INSIGHTS INTO SCHISTOSOMIASIS MANSONI PATHOGENESIS: EVIDENCE FOR BACTERIAL TRANSLOCATION, INFLAMMASOME ACTIVATION, AND UPREGULATION OF PROINFLAMMATORY CYTOKINES IN HEPATOSPLENIC PATIENTS

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IL13 drives schistosomiasis fibrogenesis, but growing evidence suggests that IL1β and IL17 contribute to severe disease. Our aims were to evaluate the immune response in patients with schistosomiasis and determine if liver fibrosis is associated with bacterial translocation, inflammasome activation, and Th17 response. Plasma samples from controls (n=30) and patients with acute (n=22), hepatointestinal (n=40), and hepatosplenic (n=26) schistosomiasis mansoni were collected. ELISA was performed for IL1β, IL5, IL6, IL10, IL13, IL17, TNFα, IFNγ, CCL11, and CCL17. Snap-frozen liver biopsies from controls (n=6) and hepatosplenic patients (n=36) were also included. Real-time PCR was performed for genes related to bacterial translocation, inflammasome activation, immune response, and fibrogenesis. Liver fibrosis was assessed by ultrasound (WHO protocol). Patients with acute schistosomiasis had higher levels of IL1β, IL5, IL6, IL10, IL13, IL17, TNFα, CCL11, and CCL17 than hepatointestinal patients or controls. Hepatosplenic patients had higher IL13, IL5, IL1β, TNFα, and CCL11, but lower CCL17 levels than hepatointestinal patients or controls. IL-5, IL-13, IL-1β, TNFα, and CCL11 positively correlated with the degree of fibrosis, while CCL17 levels were negatively correlated. Hepatosplenic patients had increased liver expression of markers of bacterial translocation (16S rRNA, LPS binding protein), inflammasome activation (NLRP3, Caspase 1, IL1β, IL18), Th1 (IL12p35, TNFα), Th2 (IL5, IL13, GATA3, CCL11, CCL17), Th17 (IL17A, IL17RC, IL17RC, IL23, IL23R, IL6), Treg (IL10, TGFβ), myofibroblast activation (αSMA, Vimentin) and collagen deposition (type I, III and VI). Bacterial translocation, inflammasome activation, Th2, and Th17 cytokines correlated with myofibroblast activation, collagen deposition, and fibrosis staged by ultrasound. Liver fibrosis in hepatosplenic schistosomiasis is associated not only with Th2 response

but also with NLRP3 inflammasome activation and Th17 immune response, probably exacerbated by bacterial translocation. Dual targeting of IL13/IL17 may benefit patients with severe disease.

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IMMUNE RESPONSE KINETICS IN NEUROCYSTICERCOSIS OVER TIME POST INFECTION USING AN ANIMAL MODEL

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Neurocysticercosis (NCC) is an infection of the central nervous system (CNS) caused by the metacéstode helminth Taenia solium. In NCC, brain lesions depend on the host-immunoinflammatory response interaction. However, it is not clear how is the inflammatory response in the early stage and throughout the infection process over time. We generated a rat model for NCC in which activated T. solium oncospheres were inoculated intracranially. 10 groups were used: 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10 and 12 months post-infection (MPI). It was shown that in parenchymal cysts of 1 MPI more than 60% of the area around the cyst present macrophages organized in palisades without fibrosis, and from 3 MPI the presence of macrophages with fibrosis begins to be observed, as the post-infection time progresses this fibrosis increases, being 40% around the cyst for the 3 MPI, in the 4 with 70% and 80% in groups of 6 MPI. Picrosirius Red staining shows that the predominant type of collagen in the fibrotic tissue for 3 MPI is type III, with green fibrosis being observed; then, as the post-infection time progresses, the presence of red/yellow type I collagen is observed with greater predominance. On the other hand, a striking characteristic of meningeal and ventricular cysts is the presence of a higher percentage of moderate to severe inflammation score of 30% around the cyst compared to parenchymal cysts with only 10% around the cyst. The microglial cells of the groups of 1 to 2.5 MPI are found forming a layer of cells around the cyst and mainly with ameboid/phagocytic morphology. While in cysts from 3 MPI was located both in the fibrotic tissue that borders the cyst and continuous to this tissue are the astrocytic cells; microglia morphology was rod-shaped for the 3 to 4 MPI; in those of the 6 and 12 MPI, the microglia had a branched/debranched hypertrophic and dystrophic morphology. Concluding that the type of cellular infiltrate, macrophages, the formation of fibrosis and glial cells participate in the modulation of the host's immune response throughout the post-infection time in NCC.

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TRANSCRIPTOMIC IDENTIFICATION OF BIOMARKERS FOR CHAGAS DISEASE PROGRESSION

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Chagas disease affects approximately 8 million individuals worldwide. Of those infected, 20-40% will go on to develop chronic Chagas cardiomyopathy (CCC) and ultimately heart failure. There is currently no way to predict which patients will develop CCC, and the mechanisms underlying CCC progression are poorly understood. This study aims to discover biomarkers of disease progression by using whole blood samples that were obtained from individuals prior to disease progression (stage A). These individuals were evaluated yearly for any electrocardiogram (EKG), echocardiogram, or symptomatic changes suggestive of CCC. We then randomly selected patients who went on to develop EKG changes to stage B heart failure (asymptomatic progressors), those who went on to develop reduced ejection fractions and symptoms of stage C heart failure (symptomatic progressors), and age and sex matched non-progressors that remained in stage A. We performed RNA-sequencing on these blood samples to investigate differential gene expression, immune cell composition and HLA type. For symptomatic progressors compared to non-progressors, we identified various differentially expressed genes (DEGs) and significantly enriched biologic processes. These pathways included muscle morphogenesis, regulation of cell-cell adhesion, and defence response to intracellular pathogens. Notably, for very early-stage progression to asymptomatic disease compared to non-progressors we also identified DEGs related to immunologic and remodelling functions, and significant increases in memory B cells, M2 macrophages and eosinophils. No significant difference was detected in HLA type with disease progression. Overall, these findings indicate RNA transcripts detected in the blood of Chagas patients can differentiate those individuals who will go on to progress in CCC from those who will not, and suggest that there are notable physiologic changes that precede clinically detectable CCC progression. Our findings may help inform screening strategies for risk of disease progression and to develop novel therapeutic strategies that target these early dysregulated genes.

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REDUCTION OF SEXUALLY TRANSMITTED INFECTIONS FOLLOWING AZITHROMYCIN MASS DRUG ADMINISTRATION FOR TRACHOMA IN NAURU

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Sexually transmitted infections (STIs) are a major public health problem globally, particularly in low-and middle-income countries (LMIC). STIs are common in the Western Pacific region, including Nauru. The strategy of syndromic STI management, relying on clinical findings alone without laboratory confirmation, has long been endorsed by the World Health Organization but misses more than 80% of asymptomatic infections, especially common during pregnancy. Screen and treat strategies are not currently affordable or feasible at scale in LMIC. In areas where trachoma or yaws are endemic, mass drug administration (MDA) with azithromycin might offer an alternative approach to the population control of STIs as well as Neglected Tropical Diseases (NTDs). In Nauru, we evaluated the impact of an azithromycin-based MDA for trachoma control on bacterial STIs in a population aged 18-29 years, by conducting a before and after community survey pre and post MDA with 8-month follow-up to determine long-term impact on genital infections. The study enrolled 381 participants at baseline and 360 post-MDA. At baseline C. trachomatis infection was diagnosed in 21.7% of participants (95% CI 17.6% - 26.3%) T. vaginalis and M. genitalium were also common (21.2% and 10.9%, respectively) as well as N. gonorrhoeae 2.7% (95% CI 1.3% - 4.9%). Eight months following azithromycin MDA a reduction in prevalence was observed in all STIs except for T. vaginalis. The relative reduction in the prevalence of C. trachomatis was 34.6% (95% CI 25.7 - 45.2) and that of N. gonorrhoeae was 66.7% (95% CI 56.9 - 76.1). This study is the first to investigate the reduction of STIs using azithromycin-based MDA in the general population, not restricted to the female population and/or pregnant women. The significant decrease in STI prevalence seen in this study 8 months after azithromycin MDA is encouraging in island populations such as this, where populations are less mobile. Azithromycin MDA is a well-established and safe intervention which has been successfully adopted for NTD control. Prospective evaluations of MDA strategies specifically targeting common STIs should be undertaken.

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THE SECONDARY EFFECTS OF IVERMECTIN MASS DRUG ADMINISTRATION DESIGNED FOR MALARIA ON ECTOPARASITIC INFESTATIONS IN MOPEIA, MOZAMBIQUE: A CLUSTER-RANDOMIZED CONTROLLED TRIAL

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Ectoparasitic diseases such as scabies are severely neglected, despite the existence of effective treatments. There is limited data on their prevalence in Africa, and no published reports assessing the prevalence of scabies in Mozambique at scale. Ivermectin Mass Drug Administration (iMDA) is currently being studied as a potential malaria vector control tool. Given the substantial overlap between populations at risk of malaria, scabies and headlice, and the known efficacy of ivermectin against scabies and headlice, it is likely that in co-endemic areas there will be collateral benefits. During a cluster randomised controlled trial (BOHEMIA), which aimed to assess the effect of iMDA against malaria, we monitored the prevalence of scabies, headlice and bedbugs. The intervention consisted of a single dose of 400 mcg/kg ivermectin given monthly to eligible humans or humans and livestock in 3 consecutive months during the rainy season. The control group received albendazole (humans only). 39 of 100 total clusters were randomly selected and monitored for ectoparasitic infestations (scabies, headlice and bedbugs) among the three study arms. Cross-sectional surveys took place in adults and children at 3 months after the first dose (1,341 participants) and in untreated children under 5 (382 participants) at 6 months. Scabies and headlice diagnosis were determined by a questionnaire and examination of exposed skin/scalp by non-experts after intense training. Bedbug infestation was based on a short questionnaire. The baseline prevalence of scabies, headlice and bed bugs were 10.14% (95%CIs 8.58-11.88), 9.80 (95%CIs 8.23-11.55) and 16.70 (95%CIs 14.15-19.52), respectively. A semi-blinded and unadjusted analysis suggests a reduction in scabies prevalence of up to 88% (RR 0.12 (95%CI 0.06-0.25) after 3 months and up to 87% (RR 0.13 (95%CIs 0.04-0.41) in untreated children after 6 months. For headlice, the data suggests a reduction of up to 74% (RR 0.26 (0.13-0.49)) and no effect in untreated children after 6 months. The data suggests no significant effect on bed bugs at any time point. A full unblinded analysis will be available during the meeting.

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ASSESSING THE PREVALENCE OF SOIL TRANSMITTED HELMINTHS AND TUNGIASIS DURING LYMPHATIC FILARIASIS SURVEILLANCE IN THE COASTAL REGION OF KENYA

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The World Health Organization encourages Neglected Tropical Diseases (NTD) programs to employ integrated approaches to disease surveys for NTDs with similar epidemiology for efficient resource utilization and to avoid duplication of efforts. During Lymphatic Filariasis (LF) treatment, albendazole is co-administered with diethylcarbamazine and, as such soil-transmitted helminths (STH) are secondarily treated. A cross-sectional survey conducted in Kilifi and Kwale counties in 330 randomly selected schools to establish if LF transmission is ongoing assessed the impact of LF treatment on STH. The survey also collected relevant WASH data and assessed the prevalence of Tungiasis, which is known to occur widely and is prevalent among school-age children. 17,602 children aged 6-7 years were tested for circulating filarial antigen using the rapid filariasis test strip. All those positive were further tested for microfilaria using microscopy. For STH and Tungiasis, 60 children per school of ages 10-14 years were randomly selected, 12 children from each of grades 4 to 8. All sampled children were asked to provide stool samples for STH testing. Their feet were further washed, dried, and carefully examined for the presence of Tunga penetrans fleas. They were also interviewed on individual WASH characteristics. LF positive results were only reported in two sub-counties- Rabai 2/1,655; 0.12% (95%CI: 0.03-0.47) and Magarini 1/1,624; 0.06% (95%CI: 0.01-0.46). All three positive cases were negative by microscopy. For STH, the highest prevalence was in Msambweni sub-county (15.1%, 95%CI: 12.2-18.6). For Tungiasis, the highest median school prevalence was also recorded in Msambweni Sub-County (6.8%, 95%CI: 5.2-8.9). However, the highest intensity of infection was recorded in Kinango Sub-County with a median of 8.0 (IQR 2.8-8.0) embedded fleas. Schools with the highest prevalence of Tungiasis were in the same wards as schools with a high prevalence of STH. This study demonstrates that implementing integrated surveys for NTDs with similar epidemiology was feasible and enabled the evaluation of Tungiasis prevalence for the first time in Kenya.

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ESTIMATING THE BURDEN OF MALARIA-HELMINTH CO-INFECTIONS AMONG CHILDREN LIVING IN A SETTING OF HIGH COVERAGE OF STANDARD INTERVENTIONS FOR MALARIA AND HELMINTHS

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Concurrent infections of Plasmodium falciparum with Soil Transmitted Helminths (STH) and Schistosoma spp are still a major public health problem among children living in sub-Saharan Africa. We conducted two prospective studies among children living in urban and rural settings of Senegal, where control programs have been sustained, to determine the prevalence of malaria-helminth co-infection. We enrolled 910 children aged 1-14 years from Saraya and Diourbel districts of Senegal in June and November 2021. Finger-prick blood samples were obtained from the children for malaria microscopy and PCR methods. Stool samples were also collected. Kato-Katz and PCR methods were used to detect STH and S. mansoni, and Merthiolate-iodine-formalin test for other intestinal protozoans. Urine samples were analyzed using a filtration test, Point of Care Circulating Cathodic Antigens, and PCR methods for detection of S. haematobium. Continuous and categorical variables were compared across the two study sites and adjusted Odds ratios were used to explore risk factors for malaria-helminth co-infections. The overall prevalence of polyparasitism with P. falciparum, STH, S. haematobium and S. mansoni among children was 2.2% (20/910) while prevalence of P. falciparum-S. haematobium co-infection was 1.1% (10/910); P. falciparum-S. mansoni 0.7% (6/910) and P. falciparum with any intestinal protozoan 2.4% (22/910). Co-infection was slightly higher among 5-14-year-old children (17/629,2.7%; 95% CI:1.43-3.97) than 1-4 years (3/281,1.1%; 95% CI:–0.12-2.32) and, in boys (13/567,2.3%; 95%CI:1.27-3.96) than girls (7/343, 2.1%; 95% CI:0.52-3.48). Children aged 5-14 years (aOR=3.37; 95% CI:0.82-13.77, p=0.09), who were boys (aOR=1.44; 95% CI: 0.48-4.36, p=0.51) and lived in Saraya (aOR=1.27; 95% CI: 0.24-6.69, p=0.77) had a higher risk of the co-infection. Living in houses with spaces between the walls and frequent contact with water were statistically significant risk

factors for malaria-helminth co-infection. These findings could help to develop and implement strategies that would lead to elimination of malaria and helminths in the study areas.

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INTEGRATED NEGLECTED TROPICAL DISEASES SURVEYS TO ASSESS IMPACT OF INTEGRATED MASS DRUG ADMINISTRATION IN VANUATU

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Soil transmitted helminths (STH), scabies and yaws are neglected tropical diseases (NTDs) endemic to Vanuatu. To control and eliminate these NTDs, the Vanuatu Ministry of Health, with the support of the non-profit organisation Bridges to Development, is implementing large-scale innovative integrated control programs including two rounds of mass drug administration (MDA) with albendazole, azithromycin and ivermectin, concurrent with active surveillance of yaws and leprosy. To monitor and evaluate the impact of this program, cross-sectional parasitological surveys will be conducted before and after MDA. A cross-sectional baseline prevalence survey was conducted in 92 villages across three provinces. In each village the aim was to recruit 100 residents of skin examination and 50 to provide stool samples. One day prior to the MDA, field teams visited selected households, sought consent, and provided a stool collection kit to be returned the following day. On the day of MDA, a nurse performed a skin examination for scabies, yaws and leprosy. The dual path platform (DPP) rapid diagnostic test (RDT) was used to confirm suspected yaws cases. Stool samples were tested for STH species using sodium nitrate flotation (SNF) technique and qPCR. At the time of writing this abstract, a total of 4815 individuals in 2 provinces participated in the baseline survey that took place in Tafea in November 2021 and Sanma in September 2022. A baseline survey is planned for Shefa in May 2023. In the first 2 provinces, the prevalence of any STH by SNF was 28.3%, Ascaris lumbricoides 16.7%, Trichuris trichuria 11.4%, and hookworm 12.1%. The prevalence of scabies was 14.0% in Tafea vs 2.6% in Sanma. Active surveillance of yaws and leprosy identified 15 cases of confirmed yaws (13 in Tafea and 2 in Sanma) and 6 cases of suspected leprosy. Our study suggests that there is a high prevalence of STH and skin diseases among Vanuatu population. The implementation of surveys integrated with MDA is a novel approach that allows more cost-efficient collection of data necessary to monitor and evaluate impact of the MDA.

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COMMUNITY DIALOGUE AS AN INNOVATIVE APPROACH TO IMPROVE THE EFFECTIVENESS OF NEGLECTED TROPICAL DISEASE (NTD) CONTROL PROGRAMS TO IMPROVE MASS DRUG ADMINISTRATION (MDA) COVERAGE FOR LYMPHATIC FILARIASIS IN BURKINA FASO

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Burkina Faso has implemented mass drug administration (MDA) for lymphatic filariasis (LF) for over 20 years in all 70 health districts (HD). Currently, 62 of the 70 districts have stopped treatment. However, LF transmission has persisted in 8 HDs despite multiple rounds of MDA with good, reported coverage and implementation of additional MDA quality improvement strategies since 2018. In order to identify the factors for the persistence of transmission, the National Neglected Tropical Disease Program (PNMTN) implemented a community dialogue in 2022 in the districts of Gaoua, Batié, Bogodogo, Ouargaye and Tenkodogo. A total of 52 villages were selected based on the following criteria: therapeutic coverage rate ≤65%, antigenic prevalence ≥2%, and accessibility from a security perspective. Data collection of the community dialogue was done through individual interviews and focus groups, which were then qualitatively analyzed by theme. In total, the dialogue was conducted in 47 of the 52 villages targeted (90.4%) due to the deteriorating security situation. The individual interviews involved 346 people, including head nurses (5.2%), community distributors (27.1%) and community leaders (67.6%); 15.3% of participants were women. A total of 92 people (47 women) participated in the focus groups. The main factors for the persistence of LF were determined to be non-adherence to treatment and missed opportunities for treatment. The reasons mentioned by participants were lack of knowledge about LF, insufficient social mobilization, visits to the home at inconvenient times by distributors, the delay in providing financial resources available to implementing actors and MDA conducted in the rainy season. Some recommendations from the community dialogue, including improved planning, social mobilization, training, supervision, and distribution, were implemented during an MDA two months later; reported therapeutic coverages increased by an average of 4% in all districts. The remaining recommendations will be implemented in 2023.

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CHARACTERISTICS OF NON-TREATED POPULATIONS AMONG SELECT NEGLECTED TROPICAL DISEASE (NTD) MASS DRUG ADMINISTRATION (MDA) CAMPAIGNS IN WEST AFRICA: RESULTS FROM MULTI-LEVEL MODELING USING COVERAGE EVALUATION SURVEYS

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Effective mass drug administration (MDA) is the cornerstone of preventive chemotherapy (PC) neglected tropical disease (NTD) programs. USAID's Act to End NTDs | West program supports Ministries of Health to eliminate or control five PC NTDs across 11 West African countries by assisting with MDAs and disease specific assessments. Coverage evaluation surveys (CES) are used to validate coverage shortly after MDA. Non-treated populations (MDA eligible people in endemic districts who do not participate in the treatment campaign) are of concern as they may enable ongoing transmission of infection. If these populations can be better characterized, programs can take more precise actions to identify and target them. Three-level (persons/households/villages) hierarchical models of non-treatment were built using Act | West CES data from six surveys (39,705 MDA-eligible respondents) conducted in 24 districts across Ghana, Niger, Senegal, and Sierra Leone. We employed a range of explanatory variables from the CES and using geospatial techniques, we estimated travel time between households and the closest health facility as an additional explanatory variable. The overall model results showed odds of non-treatment were higher among males compared to females in all age groups except under 5. The highest odds of non-treatment were observed in males compared to females in the age group 25-34 (OR=2.55, 95% CI = 2.08, 3.13). People living in household more than one hour away from the closest health facility had 1.7 times higher odds (95% CI = 1.25, 2.34) of non-treatment compared to those living closer. Not having prior knowledge of the MDA campaign was also a significant predicter of non-treatment (OR=6.45, 95% CI = 5.46, 7.62). Country-specific models indicated that the drug distribution platform and an individual's time living in the community were also significant covariates. Our findings suggest the most influential programmatic response could include implementing age and sex specific

MDA mop-up, increasing the information coming through the health system to raise awareness of MDA, and focused attention on facilities serving relatively remote areas.

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A SEMI-QUANTITATIVE DIPSTICK ASSAY IN SERUM FOR THE FOLLOW-UP OF PATIENTS WITH SUBARACHNOID NCC

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Neurocysticercosis (NCC) is one of the most frequent parasitic diseases in the human central nervous system. Clinical manifestations rely principally on cyst localization, being subarachnoid NCC (SANCC) the most severe clinical form of NCC. Taking leverage of the enormous quantities of antigens released into circulations in SANCC, we evaluated the utility of a dipstick assay based on monoclonal antibodies (mAbs) anti-T solium (TsW8 and TsW5) in serum samples of SANCC patients for the follow-up after antiparasitic treatment; and compared its performance with a standard Ag-ELISA using the same pair of mAbs . Fifteen patients were included, with a total of 45 samples collected over 3 months. Under the hypothesis that a low mAb concentration would only detect high levels of circulating antigen, whereas when antigen level decrease, it would only be detectable using high mAbs concentrations; we developed a dipstick format with two different mAb concentrations: TsW8 at 3mg/ml and 0.5 mg/ml. Our results demonstrated that initially all SANCC cases presented saturating antigen levels the new dipstick assay (3+++ intensity bands) and Ag-ELISA (Ag ratio ranging from 104.73 to 21.00). Second and third bled showed a drastic reduction in antigen levels, obtaining one (n=10) or absent (n=1) bands and negative antigen ratios ranging from 0.92 to 0.25. As shown, the presence and intensity of reactive bands in our dipstick assay correlated strongly with antigen levels measured by Ag-ELISA. This new dipstick assay is a cheap, practical and reliable tool for the follow-up of patients with the NCC type with the worse prognosis (SANCC) reflecting the efficacy of cysticidal treatment. Hopefully, subsequent work will assess whether this dipstick assay can be used with non-invasive samples such as urine and in rural cysticercosis endemic communities.

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OPTIMIZATION OF A PCR ASSAY TO DETECT URINARY PARASITE DERIVATE DNA IN PATIENTS WITH NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is one of the main causes of epilepsy and other neurological morbidity in most of the world. Definitive diagnosis is based on technically demanding and costly imaging approaches that are impractical for routine screening or monitoring treatment effectiveness. Specific molecular diagnosis of helminth-derived cell-free DNA (cfDNA) in body fluids has shown promise as a tractable approach monitoring infection status through measuring parasite cfDNA fragments in blood or urine by PCR. In this study, we explored the utility of a PCR-based detection of T. solium cfDNA for diagnosis of NCC. First, we tested the difference in stability and yield of parasite cfDNA from urine samples stored/processed under different conditions (fresh urine extracted immediately after collection, fresh urine in filter paper, frozen urine at -20C and frozen urine at -80C). Urine stored at -80°C gave the highest DNA yield and, when combined with a new 30-minute extraction protocol, requires as little as 4 ml of urine for sufficient cfDNA for analysis. We also evaluated and standardized 15 different sets of primers using urine samples from 6 subarachnoid and 6 parenchymal NCC cases. Primer pairs that resolved the amplicons pTsol9 (116 bp), TsollTS (86 bp) and Tsol13(<100 bp) demonstrated that T. solium cfDNA could pass the glomerular barrier and be detected in urine. Cross reaction analysis with T. multiceps, the closest related brain parasite in humans, revealed that none of the primer pairs generated amplicons from T. multiceps DNA. For the urine samples tested, all three primers pairs detected T. solium cfDNA; however, the pTsol9 amplicon showed the highest intensity band after electrophoresis. In a second phase of this study, we will increase our sample size to better assess the performance of the cfDNA detection system. This molecular test, based on the detection of parasite-derived cfDNA, could serve to categorize populations with viable cysts as an initial screen prior to confirmatory diagnosis and could also function as a sensitive biomarker for monitoring treatment efficacy using a non-invasive sampling method.

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DETECTION OF TAENIA SOLIUM ANTIGENS IN PAIRED SERUM AND URINE SAMPLES FROM PATIENTS WITH NEUROCYSTICERCOSIS USING THE TSW8/TSW5 ANTIGEN ENZYME-LINKED IMMUNOSORBENT ASSAY (AG- ELISA)

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Neurocysticercosis (NCC) is a frequent parasitic disease of the human central nervous system and is caused by the accidental ingestion of Taenia solium eggs. NCC is endemic in most developing countries, estimating that the third part of epilepsy cases are attributable to this parasitosis. The diagnosis of NCC is based on radiological images due to the heterogeneous clinical manifestations, which principally depend on its localization within the CNS. Detection of circulating parasite antigen marks the presence of live parasites, but it is usually assessed in serum sampling, which is poorly accepted by patients. On the other hand, urine antigen detection has been lately shown as an alternative non-invasive sample to detect parasite antigens. However, the correlation between paired samples of serum and urine has not been assessed with TsW8/TsW5 Ag-ELISA. We evaluated the correlation between paired serum and urine samples of 172 NCC patients using a T solium monoclonal antibody based enzyme-linked immunosorbent assay TsW8/TsW5 Ag-ELISA expressed as optical density (OD) and OD ratios. Study samples included subarachnoid (n=51), parenchymal (n=18) and calcified (n=103) NCC cases. Correlation between LogOD (rho=0.79) and antigen ratio (rho=0.66) of all samples was statistically significant (p=0.000). When separated by type of NCC, positive correlations were found between the urine and serum LogOD and ratio of subarachnoid (rho=0.71/rho=0.53), parenchymal (rho=0.83/rho=0.79), and calcified (rho=0.66/rho=0.64) NCC cases. Our results showed a strong correlation between paired serum/urine samples, guiding our perspective to a less invasive form of diagnosis.

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PRESENTATION, COMPLICATIONS, AND OUTCOMES OF CYSTIC ECHINOCOCCOSIS IN CUSCO, PERU

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Cystic echinococcosis (CE) morbidity and mortality are associated with size, delayed care, and cyst complications. Data on CE outcomes are scant in endemic countries. We characterized the clinical presentation, complications, and outcomes of CE in two tertiary hospitals in Cusco, Peru. We reviewed available medical records from patients discharged with a diagnosis of CE between January 2009 and December 2019. Medical records of 489 patients with over 821 cysts were included, the median age was 23 years (IQR 29), 50% were female, and 40% were referred from another health center. The most common occupations were student (43%) and homemaker (21%). Lung (64%) and liver (42%) CE were the most common. Other locations included other intraabdominal organs, brain, and pelvis. Most liver (60%) and lung (54%) CE had a diameter larger than 10 cm. Most lung (76%) and 42% of liver cysts were complicated on admission. Common complications of lung CE were hemoptysis, vomica, and bronchial fistulas. Leukocytosis (21%) and eosinophilia (10.6%) were uncommon. Surgery was performed on 72% of lung and 45% of liver cysts. Twenty-three percent of patients had a second related hospital admission and 4.7% had a third one. Three patients died in the hospital and 23.6% had a discharge status of "worse or unchanged". Patients with lung cysts (OR=1.92; 95%CI 1.07-3.44) and those reporting contact with dogs (OR 1.53; 95%CI 1.15-2.05) were more likely to have more than one admission. Patients with complicated cysts on admission (OR=1.9; 95%CI 0.99-3.66) and those treated medically (OR= 5.5; 95%CI 2.21-13.67) were more likely to meet a composite outcome of death or "worse/unchanged" discharged status. Patients receiving post-surgical medical treatment (OR=0.43; 95%CI 0.22-0.82) and those referred from another health center (OR=0.22; 95%CI 0.12-0.42) were less likely to have the composite outcome. Advanced and complicated CE were common and associated with worse outcomes. Readmission and worse/unchanged discharge status rates suggest a large burden affecting patients and the health system. Early detection and treatment may decrease the disease impact in the Cusco Region.

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DEVELOPMENT OF A HIGHLY SENSITIVE QPCR ASSAY FOR DETECTION OF ECHINOCOCCUS MULTILOCULARIS AND FURTHER MAPPING THE EXTENT OF EUROPEAN-LIKE STRAINS IN NORTH AMERICA

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Echinococcus multilocularis (Em) is a severe invasive parasitic disease. Humans are exposed through eggs shed primarily in the stool of wild canids, the definitive host. Almost all human cases of Em have been reported in Europe and Asia, despite the fact that North American strains of Em were previously known to circulate in wild canids in the Northern US and Canada. With the recent reporting of several human and canid cases of Em in Canada and the US due to a more aggressive European-like strain, we sought to develop a highly sensitive qPCR assay for detection of Em in stool samples that could be used for high throughput screening. Using RepeatExplorer, the Em genome was mined for unique, highly abundant interspersed repeats. We then developed and compared 15 new Em qPCR assays against the 5 found in the literature. The most sensitive assays were tested for cross reactivity to E. granulosus, E. ortleppi, and E. vogeli. New Em assay 17S2 was 2-fold more sensitive than any previously reported assay, had a threshold of detection of 25fg (at 97.7% sensitivity) and was specific to Em. We then screened wild canid stool samples from across the US and Canada (n=261), specifically from Virginia, Maryland, Nebraska, and British Columbia. A total of 13 samples (5%) were positive for Em. Mitochondrial sequencing is underway to determine the haplotype of these isolates. One of the positive isolates from a red fox in a Washington, DC suburb had a European haplotype at the gene loci COB and NAD2. This highly sensitive and specific qPCR assay for the detection of Em can be used to identify the prevalence of wild canid infection. Understanding the true extent of European-haplotype Em in North American wildlife will help better understand the risk to human disease and inform preventative measures.

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EVALUATION OF ETIDRONATE IN CALCIFIED CYSTS IN THE PIG MODEL OF NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is the most important factor associated with late-onset epilepsy in developing countries. Cysts in the brain go through a process of complete resolution or calcification and these calcifications would be associated with epilepsy and seizures. Bisphosphonates, such as etidronate, have been shown to have an effect in reducing the ectopic calcification process in soft tissues, which would probably cause a decrease in epileptic activity. The objective was to evaluate the calcification process in pigs treated with etidronate in a natural infection of neurocysticercosis. This was an experimental study consisting of fourteen pigs naturally infected with Taenia solium and treated with 15 mg/kg albendazole and 25 mg/kg praziquantel orally. Then the animals were divided into two groups, one treated with etidronate for 10 weeks orally (n=7) and the other control group without treatment (n=7). After 8 months, the necropsy was performed and calcifications were evident on CT scan and SEM. Inflammation and calcium deposits were assessed with H&E, Masson's trichrome, Alizarin Red, and Von Kossa stains. In naturally infected pigs, we assessed the likelihood of residual calcification calcification after 8 months in 240 cysts from ten NCC pigs treated with either antiparasitic drugs plus etidronate antiparasitic only. Etidronate was associated with a significantly lower risk (49% 67/137 vs 77.67% 80/103 RR:0.63 $p<0.05$). Calcifications in pigs receiving etidronate had a non-statistically significant reduction in density measured on CT as Hounsfield units (80.8 ± 15.5 vs 100.6 ± 31.4). On SEM, calcifications in pigs receiving etidronate demonstrated significantly lower proportions of weight (Wt%) of phosphorus (2.68 vs 4.19 $p=0.02$) and calcium (4.2 vs 8.21 $p=0.01$). Etidronate also prevented the aggregation of macrophages, which are associated with calcification. This study shows the evaluation of the calcification process in animals treated with etidronate, observing less calcification in these, serving as a basis for future drug treatments in neurocysticercosis.

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DYSREGULATED AUTOPHAGY LEADS TO AXONAL SWELLING IN NEUROCYSTICERCOSIS

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Neurocysticercosis is a central nervous system disease caused by infection with the larval stage of Taenia solium (cysticercus). We have published novel neuropathological findings in neurocysticercosis, such as axonal swellings, which other studies linked to seizures and cognitive decline, common symptoms in neurocysticercosis. As axonal swellings indicate an impairment in axonal transport and accumulation of cargos throughout the neurons, autophagy was proposed as a possible mechanism involved in axonal swelling formation. We aimed to understand the role of autophagy in the axonal swelling formations in neurocysticercosis. Using our rat model of neurocysticercosis, we analyzed secretory cysticerci antigens and different markers for autophagy, like Beclin-1, p62, and LC3B, in brain sections by immunohistochemistry. We found overexpression of autophagy markers, and this autophagy was dysfunctional where p62 was increased in the tissue surrounding the parasite, and neurons mainly overexpressed autophagy markers, unlike glial cells. Although microglia engulfed most parasite antigens, secretory cysticerci antigens were found within the neuron, which co-localized within autophagosomes. The results suggest an important role of autophagy in disease development in neurocysticercosis and may afford attention toward improved disease management.

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EVALUATION OF APOPTOSIS IN RESPONSE TO ANTHELMINTIC TREATMENT IN RAT BRAINS EXPERIMENTALLY INFECTED WITH ONCOSPHERES OF TAENIA SOLIUM

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An important cause of seizures, epilepsy and other neurological manifestations is the infection by Taenia solium, which is endemic in developing countries and currently a public health problem worldwide due to migration. In recent years, studies have increased trying to understand the pathogenesis of the disease and the host's inflammatory response using animal models. The unpredictable nature of the host's immune reaction in response to the presence of the parasite and the various pathological mechanisms that this reaction induces in the nervous system, make this a complex disease. When the cysticercus begins to degenerate due to it's development or in response to antiparasitic drugs, it triggers an exacerbated inflammatory response. This could cause damage to neuronal and glial cells, a central feature of neurodegenerative diseases, nevertheless; there are no studies in Neurocysticercosis that confirm this information. Recent evidence suggests that apoptosis process plays a key role in nerve cell death in acute and chronic diseases of the nervous system. In the present study, we proposed to evaluate whether the presence and subsequent inflammation caused by the cysticercus of Taenia solium would be associated with damage and death by apoptosis of neuronal and glial cells in an animal model. To achieve this, by the colocalization of biomarkers by immunofluorescence; The TUNEL technique and activation by Caspase-3, the presence of apoptotic cells will be determined in an animal model of NCC using laboratory rats. We found that colocalization of TUNEL essay and active Caspase-3 was performed, suggesting the presence of cell death by apoptosis, with an evident increase in rats infected with NCC, predominantly in those that were sacrificed 24 hours after treatment. In addition, an increase in immunoreactivity to the apoptotic marker Caspase-3 was demonstrated, with an increase predominant in NCC-infected rats sacrificed 24 hours after treatment. In addition, cellular colocalization of active Caspase-3 was demonstrated with GFAP and NeuN but not with Iba-1, suggesting that apoptosis mainly affects astrocytes and neurons but not microglia.

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LEAKY GUT MECHANISMS IN GIARDIASIS

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Giardia duodenalis is an intestinal parasite endemic worldwide and commonly transmitted via contaminated water. Infection in children under 2 is one of the top 5 infectious causes of childhood growth stunting. Growth faltering is a complex pathology facilitated by changes in the intestinal barrier and enzymatic deficiencies. This pathology is predictive of later delays in cognitive and motor development. However, while infection is widely associated with barrier damage in vitro, in animal models, and in patient studies, the mechanisms behind this process are not well understood. The Protease-activated receptor 2 (PAR2) has a prominent role in modulating intestinal tight junction permeability in Celiac disease. Co-culture of Giardia and Caco2 cells similarly results in altered tight junction morphology as revealed by staining for the tight junction-associated protein Zonula occludens 1 (ZO-1); these changes are reduced by treatment with a PAR2 antagonist. Effects of Giardia-induced PAR2 signaling on barrier function are being assessed further by measuring transepithelial electrical resistance (TEER) in Caco2 cells and PAR2+/- and PAR2-/- organoids cultured on transwell filters. Additionally, infected mice lacking PAR2 and fed a low-protein diet gain weight normally over time, while wildtype C57BL/6 animals under the same conditions arrest growth post infection. These data indicate that PAR2 signaling contributes to intestinal permeability defects and growth faltering. Identifying parasite factors that activate PAR2 will provide novel targets for development of pharmaceuticals and vaccines to improve child growth.

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DISRUPTION OF HUMAN LYMPHATIC EPITHELIAL CELL CONTACT INTEGRITY PROTEINS BY FILARIAL MIRNAS

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Parasitic filarial nematodes Wucheria bancrofti, Brugia malayi, and Brugia timori are the causative agents of the debilitating, yet neglected, infectious disease lymphatic filariasis. Adult worms reside in the human lymphatic system where they can survive and reproduce for 8-10 years. The worms can damage the lymphatics and cause lymphedema, however the mechanism by which this occurs is unclear. As filarial worms are in contact with lymphatic endothelial cells (LECs) we used an in vitro model to study interactions between the parasite and human LECs. Filarial worms have been shown to secrete microRNAs (miRNAs) that can be detected in the biofluids of infected animals and humans. We tested if secreted B. malayi miRNAs were involved in the damage to lymphatic cells, which could lead to lymphedema. We used miRanda, an algorithm to predict miRNA-mRNA pairs, to find potential human mRNA targets of B. malayi miRNAs that were previously found to be secreted by worms. First, we prioritized the human targets that encode proteins involved in cell-to-cell connection and the extracellular matrix: fibronectin, integrins, as well as proteins of tight junctions (claudins) and adherens junctions (VE-cadherin). We identified 2 Brugia miRNAs—bma-mir-86 and bma-mir-5864—that have potential target sites in these genes. To validate the interactions predicted and determine their effects on target genes, we treated LECs with miRNA-mimics, which mimic selected parasite miRNAs, and analyzed the expression of the human proteins to determine if there was suppression. We showed that the 2 parasite miRNAs tested significantly decreased the expression of human fibronectin and VE-cadherin. We also observed a reorganization of integrins in treated cells. As these parasite miRNAs are secreted by the worms in the lymphatics, they could participate in the

pathology by reducing cell-to-cell connection and adhesion of the cells, as well as increase the permeability of the endothelial monolayer. Defining the role filarial miRNAs play in the pathogenesis could help establish a mechanism that could be targeted therapeutically.

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A HUMAN PLURIPOTENT STEM CELL DERIVED MODEL OF THE BLOOD-BRAIN BARRIER IN CEREBRAL MALARIA

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Blood-brain barrier (BBB) disruption is a central feature of cerebral malaria (CM), a severe neurologic complication of Plasmodium falciparum (Pf) infections that presents clinically as an unarousable coma and is a significant driver of childhood mortality. The pathogenesis of CM involves sequestration of Pf-infected red blood cells (Pf-iRBCs) to the brain microvasculature. In-vitro BBB model-based studies have provided insight into CM-mediated brain injury, but limitations of these models include endothelial monolayers in the absence of cells like astrocytes and neurons and reliance on immortalized or primary brain microvascular endothelial cell (BMECs) that lack physiologically relevant barrier properties and show batch-to-batch variability. We have developed a multicellular BBB model comprised of human-induced pluripotent stem cell (iPSC) derived BMECs, neurons, and astrocytes representing a physiologically relevant BBB as determined by elevated trans-endothelial electrical resistance (TEER). Using the HB3var03 parasite strain that expresses proteins bind to endothelial cells, we conducted co-culture experiments with multiple timepoints over 9 hours. By the 6-and 9-hour timepoint, in iPSC-derived BMECs co-cultured with Pf-iRBC but not uninfected RBC controls, we observed disruptions in barrier integrity measured by TEER and confirmed by immunofluorescence imaging to visualize changes in the localization of tight junction (TJ) proteins occludin and zona-occludin-1. Western blots of BMEC lysates to determine Pf-iRBC co-culture mediated changes in TJ protein expression on BMECs, and immunoassays with co-culture supernatants to detect changes in expression of angiogenesis, and endothelial activation markers are ongoing. Furthermore, we will validate the effects of Pf-iRBC in a co-culture model of the BBB comprising of BMECs, astrocytes, and neurons to investigate neuronal injury. Upon completion, this work aims to establish the iPSC-derived multicellular BBB model as a new in vitro standard for investigating pathways underlying neuronal injury in clinical CM.

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THE BRCT DOMAIN FROM LEISHMANIA MAJOR LMJPES PROMOTES MALIGNANCY AND DRUG RESISTANCE IN MAMMALIAN CELLS

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According to IARC, 15% of cancer cases are attributable to pathogens including parasites. Epidemiological studies suggest an association between cancer and leishmaniasis. Recently, the homologue of the human oncogene PES1 was identified in Leishmania major and named LmjPES encoding a conserved protein containing a BRCT domain. This domain is a key factor in DNA damage-response checkpoints. Interestingly, previous results have demonstrated that LmjPES is involved in parasite infectivity. In addition, BRCT domain was used as a therapeutic target and new antileishmanial drug candidates were identified. Our work aimed to elucidate the hypothetical oncogenic implication of BRCT domain from LmjPES in host cells. We generated a lentivirus carrying this BRCT domain sequence (lentiBRCT) and a lentivirus expressing the luciferase protein (lentiLuc), as control, and used them to infect mammalian cells. We observed that the expression of BRCT domain from LmjPES conferred to HEK293T and NIH/3T3 mammal cells a greater replication rate and higher survival in vitro. Moreover, such lentiBRCT infected cells were less sensitive to genotoxic drugs 5-FU and etoposide. In addition, lentivirus infected cells were used to induce tumorigenesis process. The in vivo experiments showed faster tumor growth in mice inoculated with lentiBRCT respect to lentiLuc HEK293T infected cells. To shed some light on the molecular mechanisms involved in the cellular alterations described after the expression of the studied domain in mammalian cells, we performed a high-throughput RNA sequencing of LentiBRCT- and Lentiluc-infected HEK293T cells. The gene expression profiling analysis revealed that BRCT domain from LmjPES altered the expression of proliferation- (DTX3L, CPA4, BHLHE41, BMP2, DHRS2, S100A1 and PARP9), survival- (BMP2 and CARD9) and chemoresistance-related genes (DPYD, Dok3, DTX3L, PARP9 and DHRS2). Altogether, our results reinforced the idea that in eukaryotes, horizontal gene transfer might also be achieved by parasitism like Leishmania infection driving therefore to some crucial biological changes such as proliferation and drug resistance.

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SUPER RESOLUTION IMAGING REVEALS CYTOSKELETON REGULATION IN PLASMODIUM SEXUAL STAGE DEVELOPMENT

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The transmission of Plasmodium falciparum parasites from human to mosquito relies on the formation of a specialised sexual form known as the gametocyte. The gametocyte develops through five distinct morphological stages over a period of 10 days, adopting a unique crescent shape upon reaching sexual maturity. Formation of these mature stage V gametocyte is essential for transmission. The distinct morphology of the gametocyte is driven by the assembly of a dense microtubule (MT) network that assembles under an additional cisternal compartment called the inner membrane complex (IMC). In addition, the parasite also has an actin cytoskeleton which accumulates at the apical tips of the parasite and co-locates with the MT network across gametocyte development. Despite the importance of these structures to maintaining parasite morphology, we know very little about how these networks are regulated and how they work together to control gametocyte shape and transmission. In our work we investigate IMC proteins (GAPM 1-3), the actin nucleating protein formin 2 and important proteins of mitosis (centrin 1-3 and NDC80). To investigate the function of these proteins we have employed a conditional knockout approach and combined this with ultra-expansion microscopy, super-resolution imaging and electron microscopy. We show that early gametocyte have novel non-mitotic microtubules within their nuclei that bind and redistribute chromatin inside the nucleus of gametocytes. In addition, these novel MTs function in positioning the nascent IMC and subpellicular microtubules, initiating gametocyte elongation. We show that deletion of GAPM proteins ablates IMC expansion leading to an inability of the MT network to align and elongate the gametocytes. Lastly, we demonstrate that Formin 2 locates at the apical tips of the gametocyte interleaving between the actin and MT networks, stabilising the crescent shape. Deletion of Formin 2 results in a collapse of gametocyte shape. In this work we reveal a holistic picture of the function and interplay between key proteins controlling IMC, MT and actin cytoskeletons dynamics across gametocyte development.

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DEVELOPMENT OF AN IN VIVO MOUSE MODEL FOR TRANSMISSION BLOCKING STUDIES WITH HUMAN MALARIA PARASITE PLASMODIUM FALCIPARUM

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Malaria elimination/eradication will need a coordinated effort involving multiple strategies including those that interrupt transmission of malaria parasites from humans to mosquitoes. Transmission blocking drugs, vaccines and genetically modified mosquitoes represent an appealing approach. Standard membrane feeding assay (SMFA), which involves feeding mosquitoes with cultured Plasmodium falciparum gametocytes using glass membrane feeders is used as primary screen for different transmission blocking interventions (TBI). However, further development of TBI is hindered by the lack of a reliable P. falciparum small animal model to test TBI before proceeding to the controlled human malaria infection studies or field trials. To develop the mouse model for assessment of TBI we have utilized extremely immunodeficient NSG (NOD-scid IL2Rgammanull) mouse. The immunodeficiency allows the mice to be humanized by the engraftment of human red blood cells. P. falciparum asexual blood stages, when inoculated in RBC humanized NSG mice, are promptly cleared from circulation, either by macrophages or through splenic clearance. However, when we inoculated mature stage V gametocytes, they remained in circulation for at-least a week, which allows us to use these mice to feed Anopheles stephensi mosquitoes. Mosquitoes fed on NSG mice inoculated with P. falciparum mature gametocytes developed midgut oocyst and passive transfer of transmission blocking monoclonal antibody to Pfs25 (4B7) significantly reduced the transmission. To further standardize the assay, we are currently testing known transmission blocking drugs and antibodies.

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GLOBAL RELEASE OF TRANSLATIONAL REPRESSION ACROSS PLASMODIUM'S HOST-TO-VECTOR TRANSMISSION EVENT

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Malaria parasites must be able to respond quickly to their environment, including during their transmission between mammalian hosts and mosquito vectors. Therefore, before transmission, female gametocytes proactively produce and translationally repress mRNAs that encode essential proteins that the zygote requires to establish a new infection. This essential regulatory control requires the orthologues of DDX6 (DOZI) and LSM14 (CITH), which along with ALBA proteins, form a translationally repressive complex in female gametocytes that associates with many of the affected mRNAs. However, while the release of translational repression of individual mRNAs has been documented, the details of the global release of translational repression have not. Moreover, the changes in spatial arrangement and composition of the DOZI/CITH/ALBA complex that contribute to translational control are also not known. Therefore, we have conducted the first comparative transcriptomics and proteomics of Plasmodium parasites across the host-to-vector transmission event to document the global release of translational repression. Using female gametocytes and zygotes of P. yoelii, we find that over 150 transcripts are released for translation soon after fertilization, including those with essential functions for the zygote. However, we also observed that some transcripts remain repressed beyond this point. In addition, we have used TurboID-based proximity proteomics to interrogate the spatial and compositional changes in the DOZI/CITH/ALBA complex across this transmission event. Consistent with recent models of translational control, proteins that associate with either the 5' or 3' end of mRNAs are in close proximity to one another during translational repression in female gametocytes and then dissociate upon release of repression in zygotes. These interactions in female gametocytes were further validated through Structured Illumination Microscopy and Ultrastructure Expansion Microscopy. Together, these data provide a model for the essential translational control mechanisms used by malaria parasites to promote their efficient transmission.

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DYNAMICS OF ASYMPTOMATIC PLASMODIUM FALCIPARUM AND P. VIVAX INFECTIONS AND INFECTIOUSNESS TO MOSQUITO IN LOW TRANSMISSION SETTING OF ETHIOPIA: A LONGITUDINAL OBSERVATIONAL STUDY

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The natural history of Plasmodium falciparum and P. vivax asymptomatic infections and the magnitude of their contribution to onward transmission in co-endemic low transmission settings is incompletely studied. We conducted a 15-month longitudinal study in asymptomatic PCR-detected asymptomatic parasite carriage with mosquito membrane feedings every 14 days for 2.5 months and subsequent monthly parasitology assessments in Adama, Ethiopia. Transmission results were compared with passively recruited clinical malaria cases from the same setting. From 596 feeding experiments in 162 asymptomatic individuals, 0.3% (69/24,966) of mosquitoes were infected by 4 individuals. Two microscopy detectable asymptomatic P. falciparum carriers infected 18.8% (15/80) of mosquitoes and one sub-microscopic P. falciparum carrier infected 30% (14/46) of mosquitoes. No sub-microscopic P. vivax mono-infection was infectious. Among clinical cases, P. falciparum clinical patients were less infectious (2.7% infected mosquitoes, 38/1389) compared to P. vivax patients (42.4% infected mosquitoes; 1068/2519). When analyzing infection duration at a continuous scale, the median duration of infection was 33 days (IQR:15-56) for individuals who were P. falciparum microscopy positive at enrolment and 30 days (IQR:15-48) for individuals who were P. falciparum PCR positive (but microscopy negative) at enrolment. The longest infection duration we observed was 363 days. For P. vivax parasite carriers who were PCR positive at enrolment, the median duration was 33 days (IQR:15-60). We conclude that a minority of asymptomatic infections are of long duration and infectious to mosquitoes. Clinical cases are a relevant source of transmission for P. vivax.

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EFFECT OF CHLOROQUINE ON PLASMODIUM VIVAX PARASITE TRANSMISSION TO MOSQUITOES IN THE EARLY POST-TREATMENT HOURS, ARBA MINCH, ETHIOPIA

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Ethiopian malaria guidelines prescribe chloroquine (CQ) for Plasmodium vivax. Data on human-mosquito malarial parasite transmission in the initial days following CQ therapy is scarce. This study examines CQ's early transmission-blocking impact. Thirty microscopically confirmed P. vivax patients in Arba Minch, Ethiopia, participated in an open-label

experimental follow-up investigation. Participants were treated with CQ for three days and observed for 42 days. Clinical, microscopic blood film and quantitative polymerase chain reaction (qPCR) tests were performed. Anopheles arabiensis colony mosquitoes were tested using artificial membrane feeding. While nested polymerase chain reaction (nPCR) was used to measure the clearance of asexual parasites, qPCR was used to measure the clearance of mature gametocytes. 67% (20/30) were positive for P. vivax alone, 7% (2/30) for both P. vivax and P. falciparum, and 10% (3/30) were positive for P. falciparum by nPCR. Plasmodium vivax mono-infection cases confirmed by nPCR were included in the analysis. 85% (17/20) of confirmed cases were infectious to mosquitoes before treatment and 59% (10/17) after 8 and 24 hours of treatment. The median oocyst infection rate dropped from 51% (245/480 mosquitoes) (ranges: 14-83%) at baseline to 36% (209/522 mosquitoes) after 8 hours and 17% (81/440 mosquitoes) at 24 hours post-treatment. The circumsporozoite protein rate of An. arabiensis was 3% (95% CI: 1-7) before treatment, 3% (CI: 1-5) at 8 hours post-treatment, and 0.7% (CI: 0.1-2.5) at 24 hours post-treatment. Eight hours post-treatment, all patients had gametocytes and sexual parasites. After 24 hours of treatment, positive cases dropped to 50%, but mosquitoes continued to transmit parasites. On day three post-treatment, 19 of 20 patients obtained gametocyte clearance and all patients showed complete asexual parasite clearance. This finding implies that the P. vivax-positive cases continue supporting parasite transmission for at least 24 hours after treatment; therefore, protective intervention and anti-malarial medications that immediately kill mature gametocytes could be recommended.

6503

CLINICAL INVESTIGATION STUDY TO EVALUATE THE CONSISTENCY AND REPRODUCIBILITY OF TWO CONSECUTIVE MOSQUITO FEEDING ASSAYS IN ADULTS WITH VARYING PLASMODIUM FALCIPARUM GAMETOCYTE DENSITIES

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New malaria control tools are needed to prevent the transmission of parasites from host to the mosquito vector and vice versa. Infectiousness of Plasmodium falciparum gametocytes obtained from individuals to lab reared mosquitoes should be estimated and quantified in order to apply assays that are easily applicable for evaluating transmission-blocking interventions. The aim of this of this study was to establish relationship between parasite transmission from humans to mosquitoes both within a person and across persons by assessing the variation in the proportion of infected mosquitoes with at least one oocyst (oocyst prevalence) in direct membrane feeding assay (DMFA) and direct skin landing feeding assay (DSFA) performed at two consecutive time points in the same human subject with P. falciparum gametocytemia. A total of 400 adults residing in Western Kenya without symptoms of malaria were enrolled. A blood sample was tested for the presence of P. falciparum gametocytes. Subjects that tested positive for gametocytes had both direct membrane feeding assays (DMFA) and direct skin landing feeding assay (DSFA) on day 1 and day 2 to compare infection rates between the two feeds. Blood samples from 42/400 individuals testing positive for gametocytes underwent mosquito infection assays. Survival rates of mosquitoes at initial day 1 and subsequent feeding day 2 were 12.1 and 11.4 days for DSFA, and 13.2 and 11.6 days for DMFA. The mean oocyst prevalence by DSFA on days 1 and 2 was 5.2% and 2.3% on days 1 and 2; and 6.3% and 2.2% for DMFA, respectively, suggesting comparable readouts for initial versus subsequent feeding timepoints. The correlation between day 1 and day 2 and between assays was low. Exploratory analysis suggests a lower probability of infection the second day, with lower oocyst density. We will discuss the implications for future study designs in testing transmission-blocking interventions based on these results.

6504

HYPER-DIVERSE ANTIGENIC VARIATION AND RESILIENCE TO TRANSMISSION-REDUCING INTERVENTION IN FALCIPARUM MALARIA

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In falciparum malaria under high transmission, high asymptomatic prevalence co-occurs with incomplete immunity given vast antigenic variation of the parasite. The var multigene family encodes for the major surface antigen of the blood stage of infection. A field longitudinal study in northern Ghana relied on deep sampling of var sequences from individual isolates to monitor response to transient IRS (Indoor Residual Spraying) intervention. Resulting estimates of parasite population size and structure showed persistent features of high transmission regions despite considerable decrease in prevalence, consistent with a rapid rebound post-IRS. To ask whether the transmission system had been brought closer to losing its persistence, we investigate with a stochastic agent-based model (ABM) the existence of a sharp transition with intervention intensity. We also seek molecular indicators capable of revealing proximity to such a transition in the model, and apply those to the field molecular data on var genes across multiple surveys and the IRS intervention. The ABM explicitly incorporates the evolution of var genes and the acquisition of specific immunity by individual hosts. A sharp transition occurs in the model across a narrow region of intervention intensity in the capacity of the transmission system to rapidly rebound to high prevalence. Molecular indicators are identified, informative about the approach to this transition. Their application to the field data indicates that the system was brought close to transition by IRS, so that sustaining and intensifying intervention could have pushed it to a slow-rebound regime with a high probability of extinction. Our results establish a link between population dynamics of the disease and observations of parasite population genomics from the perspective of hyper-variable antigen-encoding genes. They indicate that the structure of diversity revealed via molecular surveillance can inform intervention against malaria in high-transmission endemic settings. These findings should be relevant to other pathogens with similar immune evasion strategies based on high antigenic diversity.

6505

DENGUE SEVERITY BY SEROTYPE IN 17 YEARS OF A PEDIATRIC HOSPITAL STUDY IN NICARAGUA

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The four dengue virus serotypes (DENV1-4) cause a range of clinical manifestations, from mild to severe and potentially fatal disease. Understanding dengue severity by serotype is critical, particularly in the context of the introduction of new vaccines that have differential efficacy by serotype. We studied the clinical spectrum of all 4 DENV serotypes over 17 years in the Nicaraguan National Pediatric Reference Hospital. Study participants 6 months to 14 years of age were followed during their hospital stay or as ambulatory patients. Cases were confirmed by molecular, serological and virological methods. A clinical report form with >150 variables with detailed clinical information was completed daily. Cases were classified according to the World Health Organization 1997 (Dengue Fever/Dengue Hemorrhagic Fever/Dengue Shock Syndrome; DF/DHF/DSS) and 2009 (Dengue without Warning Signs/Dengue with Warning Signs/ Severe Dengue) guidelines. A total of 2,811 participants were enrolled, with 1,570 (56%) laboratory-confirmed as DENV-positive. Of 1,355 cases with serotype result by RT-PCR, 281 corresponded to DENV1, 572 to DENV2, 466 to DENV3 and 36 to DENV4. With DENV2 and DENV4, secondary (2°) cases were more prevalent, with 478 (88.7%) and 30 (93.8%), respectively, while with DENV1 and DENV3, 136 (51.1%) and 237 (53.1%) were primary cases, respectively. Plasma leakage was associated with DENV2 (OR: 1.46; 95% CI: 1.16-1.85) and DENV3 (OR: 1.3; 1.02-1.66), with 190/572 (33.2%) DENV2 and 105/466 (22.5%) DENV3 cases resulting in DHF/DSS, respectively. Of the DHF/DSS cases, 167/178 (93.8%) of DENV2 cases were 2°, compared to 63/103 (61.2%) of DENV3 cases and 22/36 (61.1%) of DENV1 cases. Comparing serotypes, DENV2 was associated with DHF/ DSS (OR: 2.06; 1.67-2.75), while DENV3 was associated with Severe Dengue (OR: 2.08; 1.60- 2.70). Overall, we found that clinical manifestations of dengue differ by serotype and immune response, with DENV2 and DENV3 being most associated with severity. Our findings indicate that the clinical spectrum of all serotypes should be considered in the development of a safe and effective DENV vaccine.

6506

COMPARATIVE EVALUATION OF FIVE RAPID DIAGNOSTIC TESTS FOR DENGUE DIAGNOSIS

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Every year, dengue outbreaks cause substantial humanitarian and economic hardship worldwide. Dengue causes a wide spectrum of symptoms. Primary dengue can range from subclinical disease to flu-like symptoms. Although less common secondary dengue is associated with increased morbidity and mortality. Accurate, efficient and rapid diagnosis of dengue in acute stage is essential as delay in diagnosis increases the risk of severe dengue and can lead to poor disease outcome. In dengue-endemic areas, laboratories and clinics have to date relied on simple and cost-effective serological rapid diagnostic tests (RDTs) to diagnose dengue. This study evaluated the performance of five commercially available RDTs which can detect NS1 antigen and IgM/IgG antibodies: SD Bioline Dengue Duo, Atron Dengue virus IgG/IgM and Ag cassette, Standard Q Dengue Duo, Humasis Dengue combo kit and ALL Test Dengue Combo Rapid Test. Well characterized archived dengue and non-dengue serum samples at Aga Khan University, Pakistan were screened. Each RDT was evaluated separately and in combination to determine diagnostic parameters [non-structural (NS1) antigen and/or immunoglobulin M (IgM) positive]. 430 serum samples were evaluated (255 NS1 ELISA positive and 175 negative NS1 ELISA). Compared to the reference NS1 enzyme-linked immunosorbent assay (ELISA) samples, sensitivity of RDTs ranged from 69.8% to 94.12% with best overall sensitivity shown by Atron Dengue virus IgG/IgM and Ag cassette (94.12%) All RDTs showed a specificity of >99%. Atron Dengue virus IgG/IgM and Ag cassette (96.78%) had the highest diagnostic accuracy. In conclusion, Atron Dengue virus IgG/IgM and Ag cassette showed the highest sensitivity and diagnostic accuracy, while Standard Q Dengue Duo and ALL Test Dengue Combo Rapid Test showed the highest specificity. Moreover, these results confirm that combining antigen- and antibody-based RDTs can have huge value for dengue diagnosis and that very good commercial tests exist and should be used.

6507

POTENTIAL UTILITY OF CONTINUOUS PPG MONITORING IN THE MANAGEMENT OF SEVERE DENGUE

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Dengue infection can progress to shock, driven by increased intravascular permeability and plasma leakage. Management of patients with dengue shock is challenging as the risk of repeated episodes of shock (reshock) due to insufficient fluid replacement and ongoing plasma leakage must be weighed against the risk of volume overload when too much fluid is given. Therefore, a dynamic measure of intravascular volume to guide fluid management has the potential to improve clinical outcomes. We investigated the use of continuous photoplethysmogram (PPG) monitoring using a wearable device for the management of dengue in a prospective study involving 250 patients who were admitted to the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam in 2020 to 2022. Detailed clinical data were collected and PPG monitoring was performed for 24 hours after enrollment. We hypothesized that the PPG waveform can provide actionable information about a patient's volume status. The 2-hour time window preceding a reshock event, was predefined as an "empty" intravascular state, while the 2-hour time window between 1 to 3 hours following a fluid bolus, was predefined as "full". We then sampled PPG segments (1 minute duration) from these time windows and, accordingly, labelled each as "empty" or "full". Labelled segments were transformed into spectrograms and used to train and test a convolutional neural network model. There were 96 patients with sufficient data for the analysis. Data from 67 patients (70%) were used to train the model and the remaining data were reserved for testing. We repeated the analysis 3 times using 3 different patient splits. The overall performance of our model included accuracy of 0.76 (range 0.73-0.80), F1 score of 0.84 (range 0.84-0.85) and ROC-AUC of 0.77 (range 0.73-0.82). In summary, preliminary analyses suggest that information regarding intravascular volume during severe dengue can be extracted from real-life PPG recordings. Since PPG signals are measured continuously, there is the potential for dynamic guidance. We are continuing to refine our model and will present our updated analysis.

6508

METFORMIN AS ADJUNCTIVE THERAPY IN OVERWEIGHT AND OBESE PATIENTS WITH DENGUE: AN OPEN-LABEL SAFETY AND TOLERABILITY TRIAL (MEDO)

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Dengue is a major public health burden for Vietnam and globally. Patients with certain risk factors, including obesity, are at higher risk of developing severe disease. There is no antiviral for dengue and novel host-directed therapeutics are urgently needed, particularly in high-risk patients. We conducted an open-label trial using Metformin as an adjunctive therapy for dengue patients with obesity. Our hypothesis was metformin would attenuate obesity-induced lipid-inflammatory mediators, improve clinical parameters and reduce viral replication through AMPK activation and immunomodulation mechanisms. This trial recruited 120 overweight/obese patients with dengue who were admitted to the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam between 2020 and 2022. Patients were eligible for enrolment if they were 10- 40 years old, had a BMI > 25kg/m2 or BMI-for-age > 1SD, were within 72 hours of fever, and had a positive NS1 test. Sixty patients were treated with metformin (treatment group) and compared with 60 patients receiving standard of care (untreated group). Following a pilot of 10 patients given a low dose of metformin, the dosing for the remaining 50 patients was weight-based, with patients receiving either 1g or 1.5g per day in divided doses for 5 days. The primary outcome was number of adverse events (AEs) and secondary outcomes included comparisons of clinical, laboratory parameters, plasma viraemia, NS1 antigenaemia and biomarker kinetics. Majority of patients enrolled were male (68% in treatment group versus 73% in untreated) with a mean age of 18.4 ± 7.9 years in both groups. Preliminary analysis shows most of the patients developed more than 1 warning sign during their hospitalization (85% versus 88%) and 10% developed dengue shock syndrome (in both groups). Twenty-five patients (42%) had to discontinue metformin due to predefined AEs, including hypoglycemia (7%), severe diarrhea (22%), increased lactate > 3mmol/L (13%). The full trial results will be presented at the conference. ClinicalTrials.gov identifier: NCT04377451

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AFTERSHOCK: PERSISTENT INFLAMMATION AND ENDOTHELIAL ACTIVATION IN ADULT SURVIVORS OF DENGUE SHOCK

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Dengue shock (DS) is the most severe complication of dengue virus infection; the syndrome results from plasma leak through an activated, disrupted endothelial barrier and may be complicated by hyperinflammation. It is assumed that inflammation and endothelial disruption subside with clinical recovery, but no studies have followed up survivors to confirm this. We conducted a prospective observational study of adults (age≥16 years) with DS in Vietnam between 2018-2022. Patients completed the following assessments at hospital discharge, 1-, 3- & 6-months follow-up: health related quality of life (HRQOL) (EQ-5D-5L), cognitive function (Montreal Cognitive Assessment, MoCA), plasma inflammatory (IL-6, ferritin) and endothelial (Ang1, Ang2, VCAM1) biomarkers & endothelial function testing (EndoPAT). Healthy controls (HC) and survivors of septic shock (SS) participated as comparators. Survivors of DS (n=125) experienced rapid functional recovery, with median EQ-5D-5L visual analogue score >90/100 at all timepoints. MoCA scores were lower than normal (≥26) at hospital discharge (med:23/30, IQR:20-26), but scores had largely normalized by 3 months (med:27/30, IQR:25-29). However, compared to HC (n=25), DS patients had persistent subclinical inflammation (elevated IL-6 & ferritin vs HC, p<0.01 at all timepoints), endothelial activation (lower Ang1 and elevated VCAM1 vs HC, p<0.01 at all timepoints) and impaired endothelial function (median Reactive Hyperaemia Index below normal threshold of 1.67 at 1-,3-&6-months). Survivors of SS (n=26) also had persistent inflammation, with worse functional and cognitive outcomes than DS survivors. This is the first report that survivors of DS have persistent inflammation, endothelial activation, and impaired endothelial function for at least 6 months after discharge. Further study is needed to determine the duration of this phenomenon, and whether individual or repeat infections have an impact on long term cardiovascular health; if so, these findings could have important public health implications for dengue endemic regions.

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NEURODEVELOPMENTAL OUTCOMES IN TWO YEAR OLD CHILDREN BORN DURING THE ZIKA EPIDEMIC IN BRAZIL: A PROSPECTIVE COHORT STUDY

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Key questions remain on the impact of Zika virus (ZIKV) exposure on long-term developmental outcomes, especially among infants who were exposed in utero during the pandemic in the Americas but did not develop congenital Zika syndrome (CZS) at birth. Therefore, we prospectively evaluated the clinical and developmental outcomes of a cohort of children with two years of age who were born during the Zika epidemic in Salvador, Brazil. We enrolled mothers and their newborn infants at a maternity hospital between Oct 01, 2015 and Jan 31, 2016. Performed anthropometric, auditory, ophthalmologic evaluations, Hammersmith Infant Neurological Examination and Bayley Scales of Infant and Toddler Development-3 assessment. We ascertained ZIKV exposure in utero by assaying for neutralizing antibodies in sera from mothers during childbirth and evaluated the association with clinical and developmental outcomes. Among 469 children enrolled at birth, 364 (78%) completed follow-up evaluations at a mean age of 26.9 (±4.0) months. Of these, 214 (58.8%) were born to mothers with serologic evidence of ZIKV exposure. Of these, 22 (10.2%) were identified to have neurodevelopmental impairment (31.8% cognitive, 45.5% language and 22.7% motor domains). After adjusting for maternal age, ZIKV exposure was not associated with specific domain impairments but was associated with a higher risk (OR=2.36; 95% CI 1.05-5.80) for global neurodevelopmental impairment. The attributable fraction of neurodevelopmental impairment associated with ZIKV exposure was 36.0%

(95% CI 3.4 to 68.6%). Significant associations were not observed between exposure and anthropometric, auditory or ophthalmologic deficits. Our study found that ZIKV exposure in utero imparts mild neurodevelopmental deficits, primarily associated with language acquisition, in a significant proportion of children without CZS by two years of life. Given the large numbers of infants that had unapparent ZIKV exposures during the pandemic, routine screening and intervention will be needed in affected regions of the Americas to mitigate these impacts on development, especially as these children enter schools.

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PERSISTENT RHEUMATOLOGICAL DISEASE AFTER SEVEN YEARS OF CHIKUNGUNYA VIRUS INFECTION: RESULTS FROM A COHORT STUDY IN PIEDECUESTA, COLOMBIA

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Chikungunya virus (CHIKV) has circulated and caused outbreaks in the Americas region since 2014. There is a need to better characterize post-CHIKV chronic rheumatism and its impact on quality of life (QoL). The objective was to estimate the prevalence of post-CHIK chronic rheumatism in adult patients 7 years after the CHIKV outbreak (2014-2015) in Piedecuesta, Colombia.We evaluated 106 patients, 94 (88.7%) of which had symptomatic infection. The exposure was determined by RT-qPCR, IgG/IgM ELISA, or the ArboMIA multiplex immunoassay. In 2022, approximately 7 years post-infection, all patients completed a set of surveys (screening for rheumatic disorders [GALS], stiffness [MSQ], functional capacity [HAQ]), provided a blood sample, and were examined by physicians who were trained by a rheumatologist. A subgroup completed the surveys fatigue [FSS], and QoL [SF-36]. A second evaluation was performed by a rheumatologist to those patients (n=46; 43.3%) who screened positive to GALS but whose clinical findings were not associated with trauma.The prevalence of post-CHIK chronic inflammatory rheumatism (pCHIK-CIR) was 10.8% (IC95%: 5.5, 18.5) whereas 35.3% (95%CI: 26.0, 45.4) had a diagnosis of Non-inflammatory pain likely degenerative. Among patients with pCHIK-CIR, 4 (36.4%) had oligoarthritis/polyarthritis, 4 (36.4%) post-viral arthralgia, 2 (18.1%) fibromyalgia, and 1 (9.1%) fasciitis; moreover, 63.4% (n=7) of pCHIK-CIR cases had arthralgia (pain scale median=7), and the joints most affected were hands (57.1%), knees (57.1%) and feet (42.9%). A small proportion had stiffness (n=2; 18.2%; stiffness scale median=9). In addition, overall, 33.7% of participants screened positive for fatigue, whereas those with pCHIK-CIR scored lower than the recovered cases in the QoL questionnaire (medians: 37.4% vs. 49.4%, p=0.001; and 46.1% vs 55.8%, p=0.000; for mental and physical domains, respectively). This study implemented a comprehensive clinical assessment to objectively estimate and characterize the prevalence of chronic rheumatological disease attributed to CHIKV infection. These results correspond to a preliminary analysis.

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MAPUTO SANITATION TRIAL 60-MONTH FOLLOW-UP ANTHROPOMETRIC MEASUREMENTS AND CHILD HEALTH

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Safe water, sanitation, and hygiene (WASH) can interrupt enteric pathogen transmission and may improve growth outcomes in children. Growth deficits manifest as children age, with early childhood the critical window for interventions. We conducted a cross-sectional assessment of long-term growth outcomes in a cohort of children exposed to differential sanitation infrastructure from birth in Maputo, Mozambique. We enrolled 1014 children aged 1 - 60 months living in household clusters in two arms: those having received improved shared sanitation (n = 473) intervention and those from matched clusters with unimproved sanitation (n = 541) but meeting eligibility criteria for the intervention. We used standard length, height, and weight measurement methods with appropriate quality control checks to reduce measurement bias. We calculated height/length-for-age (HAZ) and weight-for-age (WAZ) and weight-for-height (WHZ) z-scores and compared them with the 2010 WHO Child Growth Standards reference dataset, utilizing the R package z-scorer. We estimated the prevalence of stunting, wasting, and underweight children in both arms. Approximately 26% (95% CI: 23%, 30%), 4.6% (95% CI: 3.1%, 6.7%), and 6.1% (95% CI: 4.4%, 8.4%) of control children were stunted, wasted and underweight, respectively, compared with 16% (95%CI: 13%, 20%), 4.6% (95% CI: 3.1%, 6.9%), and 4.6% (95% CI: 3.1%, 6.9%) of children in the intervention arm, suggesting visible reductions in stunting among children born into better sanitation conditions. Mean differences in HAZ/LAZ, WAZ and WHZ z-scores between treatment arms are shown HAZ 0.32 (95% CI: 0.129, 0.51), WAZ: 0.20 (95% CI: 0.06, 0.33), and WHZ: -0.028 (95% CI: -0.20, 0.14). We estimate that children in the safe sanitation group experienced 41% reduced odds of stunting (OR 0.59, 95% CI: 0.43 - 0.82), after controlling for age, sex, household wealth indicators, and caregiver education. Because interventions were not randomly assigned, we cannot rule out unmeasured confounding. Ongoing analyses will account for associations with enteric pathogen gut carriage to interrogate sanitation-related drivers of undernutrition.

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EFFECT OF A WATER, SANITATION AND HYGIENE PROGRAM ON HANDWASHING WITH SOAP AMONG DIARRHEA PATIENTS AND ATTENDANTS IN HEALTHCARE FACILITIES IN THE DEMOCRATIC REPUBLIC OF THE CONGO: A RANDOMIZED PILOT OF THE PICHA7 PROGRAM

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Healthcare-acquired infections are a major problem in healthcare facility settings globally. The Democratic Republic of the Congo (DRC) has over 2 million diarrhea patients admitted to health facilities annually. Health facilities can be a high-risk environment for transmission of diarrheal diseases. The objective of the Preventative Intervention for Cholera for 7 Days (PICHA7) program is to develop evidence-based water, sanitation, and hygiene (WASH) interventions to reduce cholera and other severe diarrheal diseases in DRC. This study evaluated the effectiveness of PICHA7 program delivery in increasing handwashing with soap at stool, vomit, and food related events in a healthcare facility setting among diarrhea patients and their attendants. A randomized pilot of the PICHA7 program was conducted among 284 participants from 27 health facilities from March 2020 to November 2021 in urban Bukavu in South Kivu Province of DRC. The 'Standard Message' Arm received the standard message given in DRC to diarrhea patients on the use of oral rehydration solution. The PICHA7 arm received the PICHA7 WASH pictorial communication module bedside to the diarrhea patient, and a soapy water bottle in the healthcare facility during the time of treatment. Within 24 hours of intervention delivery, three-hour

structured observation of handwashing practices at stool, vomit, and food related events (key events) was conducted in healthcare facilities of diarrhea patients and their attendants. Compared to the Standard Message Arm, there was significantly higher handwashing with soap at key events in the PICHA7 Arm (39% vs. 12 %) (Odds Ratio: 5.32; (95% Confidence Interval (CI): 2.00, 14.10). These findings demonstrate that delivery of the PICHA7 WASH pictorial communication module and provision of a soapy water bottle to diarrhea patients and their attendants presents a promising approach to increase handwashing with soap among this high-risk population in healthcare facilities in eastern DRC.

6514

THE LONG-TERM EFFECTS OF IMPROVED WATER, SANITATION, AND HYGIENE (WASH) AND IMPROVED COMPLEMENTARY FEEDING ON SCHOOL-AGE GROWTH AND DEVELOPMENT IN RURAL ZIMBABWE: FOLLOW-UP OF THE SHINE CLUSTER-RANDOMIZED TRIAL

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The SHINE cluster-randomised trial tested the effects of a household WASH intervention and/or infant and young child feeding (IYCF) on child stunting and anemia at age 18 months in rural Zimbabwe. SHINE showed that IYCF increased linear growth and reduced stunting by age 18 months, while WASH had no effects. Here, we present long-term follow-up data from 1000 HIV-unexposed children (250 in each intervention arm) who were re-enrolled at age 7 years to evaluate growth, body composition, cognitive and physical function. We measured cognition using the Kaufman Assessment Battery for Children (KABC-II) as a primary outcome, and executive function, literacy, numeracy, fine motor skills and socioemotional function as secondary outcomes. Physical function was assessed by handgrip strength, broad jump and shuttle-run test. Growth was assessed by anthropometry, body composition (using bioimpedance analysis) and skinfold thicknesses. Contemporary household socioeconomic status, demographics, nurturing, food and water insecurity were measured by a caregiver questionnaire. Data were analyzed using generalized estimating equations with an exchangeable working correlation structure to account for clustering. Of 1000 children assessed, 10 were excluded from analysis for severe disability. Children (51% female) were median 7.2 years old (IQR 7.1, 7.4). IYCF and WASH each had no effect on the primary outcome (KABC-II score) or secondary cognitive outcomes, except a small difference in socioemotional function in the WASH arms (-1.2 marks, 95%CI -2.0, -0.5, p=0.002) which remained in adjusted analyses. Children in IYCF arms had a greater handgrip strength (+0.3 Kg, 95% CI 0.0, 0.5, p=0.03), which remained in adjusted analyses. There were no significant effects of IYCF or WASH on growth or body composition measures at 7 years. Overall, long-term follow-up of a subgroup of children enrolled to SHINE showed minimal long-term effects of early-life IYCF and WASH on school-age function, despite improved linear growth following IYCF in the original trial.

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SURPRISE SOAP: EFFECT OF A NOVEL HYGIENE INTERVENTION ON OLDER CHILDREN'S HANDWASHING IN COMPLEX HUMANITARIAN SETTINGS: RESULTS OF TWO CLUSTER-RANDOMIZED CONTROLLED EQUIVALENCE TRIALS

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Children in emergencies are particularly vulnerable to infectious diseases such as diarrhoea and respiratory infections. Improving handwashing with soap (HWWS) can greatly reduce transmission, however, there is limited evidence on which approaches to child targeted HWWS promotion are effective. One recent innovation - the "Surprise Soap" intervention - was successful in a small-scale efficacy trial in an IDP camp in Iraq. This novel intervention includes transparent soap with embedded toys delivered in a short household session comprising a glitter game, instruction of how to wash hands, and HWWS practice. Whilst promising, this approach has not been evaluated at programmatic scale in a complex emergency setting. To address this gap, we conducted two cluster-randomised controlled equivalence trials, one across IDP camps in Somalia, and one in a refugee settlement in Sudan. In each trial, 200 households were randomly allocated (1:1) to receive the Surprise Soap intervention or an active comparator intervention including plain soap delivered in a short household session involving standard health-based messaging and instruction of how to wash hands. The primary outcome was the proportion of pre-specified occasions when HWWS was practiced by children aged 5-12, measured at baseline, 4-weeks, 12 weeks, and 16 weeks post intervention delivery. In both trials, we observed a large and sustained increase in HWWS in both arms (Somalia: 48 and 51 pp increase in the intervention and comparator arm, respectively; Sudan: 27 and 23 pp increase, respectively). However, there was no difference in HWWS between the two arms. In these two settings, where soap availability and past exposure to HWWS promotion was low, it appears that interventions that directly target children at the household-level and provide soap can increase their HWWS and potentially reduce disease risk. Here the Surprise Soap intervention offers no marginal benefit over providing plain soap within a household-level "standard" intervention that would justify the additional costs. Applying contextual knowledge to decisions on Surprise Soap implementation is recommended.

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EFFECTIVENESS OF SEWAGE INTERVENTION ON LEPTOSPIRA TRANSMISSION AMONG RESIDENTS OF URBAN INFORMAL SETTLEMENTS

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Leptospirosis is an environmentally-transmitted zoonotic disease that affects impoverished urban and rural populations worldwide. In informal settlements, leptospirosis is associated with precarious sanitary infrastructure. Yet, the role of sewerage in reducing Leptospira transmission has not yet been rigorously evaluated. We conducted a cluster-controlled

natural experiment in a slum community in the city of Salvador, Brazil to prospectively evaluate the effectiveness of a government sewerage intervention. We selected two intervention clusters which comprised of a regions where open sewers were closed without implanting rainwater drainage in 2018 and 2021 and one control cluster for each period, which did not receive the intervention. As part of an on-going cohort study, we performed biannual serosurveys of the study community during the study period from 2015 to 2022. Leptospira infection was ascertained by detecting seroconversion or a four-fold rise in titer during microscopic agglutination testing and used in time series analysis to estimate effectiveness of the intervention using generalized estimating equations models. Age, sex, and elevation level were used to adjust estimates. Among 1,058 residents who were enrolled and followed during the study period, the Leptospira infection rates varied between 13 and 48 per 1000 follow-up events. A significant difference was not observed in the odds of Leptospira infection between control and intervention clusters in the post-intervention period (OR: 0.78; 95% CI 0.35-1.13). After the closure of sewage, residents in intervention clusters reported frequently exposed to flooding, mud, and soil. Our findings suggest that isolated closure of human fecal sewage without implanting enclosed rainwater drainage systems was not effective in reducing Leptospira transmission. Effective interventions in high-risk slum communities must therefore incorporate multiple sanitation dimensions and ensure sustainability.

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IMPACT OF THE WASH IN SCHOOLS FOR EVERYONE (WISE) PROGRAMME ON CHILD HEALTH AND SCHOOL ATTENDANCE IN ADDIS ABABA, ETHIOPIA: A CLUSTER-RANDOMISED CONTROLLED TRIAL

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Water, sanitation and hygiene (WASH) interventions in schools (WinS) have been proposed to reduce morbidity in schoolchildren, including gastrointestinal and respiratory infection, and improve school attendance, particularly among post-menarcheal girls. However, evidence of the impact of WinS interventions on pupil health and educational outcomes has been mixed. We evaluated the WASH in Schools for Everyone (WISE) programme implemented by US-based NGO Splash in partnership with the Government of Ethiopia, which aims to achieve universal WASH coverage in schools in Addis Ababa, Ethiopia over a five-year period. We conducted a cluster-randomised trial among 60 randomly selected primary schools and randomly assigned them 1:1 to receive the intervention during the 2021/22 academic year or the following year (waitlist control). The intervention comprised WASH infrastructure improvements, including water storage and filtration, drinking water / handwashing stations and upgraded sanitation facilities, and behaviour change promotion. Within each participating school, we enrolled between 2 and 4 randomly selected classes in to reach a total school enrolment of approximately 100 pupils. Individual pupils (ages 7 - 16) were enrolled in November 2021. At four follow-up visits between March and July 2022, enumerators recorded roll-call absence, pupil-reported illness (diarrhoea, respiratory infection) and pupil-reported absence in past week among pupils present. Secondary outcomes including wellbeing and menstrual hygiene self-efficacy were recorded at the final follow-up. We found a 17% reduction in odds of pupil-reported respiratory infection in the past week during the follow-up period among pupils in intervention vs. control schools (OR: 0.83, 95% CI: 0.70, 0.99), notable in the context of the COVID-19 pandemic. No impacts on diarrhoea or absence were observed. There was evidence of greater intervention effects among boys vs. girls. The Splash intervention was delivered with high fidelity. Further analyses will explore the heterogeneity in effects and the link between compliance and observed outcomes.

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PROCESS EVALUATION OF THE PREVENTATIVE INTERVENTION FOR CHOLERA FOR SEVEN DAYS (PICHA7) WATER, SANITATION AND HYGIENE MOBILE HEALTH PROGRAM

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In the Democratic Republic of the Congo (DRC) there are estimated to be 85 million diarrhea episodes annually. Effective and scalable water, sanitation, and hygiene (WASH) interventions are urgently needed to reduce diarrheal diseases globally. Phone-based reminders of public health information have been shown to reduce disease morbidity and increase health-protective behaviors. The objective of the Preventative Intervention for Cholera for 7 Days (PICHA7) program is to develop evidence-based WASH interventions to reduce cholera and other severe diarrheal diseases in DRC. The PICHA7 mobile health (mHealth) program delivers weekly voice, text, and interactive voice response (IVR) messages to diarrhea patient households promoting handwashing with soap and water treatment and safe water storage. The randomized pilot of the PICHA7 program demonstrated this intervention was effective in increasing handwashing with soap and water treatment behaviors during the three-month program period compared to the standard message given in DRC on the use of oral rehydration solution for rehydration. The objective of this study was to assess the implementation of the PICHA7 mHealth program during this randomized pilot to determine the feasibility of delivering this program in urban Eastern DRC. This study was conducted in Bukavu in South Kivu province in eastern DRC. Three hundred fifty-six participants were in households that received weekly text, voice and IVR messages from the PICHA7 mHealth program over the 3-month program pilot. Outcome indicators included unique text, voice, and IVR messages received (fidelity) and % of unique messages fully listened to (dose). Eighty three percent of text messages were received by program households. Eighty seven percent of voice and 88% of IVR messages sent were answered by at least one household member. Ninety percent of voice messages were fully listened to, and 62% of IVR messages. These findings have shown high fidelity and dose of mobile messages delivered for the PICHA7 mHealth program, demonstrating the feasibility of delivering the PICHA7 mHealth program in our study setting in Eastern DRC.

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BACTERIAL ZOONOSES DETECTED BY 16S RRNA METAGENOMICS AMONG FEBRILE ADMISSIONS IN KILIMANJARO, TANZANIA, 2007-2009

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Bacterial zoonoses are prominent causes of severe febrile illness in East Africa. While most of these diseases are highly treatable, many require specific therapies beyond standard empiric antimicrobials. Diagnosis remains a challenge, as these fastidious or non-culturable organisms thwart conventional culture and serologic diagnosis requires convalescent sample collection. Within a well-characterized fever etiology cohort, we applied a high-throughput 16S rRNA metagenomics assay validated for targeted detection of bacterial zoonotic pathogens. A prospective cohort study enrolled pediatric and adult medical patients admitted with fever

to 2 referral hospitals in Moshi, Tanzania, September 2007- April 2009. Red cell pellets were archived at -70ºC after plasma fractionation of EDTA whole blood obtained from participants within 24 hours of admission. DNA extracts from the cell pellets were subjected to PCR targeting the V1-V2 of 16S rRNA, followed by metagenomics deep-sequencing of V1-V2 amplicons.Taxonomic identifications were analyzed after subtraction of background taxonomic identifications of ubiquitous DNA contamination from the environment. Among 788 participants enrolled the median (interquartile range) age was 20 (2-38) years, 239 (32.1%) were HIV-infected, 384 (50.4%) were male, and 314 (47.3%) lived in an urban setting. A bacterial zoonotic pathogen was detected in 10 (1.3%): 3 Rickettsia typhi, 1 Rickettsia conorii, 2 Bartonella quintana, 1 Leptospira borgpetersenii, 1 Leptospira species, 1 Coxiella burnetii, 1 sample with reads for an apparently novel organism in the Anaplasmataceae family. This targeted 16S metagenomics approach made important identifications: a potentially novel agent of anaplasmosis; and to our knowledge the first molecular evidence of R. conorii in East Africa, improving our understanding of the species responsible for spotted fever group rickettsioses in the region.

6520

DETERMINING FLEA VECTOR SUSCEPTIBILITY TO INSECTICIDES AS PART OF PLAGUE RISK MONITORING IN MADAGASCAR

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Fleas have medical importance in Madagascar in relation to human plague. Through infected bites, they transmit Yersinia pestis from rodents to humans. Two species, Xenopsylla cheopis and Synopsyllus fonquerniei, are known vectors. Insecticides are the primary response tool to control fleas; therefore, susceptibility monitoring is essential to ensure this intervention is effective. We aimed to determine susceptibility of plague flea vectors to insecticides. Between 2019 and 2022, fleas were collected alive then reared in insectary. Following WHO protocols, eighteen, twelve and ten assays were performed using fenitrothion, permethrin and deltamethrin respectively. Per assay, 40 fleas were exposed to paper impregnated with the following concentration/duration combinations: fenitrothion 1% for 5h (organophosphate), permethrin 0.75% or deltamethrin 0.05% for 8h each (pyrethroids). After 24 hours, mortality rates (MR) were recorded. Fleas were either resistant (MR < 80%), tolerant (80% ≤ MR < 98%) or susceptible (98% ≤ MR ≤ 100%). Sixteen populations (sites) from eight districts were tested. Eighteen, twelve and ten assays were performed using fenitrothion, permethrin and deltamethrin respectively. Susceptibility to fenitrothion was heterogenous but 50.0% of populations remained susceptible, two were tolerant (11.1%) and seven were resistant (38.9%). All S. fonquerniei were fenitrothion susceptible whereas X. cheopis showed heterogenous responses. Two S. fonquerniei populations were permethrin tolerant (16.7%) and ten were resistant (83.3%). Almost all districts showed permethrin resistant X. cheopis. Nine X. cheopis populations were deltamethrin resistant and one was tolerant. These findings showed heterogeneity responses to insecticides considering sites and species. All populations were non-susceptible to pyrethroids. Susceptibility to fenitrothion persisted although trends indicate resistance emergence which may be related to plague control or other usage. Monitoring flea susceptibility to insecticides should be continued to guide data driven decision making for plague control.

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RISK FACTORS ASSOCIATED WITH RURAL HOUSEHOLD FLEA INFESTATIONS IN THE PLAGUE ENDEMIC AREA OF MADAGASCAR

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Human and domestic animals may experience skin reactions and discomfort due to heavy flea bites. Some species are vectors of pathogens such as Yersinia pestis, the agent of bubonic plague. In this study, we are interested in the species composition, prevalence, abundance, seasonality, and risk factors for the host-seeking fleas infesting households in plague endemic areas of Madagascar. We used a structured questionnaire and observational checklist to collect data from households in 4 villages. Fleas were sampled during the dry and the rainy season using a candle trap for 3 consecutive nights. We used a generalized linear mixed model to identify the factors that are associated with flea abundance in households. We found that more than 98% of the households were infested by fleas, dominated by the species Pulex irritans (98.18%, n=9,352). No seasonal pattern was found in flea abundance, but the number of fleas detected per household was highly variable with an average of 37.16 fleas per household during the dry season and 45.66 during the wet season. Our model showed that flea infestation was associated with having a male head of the household (aOR=1.75), reported rodent activity (aOR=1.31), mat floor (aOR=1.98), and thatched roof (aOR=1.22). The risk increased with the number of chickens (aOR=1.03), pigs (aOR=1.07), and household size (aOR = 1.09). Head of the household education level above primary school (aOR=0.58), sleeping two stories away from the ground floor (aOR=0.81) where livestock was kept at night, and the proximity of a separated livestock housing (aOR=0.91) were found to be protective against flea infestation. High flea burden in the household motivated the use of insecticide, which may induce resistance among the vectors. Interventions targeting an increased quality of life, access to education, and security may alleviate the flea burden in rural villages experiencing high flea infestation. The human flea, P. irritans is one of the probable vectors in Madagascar and the present description of its infestation ecology is a first step toward understanding its potential role in plague transmission.

6522

SURVEILLANCE FOR METASTRIATE TICKS AND SPOTTED FEVER GROUP RICKETTSIOSES IN SOUTHERN ILLINOIS

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Reported human cases of Spotted Fever Group Rickettsioses (e.g., Rocky Mountain Spotted Fever) have been increasing in Illinois over the past few decades. The majority of SFGR cases have been reported from the southern region of the state. However, until beginning the Illinois statewide active tick surveillance program in 2019, relatively little information was available regarding population densities and SFGR pathogen prevalence in Illinois ticks, and there was a need to address gaps in understanding of human exposure risk to different tick-borne Rickettsia sp. pathogens. Based on the hypothesis that some of the reported human SFGR cases in southern Illinois could be due to Rickettsia sp. other than R. rickettsii, and possibly due to R. parkeri, we designed a sampling strategy to identify environments most likely to harbor the Gulf Coast tick (Amblyomma maculatum), the vector of R. parkeri. During targeted collection events, we also retained any other tick species encountered. Sampling yielded collections of A. americanum, A. maculatum, and D. variabilis. We collected

782 adult Gulf Coast ticks in 8 southern Illinois counties in summer 2020, a 30-fold increase over the sum total of all prior historical reports in Illinois. We tested all three metastriate tick species for Rickettsia amblyommatis, R. parkeri, and R. rickettsii. Tick infection prevalences and densities of adult and nymphal ticks were compared to the incidence of reported human SFGRs. Gulf coast ticks were strongly overdispersed, as they were found to be highly abundant in specific focal locations. Overall, 17.4% of Gulf Coast ticks were positive for R. parkeri, 48.5% of lone star ticks were positive for A. amblyommatis, and we detected no R. rickettsii in the 3,324 ticks tested. The standardized incidence ratio of SFGRs at the county level was most strongly associated with the density of R. amblyommatis-infected A. americanum nymphs and adults. Understanding the distribution of tick species and Spotted Fever Group Rickettsiae diversity in southern Illinois is essential for accurate and timely diagnosis of tick-borne disease and design of effective tick-bite prevention messaging.

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SEROLOGIC TESTING FOR THE DIAGNOSIS OF BARTONELLA INFECTIONS IN PATIENTS IN MARYLAND

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Bartonella species are gram negative, vector-borne bacteria which cause a range of human disease. Bartonella species are an underrecognized pathogen and infections are often missed by routine microbiological testing. Bartonella infections in the United States are initially diagnosed by serologic testing for antibodies to B. quintana, the causative agent of trench fever, and Bartonella henselae, the causative agent of cat scratch disease, however the number of Bartonella species that are known to cause human disease is growing each year. To better understand the prevalence and diagnosis of Bartonella infections in Maryland a retrospective analysis of all serologic testing for Bartonella species through the University of Maryland Medical System from 2020-2022 was conducted. 271 serologic tests were ordered between 2020-2022. Clinical indications for testing included homelessness, contact with cats, fever, lymphadenopathy, animal bites, and endocarditis. However, in many cases there were no clinical indications for testing. Overall, twenty were positive for IgM and/or IgG to B. quintana and/or B. henselae. Eight were positive for IgM and IgG and twelve were positive for IgG alone. While molecular testing following serologic diagnosis indicated that B. henselae and quintana along with B. rochalimae were causes of positive serologic results, several cases were complicated by false positive serology for Chlamydia, Coxiella and/or Brucella, confusing those who are unfamiliar with serologic testing causing delayed treatment. Additionally, false positive/borderline positive serologic results and/or results due to previous infection delayed treatment in cases where clinical syndromes were mistakenly ascribed to acute Bartonella infections. Results from serologic testing show that Bartonella is an important yet poorly understood human pathogen with the potential to cause significant morbidity. Lack of appropriate laboratory tests and education result in treatment delays and increased morbidity in patients with suspected Bartonella infections. Increased awareness of Bartonella as a human pathogen is imperative.

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MOLECULAR SURVEY OF ANAPLASMATACEAE AGENTS AND BARTONELLA SPP IN COATIS NASUA NASUA FROM URBAN FORESTED AREAS IN BRAZIL

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The Anaplasmataceae and Bartonellaceae families encompasses vector-borne obligate and facultative, respectively, intracellular αproteobacteria of human and veterinary medicine importance. While Ehrlichia and Anaplasma are tick-borne agents, Neorickettsia can be transmitted through the ingestion of intermediate hosts harboring trematodes infected with Neorickettsia. Depending on the species, Bartonella can be transmitted by fleas, lice, bites and scratches. This study investigated the molecular occurrence of Ehrlichia, Anaplasma, Neorickettsia, and Bartonella in coati's blood samples in Midwestern Brazil. Twenty-five out of 165 samples, 15.1%, were positive in the screening PCR based on the dsb gene of Ehrlichia spp. and were characterized using 16S rRNA, sodB, groEL, and gltA genes and the 23S-5S intergenic space region ITS. Phylogenetic analyses based on all six molecular markers positioned the sequences into a new clade, with a common origin of Ehrlichia ruminantium. Genotype analyses of 16S RNA sequences revealed the presence of two distinct Ehrlichia genotypes. Six samples, 3.6%, were positive in the screening nPCR for the 16S rRNA gene of Anaplasma spp. and were submitted to an additional PCR targeting the ITS for molecular characterization. Phylogenetic analyses based on both 16S rRNA gene and ITS positioned the Anaplasma sp. detected in the present study in a large clade with other Anaplasma sp. previously detected in ticks and wild animals and in a clade with Candidatus Anaplasma brasiliensis, respectively. Neorickettsia sp. 16S rDNA, showing high identity to Neorickettsia risticii, was detected in 6 coati blood samples. None of the coati blood samples was positive for Bartonella spp. in a combined approach using BAPGM (Bartonella AlphaProteobacteria Growth Medium) and isolation onto chocolate agar followed by a qPCR based on the nuoG gene. The present work described a putative novel Anaplasmataceae agent, namely Candidatus Ehrlichia dumleri, Anaplasma sp. closely related to the previously described Candidatus Anaplasma brasiliensis, and Neorickettsia sp. in coatis from urban forested areas in Brazil.

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DOGS AS RICKETTSIA SPP. SENTINELS IN A PERUVIAN AMAZON NATURAL RESERVE BUFFER ZONE

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Countries neighboring Peru, such as Brazil and Colombia, have reported human cases of high and mildly pathogenic Spotted Fever Group rickettsiae (SFGR), including R. rickettsii and R. parkeri strain Atlantic rainforest, respectively; however, these species have not been reported in the Peruvian Amazon basin. Dogs play essential roles in the transmission cycles of these spp, since they serve as amplifying hosts. We conducted a cross-sectional study in a rural community of Madre de Dios (MdD) to characterize the species of ticks in dogs and to determine the presence of ticks and dogs positive to Rickettsia spp. We collect whole blood and ticks (n=23) from 23 dogs living around Kawsay Biological Station, located in the Tambopata National Reserve buffer zone. We collected 23 ticks from 23 dogs, including Amblyomma ovale (n= 22) and Rhipicephalus sanguineus (n=1). We tested blood samples and ticks by real time-PCR targeting the rickettsial conserved gene gltA. We found 2 (8.2%) Rickettsia-positive dogs and 12 (54.2%) ticks. Of the 12 positive ticks, 11 were identified as A. ovale (50% of all 22 A. ovale) and one as R. sanguineus. Our results indicate that dogs living in rural areas of MdD are infected with Rickettsia spp. Moreover, we have found that, as has been reported in Brazil, A. ovale, which normally infests rodents and wild carnivores, is infesting pet dogs in MdD, bringing ticks into the households and surrounding environments. Since, A. ovale and R. sanguineus are well known vectors of two of the most important rickettsial agents, R. parkeri strain Atlantic rainforest and R. rickettsii, our results suggest these pathogens may be circulating in rural communities of MdD. This study is still ongoing, and we will sequence the positive samples to determine the circulating Rickettsia species in rural areas and also we will explore the role of pet dogs as sentinels of rickettsia infections in rural areas of MdD. The role of dogs as rickettsia sentinels has been proven in

developed countries; however, in developing countries this may be different due to different dog ecology and human-dog interactions, especially in rural areas where dogs are allowed to roam free

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BIOMETRICS DATA COLLECTION FOR TRACHOMATOUS TRICHIASIS SURGERY PROGRAM IN OROMIA, SNNP AND SIDAMA REGIONS, ETHIOPIA: LESSONS LEARNT

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Trichiasis patient identification, documenting Trachomatous Trichiasis (TT) cases known to the health system is a challenge using paper based records. Paper based data systems are vulnerable for loss, wear and tear as well as mis location, which leads to loss of medical history, making post operative follow up overtime challenging. To register all TT cases with biometrics and provide biometrically verified TT management, get real-time data for program monitoring and decision making. The paper form trichiasis patient register has been changed into digitized form using SurveyCTO (SCTO) to capture trichiasis patient records that works with or without internet connectivity. SCTO has been linked to a data system that captures unique fingerprint using scanning technology. Enrolment and identification are the two steps in the system. The system allows health service providers to identify patients any time when they seek care. 283 IECWs were trained from three regional states. A total of 6,970 patients have been enrolled into the system so far. Of which, 5,303 (76%) were enrolled through biometrics. Electronic data collection was considered as empowering by health service providers; Biometrically verifiable digital trichiasis recording system is found more convenient, reliable, accurate and timely recording and reporting system; Due the implementation of the system, no data duplication, no misuse of standard formats, no missing records, no delay of reports; Got real-time information dashboard that auto update as soon as data is submitted and is capable of transitioning into the mainstream health information system run by the Ministry of Health. The dashboard is accessible to the health systems staff, implementing partners and program leaders, which facilitated timely evidence based action and decision making. Train IECWs in Amhara region, refresh and closely support the already trained IECWs and work to simplify SCTO dataset and dashboard.

6527

SPATIAL VARIATION IN HOUSING CONSTRUCTION MATERIAL IN LOW- AND MIDDLE-INCOME COUNTRIES: A BAYESIAN PREDICTION MODEL OF A KEY INFECTIOUS DISEASES RISK FACTOR AND SOCIAL DETERMINANT OF HEALTH

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Housing quality is a well-recognized social determinant of health. Many infectious diseases of global concern are transmitted within and between households and features of the built peridomestic environment and infrastructure can promote or impede the spread of pathogens and their insect vectors. In tropical and rural regions where vector borne and neglected tropical diseases circulate, dwellings are often constructed using locally available, naturally occurring materials and traditional techniques. Disease-causing insects and microbes are well-adapted to exploit the ecological niches that such buildings provide. This study modeled spatial variation in housing material types using covariates with global coverage to map predicted coverage across LMICs. Data on materials used in construction of dwelling floors, walls and rooves were compiled from 334 nationally representative, population-based household surveys, and classified into natural, rudimentary, and finished types. A novel georeferencing methodology was developed and implemented here for the first time. A suite of time-static environmental and demographic spatial covariates in raster format were compiled based on their hypothesized associations with the outcome variables. Variable values were extracted at the georeferenced cluster locations and a Bayesian Multi-level based logistic regression approach was used to model associations and generate predictions for all LMICs at a 6km resolution. A Markov Random Field (MRF) smooth algorithm was employed to improve spatial correlation and continuity of the prediction maps. Models for wall and roof material performed better than for floors giving a precision of 0.82 for the finished category and a weighted average precision of 0.7 and 0.73 respectively. Cropland areas, urbanization, and distance to water source were important variables in all models. Resulting prediction maps enable the identification of areas of low coverage of improved housing material across large areas of Sub-Saharan Africa, South Asia, and Amazonian South America among others, and can be used to prioritize populations for housing improvements.

6528

USE OF MATHEMATICAL MODELING TO INFORM INSECTICIDE-TREATED BEDNET DISTRIBUTION CAMPAIGNS: A HAITIAN CASE STUDY

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Despite numerous natural- and human caused disasters, Haiti has made significant progress towards malaria elimination. In 2021, the number of presumed and confirmed malaria were 10642, down from over 84153 in 2010. As cases have fallen, they have become increasingly concentrated; thus, interventions such as insecticide treated bednets should be strategically targeted to reach maximal epidemiological impact. In order to identify the optimal set of communes in which bednet distribution would result in the most cases averted through the once-every-three years distribution campaign, we use a metapopulation model that was fitted on historical reported cases between 2014 and 2021 and on spatial data estimates from the Malaria Atlas Project. The model includes past bednet distributions, case management indicators and human inter-commune mobility as informed by mobile phone data. Several versions of the model are compared to evaluate the sensitivity to the input data. The fitted model was used to identify the communes in which the intervention would have the most impact at the national scale. The model ranked 125 communes, of which we selected the top 25 given the diminishing benefit of each additional commune and the defined number of bednets the country would receive. The selected communes accounted for 82% of observed cases in 2021. As this model combines the effects of connectivity, past interventions and local trends in transmission intensity, it provides a useful additional piece of information in prioritized communes for interventions such as LLIN distributions and communication campaign aiming at increasing bednet usage. The results provided insights about the impact of the targeted communes at the national scale and identified communes to be targeted with communication campaign. Finally, this calibrated model provides an additional tool to support routine campaign planning including the 2023-2026 Global Fund application.

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NET WORTH: A MODELING EXPLORATION OF COST AND COST-EFFECTIVENESS IN INSECTICIDE-TREATED NET INTERVENTIONS

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As the malaria funding envelope plateaus while burden grows and the number of people in need of protection continues to rise, it becomes ever

more crucial to ensure that every dollar spent on malaria interventions is utilized as efficiently and effectively as possible. Insecticide-treated nets (ITNs) are one of the largest line items in global malaria expenditures, making this intervention a major target for improving cost-effectiveness. This is especially true in the rapidly diversifying landscape of ITNs, with multiple novel products on the market and a growing understanding of this intervention's multifaceted nature and heterogeneous historical effectiveness. We utilized the mechanistic modeling software EMOD to explore three common operational questions across a range of transmission intensities, climates and vector mixes: First, is it more cost-effective to attain a specified coverage level by distributing more nets, or by improving the efficiency of net campaigns such that nets are more appropriately allocated? Second, at what level of insecticide resistance does it become cost-effective to move from pyrethroid-only ITNs to pyrethroid + piperonyl-butoxide (PBO) ITNs? And finally, in a situation in which one could either increase pyrethroid-only ITN coverage or maintain current coverage levels with PBO nets, which is more cost-effective? Results show that increasing campaign efficiency is more cost-effective than distributing additional nets, and that a switch to PBO nets is generally cost-effective in areas with high insecticide resistance, though the specific magnitude varies meaningfully depending on the local context. This analysis only scratches the surface of possible operational tradeoffs to explore, but demonstrates the power of modeling for optimal intervention planning and provides insight into best practices for future ITN campaigns.

6530

MULTIFACETED INTERVENTIONS FOR UNINTERRUPTED MALARIA COMMODITIES: LESSONS FROM MALAWI

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There has been significant progress in malaria control in Malawi. The malaria incidence rate reduced by almost 50%, from 407/1,000 population in 2016 to 208/1,000 population in 2022. Malaria mortality declined from 23/100,000 population in 2016 to 8/100,000 population in 2022. In fighting malaria, the Ministry of Health (MOH) implemented malaria case management and vector control programs. To support the National Malaria Control Program, in 2017, the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project made some changes to the parallel supply chain program, which was instituted in 2012 to ensure uninterrupted availability of malaria commodities. GHSC-PSM engaged third-party logistics (3PL) firms to run its in-country warehousing and distribution of malaria commodities to all the 716 service delivery points in the country. The 3PLs use all modes of transportation including boats, motorbikes, and trucks, to ensure that the products reach their destination. Further, GHSC-PSM provided a comprehensive support to the malaria program supply chain with periodic forecast reviews; developing coordinated procurement plans with other funders; procurement and delivery of malaria commodities, including pipeline monitoring, and capacity strengthening of MOH staff to manage their supplies. This multifaceted support helped the NMCP track commodities from 716 SDPs with a 92% average reporting rate in 2022 resulting in a sustained supply of malaria commodities in health facilities and communities through the parallel supply chain program. From 2017 and 2022, there has been less than 1% stockout rate of first-line malaria treatment at service delivery points and this is likely contributing to the significant decrease in the malaria burden in the country.

6531

MULTI-OBJECTIVE CALIBRATION OF THE AGENT-BASED MALARIA TRANSMISSION MODEL, EMOD, TO SYMPTOM, PARASITE, GAMETOCYTE, AND MOSQUITO INFECTION DATA FROM A TRIAL OF ASYMPTOMATIC SCREENING IN SAPONE, BURKINA FASO

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Mathematical models of malaria transmission have been used to predict the impact of various screening and treatment interventions where clinical trials may not be feasible. To make accurate predictions, models must reproduce key quantitative relationships between parasites, symptoms, gametocytes, and infectiousness within modeled human and mosquito hosts, all of which can vary between malaria-endemic settings. With many variable inputs and desired outputs, manual calibration of mathematical models is complex and tedious, making automated calibration algorithms an attractive alternative. We adopted a Bayesian optimization framework employing Gaussian process emulators to simultaneously calibrate 15 core parameters of the complex agent-based malaria transmission simulator, EMOD. These parameters describe aspects of modeled vector life cycles, parasite dynamics, human host immunity and symptom development, and vector-human interactions that are assumed to be constant across modeled settings. We evaluate each possible core parameter set against 8 fitting objectives describing key epidemiological and within-host relationships observed from field data. Compared to previous calibration approaches, ours leveraged data from the INDIE-1a trial in Sapone, Burkina Faso, which included detailed P. falciparum parasite and gametocyte data from human blood samples, and mosquito infection data from direct membrane feeding assays. We first calibrated core model parameters to data from the INDIE control arm, and then validated the effect size of simulated screening interventions in the recalibrated model against primary endpoints from the trial. This approach resulted in a better fit compared with the previous parameterization more quickly than sequential calibration approaches. The reparametrized model will be used in future modeling studies to predict the impact of proposed interventions on population-level malaria transmission.

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IMPLEMENTING A LARGE-SCALE COMMUNITY DIGITAL HEALTH PLATFORM IN MOZAMBIQUE: LESSONS LEARNT FROM UPSCALE

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From 2009 to 2016, MC tested interventions to improve the quality of care provided by community health workers in Mozambique, locally known as (APEs), including a smartphone application introduced in Inhambane province through the inSCALE project. Building from this success and in order to link APEs with the national HIS, MC worked in collaboration with the MOH and UNICEF to develop the upSCALE platform - a digital strategy to strengthen health systems and community health delivery. The upSCALE APE and supervisor apps are built using CommCare, an open source, multi-media rich software running on Android that can work offline. Dashboards on DHIS2 can then display the aggregate data for all APE monthly indicators, as outlined in the MoH's Monitoring and Evaluation plan for the APE programme.Automated performance reports on how APEs and supervisors are using the applications are emailed on a weekly and monthly basis to district, provincial and national levels.Implemented in 7 out of 11 provinces, with over 2,778 APEs and 777 supervisors using the app. MoH is planning to roll out the platform to all 8,800 APEs and 1,300 supervisors nationally by the end of 2024. Lessons learned from upSCALE implementation in large scale, we used desk review interviews from March

to May 2021 with 12 key stakeholders who had significant involvement with upSCALE. We led discussions with all of whom gave their consent for verbatim notes. We analysed notes in four categories: advocacy, engagement and acceptability; data collection and uptake; technology and usability; and ownership and sustainability. Finds shows established relationships at the beginning, accompanied by close engagement on planning promoted successful implementation; data quality and timeliness are key considerations for decision-making; linking data, uptake and use at various levels of the health system presents a challenge; the integration of data into the national health information system is key for sustainability and fostering a data-to-action the provision of equipment, is a valuable investment, training, is essential to promote accurate use of technology and knowledge retention.

6533

PREDICTIVE MODEL FOR REAL WORLD PERFORMANCE OF RAPID ANTIGEN TESTS BASED ON LABORATORY EVALUATION

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Controlling spread of disease due to infectious agents require a quick response from the public health sector. In the ongoing COVID-19 pandemic, the use of antigen tests (ATs) has shown to be an excellent tool to inform users and help mitigate the spread of the disease. In this communication we demonstrated how performance of an antigen test -- as a diagnostic in vitro device -- can be properly validated using a combination of quantitative laboratory experimentation and self-testing data from a clinical study. Furthermore, the work demonstrates that the clinical performance of an antigen test can be predicted using mathematical modeling based on laboratory validations. The proposed appraisal methodology of antigen test performance under real-world conditions could be a useful tool to inform the decision making of regulatory officials. This approach standardizes, simplifies and quickens the process of validation, analysis, and comparison of antigen rapid tests. If accepted as a standard, it will help democratize the process of compliance to show test performance to the public (and regulatory agencies) and ultimately will help with the execution of effective public health responses.

6534

EVALUATING A DHIS2 BASED PLATFORM FOR REAL TIME MONITORING OF MASS DRUG ADMINISTRATION OF NEGLECTED TROPICAL DISEASES MEDICINES: LEARNINGS FROM NIGERIA

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Mass drug administration (MDA) of Neglected Tropical Diseases (NTDs) medicines has proven to be the most effective NTD prevention strategy globally. MDA is implemented annually in endemic areas in Nigeria, where campaigns are tracked using a combination of paper and spreadsheet-based methods. This tracking system is inefficient, slow, and prone to errors. In collaboration with Nigeria's Federal Ministry of Health (FMoH), Sightsavers developed a DHIS2-based tool for real-time capture, analysis, and reporting of MDA data. We assessed the tool's accessibility, data quality, and utility for MDA planning, monitoring, and reporting, as well as its scalability regardless of funding source or location. Data was collected at the local government level (LGA), state, and federal levels during the pilot and scale-up phases using a combination of qualitative and quantitative methods. We investigated the potential for use at scale by evaluating in three Nigerian states (Jigawa, Enugu, and Kwara) with different support models and partners. The ability of DHIS2 to detect and address a variety of MDA-related technical and programmatic issues was generally highlighted as beneficial by participants. The tool reportedly improved timeliness in tracking incoming data, detecting data inconsistency and flagging data quality issues, as well as identifying areas of low coverage, informing supervisory visit decisions, and tracking drug inventory. Our findings showed that scaling-up to different settings was feasible; however, plans would need to address several challenges including insufficient funding, poor internet infrastructure, particularly in rural areas, increased workload, and high staff attrition rate from the NTD program. Furthermore, because of differences in operating models, cultural contexts, technology capacity, and levels of willingness to change, successful scale-up into new locations will not be a one-size-fits-all approach. The Nigerian FMoH has taken these findings and recommendations into account as they scale up the system across the country.

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A PROBABILISTIC FRAMEWORK OF MALARIA EPIDEMIOLOGY USING AGE OF INFECTION

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The epidemiology of Plasmodium falciparum malaria can be understood jointly through observed prevalence, parasite densities, measures of cumulative exposure, and outcomes of infection. Malaria epidemiology has proven difficult to capture using simple models because of complex, heterogeneous infection dynamics and a biased, noisy observational process. Parasite densities, which are highly variable over long infections and controlled by immunity, act as strong predictors of infectiousness, detection rates, and disease. Exposure stimulates immunity, but infections are also modified by treatment and chemoprotection, superinfection, and various sources of population heterogeneity. Immunity is presumed to develop with cumulative exposure, decreasing the 'typical' parasite density below the baseline naïve infection. To deal with all these features in compartmental models, the number of state variables would increase combinatorically and become unwieldy. Stochastic models that include all these sources of heterogeneity are complex and implemented as agent-based models to be simulated. These models are effectively black boxes and are difficult to analyze or fit to data without a heavy computational burden. Here, departing from traditional compartmental or agent-based models, we present a new, probabilistic approach using a semi-Markov framework for modeling both infection age and multiplicity of infection, which jointly can predict statistical properties of individual infections in a cohort of humans as it ages. Using the distributions of parasitemia fitted to a model of the time since first patency in malaria-naïve human subjects from the malaria therapy dataset, we can use our infection age distribution to produce a dynamic predictor of parasitemia with the effects of immunity. Ultimately, using a state-space modeling approach, we can derive equations that model the distributions of both observable (e.g., observed prevalence, fever) and unobservable (e.g., true prevalence, immunity) quantities, allowing for both qualitative analysis of the expected behavior and quantitative measures of uncertainty.

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DENGUE--AN EMERGING THREAT WORLDWIDE: A MATHEMATICAL MODEL EXPLORING GLOBAL RELATIVE RISK USING CLIMATIC, GEOLOCALIZED ECONOMIC, AND VECTOR DISTRIBUTION DATA

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Dengue is a vector-borne viral disease affecting humans that is endemic in tropical and subtropical areas worldwide. A complicated web of factors that determine disease transmission dynamics, including the human

host's infection status the age of the mosquito vector and the ingested viral dose during bloodmeal acquisition, specific viral characteristics, and environmental conditions, such as temperature and humidity. The aim is to evaluate the impact of temperature and precipitation on the global risk of dengue outbreaks at a 5x5 km2 resolution.A spatiotemporal model using an extended version of the Ross-Macdonald theory calculated a Relative Global Dengue Basic Reproductive Model (R0). It included temperature, rainfall, Aedes aegypti vector distribution, and geolocalized economic factors to evaluate disease transmission dynamics. The geolocalized economic data integrated the association between mosquito and human interaction and economic prosperity, which is heavily dependent on the availability of running water, access to air conditioning, and screens on the windows.Overall, the R0 model's projections align with the observed distribution of the Dengue virus. The Brière and Quadratic Functional forms of precipitation demonstrate widespread dengue risk throughout the year in equatorial regions and a coordinating increase in R0 values at higher latitudes in the northern hemispheres during the summer months and lower latitudes in the southern hemisphere during the summer months. The model predicts a global relative Dengue outbreak risk profile and demonstrates its spatiotemporal heterogeneity by identifying areas at risk of high virus transmission throughout the various months of the year. It shows an increase in the geographic risk during summer temperatures, demonstrating an optimal temperature and precipitation range for the genesis and proliferation of an outbreak. For simplicity, our model considers the impact of precipitation and temperature on Ae. Aegypti life cycle as independent variables. Future work should investigate their potential synergistic impact on mosquito population dynamics and outbreak risks.

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THE SINGLE PATCH PLASMODIUM FALCIPARUM APPLICATION - A TOOL FOR MALARIA MODELLING IN LMIC

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With a global push towards malaria elimination, modellers are increasingly supporting national and regional policy design in LMIC, and have the ability to contribute directly towards achieving malaria elimination in these countries. Innovations in modelling and scientific communication become necessary as timelines for decision-making vary. One such innovation is to develop user-friendly computer applications designed to allow policy-makers to run simple mathematical models and navigate the output of millions of simulations of more complex models with the aid of interactive graphs. The primary novelty is the focus on implementation and translation of the modelling results allowing policy-makers to design an elimination/control strategy incrementally by combining candidate interventions to predict the desired impact and cost. The Single Patch Plasmodium falciparum (SPPf) tool is disease modelling software that simulates Plasmodium falciparum malaria transmission for a population of interest. The software allows the user to simulate malaria policies and intervention strategies, alone and in combination, to determine the impact on malaria incidence and the cost thereof. The tool has been developed in the open-source RShiny Application framework and can be made available to the user in both an online and offline format. Beyond allowing the user to upload local data into the tool, the SPPf tool simulates key interventions such as scaling up or down of vector control activities including long lasting insecticide treated bednets and indoor residual spraying, health systems strengthening through improved access to and receipt of care, chemoprevention during pregnancy and seasonally, and the impact of the RTS,S vaccine. Both the epidemiological and cost results are available for download for further analysis. The SPPf tool has already been used to design malaria policy in South Africa, Ghana and several other settings. The principal benefit of the SPPf tool is to allow the modeller to co-design malaria policy with the decision-maker to enable true participatory modelling.

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RESPONSIBLE ACCESS TO DATA FOR ANALYSIS AND RESEARCH (HEALTH: RADAR) – A PROJECT FOR BETTER CLIMATE SENSITIVE INFECTIOUS DISEASE MODELS IN THE GLOBAL SOUTH AFRICA

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A recent literature review by the Wellcome Trust found that the majority of digital tools related to Climate Sensitive Disease Modelling (CSID) have been developed by institutions in the global North, while the major burden of disease remains in the global South. Disease models accounting for local context, diversity and culture in model development can lead to recommendations that are more implementable and acceptable to the populations on whom these models are based. This is maximised when the models and analysis are generated by modellers from the geographies under study. One of the greatest obstacles to CSID modelling in LMIC is accessibility to operationalisable datasets in a format that is digestible and acceptable to modellers and analysts. Health: Responsible Access to Data for Analysis and Research (Health: RADAR) is a project funded by the Wellcome Trust which seeks to contribute to the development of useful CSID models within an African context. The project partners include the Modelling and Simulation Hub Africa (MASHA), the Climate Systems Analysis Group (SAG), the Clinton Health Access Initiative (CHAI) and the South African Medical Research Council (SAMRC). A key project output is an open-source online resource where users can access contextually enriched data sources for climate sensitive infectious disease models. For this project, the pilot application is on Malaria in the Southern African region though the nature of the project allows for more general scope at a later stage. Another key output is the establishment of a community of users who contribute to the online resource through procedures developed over the coming years. Data included in the resource should follow certain criteria - it should be readily accessible and befitting of the context focused on by the tool and citeable. The data should be incorporated in a way which adds contextual relevance as to how it could be incorporated into a CSID model, with example code on how one might work with the data.

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A PREDICTIVE MODEL FOR NON-INVASIVE ANEMIA DIAGNOSIS

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Anemia, a disease characterized by impaired tissue oxygen supply, is a condition that affects about a fifth of the world's population and is the second leading cause of disability. Individuals in western and central sub-Saharan Africa and South Asia are disproportionately affected by anemia, with young children and pregnant individuals experiencing the highest prevalence with life-threatening consequences. The objective of this study is to develop a predictive model which accurately estimates hemoglobin concentrations from nail bed images. Predictive models, including logistic regression and random forest, are trained on a data set that maps hemoglobin concentrations to patient nail bed images. Preliminary results are promising, suggesting that these predictive models have the potential to develop a cheaper and more accessible diagnostic tool for anemia diagnosis. Future work will focus on implementing additional predictive models such as a binary classification model or deep learning to improve

predictive performance. Ultimately,these results will be used to improve point-of-care anemia diagnostics by developing a better hematology tool that is non-invasive, accurate, and affordable for low-resource settings.

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IMPACT OF GOVERNMENT-REGULATED LOCKDOWNS DURING THE COVID-19 PANDEMIC ON ACCESS TO MENTAL HEALTH SERVICES THROUGH A TERTIARY PSYCHIATRIC CARE FACILITY AND THE NATIONAL MENTAL HEALTH CALL HELPLINE IN SRI LANKA

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During the COVID-19 pandemic, many countries imposed restrictions on human mobility, limiting access to healthcare. We examined how these measures affected access to psychiatric services in Sri Lanka. We analyzed 15,122 outpatient presentations (OPs) to tertiary care psychiatric service at the National Hospital of Sri Lanka, and 56,363 calls to the national mental health helpline of the National Institute of Mental Health between 2019 and 2021. Selected presentations for pre-pandemic (01.01.2019-20.03.2020) and pandemic (21.03.2020-31.12.2021) periods were compared using Chi-Square test at a significance level of 0.05. Using the Google residential mobility index as a proxy for the intensity of community response to nationwide lockdown, we evaluated its delayed association with OPs and helpline calls using distributed lag non-linear models. Statistically significant increases in OPs were observed for females (10%), somatic (28%) and mood (10%) symptoms, and behavioral changes (18%) during the pandemic while OPs for self-harm and substance use decreased significantly by 22% and 25%, respectively. Treatment termination rate by provider was significantly higher among patients during the pandemic. Compared to pre-pandemic period, we observed a significant increase in calls for mental health concerns and a significant reduction in calls for domestic violence and alcohol use during pandemic period. Similarly, relative to the pre-pandemic period, increases in residential mobility index were associated with statistically significant increases in risk of OPs due to mood, somatic and behavioral symptoms, and self-harm with a lag of 21 days. The risk of helpline access due to mental health concerns, relationship issues, and suicidal ideation increased significantly with a lag of 3-5 days. Our findings indicate that OPs and psychiatric service provision patterns changed significantly during the pandemic. The shorter lags for helpline calls, when compared to OPs, indicate the importance of providing continued access to mental health services through telephone helplines during times of mobility restrictions and lockdowns.

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CREATING A DATA LIBRARY USING PUBLICLY AVAILABLE RESEARCH DATA ON NEGLECTED AND EMERGING INFECTIOUS DISEASES

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Neglected and emerging infectious diseases are vastly understudied due to being uncommon in high income countries and the lack of resources in low-income countries have led to underfunding for research. The goal is to search for publicly available data on neglected diseases so that researchers can utilize them to answer research questions they may have on neglected diseases. A search was conducted for data on each neglected disease through data repositories including Harvard Dataverse, Cliniclatrials.gov, zenodo.org, All of Us Cohort Study, and Data dryad.org. The research studies with data were collected and a data library was developed including each neglected disease, the name of the study, a brief description of the research, the origin of the research data, and links to the research data. The results from the search revealed that data is publicly available on each neglected disease with some diseases having more research results compared to others. A search for Schistomiasis on Harvard Dataverse yielded only 6 studies while Chagas disease generated 4694 results on research with data on zenodo.org. More than 50 studies with data on neglected diseases within the last 5 years were obtained from the online data repositories which makes the limited data available and can facilitate research.

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FEASIBILITY AND ACCEPTABILITY OF MOBILE TECHNOLOGY TO IMPROVE ONE HEALTH OUTBREAK REPORTING IN BWINDI, UGANDA

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The Bwindi Impenetrable National Park (BINP) in Southwest Uganda is an extremely dense and biodiverse forest. A highly dense human population living in proximity to forest animals results in numerous opportunities for zoonotic spillover. This work was part of NIAID CREID Network's Epicenter for Emerging Infectious Disease Intelligence (EEIDI) that investigates regional emerging infectious diseases (EIDs). A One Health, transdisciplinary strategy is used for surveillance and response for EIDs of pandemic potential.This exploratory study was undertaken as a needs assessment and acceptability study to inform a large technology-development project intended to improve data reporting and outbreak responses in areas at high risk for zoonotic spillover. Methods employed primarily focus group discussions (FGDs) in both hard-to-reach rural communities around BINP, and the urban setting of Kabale city. Though smartphone app-based technology is replacing SMS-based technology, local communities rely solely on simple button phones to communicate. This study had the goals of 1) determining the primary methods of mobile communication and 2) estimating community acceptance of a mobile reporting system to report and record location.Ten rural FGDs were conducted around BINP in 3 districts (Kanungu, Rubanda, and Kisoro), and 5 FGDs were conducted in the urban setting in Kabale district. Each FGD had 6-8 participants, totaling 102 people. With written informed consent from each participant, we recorded the discussions, translated them from the local language into English, and transcribed them. Line by line coding of major categories and themes was performed using NVivo software. This analysis revealed that all 15 FGDs reported simple button (SMS based) phones as the predominantly available cell phone type. All 15 FGDs also reported willingness to participate in a mobile outbreak reporting system and willingness to have their geolocation data reported. Communities in Bwindi have access to, and prefer, Simple button (SMS) phones. Community acceptance was very high. These results combined reveal high potential for a new mobile reporting system.

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INVESTMENT CRITERIA FOR THE DEVELOPMENT OF NEW DIAGNOSTICS

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When making decisions to invest in the development of new diagnostics, most manufacturers from high-income countries (HIC) require extraordinarily high prerequisite levels of projected annual sales, market growth and rates of return. Because of these investment criteria, medical technologies are rarely designed for use in low- and middle-income countries (LMICs). Transferring healthcare solutions and technologies from HIC to LMICs is slow, expensive and challenging if not impossible. Appropriate diagnostic products designed specifically for implementation in LMICs are best developed with local knowledge and understanding of needs, context, and available resources. For local innovation of health technologies to become a new standard, capabilities in health technology are required for needs assessment, market analysis, product design, prototyping, validation testing, manufacturing and management. The NIH-funded Center for Innovation in Point-of-Care Technologies for HIV/AIDS and Emerging Infectious Diseases at Northwestern (C-THAN) is one of the Point-of-Care Technology Research Network (POCTRN) centers of the NIH that supports biomedical engineering capacity in LMIC-centered diagnostics. C-THAN includes 9 academic centers across Africa that catalyzes innovation in diagnostic technologies through a model that enhances complementary strengths to build multidisciplinary partnerships across technology platforms, clinical, regulatory and commercialization domains with a specific focus on HIV/AIDS and emerging infectious diseases. During C-THAN's first five years, 43 projects were successfully supported, 26 involved technology development, 9 clinical validation, and 9 technology dissemination. 34% of projects have African Principal Investigators and most involve collaborations between HIC and LMIC investigators. In the next 5 years, C-THAN will emphasize specific technologic domains by establishing working groups in molecular, lateral flow, synthetic biology, and product engineering in HIV and emerging infectious diseases related diagnostics.

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CLOSE ENCOUNTERS OF THE ENVENOMATING KIND: MISSIONARIES, INSECTS, AND SNAKES DURING THE SCRAMBLE FOR AFRICA, 1885 - 1914

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Encounters with envenomating insects and reptiles of all kinds were, and remain, common in sub-Saharan regions throughout Africa. As Europeans, whether secular, military, or religious, pushed more deeply into these areas, these meetings grew increasingly likely. Missionaries who worked for the Church Missionary Society (CMS), an evangelical Anglican organisation founded in 1804, provide an excellent case in point. They provide vivid, humorous, and sometimes tragic, encounters with arthropods and reptiles. Naïve newcomers, blissfully ignorant of hazards that might await them in the bush, faced particular risk. Relying on published and archival contemporary accounts by CMS missionaries during the late 19th century Scramble for Africa, this presentation will highlight encounters, both comical and tragic, with envenomating insects in sub-Saharan Africa.

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IMPACT OF AN ANCILLARY CARE POLICY DURING AN EBOLA VACCINE TRIAL IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Between 2019 and 2022, the Universities of Antwerp (Belgium) and Kinshasa (DRC) conducted an Ebola vaccine trial (clinicaltrials.gov: NCT04186000) in the remote area of Boende in DRC, characterized by insufficient access to essential health care and a previous Ebola outbreak. After the trial started, a policy with decision algorithm was developed to support participants' concomitant medical events. To evaluate its impact on the management of related and unrelated (Serious) Adverse Events ((S) AE), we assessed for each event reported if and which type of support was provided. Potential outcomes were administering medication, direct payment or reimbursement of medical costs, or no support possible. Data was summarized using descriptive statistics. In total, 629 AE and 62 SAE were reported; the majority (613 and 58 respectively) were unrelated to the investigational product or to trial participation. Medication from the study pharmacy was administered to 555 AE and 18 SAE. Additionally, for 155 cases the medical costs were directly covered by the study budget. Reimbursements were provided for 20 AE and 24 SAE, but for 17 AE and 24 SAE this was impossible. With AE, treatment consisted of medication (from multiple sources) in 611 cases, 32 were hospital consultations. The remaining 12 were managed otherwise, e.g. via blood checks, observation, or surgical interventions. With SAE, 52 participants were hospitalized, 50 were treated with medication and 13 received surgery. The policy's largest impact lays with the provision of medication, offered directly or reimbursed when coming from other sources. Study pharmacies can thus contribute majorly to participant care. Financial support, although not the largest support outcome, had a considerable impact on reducing participants' out of pocket payments for health care. Unsupported medical costs were mostly due to (unrelated) events occurring prior to policy implementation, or to the absence of documentation. This underlines the importance of planning an ancillary care policy upfront, and of informing participants at recruitment in order to adequately address their health needs during research.

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THE SOUTH AND SOUTHEAST ASIAN COMMUNITY BASED TRIALS NETWORK (SEACTN)

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The South and Southeast Asian Community-based Trials Network (SEACTN) was launched in October 2019 to establish the foundational infrastructure for monitoring the incidence, causes and outcomes of febrile illnesses in rural communities in these regions, and later the trialling of interventions delivered by village health workers and rural clinics to improve their diagnosis and treatment. SEACTN activities span approximately 750 villages across five South and Southeast Asian countries (Bangladesh, Myanmar, Laos, Cambodia, and Thailand). It is a uniquely multi-national network with governmental, non-governmental, and academic partners focused on rural and remote healthcare provision in areas often neglected by the health system, and with data being collected electronically and collated in real time. As of March 2023, over 60,000 patients with a febrile illness have been recruited in these remote and underserved communities, as well as over 2100 patients admitted in higher level facilities. Multiplex serological and molecular assays have been developed to establish the causes of illness in these patients. In parallel, over a thousand deaths have been investigated with verbal autopsies, and household health surveys are being conducted in hundreds of villages. This is providing an unprecedented account of the incidence, morbidity and mortality associated with acute febrile illness as well as other causes of morbidity and mortality in rural South and Southeast Asia. This will support evidence-based decisions as to which interventions are likely to have the largest positive impact on population health in these remote, underserved, and understudied communities and these interventions will later be trialled in the same network. This session will provide an overview of SEACTN and interim findings on presenting syndromes and outcomes in the community and hospital-based cohorts.

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FEEDBACK FROM THE FAMILY FOLLOW-UP SESSIONS WITH DECEASED FAMILIES TO SHARE THE CAUSE OF DEATH REPORT: LESSON LEARNT FROM THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) PROGRAM IN BANGLADESH

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In Bangladesh, determination of cause of death (CoD) is often imprecise due to under-resourced diagnostic facilities and culturally low acceptance of full autopsy. The Child Health and Mortality Prevention Surveillance (CHAMPS) offers minimally invasive tissue sampling (MITS) at Baliakandi sub-district and Faridpur district to identify the cause of stillbirth and of <5 deaths. The team promised families to return the CoD report determined by an expert panel within 120 days of the death, but if delayed team informed them the cause of delay. The CoD reports were prepared in a descriptive format and a trained, gender balanced team including a physician and community engagement staff shared the report to families in their home through an interactive session. To make it more effective, we observed 110 sessions between 2018 to 2020 and documented participants' acceptance, queries, opinions and our team's responses. The parents, key decision makers, relatives and some neighbors attended the sessions with duration of 35 minutes. Families generally appreciated that our team returned to them with CoD report. In the initial sessions, families requested to share the case specific preventions. Subsequently, the panel prepared cause specific and general prevention messages that the team shared with families. Although families accepted the report; some perceived that the child death was expected as some maternal factors mentioned as CoD i.e. high blood pressure, diabetes and domestic violence. After explaining how such conditions were treatable, families stated that now they realized the death occurred due to their negligence, not sending mother for antenatal care and some families argued, the death occurred due to physicians' negligence. Families common queries were how to prevent future deaths and how CHAMPS can support mother during subsequent pregnancies i.e. for treatment and team explained the need for ANC and CHAMPS could support mother to receive it in CHAMPS facilities. Our findings suggest that such interactive session could sensitized families about CoD and need for ANC or required treatment during pregnancy to prevent unwanted child death.

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HOW DO SUBSTANDARD AND FALSIFIED ANTIMICROBIALS AFFECT THE EMERGENCE AND SPREAD OF ANTIMICROBIAL RESISTANCE?

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Approximately 10% of antimicrobials used by humans in low- and middle-income countries are estimated to be substandard or falsified (SF). In addition to their negative impact on morbidity and mortality, they may also be important yet neglected drivers of antimicrobial resistance. Despite concern over their potential role in the emergence and spread of antimicrobial resistance, and the consequences this would have on public health, our current understanding of this relationship is rudimentary. In this study, we used mathematical models to examine the relationship between SF medicines and antimicrobial resistance. Combining observed distributions of active pharmaceutical ingredients in randomly sampled antibiotics with different assumptions about the relationship between dosing level and resistance emergence, we quantified the expected rate of population level resistance emergence. Results suggested that when ~10% of medicines are SF, the effect on resistance may be relatively small. However, in pockets where SF medicines are more common, representing ~50% or more of antimicrobials, SF medicines may have a substantial effect on resistance emergence. Second, we combined these outputs with epidemiological models to understand the role that both transmission of resistant microbes and heterogeneity in the frequency of SF medicines play in driving the spread of resistance. This suggested that those pockets with higher frequencies of SF medicines have the potential to drive resistance in other areas too. Together, our results add to our understanding of this important and neglected global health problem, and provide a framework for future work assessing the importance of different intervention points to reduce the impact of SF medicines on resistance.

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THE DEVILS INVADE THE HOUSE THROUGH THE HOLES IN THE BAMBOO BOOTH: A NARRATIVE OF LOKU AND TAKAYA FEVER ILLNESS AMONG CHILDREN IN EASTERN INDONESIA

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Fever is the most prevalent presenting ailment during childhood. On the eastern Indonesian island of Alor, the Abui people recognize two fatal fever-

related folk illnesses called Loku and Takaya. From June 2021 to July 2022, an ethnographic study was done using in-depth interviews, participant observation, and informal interactions. Following the ethnographic work, census, and behavioral surveys were carried out to measure the impact of distance to a health facility and degree of illness on treatment seeking behavior for fever. The study explored how people perceive and seek treatment for childhood fever. Five individuals were purposively chosen from 50 key informants. The narratives of two eminent healers and three mothers of feverish children illustrate the cultural understandings of febrile illness. The mothers consulted traditional healers and home remedies or holy water were offered. When illness progressed to severe, mothers acknowledged that the child may need to be admitted to a health facility. However, cost and poor service quality were cited as impediments to that treatment-seeking. Consequently, mothers often opted to care for their children at home, even understanding the danger that imposed. The healers believed both Loku and Takaya would be diagnosed as malaria at the health facility. Yet, they believed that antimalarials are unable to cure due to its supranatural causes. In summary, traditional understanding and management of febrile illness and treatment seeking behavior within this impoverished rural community continues and leads to potentially dangerous delays in treatment of feverish children. Health promotion and community engagement by public health workers who understand local perceptions of fever are more likely to devise more effective health interventions and mitigate preventable infectious harm to Abui children.

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PREVALENCE OF ANTIBIOTIC USE AMONG THREE SELECTED TERTIARY LEVEL HOSPITALIZED PATIENTS, A POINT PREVALENCE SURVEY FINDING IN BANGLADESH

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Irrational use of antimicrobials in both humans, animals, and the food chain led to the emergence of antimicrobial resistance (AMR). Due to antibiotic resistance, patients are more likely to remain infectious for a longer time, increasing the risk of spreading resistant microorganisms to others. For supporting antibiotic stewardship interventions, the World Health Organization (WHO) categorized antibiotics according to AWaRe (Access, Watch, Reserve) classification. We aimed to describe the prevalence of antibiotic use (ABU) as stated by AWaRe classification in tertiary level acute care hospitals in Bangladesh. A point prevalence survey (PPS) was conducted adopting WHO PPS design among inpatients of three tertiary level public hospitals in Bangladesh from June to September 2022. Among the enrolled 1634 inpatients, 52% (860) were female and 66% (1093) were from the 15-64 years age group. Nearly, 75% (1241) of patients received at least one antibiotic during the survey period. Proportioning for different departments, 90% of the patients from burn ward, 87% of pediatric, 75% of gynae and obstetric, 72% of surgery, and 69% of medicine wards received at least one antibiotic. Third-generation cephalosporins (43%), imidazoles (15%), penicillins (13%), aminoglycosides (8.5%), and second-generation cephalosporin (8%) were documented as top 5 antibiotics. Different group of antibiotic usage at the same time was a common phenomenon. In the course of a single admission patients received ranging from single to seven antibiotics. Overall, 63% of Watch, 36% of Access, and 1% of Reserve group antibiotics were used for treatment. The use of watch group antibiotics is quite high in public hospitals. Our PPS findings underscores the need for urgent nationwide antibiotic stewardship progam for physicians along with development of disease specific and department-wise standard treatment guidelines and in-service training on ABU for the containment of AMR.

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IMPROVING MALARIA COMMODITY ACCOUNTABILITY: - THE CASE OF MALAWI

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In Malawi, before 2016, reports showed limited availability of malaria medicines with 10% facilities reporting stock out of first line malaria treatment. The discrepancy ratio between the number of commodities issued and the number of cases treated was also high (1.53 compared with 1.15 target); the base line documented that 10,178,5929 treatments were issued to treat 6,647,163 cases. The potential factors contributing for this discrepancy were identified as poor recording and pilferage at treatment site level. The USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM), project devised a Commodity Accountability and Performance Tracking (CAPeT) initiative. This initiative targets 30-60 health facilities with high discrepancies based on data analysis on malaria cases and first-line treatments reported through District Health Information Software 2 (DHIS2) and Open Logistics Management Information System (OpenLMIS) quarterly. It identifies the factors (such as missing records and data aggregation errors) responsible for the discrepancies and offers solutions at various levels of implementation to address these factors. GHSC-PSM engages facility staff to verify reports and review performance, identifying discrepancies as a measure of accountability and developing action plans shared with the district and central-level health offices for further follow-up. Results from the activity show a general decrease in the discrepancy ratio of 1.38 (2019), 1.26 (2020), 1.20 (2021), and 1.23 (2022). The proportion of facilities with a discrepancy ratio of less than or equal to 1.15 increased from 10% (3/30) in the initial visit to 50% (15/30) in the revisit. Similarly, the average national discrepancy ratio reduced from 1.53 before 2016 to 1.23 in 2022. Results showed that ensuring the accountability of health commodities in the supply chain plays a critical role in improving the availability of life-saving drugs at service delivery points, as evidenced by consistently low stock-out stock rate (<1% for ACT) and decreased discrepancy ratio.

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ANTIMICROBIAL STEWARDSHIP IN SOUTH ASIA: A SYSTEMATIC REVIEW OF QUALITATIVE LITERATURE

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Antibiotic resistance is a global public health crisis. Effective antibiotic stewardship requires an understanding of the factors and context that contribute to inappropriate use of antibiotics. The goal of this qualitative systematic review was to synthesize themes across levels of the social ecological framework that impede antimicrobial stewardship in South Asia. In July 2022, a systematic search was conducted using the electronic databases Medline and Embase. Search terms were identified a priori, based on eligibility criteria of methods (qualitative), location (eight countries of South Asia), topic (antimicrobial and antibiotic stewardship; drug resistance), and English language. 130 articles were identified; after removing duplicates (n=11) and excluding articles that did not meet eligibility criteria (n=96), 34 articles were included in the review, with publications ranging from 2010 to 2022. Methodological quality was assessed using the qualitative Critical Appraisal Skills Program checklist. The studies represented six countries in South Asia, and included data from patient populations, health care providers, community members, and policy members. For each paper, a summary memo was written to extract the factors that impede antimicrobial stewardship. NVivo software was then used to code the memos; codes were organized by levels of the social

ecological framework. Themes emerged at the level of the individual patient (access to medical care, patient expectations, rationing of antibiotics, and perceived value of antibiotics), the formal provider (antibiotics as the first line of therapy, gaps in knowledge and skills, and financial or reputational incentives), the clinical setting (lack of resources, and poor regulation of the facility), the community (informal drug vendors, and social norms), and policy (lack of legislation, and poor implementation of existing policies). The findings highlight the importance of working across multiple sectors to build commitment for antibiotic stewardship in South Asia.

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A PHYSICIAN-LED PRIMARY PREVENTION CARE ON RISK OF CARDIOVASCULAR DISEASE: A RANDOMIZED CONTROLLED TRIAL (PRIMCARD STUDY)

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Cardiovascular diseases account for more than 36% of deaths among adults younger than 60 years in Nigeria. The WHO advocated primary prevention care as the cheapest and most cost-effective approach to managing cardiovascular risk. Even with standard guidelines, caregivers, especially physicians are yet to accept primary prevention in practice. Major barriers include its time-consuming nature and low yield of immediate effects. This study compared the effects of physician-led primary prevention care versus usual care on cardiovascular risk reduction among at-risk institutional workers.A parallel randomized control trial was conducted. A total of 223 respondents with moderate and high risk were enrolled and randomized into physician-led intervention (n = 118) and usual care (n = 105) and followed up for six months. Respondents in the intervention arm were offered a physician-led total cardiovascular risk management approach, while the control arm continued with their usual care. The primary outcome measure was cardiovascular risk score while secondary outcome measures were: blood pressure, fasting blood sugar and body mass index and waist-to-hip ratio. Data were analyzed using descriptive statistics, paired t-test and independent t-test at α0.05.Respondents were similar in both arms for baseline sociodemographic, behavioral and cardiometabolic characteristics. Between groups, the intervention arm achieved greater reduction in blood sugar and BMI, with a mean difference of -13mg/dl and -0.6kg/m2 respectively; there was a marginal mean difference in CV risk score of -0.1% with the number needed-to-treat being ten. Within the groups, the intervention arm demonstrated significant effects on systolic blood pressure(5.0mmHg), blood sugar(9.8mg/dl), and BMI (0.8kg/m2) at endline. The control arm only affected the systolic blood pressure(8.6mmHg).The physician-led primary prevention intervention was effective in reducing individual cardiovascular risk factors and may serve a beneficial prophylactic effect on the reduction of absolute cardiovascular risk at a population level.

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HYDROCEPHALUS - TWENTY YEAR TRENDS IN UGANDA

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Hydrocephalus is a life-threatening condition due to excessive accumulation of cerebral spinal fluid within the brain's fluid spaces (ventricles). Untreated progressive hydrocephalus in children below two years of age leads to further brain damage, resulting in the majority dying and survivors left with severe cognitive and physical disabilities. It is thus critical to access early proper neurosurgical treatment in order to prevent the long-term deleterious effects and complications. Hydrocephalus is an underrecognized global health problem, and a major cause of childhood disability worldwide; with more than 400,000 new cases occuring annually; 100,000 of them from sub-Saharan Africa alone. These are additionally faced with the challenges of poverty, limited access to care, and low advocacy. Uganda is a low-income sub-Saharan country with high rates of both congenital and acquired hydrocephalus.CURE Uganda is a center of excellence for peadiatric neurosurgery treatment, training and research. Located in the Eastern part of the country, it is the main referral center for patients all over the country with hydrocephalus and spina bifida, including neighboring ones like Kenya, Tanzania, DRC, Rwanda, and South Sudan.It's estimated that 3,600 - 5,400 children in Uganda are born with or acquire hydrocephalus each year or 2 to 3 / 1,000 births (based on 1,800,000 new births per year). CURE Uganda is currently providing surgery for only approximately 20-30% of the estimated annual country need. Over the past two decades (2001-2020), CURE Uganda has provided care for 10,919 children with hydrocephalus (74%) and spina bifida (26%). The majority of the causes of Ugandan infant hydrocephalus are neonatal infections (67%) and spina bifida; both of which are preventable. The early neonatal infections have been attributed to the bi-annual rainfalls; and have a spatiotemporal distribution although the exact pathogenesis is not very clear. The recent novel discovery of the pathogens presents the perfect opportunity for preventative strategies in tropical medicine that will have huge impacts in addressing these growing disparities in global health.

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MALAWI INTEGRATED TYPHOID CONJUGATE VACCINE CAMPAIGN AND ROUTINE INTRODUCTION

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It is estimated that in Malawi in 2017, for all ages, there were 32,747 typhoid cases (191 cases per 100,000), 435 deaths, and 32,787 disability-adjusted life years lost to typhoid. Sixty-one percent of all cases and 65% of all deaths were in children under 15 years. The Ministry of Health in collaboration with its partners, will conduct an integrated Typhoid Conjugate Vaccine (TCV) and Measles Rubella (MR) vaccination campaign and later introduce TCV into routine immunization. The main objective for TCV introduction is 1) To provide typhoid vaccine to all the children aged 9 months to 14 years through the campaign by reaching ≥ 95 % of the target population 2) To introduce TCV into routine immunization at age of 9 months by targeting at least 80% of eligible children aged 9 to 23 months at their 9 month immunization visit. The integrated TCV MR supplemental immunization activity (SIA) will be conducted for five days in April 2023.In addition, bivalent Oral Polio Vaccine (bOPV) and Vitamin A will be administered to children aged 0 - 59 months and 6 to 59 months respectively. There will be static, outreach clinics and mobile sites that will be opened for five days. Static sites are located at permanent government and private health facilities which will also serve as storage and distribution points of vaccines and other supplies to outreach sites. The rationale for the for the integrated SIA is; 1) To efficiently use of scarce human, financial resources and easier logistics 2) a high demand for one intervention can boost coverage of others given at same time 3) to reach the marginalized with more services 4) to respond to the public's demands for broader services during campaigns 5) for easier management of logistics and management. The campaign is currently planned whilst Malawi is battling cholera and polio outbreaks which could contribute to staff fatigue and poor quality of services. There could be challenges establishing causality when serious adverse events following immunization occur due to similar administration routes. Flooding caused by climate change will decrease access to vaccines whilst increasing transmission of waterborne diseases such as typhoid.

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THE NUTRITIONAL IMPACT OF THE COVID-19 PANDEMIC ON YOUNG CHILDREN IN PERI-URBAN PERU: A MIXED METHODS STUDY

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Peru has experienced immense suffering due to the Covid-19 pandemic, with the highest per capita Covid-related mortality in the world. In peri-urban areas, strict control measures and loss of work in the informal sector affected already vulnerable communities' ability to seek healthcare and provide nutritionally adequate food to their families. The goal of this study is to assess the pandemic's impact on child nutrition in peri-urban Lima by (1) examining the prevalence of household food insecurity and stunting, as compared to pre-pandemic levels; and (2) qualitatively exploring caregivers' experiences feeding their children since March 2020. The study employed three data collection methods. First, field workers administered a structured questionnaire to 300 caregivers of children 6-23 months of age to assess socio-economic status, food insecurity, and infant and young child feeding practices. Second, anthropometric measurements (weight and length) were taken for each. Third, in-depth interviews were conducted with a subset of 30 caregivers. Data are being analyzed for key trends and themes using Stata 16 and Dedoose. Preliminary statistical analyses indicate that 79.0% of participating households are moderately or severely food insecure according to USAID's Household Food Insecurity Access Scale, and that 10.3% of children 6-23 months of age are stunted. Future analyses will compare these data to data collected during a 2016-2019 cohort study in the same setting to estimate the pandemic's effects on food insecurity and child growth. Qualitative data analysis will shed light on how economic factors, food access, the healthcare system, and interruptions in social assistance programs affected child feeding during the early stages of the pandemic, as well as the coping strategies that caregivers have developed. In conclusion, study findings will contribute to our understanding of how low-resource, peri-urban households have been affected by the pandemic and its aftershocks, and how officials may better safeguard child health and nutrition in their responses to future public health emergencies.

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CONTRIBUTION OF VERBAL AUTOPSY INFORMATION TO CAUSE OF DEATH ATTRIBUTION AMONG CASES UNDERGOING MINIMALLY INVASIVE TISSUE SAMPLING: FINDINGS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) BANGLADESH

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Postmortem examination is a gold standard procedure for determining the cause of death (CoD). CHAMPS uses minimally invasive tissue sampling (MITS) with other information to assign specific CoD to stillbirths and under-five children. A panel of clinical and laboratory experts reviews each case's histology, laboratory, medical records, including maternal clinical records, if available, and a verbal autopsy (VA). The panel assigns underlying, immediate, morbid, and maternal conditions attributed to the death, including prevention recommendations. In this study, we examined how and to what extent VA data contributed to understanding CoD. From December 2022 to February 2023, the panel reviewed all existing data except the VA for 25 cases (7 were stillbirths and 18 neonatal deaths) and assigned CoD, maternal condition, and preventive actions. Then the panel re-evaluated the case, including the VA, and identified changes to CoD with this additional data point. After reviewing VA data for stillbirths, the underlying cause remained the same. However, a maternal condition was identified for one where maternal clinical record was missing, and the panel revised their prevention recommendations in 29% (2/7) cases. VA data changed the causal chain in 28% (5/18) of neonatal cases. In two cases, the lung histology was unremarkable, and the panel assigned underlying CoD as intrauterine hypoxia based on medical records. After reviewing the VA, CoD was changed from intrauterine hypoxia to sepsis and respiratory distress syndrome. A morbid condition was added in 11% (2/18) cases and excluded in one case. In 33% (6/18) cases, a maternal condition was detected. For one case, the condition was revised from oligohydramnios (identified through ultrasound record) to premature rupture of membrane. Overall, the VA data were a helpful adjunct to understanding CoD for stillbirths and early neonatal deaths, especially for deaths with no or poor clinical or laboratory records. In the context of poor medical records, VA advances the accuracy and completeness of MITS procedures for CoD determination in stillbirths and neonatal deaths.

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ASSESSING THE ESSENTIAL DATA SOURCES FOR PRECISE CAUSE OF DEATH DETERMINATION USING MINIMALLY INVASIVE TISSUE SAMPLING: FINDINGS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) BANGLADESH

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CHAMPS is a multi-country project aimed at determining the precise causes of stillbirths and under-five child deaths. CHAMPS utilizes various data sources including maternal and child data abstracted from medical records, histopathology, microbial culture, and molecular detection using multiple specimens, postmortem examination, and verbal autopsy (VA) for the determination of the cause of death (CoD). The aim of this study is to assess the contribution of each data source to increase the competence of the CoD determination process which is essential to develop actionable prevention strategies. From March 2018 to February 2023, an expert panel of pediatrician, neonatologist, obstetrician, pathologist, epidemiologist, and microbiologist reviewed 535 deaths and assigned CoD to 529 (99%) cases in Bangladesh. Of these, 51% (275/535) were stillbirths, 43% (228/535) were early neonatal deaths (0 to 6 days), and 6% (32/535) were child deaths (7 days to under 60 months). Maternal clinical abstracted data was used to detect maternal conditions directly attributed to causing death in 69% (191/275) of stillbirths and 51% (117/228) of early neonates. Child clinical abstracted data contributed to understanding the causes of early neonatal and older child deaths in 59% of cases and 75% (24/32) of cases, respectively. Histopathology reports contributed to CoD determination in 52% of stillbirths and 59% of early neonates. Infection was the cause of stillbirths and under-five child deaths in 12% of cases where postmortem culture (64/535) and molecular detection (66/535) assisted to identify pathogens. In 74% of stillbirths and 58% of early neonatal deaths, VA data aided in detecting maternal conditions. Also, VA data contributed to ascertaining the causes of child deaths in 68% (22/32) of cases. Due to the inconclusiveness of data, CoD could not be assigned for only 1% (6/535). The study highlights the contribution of each data source to determining a definitive CoD. However, it is contingent upon the extent to which the data is available, reliable, and comprehensive.

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DETERMINANTS OF NEONATAL MORTALITY IN RIVERCESS: SECONDARY DATA ANALYSIS OF NEONATAL DEATH IN HEALTH FACILITIES IN RIVERCESS, 2016-2020

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Globally more than 6.3 million young adolescents and children died regularly from neonatal death causes. About 2.6 million newborn die in their first 28 days of life annually. Most newborn deaths, about 99% happen in countries that had limited income. Increased access to skilled birth attendants is another strategy that had been implemented in the reduction of newborn rate in Liberia. Liberia had made substantial improvement towards the decrease of neonatal death since 1970 till today's date. The research seeks to estimates live births and deaths of neonates in health facilities in Rivercess from 2016-2020. The research was conducted using a quantitative approach. Data was collected through reviewing the health facilities Health Management Information System (HMIS) report and neonatal deaths audit forms that were used by the twenty health facilities in Rivercess. The study population encompass all live born neonates and neonatal deaths records. The results revealed that the overall neonatal mortality rates (NMR) in Rivercess was 94 deaths per 11313 births or 8.3 per 1000 live birth of children occurred within the 5 year period preceding the study. The total number of neonatal deaths over this period was 94. The research revealed that neonatal deaths were most common among neonates born asphyxiated and with difficulty breathing. However, neonates who died at an early age were asphyxiated than neonates who died at late age. Another factor which was significantly associated with neonatal death at later ages was neonatal infection. The need to implement facility based newborn care interventions particularly educating midwives, nurses and traditional birth attendants about safe delivery practices is limited and therefore need improvement. Additionally, MoH should put in place a timely referral system and retain healthcare providers especially midwives to manage delivery complications and need to implement effective interventions to reduce risk of neonatal death in Rivercess.

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PROGRESS VS PERSISTENT CHALLENGES- WHAT WE HAVE HEARD: CHALLENGES AND OPPORTUNITIES

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The rate of maternal mortality in Liberia has been and still is one of the highest in the world. In contrast, the rate of neonatal mortality in Liberia—which had been one of the highest globally—has steadily reduced over the last decade. This study aims to synthesize existing evidence on the current state of maternal and neonatal health in Liberia, including approaches to intervention. In-depth interviews were conducted with a range of key stakeholders in Maternal and Neonatal Health in Liberia. These included policymakers in Monrovia, service providers in government facilities/NGO programs, community health workers and community leaders. Additionally, a series of Focus Group Discussions (FGDs) in communities across three of the most affected counties were conducted to explore perspectives regarding maternal and neonatal health in Liberia. Thematic content analysis was to determine emerging themes and Nvivo 12 software was used to structure the analysis. Key themes emerged around challenges to receipt and delivery of high-quality maternal and neonatal health in Liberia, as well as advances that have led to improvements in care. These included 1) Financial constraints exist due to disparate yet insufficient funding across multiple sources: the government, development partners and out of pocket expenses (OOP). 2) Management, accountability, and leadership in healthcare are clearly defined as priorities but not monitored. Policy documents provide clear descriptions of the authority, responsibilities, and competencies for leadership roles at all levels of the health system in Liberia. However, there seems to be a disconnect between what the policies state and the actualities due to a lack of leadership, political will, management skills, coordination and monitoring and evaluation 3) Health facilities, infrastructure and accessibility are generally poorly maintained. 4) Human resource capacity and training is limited due to relatively low numbers of trained health workers compromise adequate coverage in remote areas

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ASSOCIATED FACTORS WITH THE POOR PERFORMANCE OF THE MATERNAL DEATH SURVEILLANCE SYSTEM IN CAMEROON, 2020-2022

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In 2014, Cameroon decided to reduce preventable maternal mortality. Surveillance data reviews shows under-reporting. We aimed to identify factors associated with poor performance of Maternal Death (MD) surveillance in Cameroon. An analytical cross-sectional study was conducted in all 10 regions from January 2020 to June 2022. A multi-stage stratified sampling helped to include randomly 13 urban and 13 rural Health Districts (HD). Health facilities (HF) were divided into six categories: all category 1-3 and 2 in category 4-6 per HD were included. Two quarters/villages were randomly chosen in Health Area (HA) hosting the mean HF. All consenting Traditional, religious and administrative leaders, Community Health Workers (CHW), traditional birth attendants and tradipratician were interviewed. Health care workers (HCW) were randomly included depending on the units. The 2001 CDC guidelines of Robert German group work was used to evaluate attributes of MD surveillance system. A KAP survey of community actors was done throw a pre tested questioner. Kobo collect software helped for data collection and Excel software for analyses. OR (CI: 95%, P<0,005) used to identify associations. A total of 2425 people were interviewed, with 1356(56%) female (F/H sex ratio of 1:1). The median age was 34(15-85) years and 1285(53%) aged 25-40 years. HCW were 1106(46%) and CHWs 1041(43%) of the interviewed. DHIS2 recorded 3046 MDs but only 1964(64.5%) were founded in HF's registers. MD causes were mostly unknown, with 80(21%). Littoral region had highest maternal mortality rate either 380 MD for 100000 live births. The surveillance system was moderately simple, unacceptable and sensitive. The promptness and completeness were acceptable. Only 6681(55,8%) MD were reviewed with 29(28%) review's recommendations fully implemented. The MD surveillance system sensitivity is significantly associated with the area (urban or rural) of implementation (OR=1.534; CI: [1,18-1,99]; P<0.001). The MD surveillance system shows globally shortcomings. We recommend training all level actors, surveillance tools elaboration, and resources allocation for activities.

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ASSESSMENT OF KNOWLEDGE, ATTITUDES, AND PRACTICES (KAP) TOWARD COVID-19 IN KINSHASA, DRC

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The Democratic Republic of the Congo (DRC) has reported fewer COVID-19 cases and deaths compared to other countries. Determining the community-level prevalence of infection, knowledge, and behaviors that may mediate transmission is essential for improving COVID-19 control measures. The Seroepidemiological Insight into COVID-19 transmission in Africa study (SICA) aims to measure host and ecological factors influencing incidence in Kinshasa Province, DRC. This sub-study assessed the knowledge, attitudes, and practices (KAP) surrounding COVID-19. SICA study participants >15 years were administered a KAP survey. The World Health Organization Social and Behavioral Insights on COVID-19 Data Collection Tool (SBI Tool) was adapted, and included six sections: knowledge of transmission and symptoms, perceived risk and impact, prevention practices, prior illness and testing, trusted information sources, and vaccination. The frequency and proportions of the KAP indicators were calculated. From August to September 2022, 420 participants were interviewed. The median respondent age was 42 years, and 254 (61%) were female. Only 12% rated their knowledge of COVID above average, but the knowledge of one or more specific symptoms of COVID was high (86%). The two most common symptoms mentioned were cough (71%) and fever (59%). Almost three-quarters of participants (72%) considered COVID-19 a problem for their community. Most respondents (72%) reported currently practicing preventative measures, the most common of which were wearing a mask (58%), hand washing (40%), avoiding shaking hands (25%), and physical distancing (23%). Twenty-three percent of respondents reported receiving the COVID vaccine. Of those not yet vaccinated, 40% reported that they would not be vaccinated against COVID-19 in the future, due to a lack of confidence in all vaccines (43%) and unsure of its efficacy (38%). Despite self-reporting a low knowledge of COVID-19, this study population had a good level of knowledge about COVID-19. However, improvements in attitudes and practices toward preventative behaviors could further reduce transmission during seasonal peaks.

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PROFILING THE QUALITY OF LIFE OF SLUM RESIDENTS DURING THE COVID-19 PANDEMIC, AND THE EFFECTS OF SOME SOCIO-DEMOGRAPHIC AND ECONOMIC MEASURES

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Brazil has recorded over 36 million cases and 650,000 deaths due to COVID-19 and remained the most affected country in Latin America. Efforts targeted at stemming transmission through non-pharmaceutical interventions (NPIs) have impacted on the socio-economic status of slum populations, however, little is known on their impact on the quality of life (Qol). We describe the Qol of residents in one of the largest slum communities in the city of Salvador, Brazil, and explored the effects of socio-demographic and economic predictors on QoL during the pandemic. We performed a cross-sectional study between November 2021 and July 2022, and administered questionnaires to obtain information on demography, employment, income, access to COVID-emergency and family support fund, food insecurity, physical health and mental health. We explored the effects of socio-demographic and economic data on physical and mental health scores using generalized linear mixed models. Among the 907 eligible participants, 633 (69.8%) with age greater than 18 years were recruited (61% females; 39% males). Unemployment rate increased from 49.9% before the pandemic to 87.8% during the pandemic. Only 53.6% received COVID-emergency funds, and 67.3% reported lack of food. Regression models found that physical health was significantly associated with age, education and losing a job during the pandemic. Scores for physical health were significantly low among participants aged 41-60 (-4.10, 95CI: -6.21, -1.98, p<0.01), those who had no formal education (-16.34, 95CI: -25.77, -6.91, p<0.01), and those who lost their job (-2.21; 95CI: -4.15, -0.26, p<0.01). In contrast, mental health was significantly associated with age and gender, with lower scores among females (-5.09; 95CI: -3.02, -3.12, p<0.01) and participants above age 60 (-0.20; 95CI: 3.69, 4.43, p<0.01). The lower quality of life observed in our study, especially for adults, females and those who have lower school attainment, supports the importance to sustain and increase the coverage of financial aids in these slums, in addition to interventions targeted at improving school enrollment and food insecurity.

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AN IN -SILICO APPROACH ON THE EFFECT OF LOPHENOL AND ITS DERIVATIVES ON PANCREATIC LIPASE, ALDOSE REDUCTASE AND DIPEPTIDYL PEPTIDASE-IV AS POTENTIAL TARGET FOR DIABETES MELLITUS(TYPEII)

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Diabetes mellitus is a metabolic disorder that is characterized by persistent hyperglycaemia. Aloe vera has been reported to have anti-hyperglycaemic effect on diabetic patients which is reported to be due to the presence of phytosterols. The protein receptors: pancreatic lipase, aldose reductase and dipeptidyl peptidase-IV were retrieved from the PDB. Their energy was minimized using Gromacs. The targeted phytosterols of aloe vera was retrieved from PubChem and virtually docked against the targeted protein receptors using AutoDock Vina. The drug likeness and the pharmacological profiling of lophenol, methylene lophenol, methylene cycloartanol, ethylidene lophenol and ethyllophenol were evaluated using Lipinski rule of 5 and ADMET properties. Results of the pancreatic lipase, aldose reductase and dipeptidyl peptidase-IV after the molecular dynamics showed the energy of the three protein receptors were reduced and was found to be stable. All the ligands that were docked was found to have binding affinities between -6.8 and -9kcal/mol and docked firmly to the protein. All the ligands were found to be drug-like except for methylene cycloartanol that violated two rules of Lipinski rule of 5.

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EVERY CASE CONFIRMED: EXPANDING UGANDA'S INTEGRATED COMMUNITY CASE MANAGEMENT THROUGH INNOVATIVE PARTNERSHIP

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Uganda is aiming for 100% success in parasitological confirmation of all suspected malaria cases before prompt and accurate treatment of positive cases with ACTs, at all levels of care. For community based health care, the Ministry of Health has adopted a strategy for integrated community case management (iCCM) to facilitate access to and reduce the treatment gap for malaria, pneumonia and diarrhea, a strategy proven to reduce severe illness and death. The iCCM program uses ACTs to treat malaria after confirmation with malaria RDTs, amoxicillin for prompt treatment of pneumonia and oral rehydration solution and zinc for the management of diarrhea at the community level. Every district in Uganda is expected to employ iCCM per the national strategic plan, but many gaps remain, even in high burden districts-- particularly after unexpected early withdrawal of bilateral funding for iCCM in 27 districts in 2021. Uganda's funding for

iCCM through the Global Fund 2020-2023 provided only for ongoing supervision and supply, and not for start-up training and equipping. In 2022, the National Malaria Control Division (NMCD) partnered with The Rotary Foundation, the Muyenga Rotary Club, the Oklahoma Rotary Club, Malaria Partners International, The Aids Support Organization (TASO), World Vision, Pilgrim Africa and the Bill & Melinda Gates Foundation to start up iCCM in Katakwi District, a high transmission district in NW Uganda, by training and equipping 1100 community health workers. This unusual partnership, in which iCCM scale-up was funded by three partners new to malaria implementation funding in Uganda, required coordination with, and adjustment of, the country's current Global Fund grant (2020-2023) and the cooperation of all its sub-recipients for its success. NMCD program staff were able to arrange this, and in early 2023, after successful scale up in 2022, iCCM in Katakwi was sustainably transitioned to ongoing support through Uganda's Global Fund grant, proving a model for successful large-scale engagement of Rotary in creatively aiding in the achievement of national malaria reduction strategic goals.

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FEASIBILITY OF A SOUTH SOUTH NORTH COLLABORATION ON IMPLEMENTING A STUDY TO COMPARE VACCINATION COVERAGE SURVEY METHODS: CASE OF DEMOCRATIC REPUBLIC OF CONGO AND CENTRAL AFRICAN REPUBLIC

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In 2018, the World Health Organization (WHO) established a revised method for assessing vaccination coverage using either a one-stage or two-stage cluster sampling design. This WHO method is considered as a gold standard to assess vaccine coverage. However, the method requires a large number of small clusters which makes the technique prohibitive when sub-national estimates are wanted in low- and middle-income countries (LMIC) such as the Democratic Republic of Congo (DRC) and Central African Republic (CAR), highlighting the need to evaluate alternative coverage survey methods. We describe the feasibility of a South-South-North (S-S-N) collaboration in implementing a study to compare the WHO method with alternatives methods, including Lot Quality Assurance Sampling (LQAS) method, the WHO method modified by the Kinshasa School of Public Health (KSPH), and a grid-based Geographic Information System (GIS) method, in terms of efficiency, cost and time. We used a participatory approach whereby the team from KSPH in DRC and the team appointed by the Ministry of Health in CAR, with technical support from the training program of the University of California Los Angeles in DRC (UCLA-DRC) set a collaborative network through both online and in-person meetings. The team developed the study protocol and had it approved by both local ethic committees. Joining expertise from all collaborators, the teams produced mapping for application of the GIS method in DRC and CAR. As of March 20, 2023, two meetings - one in each country had been held, protocols had been approved and the DRC team was preparing for field deployment. Deployment in CAR will follow - with all collaborators involved. The teams will thereafter jointly proceed to data management, analysis, and dissemination The S-S-N collaboration was feasible with involvement of local stakeholders and was an important way for both LMIC countries to share their experience in implementing coverage survey.

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DISTRIBUTED MANUFACTURING STRATEGIES TO CIRCUMVENT SUPPLY CHAIN COMPLEXITIES, LOWER COST, AND INCREASE ACCESS TO COMPOSTABLE MENSTRUAL HYGIENE PRODUCTS

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Agaves are robust, drought-tolerant plants that have been cultivated for their high-strength fibers for centuries and they hold great promise as a crop in the face of increasing water scarcity associated with a warming planet. Meanwhile, millions of women lack access to sanitary products to safely manage their menstruation particularly in LMIC countries characterized by a dry climate. To address this issue, we show a processing route (involving mild delignification and mechanical fluffing) that transforms the leaves of succulent Agave sisalana into a highly absorbent and retentive material. We find that this process leads to a material with an absorption capacity exceeding those found in commercially available menstrual pads. We show that the carbon footprint associated with this process is comparable with common alternatives with the added benefit that it can be carried out at small scales while remaining environmentally sustainable. This work paves the way for developing partnerships between technologists, agriculturists, and entrepreneurs to enable sustainable manufacturing of compostable menstrual pads rooted in the communities.

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SOCIAL DETERMINANTS OF COVID-19 VACCINE ACCEPTANCE AND UPTAKE IN A BRAZILIAN SLUM COMMUNITY: A LONGITUDINAL TIME-TO-EVENT STUDY

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Slum residents are at high risk for involuntary COVID-19 exposure and are the least likely to access medical care, thus making vaccine-driven prevention critical in this at-risk population. Despite robust vaccination campaigns in Brazil, uptake and timing continue to be influenced by social factors and contribute to health disparities. To address this, we conducted a sequential survey in a cohort of 952 residents of an urban favela in Salvador, Brazil where participants were interviewed in 2020, before vaccines were rolled out, and in 2022. We collected data on demographics, social characteristics, and COVID-19 vaccination status and intent. Primary series uptake was high (87% for 1st dose and 85 % for 2nd dose among those eligible); however, booster uptake was lower (63% of eligible population) at the time of the second interview, suggesting a decreasing interest in vaccination. To account for both vaccine refusal and delays, we conducted a Cox time-to-event analysis of dose uptake using sequential independent outcomes. Exposure times were determined by dose eligibility date to account for age and comorbidities. Intent to vaccinate in 2020 was associated with higher vaccination rates for the 1st (0.257, CI: [0.063, 0.452]) and 2nd (0.301, CI: [0.068, 0.534]) doses. We also found that uptake was associated with a better physical health score (0.147, CI: [0.014, 0.280]) for the 3rd dose. Men were less likely to receive the 1st dose (-0.244, CI: [-0.413, -0.075]), and 2nd dose uptake was lower for employed participants (-0.250, CI: [-0.443, -0.057]). The results show that vaccination beliefs in 2020 are still associated with uptake, suggesting a level of crystallization of COVID-19 beliefs that was not addressed by subsequent campaigns. The fact that healthier and unemployed individuals are more likely to receive certain doses may suggest that those factors ease navigating the vaccination system or are associated with receptivity to

health messaging. Gender also plays an important role. The data, together with qualitative evidence from the community, offers policy lessons to build a long-term COVID-19 vaccination strategy beyond availability.

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MEASLES OUTBREAKS IN REGIONS NEIGHBORING ARMED CONFLICT ZONES; EXPERIENCES FROM THE WEST REGION OF CAMEROON, 2018 TO 2022

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In 2019, a nationwide measles/rubella vaccination campaign was organized in Cameroon. However, in 2022, 67 districts reported measles outbreaks. The West region (WR) reported outbreaks in seven districts among which four border the Northwest region (NWR). Since 2016, an armed conflict in the NWR and Southwest region has caused massive influx of people into the WR. Population displacement negatively affects routine immunization and favors outbreaks. We therefore aimed to determine factors associated with measles outbreaks in the WR of Cameroon. A retrospective study of the West regional surveillance data was carried out from 2018-2022. Data on the classification, demographics and vaccination status of measles cases were retrieved. Data was analysed and trends, seasonality by moving means method and Odds Ratios (OR) were determined and; logistic regression used within 95% confidence limits. A total of 878 cases were reported from 2018-2022. The number of cases/years progressively increased from 106 in 2018 to 309 in 2022. The median age was 34 months (2 months – 57 years), 55% were male and a majority (74%) lived in rural areas. Seventeen percent (n=149) of cases were laboratory confirmed while 30% (n=271) were epi linked; 2.4% (n=21) were Rubella cases. About half (n=441) had received at least one dose of measles containing vaccine. Through the years 60% of symptom onset occurred during epi weeks 1 and 13 with a peak at week 11. Trends showed seasonality. Risk factors identified were living in a health district neighboring the NWR, OR 5.7 (95%CI, 3.7- 8,7) and being unvaccinated OR 5.8 (95%CI, 4.1- 8.4). In conclusion, population displacement due to the armed conflict in the NWR has created pockets of susceptible children in the WR. Periodic intensification of routine immunization should be organized in the affected districts while emphasizing on vaccination in hard-to-reach populations.

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HEAT EXPOSURE AND IMPACTS ON HEALTH AND PRODUCTIVITY OF READY-MADE GARMENT WORKERS BANGLADESH: A QUALITATIVE STUDY

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The ready-made garment (RMG) sector is key to growing Bangladesh's economy, providing export opportunities and employment for its majority female workers. To ensure sustained productivity and a thriving workforce, workplace hazards like heat, must be acknowledged, assessed and managed. The existing heat experienced in the sector is set to worsen as temperatures in the country increase due to global warming. For example, under a high emissions scenario (i.e. RCP 8.5) the estimated average annual temperatures will increase by 3.9 degreeC by the end of this century. This study highlights the impact of heat on health and productivity and explores heat management through the eyes of workers, managers and other sector stakeholders. Qualitative data were collected from workers of two RMG factories in Dhaka in 2022 to identify perceived heat related health and productivity impacts and explore barriers to workers accessing cooling options and heat-related medical care. Key-informant-interviews were conducted with factory officials, onsite health professionals, government officials, the RMG peak body, and NGOs. Workers and health professionals attribute symptoms like headaches, dizziness, fatigue and nausea to heat during summer months. Factory health professionals also observed high blood pressure in workers during summer and other informants identified higher absenteeism in summer. Heat was identified as an important influence on productivity by workers themselves and others working in or with the sector. Workers felt a high degree of pressure to meet daily quotas and the impacts of heat on worker performance and subsequent productivity were identified by workers, managers and health professionals. This production quota pressure also impacted on workers taking rests or hydrating sufficiently – both of which are important heat mitigation strategies. Factories provide some medical services including dedicated infrastructure, though during the hottest periods, they were reported to be insufficiently cooled. The key-informants ranked improved ventilation and space cooling solutions as the most feasible heat mitigation strategies.

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TOO HOT FOR BED NETS IN A CHANGING CLIMATE: SPATIAL ANALYSIS AND RISK MODELLING OF MALARIA INDICATOR SURVEY DATA IN SUB-SAHARAN AFRICA 2018-2022

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Bed nets are a cornerstone of malaria control. However, with increasing global temperatures driven by climate change, survey participants in the Malaria Indicator Survey (MIS) now select "too hot" as a key reason for not using a bed net. This study aimed to examine the factors associated with selecting this reason at a community and household level in Sub-Saharan Africa. MIS data from 2018-2022 were reviewed for survey questions related to temperature factors and bed net usage. All countries in Sub-Saharan Africa with georeferenced MIS data since 2018 were included. The "too hot" for a bed net response proportions were summarised. The spatial distribution of this response was analysed, and the Getis-Ord Gi* statistic used to detect significant clustering of high values (hot spots). Regression analysis was conducted at two spatial levels with various environmental covariates. First, temperature, rainfall, humidity, and elevation data were used to determine the ecological factors associated at a community level. Second, data on building materials (e.g. mud, tin), access to electricity, and ownership of electric fans were used to determine the characteristics at the household level. MIS data from seven (44%) of the 16 countries surveyed had responses including "too hot" for a bed net, with a marked difference in the proportion of this response: Ghana (25%), Nigeria (16%), Senegal (4.8%) and Mali (1%). In Nigeria, for example, there was significant spatial clustering (Z-score = 3.69, P-value <0.001). Survey participants in the south, particularly the Akwa Ibom region, were four times more likely to have a "too hot" response than further north. This region had the highest average temperature and precipitation ranges and a statistically significant negative correlation with electric fan ownership. Further spatial and regression analyses are underway in all countries and will be presented in full. The possibility that global warming plays a role in the non-use of bed nets is alarming, and more information is needed to better understand the problem's scale. This may help national malaria programmes to develop strategies to overcome this challenge.

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CLIMATE CHANGE ADAPTATION MEASURES INFLUENCE HOUSEHOLD FOOD INSECURITY IN SOUTHERN ETHIOPIA

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As part of the project "Co-producing Gender-responsive Climate Services for Enhanced Food and Nutrition Security and Health (COGENT)" project in Ethiopia and Tanzania, we evaluated how the variation in rainfall and potential climate change adaptation measures influence household food insecurity. We did a quarterly survey involving 910 households from nine randomly selected rural kebeles (lowest political administration unit) in the Boricha district between June 2021 and March 2022. The data were collected using pretested, structured questionnaires, and potential causal

links between weather variability, such as rainfall, and food insecurity were measured after controlling for possible confounding variables. The household food insecurity rate (HFI) was highest in June (89.3 %) and lowest in December (67.7 %) after the harvesting season. Months with high rainfall were followed by improved food security, coinciding with increased household wealth. Furthermore, the average Body Mass Index (BMI) in September was the lowest, followed by an increment of 0.35 in December 2021. Households whose heads had not attended formal education [Adjusted Odds Ratio (AOR) 6.02, 95 % confidence interval (CI) 4.70, 7.71], had low-income (AOR 1.30, 95 % CI 1.07, 1.57), households with poor dietary diversity score (AOR 1.43, 95% CI 1.21, 1.63), who were not beneficiaries of the Food safety net programme (AOR 1.77, 95 % CI 1.51, 2.01), and who were not members of the community-based health insurance (AOR 3.49, 95 % CI 2.83, 4.30) had higher risks of food insecurity. Our study shows that better education, higher economic status, participation in the Food safety net programme and community-based health insurance membership reduce the population's vulnerability to food insecurity.

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LABEAUD LAB WASTE AUDIT

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Reducing medical waste is a critical mitigation strategy to reduce health care's contribution to greenhouse gas emissions. In order to understand our lab's waste generation, we conducted a waste audit in our laboratory at the Stanford School of Medicine in the Division of Pediatric Infectious Disease. For two weeks (16-27 January 2023) waste was collected and sorted into three categories (recyclable, compostable and landfill). All waste was then weighed using Fisher Science Education precision balance and Tanta BVB-800 scale equipment with a resolution of 0.1 lb. Two authors were present and led all waste sorting and weighing. All study personnel wore isolation PPE throughout the waste audit and upon completion of the waste audit; all waste was disposed of in compliance with Stanford Environmental Health & Safety policy. Over the two weeks of the study period, we generated a total of 716 gr (24%) of compostable waste and 1316 gr (43%) of recyclable and 995gr (33%) landfill waste. Cardboard boxes, pipette tips, tubes (PCR, conical), gloves, gallon-size liquid containers, and pipet tip boxes were the largest categories comprising 597gr, 546 gr, 406.9 gr 359 gr, 200 gr and 200 gr, respectively. Cardboard boxes comprised 75% of our compostable waste, followed by paper towels (10%). Bio-hazardous solid waste made up 100% of our landfill category. Hazardous waste disposal costs 10–20 times more than non-hazardous waste disposal and our study revealed that one third of our waste was considered hazardous. Other studies have documented 20 - 34% of healthcare waste (HCW) is infectious and hazardous, similar to our results of 33%. Although this audit was performed during a period when fewer individuals were actively working in the lab, we are using this data to first educate ourselves on our waste generation and management, and to highlight opportunities to encourage reuse and decrease waste streams significantly.

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ASSESSING DISTRIBUTIONAL CHANGES OF BULINUS TRUNCATUS, INTERMEDIATE SNAIL HOST OF SCHISTOSOMA HAEMATOBIUM, UNDER CLIMATE CHANGE USING AN INTEGRATED APPROACH

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Climate change influences species' distributions, including those of disease vectors and their associated diseases. However, accurate range shift predictions remain scarce due to a lack of ecological data on most of these species. Bulinus truncatus is an intermediate snail host of Schistosoma haematobium and Schistosoma bovis, causing human and animal schistosomiasis, respectively. It's broad distribution represents the maximum geographic spread of schistosomiasis in Africa, Europe and the Middle East. There is, however, a general lack of data on the ecology of B. truncatus, precluding reliable forecasts of this species' distribution and the associated schistosomiasis risk under climate change. Here, we performed experimental tests with 2500 second generation snails from different field-collected origins (France, Senegal and Zimbabwe), subjecting them to chronic temperature treatments ranging from 4°C to 36°C. Life-history and physiological data were collected on the performance of the snails at each temperature. The data shows that cold origin snails have faster growth rates overall, and that warm origin snails have higher mortality rates at warm temperatures that might be offset by their increased fecundity. The warm origin snails had a higher available energy budget, lower respiration rates and lower hemoglobin levels than cold origin snails, indicating a more efficient energy use at high temperatures. They also showed a stronger immune response, which could translate in a stronger defense response to parasite infections. Furthermore, population genetic analyses based on 4913 single nucleotide polymorphisms show a high genetic differentiation between snail origins that can be linked to adaptation to local climatic conditions. All collected data is used to assess the species' distribution at present and in the future using mechanistic niche models that are compared to more established correlative niche models. The mechanistic niche models consider the differences in life history traits between different origins and the implications on B. truncatus distribution and the associated schistosomiasis risk.

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THE PLANETARY CHILD HEALTH AND ENTERICS OBSERVATORY (PLAN-EO): AN INTERDISCIPLINARY RESEARCH INITIATIVE AND WEB-BASED DASHBOARD FOR MAPPING ENTERIC INFECTIOUS DISEASES AND THEIR RISK FACTORS AND INTERVENTIONS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Diarrhea remains a leading global cause of childhood illness and is caused by various species of climate-sensitive pathogens. The emerging Planetary Health movement emphasizes the interdependence of human health with natural systems, with much of its focus on infectious diseases and their interactions with environmental and human processes. Meanwhile, the era of big data has transformed the curation, aggregation and dissemination of health information engendering a public appetite for open access, web-based repositories of infectious disease data. However, enteric infectious diseases (EID) have largely been overlooked by these developments. The Planetary Child Health and Enterics Observatory (Plan-EO) is a new initiative that builds on existing partnerships between epidemiologists, climatologists, bioinformaticians, and hydrologists as well as investigators in numerous low- and middle-income countries (LMICs). Its objective is to provide the research and stakeholder community with an evidence base for the geographical targeting of EID-specific child health interventions. The initiative will produce, curate, and disseminate spatial data products relating to the distribution of enteric pathogens and their environmental and sociodemographic determinants, making them available to decisionmakers via an online dashboard. To date Plan-EO has compiled microdata from 23 studies with ~80,000 diagnostic results from 35,000 children aged 0 - 59 months at sites in 24 LMICs and georeferenced to over 9,000 unique locations and outreach to additional studies is ongoing. An initial published analysis of Shigella has yielded detailed prediction maps and insights into the mechanisms underlying transmission. These approaches will be extended to other pathogens and their findings used to assess their relative sensitivity to changes in climate compared to other determinants such as sanitation improvements. Plan-EO will eventually develop a scenario-

based framework to support decision-making, resource allocation and identification of priority populations for targeting EID-specific interventions such as novel vaccines.

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ADAPTING TO CLIMATE CHANGE IN SUB-SAHARAN AFRICA: ONE MALARIA INTERVENTION AT A TIME

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Climate change is making malaria-endemic countries especially vulnerable and causing operational challenges for National Malaria Programs (NMPs). Unprecedented fluctuations in rainfall and extreme weather events are changing the seasonality and distribution of Anopheles mosquitoes and transmission patterns of malaria - a disease that caused 593,000 deaths and 234 million cases in sub-Saharan Africa in 2021. We present here climate-related actions that have been integrated in malaria prevention and control programs in several countries, that were designed to adapt to the shift in climate so as to keep effective interventions. In Madagascar, mosquitoes are biting earlier and longer than before (~ 4-fold increase in biting rate). To adapt, the NMP targeted messaging to address population behavior to consistently use insecticide treated nets regardless of the temperature. Several districts in Senegal added another round of seasonal malaria chemoprevention (SMC) in order to account for the 1-month shift in the rainfall peak and/or longer rainy season where total rainfall at the end of the season in October were, on average, 13 mm above normal in the past 3 years. Proactive community case management operations were increased from 6 months to year round in 5 districts. The Zambia NMP prioritized IRS in flood prone communities before the onset of the rainy season and front loaded essential medicines to 140 out of 3,000 health facilities to increase resilience of communities that become inaccessible during the rainy season and avoid interruption of services. These operational challenges affect NMP budgets and personnel needs. Hence, highlighting the need for monitoring climatic indicators (ie. rainfall and temperature) alongside malaria incidence to identify correlations between climate related events and malaria incidence and implement early warning systems. These systems can better inform NMP decision-making to ensure effective interventions. Ultimately, NMPs need budget flexibility and better access to temperature and rainfall data to make evidence-informed decisions to improve prevention and control interventions.

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MALARIA MANAGEMENT IN AN ERA OF CLIMATE CHANGE

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Africa has experienced temperature increases 1.5 faster than the global temperature . For malaria elimination, strategies and opportunities in mitigating the impact for the most vulnerable populations requires an understanding of the climate change. A pragmatic approach has been used to inform the Climate changes and the relationship with malaria. How rapid diagnostics can influence malaria diagnosis? Implications of early diagnosis to address the spread of malaria. The UN has presented the argument, leading to the increase in the literature around climate events and the complex relation with malaria. The literature has noted substantive arguments that climate change as noted in the last 10 years may impact vector borne diseases especially Malaria. The World Bank has been capturing trends that have monitored temperature changes yearly and seasonally. The question arises: is this adequate in addressing an increase in Malaria and other vector borne diseases? Early diagnosis to address the spread of Malaria, especially, during climate events during seasonal - or approximately 4 months post heavy rainfalls and/or temperatures that cause high precipitation. This includes an increased budget allocations for widespread and real-time testing in affected geospatial areas. There is thus a conclusive argument that increasing RDT testing may be an opportunity for countries to address climate changes. Noting, the elements contributing to an increase in malaria prevalence, governments cannot be complacent around the issues of climate change and the health associations. There needs to be an intention to prepare budgets, programs, and implementation of malaria RDTs. Abbott Rapid Diagnostics has sought to understand this issue and aims to accelerate and cement the implemental intervention that moves the dial gauge towards malarial elimination. Furthermore, supporting the monitoring of malaria prevalence to strengthen programs. Malaria control programs will demand timely responses to mitigate negative impacts on populations and their health.

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FROM FOOD SECURITY TO PUBLIC HEALTH - HOW CLIMATE INFORMATION CAN BE USED IN EARLY WARNING SYSTEMS AND PREPAREDNESS FOR DISEASE THREATS

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Climate change has been called the biggest global health threat. Rising temperatures, increased incidence of severe weather, and shifting precipitation patterns can increase disease transmission, create the conditions for existing and emergent pathogens to thrive, and exacerbate disease burden on human populations. This is especially true in countries that suffer from myriad climate-sensitive health challenges and lack the information, resources, or capacity to fully address these challenges. In Somalia and Mozambique, the United States Agency for International Development (USAID) is implementing a set of pilot projects to expand the use of health data in the Famine Early Warning System Network (FEWS NET), a leading provider of early warning and analysis on acute food insecurity around the world. Each pilot spans eight months. Multisectoral data, including climate data, will support decision-makers and health practitioners to access information about how climate change impacts public health risks. The FEWS NET Health Threat Extension pilot activity results from a partnership between USAID, the National Oceanic and Atmospheric Administration (NOAA), and the United States Geological Survey (USGS). The following USAID Bureaus jointly manage the pilots and offer technical support: Development, Democracy, and Innovation; Global Health; Africa; and Humanitarian Assistance. Lessons learned from these pilots can be used to extend efforts and to include additional data to inform climate-sensitive health threats and regions. Pilot activities aim to emphasize the role and importance of a One Health approach to inform sustainable development efforts and can contribute to ongoing early warning systems for preparedness and response to disease threats.

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COVID-19 VACCINE BOOSTER DOSE UPTAKE AMONG A COHORT OF HEALTHCARE WORKERS IN BANGLADESH

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The WHO recommended COVID-19 vaccine booster dose for high-priority groups, including healthcare workers (HCWs). We explored COVID-19 vaccine booster dose uptake among front-line HCWs in Bangladesh. icddr,b in collaboration with the Communicable Disease Control of DGHS,

established a cohort of HCWs to record COVID-19 illness prospectively. The cohort enrolled HCWs from purposively selected 20 hospitals of four divisions across Bangladesh. At enrolment, we collected HCW's demographics, COVID-19 infections since the start of the epidemic, and vaccination records. The study physician followed the enrolled HCWs biweekly and recorded any change in vaccination status, including booster uptake. We summarised the data using frequency and percentages. Between July 2021-March 2023, the cohort included 3684 HCWs: nurses (1763), doctors (810), ward boy/Aya (439), health assistants (226), cleaners (155), community health care providers (125), medical technologist (108), lab attendant (30), receptionist (17), and ambulance driver (12). The median age of the HCWs was 35 years (IQR, 29-44), and 67% (2,465/3,684) were female. Overall, 90% (3,309/3,684) of the HCWs completed the primary series (first and second doses) of the COVID-19 vaccine. However, only 55% (2,020/3,684) of the HCWs received the first booster dose (third dose), and only 24 of them reported receiving the second booster dose (fourth dose). 55% (446/810) doctors and 54% (968/1,763) nurses received the first booster vaccination. The booster uptake was higher among lab attendants (93%) and medical technologists (76%) and lower among receptionists (29%) and cleaners (37%). HCWs in primary health facilities (68%) had a higher booster uptake compared to those in secondary (54%) and tertiary-level facilities (51%). The overall COVID-19 vaccine booster uptake among front-line HCWs in Bangladesh remains suboptimal. Identifying the reasons for low booster dose uptake and implementing a tailored vaccine program to address those factors can safeguard HCWs and maintain critical health services during future waves of SARS-CoV-2.

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ADAPTING SUB-NATIONAL PUBLIC HEALTH EMERGENCY MANAGEMENT: THE MBALE REGIONAL EMERGENCY OPERATIONS CENTER EXPERIENCE IN EASTERN UGANDA

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The COVID-19 pandemic has tested the capacity for emergency responses in low- and middle- income countries (LMICs), which has highlighted the importance of local public health interventions. Uganda has a robust national response coordination mechanism; however, limited capacities exist at the sub-national level. In 2020, the Uganda Ministry of Health established the Mbale regional emergency operations center (REOC) to coordinate responses to public health and natural disasters in eastern Uganda. The Mbale REOC multidisciplinary regional response team works closely with the Ministry of Health, regional referral hospitals, implementing partners, and academia. We aimed to describe the experience of the Mbale REOC over the 3 years from inception including during the COVID-19 pandemic. We conducted a qualitative study including a review of key documents and reports, and semi-structured interviews of participants involved in the establishment of the Mbale REOC and subject matter experts. We used a thematic approach and framework analysis using NVivo 12 software to analyze qualitative data. After the establishment of the Mbale REOC, complete daily regional surveillance reporting increased from 43% to 93%. Over 12 months, the REOC conducted on average 15 partner coordination meetings. The REOC supported 16 districts with logistics and inventory management including coordination of material supply transfer between districts. The REOC provided training in laboratory outbreak monitoring and evaluation to 21 regional trainers, 72 district mentors, and 256 facilities. The REOC established a mobile laboratory in the region that reduced COVID-19 PCR sample result turnaround time from ≥7 to ≤2 days and increased the number of tested samples from 200 to 500 per day. The Mbale REOC improved the sub-national response to infectious diseases outbreaks and disasters in eastern Uganda and was recognized by the Ministry of Health as a model for sub-national public health emergency management. A regional REOC strategy could be adopted by other LMICs to build local public health emergency response capacity.

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AN ASSESSMENT OF RESEARCH, SURVEILLANCE, LABORATORY, AND OUTBREAK RISK MANAGEMENT CAPACITIES FOR NIPAH AND AVIAN INFLUENZA VIRUSES IN BANGLADESH

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In 2021, as part of USAID STOP Spillover activities in Bangladesh, and based on priorities established by stakeholders, we assessed research, surveillance, laboratory, and outbreak risk management capacities for avian influenza virus (AIV) and Nipah viruses (NiV) to appraise the current capacity of different institutions within the country. Both in-person and virtual meetings were arranged for data collection using structured and semi-structured questionnaires. We conducted 49 interviews with stakeholders from government and research organizations, and academia. We collected data on six research projects and three surveillance systems focusing on NiV, 11 surveillance systems and 16 research projects for AIV. Gaps for AIV surveillance include a lack of community-based, farm-based, and wild bird surveillance and the unavailability of sustainable funding. Lack of community-based surveillance, limited integration of human and animal data, and donor-dependency for funding were the gaps in NiV surveillance. Transmission dynamics and spillover risks for both pathogens are understudied. The causes of Nipah's high case fatality rate are yet to be explored. Six laboratories were reported as capable of testing samples for AIV, while the NiV can be tested in only two laboratories. None of these laboratories has BSL-3 facilities. These laboratories reported inadequate sample storage facilities, a lack of skilled human resources, and funding challenges. One government organization conducts outbreak investigations of different zoonotic diseases with the support of other government and research institutions and development partners. Sampling wild birds and nearby poultry to compare strain similarity and estimate the frequency of spillover events is needed to understand AIV transmission dynamics. Community-based surveillance of NiV is necessary to detect missing cases and understand the spillover of these viruses from animals to humans. Increased laboratory capacity, including a BSL-3 laboratory in the country, is required for rapid diagnosis and control measures for infectious disease outbreaks.

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COVID-19 VACCINE ACCEPTABILITY AMONG HEALTH WORKERS IN THE DEMOCRATIC REPUBLIC OF CONGO

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COVID-19 vaccination coverage in sub-Saharan Africa countries has lagged behind the rest of the world, with the Democratic Republic of Congo (DRC) having one of the lowest rates. Health workers are a high-risk exposure group and key actors in vaccination response and risk communication. The objective of this study was to conduct a survey among health workers in

seven DRC provinces, and determine factors associated with COVID-19 vaccine acceptance. This survey was administered from January to October 2022 and included questions on demographics and health history, COVID-19 vaccine uptake, risk perception and exposure to COVID-19, confidence in the COVID-19 response, reasons for acceptance or rejection of the COVID-19 vaccine, exposure to information about COVID-19 and intention to self-vaccinate. Health facilities were selected through simple random sampling, and convenience sampling utilized to administer the questionnaire to personnel in health facilities. A total of 5,102 health worker responses were collected. Results showed while 75.9% of respondents perceived a moderate or high risk of contracting COVID-19, almost half reported receiving at least one dose of the COVID-19 vaccine. Differences in vaccine coverage varied across provinces with significant factors amongst vaccinated health workers in age, gender, occupation, rural settings, and having received other adult vaccines. Among vaccinated health workers, the most frequently reported reason for vaccine acceptance included protection of oneself and others, whereas the top reasons for refusal among non-vaccinated was insufficient safety data, concern about side effects, and vaccine effectiveness. As influential community members, health workers' reasons for acceptance and refusal of the COVID-19 vaccine can help inform strategies to improve vaccine uptake among the general population. Risk communication and engagement efforts among health workers in DRC should emphasize COVID-19 vaccine safety and efficacy as potential opportunities for improving uptake.

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NATIONAL AND SUB-NATIONAL AUTHORITIES' DECISION-MAKING PROCESSES DURING THE COVID-19 PANDEMIC: LESSONS FROM NIGERIA

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Public health decision-making during the COVID-19 pandemic was challenging for decision-makers due to the dynamic epidemiological situation combined with time constraints and immense public pressure. In this study, we analyzed the process of COVID-19 response decision-making in Nigeria. We undertook a desk review to gather information on the country's context and conducted a series of key informant and focus group discussions with a range of stakeholders including national and sub-national officials, civil society representatives, development partners, and academics in Nigeria. Several important themes and perspectives emerged through this analysis. First, Nigeria's previous experiences responding to disease outbreaks provided lessons for establishing health emergency decision-making structures and mechanisms. Second, the establishment of high-level decision-making taskforces at both the national and subnational levels facilitated coordination among different levels of government. However, there is a need for enhancing collaboration due to the emergence of conflicts between levels of government, hindering a cohesive and coordinated pandemic response. Additionally, while decision-makers relied on input from academic experts and civil society members as part of advisory bodies, stakeholders emphasized the need for additional efforts to engage partners and actors in decision-making processes, particularly during the early preparedness and response stages of a health emergency. Third, adapting decisions to account for emerging technical information and the social and economic context enabled the response to be context specific and evidence based. However, more efforts are needed to ensure that decision-making is inclusive, equitable and transparent, to help improve public trust in governance processes, thus increasing compliance with public health measures. By understanding the process of decision-making during health emergencies, we can identify opportunities to improve and strengthen pandemic preparedness efforts.

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GLOBAL ARBOVIRUS INITIATIVE: TACKLING MOSQUITO BORNE VIRUSES WITH EPIDEMIC AND PANDEMIC POTENTIAL

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The risk of emergence and re-emergence of arboviruses with epidemic and pandemic potential has increased as a global public health threat and will continue to do so in the years to come. The geographic range of arboviruses will also keep extending due to increased human movement, urbanization, climate change with environmental adaptation and uncontrolled expansion of mosquito vector populations. WHO has been working on strategic plans for multipathogen pandemic preparedness and response for health emergencies to strengthen capacities in vulnerable countries from local to national, regional, and global levels. In March 2022 WHO and partners launched the Global Arbovirus Initiative, comprised of six pillars: 1)Monitoring risk and anticipation; 2)Reducing epidemic risk; 3) Strengthening Vector Control; 4)Preventing and preparing for pandemics; 5)Enhancing innovation and new approaches; and 6)Building a coalition of partners. This initiative is convening partners across multiple sectors including health, agriculture, urban administration, and environment, as well as national, academic and private sector partners to forge a collaborative approach that builds on existing disease-specific programs to strengthen national integrated arbovirus disease programs. This will enable optimal use of limited resources to achieve the greatest impact. Epidemic response must be grounded in strengthening of ongoing national efforts to surveil for and respond to endemic transmission and localized outbreaks. Over the first year since the launch of the Initiative, WHO and collaborators have progressed in developing integrated risk maps for Aedes-borne arboviruses, appointed regional arbovirus consultants to drive implementation at regional level, and worked with WHO Regional Offices and Member States to adapt the approach to their specific priorities, frameworks, and needs. The successful implementation of the Initiative hinges on continued and political will, development of a sustainable funding model, and ever greater collaboration by partners to advance the objectives of pandemic preparedness and reduction of disease burden.

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DESIGN AND STANDARDIZATION OF MOLECULAR SYSTEMS BASED ON CRISPR-CAS TECHNOLOGY FOR THE IDENTIFICATION OF GENES ASSOCIATED WITH ANTIBIOTIC RESISTANCE

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Design and standardization of molecular systems based on CRISPR-Cas technology for the identification of genes associated with antibiotic resistanceEscherichia coli bacteria are commonly found in both community and hospital environments, where they can cause infections and develop antibiotic resistance. Recent studies have reported high prevalence of the resistance genes CTX-M-15 and floR, indicating the rapid dissemination of resistance genes that should be closely monitored. CRISPR-Cas12a technology has successfully detected carbapenem resistance genes and even viral sequences. In this study, we optimized the PCR-CRISPR-Cas12a system as a proof-of-concept for detecting the CTX-M-15 and floR resistance genes in E. coli. Locally produced Cas12a and Taq Polymerase proteins were used for this purpose, and E. coli isolates were obtained from 40 positive and negative samples that were confirmed by targeted sequencing. Taq Polymerase was used at 1 ng/ µl in 25 cycles for conventional PCR, while 2 crRNA were designed per resistance gene for the CRISPR-Cas system. The PCR-CRISPR-Cas12a system can detect up to 2 pg/µl of total DNA. The results compared with susceptibility tests

such as microdilution and disk diffusion and achieved a concordance index by Kappa ranging between 0.8 and 0.9, categorized as excellent. Unfortunately, in most low-resource laboratories only tests such as antibiograms are currently available. These laboratories may not have the financial resources to purchase and maintain high-tech equipment, such as next-generation sequencing platforms, which are commonly used for monitoring antimicrobial resistance. Therefore, technologies that use basic equipment such as PCR-CRISPR-Cas12a would help shorten the technical gap for early and timely detection of antimicrobial resistance. The implementation of this system can greatly support the One Health approach, which recognizes the interconnectedness of human, animal, and environmental health. Contributing to the surveillance of antibiotic resistance in both human and animal populations, as well as in environmental reservoirs in order to mitigate their spread.

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EFFECTS OF INTERPREGNANCY INTERVAL AND MATERNAL AGE ON GESTATIONAL DIABETES MELLITUS: FINDINGS FROM CHAMPS PREGNANCY SURVEILLANCE IN BANGLADESH

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Gestational diabetes mellitus (GDM) is a disorder of glucose intolerance that arises for the first time during pregnancy and is a significant health concern during pregnancy in Bangladesh. The relationship between maternal age, interpregnancy interval, and GDM remains unclear due to limited inference with small sample sizes, hospital-based cohort, and biased interval measurements (birth-to-birth intervals rather than birth-to-conception). Understanding the relationship would help healthcare providers to identify high-risk women and provide appropriate interventions. Child Health and Mortality Prevention Surveillance (CHAMPS) is conducting pregnancy surveillance in Baliakandi, a rural sub-district of Bangladesh, which tracks every pregnant woman to identify any health-related complications and outcomes. This analysis examined the association of interpregnancy interval and maternal age on GDM using multivariate logistic regression adjusted for other covariates such as socioeconomic status and education. We collected demographic and pregnancy data of all mothers who had two consecutive deliveries with at least 28 weeks of gestation in Baliakandi, Rajbari District, between February 2017 and February 2023. A total of 3168 women had ≥ 2 viable births, and among them, 2697 women were included after excluding previous diabetes and unknown GDM (15%) in the index pregnancy. Interpregnancy interval was measured in months difference between last delivery and next conception. Intervals were categorized as <6, 6-11, 12-17, 18-24 (reference), >24 months, and maternal age as <18, 18-24 (reference), >24 years. A total of 33 (1.3%) women had GDM in the subsequent pregnancy. A very short interval (< 6 months) is significantly associated with higher odds of GDM in the subsequent pregnancy (adjusted odds ratio [aOR]: 3.80; 95% CI: 1.14-12.65). Additionally, compared to women aged 18-24 years, women older than 24 years had higher odds of developing GDM (aOR: 3.48; 95% CI: 1.84-8.98). An integrated strategy combining intensive health education for longer intervals and early detection of GDM among older pregnant women should be strengthened.

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USE OF STOCHASTIC BRANCHING PROCESSES TO ESTIMATE THE EMERGENCE OF MPOX IN NORTH CAROLINA

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Emerging and re-emerging zoonotic infections are often self-limiting with the first transmission event ending prior to onward transmission. However, substantial heterogeneity may exist in secondary transmission chains allowing for subsequent epidemic growth and host adaptation to occur. Detection of emerging and re-emerging pathogens is subject to series of delays including the time between infection and symptom identification seeking testing, and ultimately the time between subsequent infections all of which obfuscate the index case. Understanding the likely time period of the initial emergence has important implications on subsequent public health interventions to limit an outbreak. In our analysis we estimate the most likely period of the initial emergence and we explore the role that different estimates for the basic reproduction number (R0) may have using the observed case rates, epidemiological parameters, and delay distributions from the 2022 Mpox outbreak in North Carolina. Using stochastic branching processes fit using a range of reported R0 values, we find that the first likely case of Mpox in North Carolina occurred between June 9, 2022, and June 23, 2022, compared to the first official reported case on June 23, 2022, indicating that it took 0-14 days before detection. Additionally, we observed that R0 values slightly above one were associated with longer estimated detection delays. These findings have implications for public health measures, as future outbreaks may be more likely to be seeded from these emergences. Estimates of the date of the first likely introduction of a pathogen can improve contact tracing, assist in targeting higher risk population for education and outreach, and inform other public strategies. Future evolutions of this approach could consider the role of mobility and contact patterns. These methods are applicable to other emergent pathogens with maximum benefit during the early transmission period among closed communities with high contact rates.

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A FRAMEWORK FOR PATHOGEN SELECTION USING TAQMAN ARRAY CARDS FOR SURVEILLANCE OF ACUTE FEBRILE ILLNESS IN NIGERIA

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Acute febrile illness (AFI) is a common reason for seeking medical care in many low- and middle-income countries. However, in malaria-endemic countries like Nigeria, AFI is commonly misdiagnosed as malaria, partly due to widespread limitations in laboratory diagnostics capacity. This hinders disease surveillance and delays outbreak detection, reporting, and response. Of particular concern are the endemic, reemerging and novel infectious diseases of public health importance, also presenting as AFI, that can go undetected. We began the Surveillance of AFI Aetiologies in Nigeria (SAFIAN) study using TaqMan-Array Card (TAC). TAC is a simple-to-use, customizable tool, which allows for accurate and simultaneous screening of 11 to 380 genetic targets, within a single assay. Although AFI is a common research focus, the literature is limited in methods for how to select which pathogens to include in these screening efforts. Due to the increased interest in AFI research/surveillance, and new commercially available multiplex tools, such as TAC, we developed a rapid model for pathogen selection for extensive screening efforts proposed by studies like SAFIAN. We used a 5-point stepwise process to identify 24-30 pathogens for inclusion in our customized TAC panel. First, we defined the study objectives and pathogen inclusion criteria: pathogens of high epidemiologic consequence, high morbidity/mortality, and priority diseases in other regional AFI studies. We aimed to provide a diverse representation

of pathogens (e.g., viral, protozoan, bacterial), with the potential for transmission in Nigeria. Next, we identified data sources for each criterion. Then we evaluated each pathogen's potential for transmission based on prevalence and routes of transmission in our study population. We designed scores based on data sources. Finally, we identified the final selection criteria to achieve the required number of targets. Based on this process, we evaluated 77 potential pathogens and customized a TAC panel with 26 targets. Our model for pathogen selection may be useful for others designing customizable tools for similar AFI screening efforts.

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ESTABLISHING THE SPATIAL DISTRIBUTION OF CIRCULATING ARBOVIRUSES IN URBAN AND RURAL LIBERIA

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Given the high number of arbovirus outbreaks in West African nations, as well as Central Africa, it is implied that mosquito- and tick-borne viruses account for a large proportion of non-malaria febrile illnesses in Liberia. Such etiologies are severely under-reported as they are frequently undiagnosed, misdiagnosed, or not recognized (if asymptomatic). Using a multiplex immunoassay based on high-quality, immunodominant antigens, our primary goal is to establish a spatiotemporal baseline of arbovirus exposure in Liberia. Approximately 600 human serum samples collected throughout the country, from communities with varying levels of urbanization, were analyzed for IgG reactive to nine common flaviviruses, alphaviruses, and bunyaviruses detected elsewhere in West Africa. Preliminary data indicate a higher seroprevalence of DENV-2 in urban counties and CHIKV in rural counties. Results generated through this study will help establish a baseline of infection which can be used to guide government policy in resource allocation and animal husbandry practices. Additionally, the success of this testing platform in generating accurate and reliable data validates the use of our thermotolerant, rapid, sample-sparing, and high-throughput bead-based multiplex immunoassay in outbreak situations, especially in the field as part of a mobile laboratory.

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EVALUATION OF ENVIRONMENTAL POLIO SURVEILLANCE SYSTEM IN GREATER ACCRA REGION, GHANA, 2021

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Since July 2019, thirty-one cases of circulating Vaccine Derived Polio Viruses (cVDPV) have been confirmed in nine out of 16 regions in Ghana, while two regions recorded environmental events. The Polio Environmental Surveillance (ES) system has been a remarkable tool for detecting poliovirus given its ability to highlight the spatial and temporal extent of viral circulation. Ghana started ES in 2018 to compliment Acute Flaccid Paralysis surveillance in the polio eradication efforts. We evaluated the ES system in Greater Accra Region to assess its attributes, usefulness and performance in meeting its objectives. The system's operation was evaluated from 2019 to 2020, using the Updated CDC Guidelines for Evaluating Public Health Surveillance Systems. Interviews, records review and observations were employed to assess the system's attributes and usefulness. We performed summary descriptive statistics on quantitative data and direct content analysis on qualitive data. Of the 140 samples collected within the period, 19 (13.6%) cVDPV-2, 8 (5.7%) orphan Vaccine Derived Polio Virus (oVDPV) and 59 (42.1%) Sabin-like viruses, were recorded with a positive predictive value of 22.1% (19/86). Timely processing and reporting from laboratory to next levels was done for all samples (144/144) with regular feedback from partner organizations. The system was well funded and well-staffed; however, site location was not adequately distributed in the region. Data completeness was 98% (141/144) and consistency was 100% (laboratory and surveillance data). Surveillance data informed initiation of reactive polio immunization campaigns nationwide. The ES system is achieving its objectives. It is useful, sensitive, stable and of good data quality. Representativeness needs improvement.

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ASSESSING REALIZED AND POTENTIAL NICHE OF PATHOGENS OF PUBLIC HEALTH IMPORTANCE TO DESIGN SURVEILLANCE TOOL FOR ACUTE FEBRILE ILLNESS IN NIGERIA

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The Surveillance of Acute Febrile Illness (AFI) Aetiologies in Nigeria (SAFIAN) study aims to support disease surveillance systems and global biological threat reduction efforts by detecting and monitoring pathogens among AFI presenting patients at two hospitals in Nigeria, both low resourced settings, with limited laboratory diagnostic tools. To maximize screening of potential pathogens among these populations, we are using the TaqMan-Array Card (TAC). This simple-to-use, customizable tool allows for accurate and simultaneous screening of 11-380 genetic targets, within a single assay, a target number which would otherwise be labor, time and cost prohibitive. There are innumerable pathogen target options for TAC and selection must be performed in accordance with study goals. To optimize the use of this tool, we sought to include only pathogens with transmission potential in the population. We conducted a literature review of 77 AFI-causing pathogens of public health importance and evaluated each for both the potential and the likelihood of pathogen detection in the study population. Binary (yes/no), tiered criteria in this assessment are 1. Capable of human-to-human transmission, 2. Previous detection (molecular, then serological) in humans, 3. Previous detection (molecular, then serological) in animals, 4. Presence of the host/reservoir, and 5. Ecological suitability for host/reservoir in Nigeria. Pathogens marked "no" for all criteria, we excluded from our AFI TAC-panel. Pathogens marked "yes" early in the tiered assessment, e.g. SARS-CoV-2 (1-human-to-human-transmission) or malaria (2-previous molecular detection in humans) were considered more likely to be detected. Pathogens marked "yes" lower in the assessment, e.g. O'nyong-nyong virus (4-vector present in Nigeria) or Bacillus anthracis (3- previous serological detection in cattle) were determined to have detection potential in our study, but that this detection would be novel or unexpected. This assessment helped us prioritize pathogen selection for inclusion in our AFI TAC panels based on their potential for detection in the study population.

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COMMUNITY-BASED SURVEILLANCE FOR INFECTIOUS DISEASES AMONG DISPLACED POPULATIONS IN IRAQ: EXPANDING BEYOND THE COVID-19 RESPONSE

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While common in sub-Saharan Africa and Asia, community-level disease surveillance does not occur in Iraq. During outbreaks, timely detection is imperative for slowing transmission - critically so in densely populated areas or displaced populations. Early warning through community-based surveillance (CBS) can help. CBS was first implemented in 4 IOM-supported IDP camps in Iraq in response to COVID-19. Building on that success,

CBS was expanded to include 8 additional diseases/conditions of concern: acute watery diarrhea (AWD), acute flaccid paralysis (AFP), Crimean-Congo hemorrhagic fever (CCHF), leishmaniasis, measles, rabies/animal bites, and scabies (based on recent outbreaks or impact on displaced populations), and suspicious community death. Six IDP camps were selected for expanded CBS activities (4 original+2 new locations). Qualified residents were hired as Community Health Promoters (CHPs). Field team size was specific to each camp (SPHERE standards=1 CHP/1000 people; n=30 CHPs [15 teams of 1 M/1 F]). Each team received a smart phone for reporting through KOBO. Working hours aligned with primary health care center (PHCC) hours. Active case finding, event-based surveillance, and misinformation tracking were conducted through interviews with consenting heads of households. Community alert definitions were used where available (e.g., AWD, measles, etc.) or developed for this context (e.g., CCHF). Community alert definitions were piloted among CHPs using fictional examples. There was moderately good agreement among CHP answers (Krippendorff's alpha=0.775); CHPs erred on the side of caution and referred for evaluation at PHCC when not necessary. CHPs were also trained on symptoms, transmission, and prevention; KOBO data collection tool; and respectful communication in December 2022 with refresher trainings in late February/early March 2023. Expanded CBS reporting began in early March 2023 and remains underway through at least September 2023, with summary surveillance data available weekly. Ongoing phone surveys seek to understand CBS acceptability among camp residents and their experiences with the program.

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SCALABLE DISTRIBUTED MANUFACTURING OF POINT-OF-CARE MOLECULAR DIAGNOSTICS IN THE GLOBAL SOUTH

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As climate change and land-use changes increase the risk of environmentally mediated infectious diseases in the Global South, innovative solutions that synthesize policy, economics, and bioengineering are necessary to ensure that equitable and quality healthcare reaches low-resource settings (LRS). Currently, to diagnose and monitor vector-borne and transmissible pathogens, LRS are forced to rely on foreign supply chains to deliver expensive, proprietary consumables. The lack of autonomy and agility of LRS to respond to outbreaks is partially due to inequitable distribution of diagnostic manufacturing capacity, which is concentrated in the Global North. Commercial molecular diagnostics rely on expensive, proprietary reagents and highly technical processes, providing a barrier to local manufacturing of diagnostics in LRS-a crucial requirement for building and maintaining healthcare capacity affordably in any region. To completely transform access to sensitive molecular diagnostics, build capacity for infectious disease surveillance, and reduce carbon-intensive cold-chain shipments, we propose a decentralized model for commerce known as distributed manufacturing. We are developing a circular manufacturing pipeline that requires minimal infrastructure and will yield open-access room-temperature stable reagents for loop-mediated isothermal amplification (LAMP). The reagents are integrated into a point-of-care, sample-to-answer modular molecular diagnostic device called SnapDx, which does not require electricity or external equipment. SnapDx can detect SARS-CoV-2 in patient saliva samples, with a limit of detection, sensitivity, and specificity of 1875 copies/µL, 82.7%, and 95.8%, respectively. Further, SnapDx is compatible with various biofluid samples and reprogrammable to fit the disease profile of different LRS. Scalable distributed manufacturing of SnapDx will democratize diagnostics, enable surveillance of neglected and emerging infectious diseases, and increase the number of healthy life years globally.

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SOCIODEMOGRAPHIC, CLINICAL AND PROGRESSIVE PROFILE OF CHILDREN FROM 06 TO 59 MONTHS HOSPITALIZED FOR SEVERE ACUTE MALNUTRITION AT THE THE REGIONAL HOSPITAL OF BOUNDIALI.FROM JANUARY TO SEPTEMBER 2022

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Severe acute malnutrition is a major public health problem in several countries around the world & is a priority in the Sustainable Development Goals. Constituting one of the leading causes of morbidity & mortality of children under 5 years of age. In Côte d'Ivoire the prevalence of Severe acute malnutrition has stagnated for more than fifteen years at around 7%. The scale of Severe acute malnutrition in the Bagoué region & the low documentation on this subject in this region led us to conduct this study to determine the sociodemographic, clinical & progressive profile of children from 6 to 59 months hospitalized for Severe acute malnutrition at the Regional Hospital of Boundiali. We have conducted a cross-sectional descriptive study from January to September 2022 on a comprehensive sample of 109 children from 6 to 59 months hospitalized at the Regional Hospital of Boundiali. The mean age was 19.7 months with 76.15% who were between 12 & 59 months old; The sex ratio was 1.1 & 61.4% lived in rural areas. Marasmus was found in 79% & kwashiorkor in 21% & as associated pathology we noted that 28.8% had malaria, 27.1% had acute respiratory infection, 18.6% had severe anemia, 18.6% had diarrhea & HIV infection was noted in 5.08%. The average length of hospital stay was 6 days & Severe acute malnutrition was stabilized at 46.8% & 8.3% had died. In conclusion, severe acute malnutrition in children from 6 to 59 months of age remains a concern in hospital environment. The analysis of the associated factors through subsequent studies will make it possible to better clarify the causes & consequences of this malnutrition.

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PREVALENCE AND FACTORS ASSOCIATED WITH MATERNAL AND NEONATAL SEPSIS IN SUB-SAHARAN AFRICA, A SYSTEMATIC REVIEW AND META-ANALYSIS

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Reducing maternal and newborn mortality is a key component of Sustainable Development Goal (SDG) 3. Sub-Saharan Africa, with a maternal mortality ratio estimated at 542, remains the region with the highest maternal mortality ratio. Maternal and Neonatal sepsis constitute a major cause of mortality and morbidity. In the low- and middle-income countries (LMICs), more than 95% of maternal deaths more than half of neonatal deaths due to sepsis. There is little data on its prevalence and associated factors in Saharan Africa. Understanding these factors will help to guide interventions, and deployment of community-based initiatives to prevent maternal and neonatal sepsis in sub-Saharan African resource constrained context. Using Prisma guideline, we have reviewed studies from different databases from January 2012 to November 2022. After checking and applying the inclusion and exclusion criteria, the selected studies was independently assessed for quality and risk of bias by 2 researchers. Stata 17 was used, and the grouped prevalence was calculated. Heterogeneity was examined using the Q-statistic and the I2-statistic. Thirty-four studies were included in this systematic review and meta-analysis. The global prevalence of maternal and neonatal sepsis in sub-Saharan Africa was respectively 71% and 56% respectively 70%. However, a heterogeneity of prevalence was observed. For maternal factors, the highest prevalence was

observed for urinary tract infection (90.5%) and the lowest prevalence was observed for caesarean delivery (58.3%). For neonatal factors, the highest prevalence was observed for intrapartum fever (80.8%) while the lowest prevalence was observed for caesarean delivery (37.7%). The prevalence of maternal and neonatal sepsis in sub-Saharan Africa is high. There was a variability on the prevalence depending on the factors. The scarcity of data and studies may explain the heterogeneity.

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IMPACT OF COVID-19 INFECTION ON PREGNANCY AND NEONATAL OUTCOMES EVIDENCE FROM A SUB-COHORT OF PREGNANT WOMEN FROM THE AMANHI-COVID-19 STUDY

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The full extent of the effects of COVID-19 on maternal and fetal health is not yet fully understood. Some studies suggest pregnant women with COVID-19 may be at higher risk for certain complications, including preterm birth, preeclampsia, and cesarean delivery. The AMANHI-COVID-19 study aimed to determine the incidence and factors associated with adverse outcomes among COVID-19-positive pregnant women or recently delivered women in a suburban area of Karachi. From March to December 2021, 410 women (pregnant or delivered within 60 days) were enrolled. Detailed information was collected on prior and concurrent pregnancies and illnesses, along with anti-SARS-CoV-2 antibody testing. Monthly information was collected on COVID-19 symptoms, pregnancy complications, and hospital records. Women were visited within 10 days of the end of gestation to ascertain outcome, peripartum details and collection of blood samples. Roche Elecsys immunoassay was used to detect anti-SARS-CoV-2 antibodies in the samples. The prevalence of COVID-19 among pregnant women was 57.3%. Pregnant women who were seropositive for COVID-19 had higher rates of miscarriage (18.1%) and stillbirth (3.6%) compared to non-reactive women (10.7% and 1.5%, respectively). The results of the study suggest that there may be a possible association between exposure to COVID-19 and adverse birth outcomes. Specifically, the odds of being seropositive and having a miscarriage were 1.9 times the odds of having a live birth (95% CI: 1-3.8). The odds of stillbirth among those exposed to COVID-19 were 1.8 times greater than having a live birth (95% CI: 0.5-7.5). This study found no significant association between socioeconomic status, age, education and parity. The study demonstrated that seropositivity during pregnancy increases the risk of adverse pregnancy outcomes. They must adhere to recommended guidelines to mitigate their risk of contracting the virus, including social distancing measures, face masks, and vaccination to reduce the likelihood of infection.

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DEVELOPING LABORATORY INFRASTRUCTURE AND TECHNICAL CAPACITY TO ADDRESS INFECTIOUS DISEASES IN EQUATORIAL GUINEA

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The increasing prevalence of emerging and re-emerging infectious diseases in Equatorial Guinea necessitates the establishment of high-quality clinical research laboratories. This study outlines the process of developing and strengthening the Baney clinical research laboratory on Bioko Island, with the goal of creating a gold standard, reference laboratory for infectious diseases in the country. Inaugurated in early 2019, the Baney Lab was initially built to conduct malaria clinical trials but had to pivot due to the COVID-19 pandemic. Through a collaboration between MCD global, Sanaria Inc, Ifakara Health Institute, Swiss Tropical and Public Health Institute, and the Equatorial Guinean government, the laboratory infrastructure and staff technical capacity were significantly improved. Key methods included the installation of advanced molecular biology analyzers, development of standard operating procedures, and staff training. The Baney Lab demonstrated remarkable adaptability and resilience by swiftly transitioning from malaria research to addressing COVID-19 and other infectious diseases, becoming a testing reference lab for all of Equatorial Guinea and gaining WHO certification as a regional reference laboratory. This study shares the experiences and challenges faced during the transformation of a basic laboratory into a high-quality, internationally recognized research facility, highlighting the importance of developing robust laboratory infrastructure and technical capacity to effectively and rapidly address diverse infectious diseases in Equatorial Guinea.

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USING SOCIAL LISTENING METHODS TO UNDERSTAND COVID -19 VACCINATION IN THE DEMOCRATIC REPUBLIC OF CONGO

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Social media creates opportunities to stay informed, but has also enabled and amplified the current infodemic that continues to undermine the COVID-19 response and vaccination campaign in the Democratic Republic of Congo (DRC). As of 5 March 2023, 12.7% of the Congolese population has received a COVID-19 vaccine. With the increasing influence of social media platforms like Twitter and Facebook, social media interactions concerning COVID-19 vaccination topics have increased remarkably. This work aims to assess COVID-19 associated posts and track rumors related to vaccination utilizing social listening techniques. Social media posts on Facebook and Twitter were analyzed from 04 September 2021 to 02 September 2022, using Brand24 and 10 keywords (e.g., "Covid-19", "Astrazeneca") associated with COVID-19 vaccination to measure engagement, sentiment (i.e positive, neutral, negative) and frequency of COVID-19 related themes in DRC. A total of 9,326 posts were identified and coded by overall theme (e.g., suspicion about vaccine/COVID-19 information, perception of COVID-19 risk). The suspicion of COVID-19 vaccine posts included any post in which a respondent was suspicious of the vaccine, safety, origin, intention to vaccinate or any information about COVID-19. The perception of COVID-19 risk post included any discussion of the severity of COVID-19 related risk of infection, death or any negative outcome. The majority of posts came from Facebook (78.4% vs 21.6% on Twitter). Facebook had more negative posts compared to Twitter (78.7% vs 55.2 %). Nearly three-quarters of all posts were negative (73.6%), while 21.2% were positive and 5.2% were neutral. The most common theme identified on Facebook was COVID-19 information and vaccine suspicion (21.1%). The most common theme identified on Twitter was the perception of COVID-19 risk (16.4%). Given the vast reach of social media worldwide, this novel social listening methodology is an innovative way to identify public sentiment related to health emergencies to inform response activities and campaigns to address misinformation and boost public confidence in health responses.

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GLOBAL HEALTH CHALLENGES OF INFLUENZA SENTINEL SURVEILLANCE COLLABORATION NETWORK

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Developing effective health protection surveillance is critical for enhancing global health. The Armed Forces Research Institute of Medical Sciences (AFRIMS) has coordinated and enabled collaborations with international partners to expand a network of influenza surveillance throughout South and Southeast Asia since 2005. These sites provide the capability to rapidly identify influenza and quickly disseminate information among partners. In order to develop baseline data to more fully understand the current epidemiology situation, determine the seasonal and regional genotypes of influenza disease, and enhance outbreak response capability. AFRIMS established a network for influenza disease surveillance in Bhutan, Cambodia, Nepal, the Philippines, and Thailand. More than 100 field locations collected data and samples from patients meeting criteria for influenza-like-illness. Rapid testing for influenza A and B is performed in the field as the first step followed by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) for influenza A (pdmH1, H3) and B. Some samples were transported to AFRIMS, where confirmation of all rRT-PCR was performed with virus sequencing performed as warranted. In addition, sequencing and drug resistance analysis is provided to all surveillance station and regional partner collaborators giving participating healthcare providers feedback on the influenza viruses circulating. Including surveillance activities from JAN 2009 through DEC 2022, AFRIMS partners collected and tested a total of 75,141 patients. To date, 37.4% of these samples tested positive for influenza A and/or B. Influenza A was the most common type accounting for 67.2% of the influenza positive samples. Sub-typing of influenza viruses detected 9,783 (13.0%) A/H3; 9,016 (12.0%) A/H1; 46 (0.1%) A/Unsubtyped; 9,123 (12.1%) B; and 94 (0.1%) Co-infected A and/or B. AFRIMS and its collaborating partners in South and Southeast Asia continue to contribute to global knowledge of influenza infections via sample collection, laboratory testing, storage, surveillance and performing and disseminating epidemiological studies.

6600

COMPARISON OF PLAQUE REDUCTION NEUTRALIZATION TEST AND MULTIPLEX ARBOVIRUS IGG DETECTION TEST FOR DETECTION AND DIFFERENTIATION OF IGG RESPONSE TO ZIKV AND DENV

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Arthropod-borne viruses (Arboviruses) cause many emerging and re-emerging diseases. The window of detection for many of these viruses using molecular assays is short, and hence serology plays a vital role in diagnosis and surveillance. The serological methods are limited due to cross-reacting antibodies; therefore, the PRNT is the gold standard for antibody detection. We have validated an 18-plex arbovirus IgG detection assay that detects antibodies to ten arboviruses using 38 PRNT-positive samples. The multiplex arbovirus IgG assay uses optically coded magnetic microspheres to immobilize NS1 and envelop protein antigens from 10 different arboviruses, namely, Zika (ZIKV), Dengue all four serotypes (DENV 1- 4), West Nile (WNV), Japanese Encephalitis (JEV), Yellow Fever (YFV), Tick-Borne Encephalitis (TBEV), and Chikungunya (CHIKV), to interrogate IgG responses in exposed serum or plasma. This 18-plex assay also includes five internal controls that assure the assay and reagent performance. The 38 samples included 17 serum samples, of which 10 were convalescent dengue samples collected between 2009 to 2015 from returning travelers. We also tested 21 plasma collected during the ZIKA pandemic of 2016. These samples were also tested using a 7-plex SARS-CoV-2 IgG multiplex panel. We found 100% agreement between the two tests qualitatively for DENV. The PRNT serotyping results matched in 8/10 samples. The PRNT titer positivity to ZIKV NS1 antigen was negative in these samples, although the envelop protein reactivity was positive in all ten samples. A serology assay based on whole virus particles or envelop protein from ZIKV may give false positive reactivity with DENV-infected samples. In these samples, no PRNT results for ZIKV were available. In 28 ZIKV-positive samples, the PRNT and multiplex assay matched in 27/28 samples completely. One instance was discrepant as it was found reactive with one out of three ZIKV antigens used in this assay. Multiplex SARS-CoV-2 IgG tests shows100%. In conclusion, this limited validation of the 18-Plex arbovirus IgG assay shows excellent agreement with PRNT.

6601

US SURVEILLANCE OF NEGLECTED TROPICAL DISEASES - A MISSED OPPORTUNITY FOR SURVEILLANCE OF NEGLECTED TROPICAL DISEASES

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Neglected tropical diseases (NTDs) are a grouping of diseases common in low-income populations of Africa, the Americas, and Asia. Some NTDs are associated with significant morbidity and mortality and have a severe impact on communities and economies. These diseases are neglected in part becuase they are not considered major concerns in wealthy countries; however, conducting research is often challenging in high-prevalence low and middle income countries due to poor infrastructure, lack of electronic health systems, etc. Surveillance of NTDs in developed countries, such as the U.S., is often irregular, despite the prevalence of disease, health burden, and outbreak potential. The Centers for Disease Control and Prevention (CDC) list 17 NTDs. We conducted a review of state department of health (DOH) websites to describe surveilance of CDC-defined NTDs and case numbers from available. Our review identified nationally reportable 4 NTDs (human cases reported to the CDC in 2019: chikungunya n=192, dengue n=1414, Hansen's disease n=77, rabies n=0). 6 other NTDs were reportable to 1 DOH (Chagas disease in 8 states; cysticercosis/teniasis in 6 states; scabies in 3 states; soil-transmited helminths in 1 state; echinociccosis in 1 state; African tryptanosomiasis in 1 state). Based on the review of available data, the case counts in 2019 include Chagas n=35; cysticercosis n=31; teniasis n=3; echinococosis n=1; soil-transmitted helminths n=14. DOHs varied widely in reportable NTDs; some states explicitly specified diseases, whereas others may report NTDs under categories such as 'diseases of public health importance'. Public-facing data availability was variable; some DOHs presented surveilance data in downloadable format for easy analysis. Others report cases in PDFs, while some states' data were only available upon request under the Freedom of Information Act, i.e. echniococcosis in Idaho. The lack of reporting requirements for NTDs, with only 4 of 17 reportable nationally and 10 reportable nowhere, is a missed opportunity to better understand NTDs, conduct research, and prepare for future outbreaks.

6602

SCALE UP FOR IMPACT IMPROVING COVID-19 ANTIGEN RAPID DIAGNOSTIC TESTING IN NIGERIA

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Continuous testing of people is essential to preventing the spread of the coronavirus disease 2019 pandemic, In Nigeria, only 1.6% of the population had been tested for COVID 19 since the pandemic commenced in Nigeria, staggering low compared to other countries in Africa and across the globe and below the WHO benchmark for testing of 200,000 per week. Despite collective enormous investment and effort by the Government of Nigeria and partners, testing remains suboptimal in Nigeria due to lack of access to testing. Rapid scale-up of testing capacity for COVID 19 is therefore crucial at all levels of the health care system. A total of 280 volunteers were recruited across eight states in Nigeria to scale up testing in communities and health facilities using COVID 19 Ag Rapid Diagnostic Test. The volunteers were trained on safe sample collection using RDT kits, handling of positive samples, testing workflow and interpretation of test results. We ensured aavailability of adequate and appropriate biosafety measures including waste management and infection prevention and Control measures. Strategies for testing includes mobile outreach testings, religious centers, community testing and facility-based testing. At all points quality assurance measure were put in place and test results were captured real time using the electronic case investigation forms and integrated real time into the National surveillance data base. Overall, total of 394,000 COVID 19 antigen rapid diagnostic test was conducted with 146 positive samples giving a test positivity rate of 0.04%. Genomic sequencing conducted on positive samples revealed 100% omicron variant. Timely and accurate testing is an essential tool in preventing the spread of COVID 19 and must be implemented strategically. This finding reveals the impact of leveraging resources to strengthen the country's capacity for detection of COVID 19 and other epidemic prone diseases.Key words: Scale up, COVID-19 prevention, Antigen Rapid testing, Nigeria

6603

FILLING THE INFORMATION GAP: FIND MPOX TEST DIRECTORY AND PERFORMANCE EVALUATIONS

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The 2022 global mpox outbreak spurred rapid development of commercial diagnostics. However, there was no central location where users could access information on the availability of mpox diagnostic tests. Furthermore, limited data on test performance, particularly for tests suitable in decentralized settings, posed a barrier to implementation. FIND aimed to fill this information gap through development of a global mpox test directory and independent performance evaluations of point-of-care (POC) diagnostics. From August 2022, FIND gathered information on mpox diagnostics through landscape review of various sources. We also put out a call for expressions of interest (EOI) to identify POC-appropriate antigen lateral flow tests (LFAs) and nucleic acid tests (NATs) for performance evaluation, selecting suppliers based on reported analytical and clinical performance, ease of use, and distribution in low- and middle-income countries (LMICs). As of 19 February 2023, we registered 119 commercially available mpox tests in the test directory: 87 (73%) NATs and 32 (27%) immunoassays (IAs) targeting mpox antigen (n=18), mpox antibodies (n=13), or mpox antigen + antibodies (n=1). Thirty-two (27%) tests are considered POC, including 18 antigen-based IAs, 11 antibody-based IAs, 1 antigen + antibody-based IA, and 2 NATs. In response to the EOI, we received 50 eligible submissions (33 LFAs and 17 NATs); 3 POC LFAs and 2 near-POC NATs were selected for evaluation. For performance evaluations, which will start in early 2023, we engaged qualified sites in Central Africa (n=2) and Europe (n=1) and established protocols for analytical and clinical evaluation of selected tests compared to laboratory-based PCR on skin lesion specimens. Results are expected in the end of 2023. Information on test availability and performance evaluations are essential to controlling outbreaks such as mpox, with POC tests especially important for diagnosis in decentralized settings in LMICs. The FIND mpox test directory and ongoing POC test evaluation will enable us to generate and share performance data on mpox diagnostics with the global community.

6604

PRELIMINARY INVESTIGATIONS OF THE MICROBIAL INTERACTIONS IN THE GUT OF POTENTIAL VECTORS OF LEISHMANIA CHANCEI IN GHANA

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The endosymbiotic relationship in the insects' gut microbial community contributes to the insects' physiology and vectorial competence. This has the potential for disease control in vectors. Cutaneous leishmaniasis (CL) in Ghana is caused by a new species Leishmania (Mundinia) chancei and has been endemic in the Volta Region of Ghana since 1999 with unknown vectors. Previous laboratory investigations showed that L. (Mundinia) chancei colonizes and replicates in the gut of Culicoides sonorensis, but could not persist beyond the blood meal stage in the gut of Lutzomyia longipalsis. This study sought to investigate endosymbionts present in the guts of Culicoides biting midges and sandflies caught in the CL endemic communities in Ghana that may promote or prevent the survival of Leishmania parasites and contribute to disease transmission and cutaneous lesion exacerbation. A total of 135 sandflies and 410 biting midges were caught by light traps in leishmaniasis endemic communities in Ghana. Flies were pooled in groups of 5 for sandflies and 10 for biting midges and further subjected to DNA extraction. Using both universal and specific 16S bacteria primers, the extracted DNA was subjected to PCR screening for bacteria (Wolbachia, Ochrobactrum, Ehrlichia, Tsukamurella). Of 27 pools (135) of sandflies, 5 (19%), 27 (100%) and 3 (11%) were positive for Wolbachia, Ehrlichia and Tsukamurella respectively. Out of 41 pools (410) of midges, 5 (12%), 11 (27%) and 6 (15%) were positive for Wolbachia, Ehrlichia and Tsukamurella respectively. The Leishmania parasite DNA was amplified in 37% of sandfly pools and 7% of the biting midges' pools. Further genomic analysis such as the sequencing of amplicons is being carried out to provide sufficient data to support this study of the gut microbial community and to ascertain the relationships between the insect and its microbiome.

6605

SAND FLY SURVEILLANCE IN LEISHMANIASIS ENDEMIC AREAS IN CENTRAL HONDURAS

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Leishmaniasis is a serious health problem in Honduras where cutaneous and atypical cutaneous cases are predominant, yet visceral cases are also present. Information about sand fly vector species is limited, particularly in the central region of Honduras. The aim of this study was to identify sand fly species found in leishmaniasis-endemic areas in central Honduras, and screen them for infection with Leishmania parasites. Sand flies were collected in Comayagua (17 sites), Francisco Morazán (2 sites) and Cortés

(1 site) departments from 2018-2022 using CDC light traps. Specimens were identified using taxonomic keys at the U.S. Naval Medical Research Unit No. 6 Entomology Laboratory on Soto Cano Air Base in Comayagua. Females were processed using a modified protocol that allowed for molecular testing and males were clarified with 20% KOH, eugenol-lactic acid (1:1). Unfed females were pooled (1-10 /tube) and PCR-screened for Leishmania minicircle kinetoplast (kDNA). Lutzomyia DNA was confirmed by 12S ribosomal PCR. A total of 978 sand flies (686 males, 292 females) belonging to 13 species were collected: 485 from Comayagua (14/trap), 474 from Francisco Morazán (59/trap) and 19 (19/trap) from Cortés. The most abundant sand fly species in Comayagua and Francisco Morazan were Lu. longipalpis (61.3%) and Lu. evansi (26.3%); Lu. (Coromyia) spp., and Lu. cruciata were also recorded in both departments (<4%). Lutzomyia panamensis was the only species collected in Cortes and was also present in Comayagua. A sub-set (28-100%) of female sand flies (112 unfed, 28 blood-fed) from each department was screened for Leishmania DNA; all samples were negative. We recorded for the first time the presence of Lu. longipalpis, the main vector of L. infantum, and the secondary vector Lu. evansi in 7 and 4 sites in Comayagua department, respectively. Atypical cutaneous leishmaniasis cases reported by the Honduran Ministry of Health in Comayagua suggest the presence of L. infantum in this region. Future studies will further characterize sand fly vector species, Leishmania clinical isolates and potential reservoirs in Comayagua department.

6606

TOWARDS A HOST-TARGETED INSECTICIDE STRATEGY: TRYPANOSOMA CRUZI INFECTION AND HOST FEEDING PATTERNS OF TRIATOMA DIMIDIATA IN A REGION WITH PERSISTENT CHAGAS DISEASE

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Chagas disease, caused by Trypanosoma cruzi, affects 6 to 7 million people worldwide. The goal is to eliminate transmission of this neglected disease by 2030. The main vector in Central America is Triatoma dimidiata, an insect that can be found from Mexico to the north of Peru. Studies in Guatemala show that vector control interventions, including plastering and residual indoor insecticide applications, decreased household infestations of T. dimidiata, but did not eliminate populations. There are regions where vectors persist despite multiple interventions. During June-August 2022, we conducted entomological surveys in 76 households from a region with persistent infestation in Comapa, Department of Jutiapa, Guatemala. Indoor walls and floors were swabbed to detect parasite and triatomine DNA as an independent metric of infestation. For sampled communities, the triatomine infestation index (presence of any life stage) was 26.3%, and the colonization index (presence of immature insects) was 18.4%. Of 86 triatomines, we found that 66% were recently fed. We will characterize the infection prevalence and circulating discrete typing units of T. cruzi using multiplex real-time PCR. We will identify the triatomine host feeding patterns by amplifying the vertebrate cytochrome B gene followed by amplicon deep sequencing. Previous PCR-based blood meal studies of T. dimidiata in Guatemala reveal the predominant hosts included chickens, rats, mice, dogs, ducks, and humans. Our study aims to provide complementary information regarding hosts and transmission cycles in this region. In a One Health approach, we intend that these studies will form the basis for deployment of host-targeted insecticides to the highly utilized vertebrate hosts (e.g., dogs, chickens) to suppress vector populations and protect human health.

6607

ASSESSING KNOWLEDGE ABOUT TICKS AND TICK BORNE DISEASES AMONG INDIANA HEALTHCARE PROVIDERS AND EXTENSION PROFESSIONALS

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The risk of tick-borne diseases (TBDs) has increased with the expanding geographic range, altering seasonal activity, and introduction of invasive ticks in Indiana. When tick control and prevention are underserved, prompt and proper diagnosis and treatment can reduce the TBD threat and disease severity, making it important for authorities, especially healthcare professionals, to stay informed about the tick vectors, associated diseases, and TBD diagnoses and treatment options in their locality. However, there is currently a lack of information about the knowledge of ticks and TBDs and diagnostic proficiency of Hoosier healthcare and extension professionals. To address the gap, we conducted an anonymized Qualtrics survey, distributed via emails to subscribers of 'Purdue University Agricultural Extension Educators' and 'Indiana State Department of Health Physician Network' distribution lists. Our survey comprised 24 discrete or ordinal questions, and one open-ended question, and received responses from 597 participants. We used chi-square and ANOVA tests to assess for significant differences in knowledge scores among demographic groups. Further analysis to identify important predictors of knowledge score gaps is ongoing. Results, to date, shows that while 87.6% of respondents recognized the importance of early removal of ticks to reduce TBD transmission and the association of 'bulls eye' with Lyme disease, only a small percentage correctly identified tick species capable of transmitting diseases in Indiana (25.6%); describe the geographic distribution of Lyme disease and Ixodes scapularis within the state (29.3 and 40.4%, respectively); and name all the endemic TBDs in the state (1%). Aggregate knowledge scores varied significantly based on factors such as respondents' credentials, area of specialty, years of experience, self-identification as a tick expert, and use of online resources to obtain information about ticks and TBD diagnosis. Our findings indicate the need for education and training interventions to improve the knowledge and preparedness of healthcare professionals in Indiana to mitigate the threat of TBDs.

6608

TICK AND INSECT CELL LINES FROM THE TICK CELL BIOBANK FACILITATE ISOLATION OF WOLBACHIA AND OTHER OBLIGATE INTRACELLULAR BACTERIA ORIGINATING FROM MULTIPLE VECTOR SPECIES

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Research into obligate intracellular bacteria in vectors faces particular challenges associated with the need for suitable host systems, whether in vivo (live vertebrates and/or arthropods) or in vitro (cell culture). The Tick Cell Biobank houses the world's largest collection of tick cell lines, as well as a growing collection of new insect cell lines, representing many taxa of importance to tropical medicine. This allows us to conduct studies on the susceptibility of a variety of arthropod cell lines to intracellular bacteria of diverse origins. In general, such bacteria can grow in cells of a much wider range of host species in vitro than in vivo, encompassing cells from both natural hosts and arthropods unlikely to be encountered in nature. Here we present two examples. (1) The genus Ehrlichia contains several tick-borne human or veterinary pathogens including Ehrlichia ruminantium. In vitro, E. ruminantium grows in cell lines derived from not only its vectors, Amblyomma spp., but also multiple other non-vector species (e.g., Dermacentor and Ixodes spp., and the one-host tick Rhipicephalus microplus, which was recently reported to support transovarial transmission of E. ruminantium). (2) Wolbachia symbionts are found in around half of all known terrestrial arthropods in which they are best known as reproductive parasites causing cytoplasmic incompatibility and other phenotypes. Wolbachia is not confirmed to infect ticks; detection in ticks is usually

associated with the presence of parasitic wasps or nematodes. However, tick cell lines support growth of several strains of Wolbachia originating from insects. We summarise how insect and tick primary cultures and cell lines have been used to isolate Wolbachia strains wPip and wPap from Culex pipiens mosquitoes and Phlebotomus papatasi sandflies, respectively, and wCfeF and wCfeJ from Ctenocephalides felis fleas (vectors of bartonelloses and rickettsioses). Moreover, we report use of diverse arthropod cell lines to separate a mixture of wCfeF and wCfeJ from an originally co-infected tick cell culture, allowing the successful generation of complete genome assemblies for both strains.

6609

IMPROVING DISTRIBUTION MODELS OF SPARSELY DOCUMENTED DISEASE VECTORS BY INCORPORATING INFORMATION ON RELATED SPECIES VIA JOINT MODELING

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A key component of understanding the risk of exposure to vector-borne diseases is accurate classification of the spatial distribution of their vectors. Standard species distribution models are applicable to vector species that are well-documented, but may produce biased or inaccurate results for species for which data are limited. In light of global change, vectors that are currently not well-documented, due to either a lack of established presence or lack of current public-health relevance, could become increasingly important. Therefore, it is vital that we have tools to estimate the spatial distributions of these vectors. A key assumption that allows us to leverage additional information on sparsely sampled vectors is that the environmental niches of evolutionarily related species are not completely independent, nor are the spatial distributions of vectors and the pathogens they transmit. One tool that allows us to exploit these relationships is joint hierarchical modeling. In this work, we evaluate whether joint hierarchical models of multiple vectors and human diseases improve distribution estimates of sparsely sampled vectors. Further, we aim to determine if there is an optimal taxonomic level to pool vector species within our modeling framework. We first fit our models to an empirical dataset of ticks and tick-borne disease within Florida, then utilize simulations to test the generalizability of our results and our understanding of their underlying causes. When fit to empirical data, the average accuracy of the estimated distributions for a sparsely-sampled species was 0.691 for the pooled models, compared to an accuracy of 0.364 in the single model. When fit to simulated data, the average R2 between the true and estimated distributions of a sparsely sampled species was 0.38 in the pooled models, compared to an R2 of 0.01 in the single model. While we could not detect a definitive optimal level of taxonomic pooling, current results demonstrate that, via limiting overfitting, joint hierarchical models improve distribution estimates of sparsely sampled vector species.

6610

ANALYSIS OF BLACK FLY ENTOMOLOGICAL SURVEILLANCE FOR ONCHOCERCIASIS ELIMINATION IN SEVEN NIGERIAN STATES

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Entomological surveillance is critical to onchocerciasis elimination. WHO criteria to stop mass drug administration (MDA) in endemic areas requires 6000+ Simulium damnosum sl black flies with an Onchocerca volvulus-infection prevalence significantly <0.05%. Collections by human landing catch (HLC) and Esperanza Window Traps (EWT) are labor and resource intensive. The Carter Center partnered with State and Federal Ministries of Health to collect black flies in seven states in central and southeastern Nigeria at sites selected by the National Onchocerciasis Elimination Committee (NOEC) and supplementary prospected sites. We analyzed fly data from stop-MDA assessment or post-treatment surveillance (PTS) from 2014-2022 to determine the most productive methods and seasons of captures. At least one month of adult black fly data was reported for 314 sites: 2,765 monthly counts from HLC and 1,742 monthly counts from EWTs, which were introduced in 2016. Despite most sites being selected as high-risk first-line villages near rivers supporting breeding, no Simulium flies were ever captured at the majority (n=166, 52.9%) of sites. At productive sites, the number of flies per month was right skewed, with an average of 69.0 flies/month (range 0-2938, s.d. 240) but 0 flies in 52.3% of monthly collections. EWTs were less productive than HLC; in sites and months where both were used, HLC produced 2.0 times as many flies as EWTs. Earlier years targeted rainy season months (~June to November); the NOEC later recommended 12 full months for more comprehensive analysis. Flies were thus collected from July 2021 to June 2022. The average count from productive sites dipped to a minimum of 37 in January but peaked in February and March at 130 and 134 flies, respectively. In 2021-2022, only 82 (35.5%) of 231 sites across 5 states were productive, and 56.0% of 56,762 total flies were captured at just 4 sites. These results reveal extreme variability in black fly yields from predicted high risk sites. Understanding the ecological predictors of the most highly productive sites could improve both the representativeness and efficiency of fly collection for program monitoring.

6611

EFFICACY OF A PERSONAL INSECT REPELLENT KIT PERIMETER CONFIGURATION AGAINSTIXODES SCAPULARIS FEMALE TICKS IN AN ENCLOSED PEET GRADY-STYLE CHAMBER

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Tick-borne diseases (TBDs) are a burden for human and animal health. Prevention of TBDs relies mainly on the prevention of tick bites. Effective tick-bite prevention methods such as EPA-approved topical repellents, permethrin-treated clothing, and thorough tick checks are currently available. However, there is limited user compliance; thus, new bite-prevention technologies are needed. Furthermore, there are no commercial passive spatial devices for area protection against tick bites. To fill this gap, Widder Brothers developed the Personal Insect Repellent Kit (PIRK), a passive, lightweight device containing transfluthrin. In 2018, we started our collaboration with Widder Brothers to test the PIRK against three tick vectors of public health importance, Ixodes scapularis, Dermacentor variabilis, and Amblyomma americanum. Our previous studies demonstrating the contact and short-range spatial efficacy of the PIRK against Ixodes scapularis ticks will be briefly reviewed. In this study, we tested the capability of a PIRK perimeter configuration to act as a tick barrier in an enclosed Peet Grady-style chamber. In this assay, ticks are placed close to the PIRK perimeter and exposed for two hours. Tick behaviors and location in the test arena were recorded during exposure, and ticks were assessed for KD and mortality post-exposure. More than 90% knockdown was obtained at 1 and 2hrs post-exposure, and 90% mortality at 48hrs post-exposure. These data indicate the potential of a PIRK perimeter configuration to protect an area from ticks when at a close distance from the device. Ongoing studies to investigate the dimension of the area protected by the device and assess the perimeter device under semi-field conditions and determine suitability as a limited outdoor device, will be discussed.

6612

ADAPTING VECTOR SURVEILLANCE SURVEYS USING BAYESIAN EXPERIMENTAL DESIGN: AN APPLICATION TO AN ONGOING TICK MONITORING PROGRAM IN THE SOUTHEASTERN UNITED STATES

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Recent decades have seen an expansion of medically important ticks and their associated pathogens throughout North America. A critical step in the prevention of tick-borne diseases is establishing the geographic and temporal extent of host-seeking ticks. However, such data are generally incomplete or entirely lacking in many areas, particularly when considering a spatio-temporal scale which is fine-grained enough to meaningfully establish risk of human exposure. Unfortunately, local vector-control agencies frequently lack the awareness and resources to perform the regular, systematic surveillance that such data demands. While statistical modeling can help address gaps in tick distribution maps, these models require sufficient high-quality data to reduce prediction uncertainty to an acceptable level, in order to reliably assess risk and inform policy. Here we demonstrate the promise of Bayesian Experimental Design to maximize the effectiveness of surveillance and control programs given limited resources. Using previous surveillance data as input, this framework allows us to identify future survey times and locations which minimize the uncertainty in current tick distribution maps. We apply our methods to an ongoing tick surveillance program in South Carolina state parks, and propose novel design criteria specifically tailored to public-health priorities. Our design analyses are complemented by an extensive model comparison study, where competing mixed-effects models widely used in the literature are evaluated based on model complexity and goodness-of-fit.

6613

INDOOR RESIDUAL SPRAYING HAS REDUCED SANDFLY ABUNDANCE AND INCIDENCE OF VISCERAL LEISHMANIASIS IN THE INDIAN SUB-CONTINENT

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Control efforts towards reaching elimination of visceral leishmaniasis (VL) on the Indian sub-continent mainly consist of detection and treatment of cases and indoor residual spraying (IRS). While IRS constitutes over 3/4 of the overall control budget, its impact on vector abundance and VL transmission has not been conclusively established. To address this, we analysed indoor vector abundance data collected from 8 endemic blocks in India (2016-2022), block-level VL case numbers from the KAMIS registry (2013-2021), and IRS quality assurance data as measured by high-performance liquid chromatography (2017-2019). Using statistical and mathematical modelling, we investigated whether sandfly abundance in sentinel sites in India changed as a result of IRS, and whether the decline in VL case numbers was in line with trends in sandfly abundance, accounting for changes in case detection rate over time. Between 2016 and 2022, a total of 229,896 sandflies were caught in CDC light traps, situated in 913 indoor living spaces across 50 villages and 8 blocks. Across the 165,189 data records (up to 4 per month per trap), vector abundance showed a declining trend over the years and was highly seasonal, typically peaking around July. In 4 blocks where IRS was started or stopped during the study period (as part of the national control program), IRS reduced sandfly abundance by 27% (95%-CI: 21%-33%) on average. In 3 of these blocks, this reduction ranged from 27% to 34%; in the fourth block, the reduction was not significantly different from zero. Concentrations of insecticides on walls were not significantly associated with the degree of reduction in vector abundance. Model-predicted trends in VL case numbers, which accounted for trends in vector abundance and case detection delays, closely followed reported case numbers. In conclusion, IRS is very likely to have contributed to reductions in sandfly abundance, although there was a strong secular declining trend in sandfly abundance across all blocks, regardless of IRS status. Trends in vector abundance explain observed declines in VL case numbers, even when correcting for temporal changes in case detection rate.

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DISTRIBUTION OF FRESHWATER SNAILS VECTORS FOR THE TRANSMISSION OF URBAN SCHISTOSOMIASIS IN THE ABUJA, FEDERAL CAPITAL TERRITORY, ABUJA, NIGERIA

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Freshwater snails belong to the class of highly infective flukes of medical and veterinary importance. The infections caused by them are widespread and prevalent in ponds, streams, marshes and lakes contaminated by faeces or urine of infected humans and animals where they breed. We determined the presence and distribution of freshwater intermediate snail hosts of schistosomes in an endemic urban area of Abuja, the Federal Capital Territory (FCT), Nigeria. Eight sampling locations in four districts [Area 1 and 2 (Garki district), Jahi 1/2 (Kado district), Karu 1/2 and City College (Nyanya district) and Central Mosque river (Central Business district] were sampled. Snails were prospected for and processed using standard techniques. Identification was done to species level based on the shell morphology using the identification keys of Brown Kristensen (1993). Each species was counted to determine the number collected in time and space. A total of 1,225 freshwater snails belonging to eight species in four families were collected. members of the family planorbidae (60.6%) with B. truncatus (24.8%) were most abundant. Freshwater snail species were found in all the water bodies in this study but the Central Business District recorded the highest number (40.0%). More Freshwater snail species were collected from streams 1,018 (82.4%) than ponds 207 (17.6%). Fresh aquatic leaves and stems (46.3%) were preferred attachment surfaces in this study. This study shows that Freshwater snail intermediate hosts of trematodes are present in urban Abuja in FCT and suggests possibility of high cases of human and animal schistosomiasis in the area; this calls for an urgent need for adequate environmental management, behavioural change modifications and snail control measures in Abuja alongside mass administration of Praziquantel.

6615

CLIP RNAI SCREEN: UNVEILING THE PROTEASE NETWORK THAT REGULATES HUMORAL IMMUNITY IN ANOPHELES GAMBIAE

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The mosquito immune system is required for mosquito survival and limits vector competence. To optimize mosquito fitness, the immune system is tightly regulated to balance resistance to pathogens and limiting self-harm. To fight pathogens that invade their body cavity, mosquitoes activate humoral immune responses such as opsonization, melanization, and antimicrobial activity via Toll pathway activation. In insects, these immune reactions are regulated by proteolytic activity through cascades of Clip-domain containing serine proteases (cSPs) and their non-catalytic homologs (cSPHs), together known as CLIPs. In this study, we developed a functional genetic analysis pipeline to assess the impact of 90 of the 109 annotated CLIPs on hemolymph antimicrobial activity and melanization in Anopheles gambiae mosquitoes. A zone of inhibition assay (ZOI) coupled

with RNAi was used to identify the contribution of CLIPs to hemolymph antimicrobial activity after Micrococcus luteus challenge. We combined this assay with established protocols that assess the contribution of CLIPs to melanization by quantifying melanotic mosquito excreta, allowing us to measure the impact in these two immune responses simultaneously. With this screen, we identified six CLIPs required for, and two CLIPs as inhibitors of antimicrobial activity. Furthermore, we identified 13 CLIPs required for and five CLIPs as inhibitors of melanization, confirming published results and expanding the canon of melanization regulators by seven CLIPs. Among the identified regulators, a single protein (CLIPB10) was required for both melanization and antimicrobial activity, suggesting limited crosstalk between the pathways controlling these immune responses. Importantly, this study demonstrated for the first time that CLIPs are involved in regulating antimicrobial activity in An. gambiae. Together, our results unveil an unprecedented complexity of immune regulation by proteases, suggesting that protease cascades in An. gambiae mosquitoes form a complex regulatory network with little redundancy and distinct sub-networks upstream of individual types of immune responses.

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IMPACT OF ARBOVIRUS INFECTION ON THE HOST-SEEKING BEHAVIOUR OF AEDES AEGYPTI MOSQUITOES

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Vectorial capacity can be defined as the efficiency of a mosquito to transmit a pathogen. It relies on several factors, including vector competence, feeding preference, survival, and host-seeking behaviour of mosquitoes. Arbovirus infection can (in-)directly impact these factors. Previous studies have shown that Aedes aegypti mosquitoes infected with dengue virus increase probing and locomotor behaviour. However, the impact of arbovirus infection on host-seeking behaviour is poorly understood. Earlier work showed that West Nile virus decreases host-seeking behaviour of the Culex pipiens mosquito, but we do not know whether this is a common phenomenon for other interactions among mosquito and arbovirus species. Therefore, the objective of this study was to unravel the effect of alphavirus (chikungunya and Mayaro viruses) and flavivirus (Zika virus) infection on the host-seeking behaviour of Ae. aegypti mosquitoes. To test this, we injected Ae. aegypti mosquitoes with chikungunya, Mayaro and Zika virus and incubated them for 8-10 days. Next, we released these mosquitoes in a one-port olfactometer in our BSL3-facility. After having exposed mosquitoes to human odour cues in this set-up, saliva samples were collected, and infection rates and transmission rates were calculated. In addition, we simultaneously ran a survival experiment, investigated the mosquito's propensity to feed, and evaluated time spent in flight to test effects of arbovirus infection on these parameters as well. Altered vector behaviour can have a major impact on disease transmission risk, and depending on its precise effects, either under- or overestimate the transmission of arboviruses.

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METATRANSCRIPTOMIC APPROACH TO CHARACTERIZE MICROBIOTA AND BLOODMEALS IN ANOPHELES DARLINGI FROM COLOMBIA

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Mosquitoes are holobiont organisms harboring diverse microorganisms which may play a role in host biology. Little is known about the microbial composition of malaria vectors from the Neotropics. The emergence of the next generation sequencing allowed obtaining sequence data from the mosquito, its microbiota and even identify its bloodmeal sources. This study aimed to characterize the bacterial and fungal communities, in addition to bloodmeals in the main malaria vector Anopheles darlingi using a metatranscriptomic approach. The mosquitoes were collected in three malaria endemic regions of Colombia, Bajo Cauca (BC), Pacific (PAC) and Amazon (AM). The An. darlingi were grouped into pools. RNA was extracted and cDNA libraries were prepared. RNA-seq was performed on the Illumina Nova Seq 6000 platform. Sequencing quality was determined with FastQC and host reads were excluded from analysis, contigs were assembled in MetaSPAdes. BLAST against SSU and LSU SILVA database was performed to identify bacteria and fungi, and against vertebrate COI and Cytb database to identify bloodmeal sources. Identification results were confirmed in NCBI non-redundant database. A total of 303 contigs were assigned to bacteria and 29 to fungi. The Proteobacteria (58.09%) and Actinobacteria (16.50%) phyla were the most abundant. Some of the sequences detected include, Moraxella osloensis, Serratia marcescens, Asaia bogorensis, Asaia krungthepensis and Thorsellia anophelis, which have been previously reported in mosquitoes. Regarding the fungi, the Ascomycota and Zoopagomycota phyla were the most abundant. The blood meal analysis identified sequences from Homo sapiens and Canis familiaris with more than 99% of nucleotide identity. These results indicated the utility of the metatranscriptomic approach for identifying the microbiota composition and bloodmeal source in a single assay and the information obtained could be useful in public health.

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CAN THE ANOPHELES FUNESTUS FEEDING RATE IMPROVE ON AN ARTIFICIAL MEMBRANE FEEDING SYSTEM?

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Malaria is the most severe vector-borne disease caused by the Plasmodium parasites and transmitted by Anopheles mosquitoes. Laboratory-reared anophelines are essential to advance research to reduce or eliminate malaria. The success of laboratory rearing as well as studies on parasite-mosquito transmission are advanced by using artificial membrane feeding systems. This will require the optimisation of mosquito feeding which will ensure that an optimal number of mosquitoes feed to maximise research sample sizes available for analysis. In this study, various parameters such as age of the mosquito, duration of starvation, method of starvation, volume of blood meal, duration of feeding, type of artificial membrane and feeding in the light or dark were evaluated to determine their impact on the feeding rate in a main African malaria vector, Anopheles funestus. By optimising the artificial membrane feeding parameters, an increase in the feeding rate of the An. funestus mosquitoes was observed. The results obtained from these parameters increased the feeding rate of the An. funestus above 50%. However, feeding rates were not significantly increased by the mosquito density, the addition of lactic acid to the blood meal, duration of feeding or the volume of blood. Furthermore, this study allows for successful adult feeding during laboratory rearing as well as opens research revenues that are dependent on blood feeding such as transmission-blocking studies, endectocide studies, etc.

6619

REVEALING FUNCTIONS OF HEMOCYTES AFFECTING PLASMODIUM FALCIPARUM INFECTION IN ANOPHELES GAMBIAE

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Malaria is one of the most devastating human diseases. However, in the last few decades, a significant decrease in the number of cases and deaths has been achieved, largely thanks to strategies focused on vector control. Mosquitoes have an efficient immune system, which protects them

against a variety of pathogens, including Plasmodium. Hemocytes are considered super immune cells because they can eliminate microorganisms through cellular and humoral mechanisms, and they are responsible for the production of several anti-Plasmodial factors. However, most of the research on hemocyte's role in fighting Plasmodium has been conducted using rodent malaria models. In the current research, we studied the function of An. gambiae hemocytes against the human malaria parasite P. falciparum. We found that hemocyte depletion results in a reduction in the number of oocysts in the mosquito midgut. In addition, we observed a high mortality rate of hemocyte-depleted mosquitoes upon infection, which is linked to blood feeding. Interestingly, hemocyte depletion increases the bacterial load in the midgut (microbiota), which, however, is not causing the high mortality. We do observe a loss in the midgut epithelium integrity independent of microbiota upon hemocyte depletion, which could result in uncontrolled cell death. We hypothesized that hemocytes are a key factor in controlling midgut epithelium integrity, which is important for the establishment of infection and development of P. falciparum. Here we present evidence that suggests new roles of hemocytes in the midgut physiology of mosquitoes, that could indirectly impact the permissiveness of mosquitoes to P. falciparum. A better understanding of hemocytes' function in human pathogen infection could allow the development of new strategies for the control of vector-borne diseases by using genetic engineering technologies.

6620

EFFECT OF SPERMATHECAL PROTEINS ON SPERM SURVIVAL AND FUNCTION IN THE YELLOW FEVER MOSQUITO AEDES AEGYPTI

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As the primary vector of Zika, chikungunya, yellow fever and dengue viruses, the Aedes aegypti mosquito affects the lives and livelihoods of millions globally. Control of these disease vectors is compromised by the increasing prevalence of chemical insecticide resistance. Strategies to replace or reduce populations through release of modified males show promise, but their success relies heavily on a complete understanding of mosquito mating biology. For Ae. aegypti, a successful mating provides females with enough viable sperm for a lifetime of producing offspring. Disruption of the mechanisms of sperm transfer and storage provides a tantalising target for novel mosquito control interventions. Here, we used RNA-seq data to screen for molecules putatively involved in promoting sperm survival and performed functional assays using RNAi-mediate gene silencing and CRISPR-based gene knockouts on the most promising candidates. Analyses of the post mating response showed that disruption of key serine proteases had a major effect on female mating phenotypes.

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NEUROPEPTIDE REGULATION OF FEMALE MATING BEHAVIOR IN AEDES AEGYPTI MOSQUITOES

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Female Aedes aegypti mosquitoes are the primary vectors of human disease-causing viral pathogens throughout the world. Methods to control disease rely on disrupting mosquito mating and reproduction to reduce population size. However, the signaling pathways and neural circuits that regulate female mating behavior in this species remain poorly understood. Female Ae. aegypti generally only mate once. During mating, the male transfers seminal fluid peptides and proteins to the female that act on cognate receptors in the female to suppress her mating receptivity, ensuring she rejects mating attempts from all subsequently-encountered males and only produces offspring from the first male. Our group previously identified a male-derived neuropeptide, Head Peptide I (HP-I), and cognate G protein-coupled receptor, NPY-like Receptor 1 (NPYLR1), capable of enforcing short-term (<24 hours post-mating) mating receptivity suppression. Our work focuses on identifying the cells that express npylr1 and testing the functional necessity and sufficiency of these cells in suppressing mating receptivity at the behavioral level on both short and long timescales. Using a genetic approach, we are anatomically mapping the cells that express npylr1 and determining if constitutively silencing and optogenetically activating these cells is capable of modifying female mating receptivity. The relationship between short-term and lifetime suppression of mating receptivity is poorly understood, and our experiments will provide the first map of female mating circuitry and insight into whether short and long-term changes in mating receptivity utilize shared neural circuits. Understanding the basic mechanisms of mating regulation is critical for creating new mosquito control methods and ensuring the continued efficacy of existing methods.

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EXPLORING NON-CODING RNAS FOR PATHOGEN BLOCKING IN MOSQUITOES

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Mosquitoes are vectors of a variety of pathogens that they transmit to humans via biting, and mosquito-borne diseases threaten more than 40% of the global population. Malaria caused by Plasmodium parasites is transmitted to humans by Anopheles mosquitoes, while Aedes species transmit viral pathogens, such as dengue and zika virus. Due to the lack of vaccines, effective therapies and emerging insecticide resistance, transmission blocking in the mosquito is emerging as a promising additional approach to encounter this threat. Apart from their physical barriers, mosquitoes rely on their innate immune system to confront pathogens. Multiple key players of the immune signaling pathways act as restriction factors during the infection cycles in the mosquito, while some mosquito genes serve as host factors facilitating pathogen infection. The main defenses are orchestrated by signaling pathways which result in various responses including lysis, encapsulation, melanization, phagocytosis and anti-microbial peptide production. Non-coding RNAs (ncRNAs) including the small non-coding RNAs (sncRNAs, <200nt long) such as siRNAs, miRNAs and piwiRNAs and the long-non-coding RNAs (lncRNAs, >200nt long) regulate gene expression, hence adding an extra layer of complexity to vector competence. They may regulate immune defenses against pathogen infection, as indicated by their differential expression upon pathogen infection. LncRNAs in particular regulate many biological processes, with existing evidence for their implication in D. melanogaster antiviral immunity. We have shown that several lncRNAs modulate ZIKV infection and reproduction, and could therefore play roles in regulating immunity-reproduction tradeoffs. In our quest to explore the use of non-coding RNAs for disease control, we have also assessed the potential of small activating RNAs (saRNAs) to augment immune responses to pathogen infection. Non-coding RNAs have not been extensively explored with regards to vector-borne disease control, and we show that they represent useful tools to be harnessed for pathogen transmission blocking strategies of public health significance.

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NEW ASPECTS OF SPOROZOITE AND ANOPHELES SALIVARY GLAND INTERACTIONS

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Here, we investigate the interaction between the Plasmodium parasites and mosquito salivary glands. Using high-resolution label-free proteomics, we compared the salivary gland protein landscape of P. berghei-infected and non-infected Anopheles gambiae, as well as the composition of saliva collected from non-infected and P. berghei- or P. falciparum-infected mosquitoes. In the salivary gland proteome, we found that sporozoite infection upregulated proteins across multiple functional families, including lipid and iron transport, metabolism, and immunity, particularly within the melanization pathway. Interestingly, the melanization of sporozoites inside

the salivary glands has never been reported, suggesting that the parasite evades melanization through an unknown mechanism. Conversely, the saliva proteome showed that sporozoite infection depletes certain groups of proteins, remarkably immune proteins. Using confocal and transmission electron microscopy, we observed that some of these immune proteins are expressed in the salivary gland cells and accumulate on the surface of sporozoite bundles in the gland secretory cavities. Moreover, we observed profound morphological changes in the saliva confined into the infected secretory cavities, which could impact the secretion and activity of salivary gland proteins. Overall, this work sheds light on new aspects of a still poorly understood step in the parasite life cycle.

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ANALYSIS OF THE GENITALIA ROTATION IN THE MALE MOSQUITOES CULEX PIPIENS

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Culex pipiens is a major vector of arbovirus and other human diseases. This species' populations have developed insecticide resistance, necessitating the development of alternate vector control strategies, such as the sterile insect method (SIT). This approach requires an understanding of the physiological factors behind male Culex pipiens sexual development, such as the rotation of their genitalia. The objective of this study was to qualitatively and quantitatively examine genital rotation in male Cx. pipiens, since it is an essential indicator of sexual maturity. The genital rotation rate was significantly affected by temperature variations (either 18°C, 22 °C or 25°C), with the rate increasing as the temperature rose. This research contributes to our understanding of the male biology of Cx. pipiens. Understanding and controlling the pace of sexual maturation in males has implications for the timing of the release of sterile males, which is essential for the sterile insect approach.

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IN SILICO DATA MINING REVEALS IMPRESSIVE DIVERSITY OF ANTIMICROBIAL PEPTIDE-CODING GENES IN MALARIA VECTOR ANOPHELES GAMBIAE

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Malaria remains a major concern in global public health. The extent of malaria worldwide, thelimitations of current control methods, and the urgent need for new chemoprophylactic andchemotherapeutic agents foster the investigation of new drug pipelines that improve or evenreplace current treatment strategies. Antimicrobial peptides (AMPs) have shown to be promisingcandidates to target malaria parasites due to broad diversity of mechanisms of action, plasticity totune activity through amino acid substitutions and the existence of distinct methods for generatinga diverse range of analogs. AMPs can also be envisioned to target parasites within mosquito hosts.Upon Plasmodium infection, dozens of host effectors are recruited to inactivate parasites,including different families of naturally encoded AMPs. Although a few classes have beendescribed to inhibit sporogonic stages of Plasmodium in mosquitoes, our understanding of themolecular diversity and function of AMPs in the major malaria vector An. gambiae is largelylacking. We have initiated a study on the discovery of novel mosquito AMPs through acomprehensive in silico survey. Data mining on publicly available An. gambiae genome revealedan impressive diversity of over 30 potential novel gene-encoded AMPs, including at least 8multigenic families. Spatial-temporal transcript distribution was analyzed by qPCR in distinctmosquito tissues and developmental stages, along with their response to bacterial stimuli and to P.falciparum infection. Additionally, the participation of AMPs during parasite infection wasstudied in vivo by RNAi-mediated gene silencing. To reveal their biological functions, 12 peptideswere selected for in vitro activity testing against a panel of bacteria, fungi, viruses, and distinctPlasmodium stages. The discovery of new classes of AMPs was further supported by theidentification of ortholog genes in at least 5 mosquito species. Our study provides the first steptowards the expansion of AMP repertoire in medically relevant mosquito species and paves theway for the development of novel strategies to mitigate the impact of vector-borne diseases.

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IDENTIFICATION OF METABOLOMIC PROFILE OF MOSQUITOES ANOPHELES SPECIES DIET BY ULTRA HIGH PERFORMANCE LIQUID CHROMATOGRAPHY MASS SPECTROMETRY TECHNIQUE IN LIMA PERU

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Malaria is an infectious disease transmitted by mosquito vectors of the family Culicidae of the genus Anopheles. The mosquitoes need a source of nutrients such as carbohydrates, lipids, amino acids to develop physiological activities like parity, longevity, survival and vectorial capacity. The mosquito's crop is part of the digestive system, which plays an important role as a reserve prior to the digestion of consumed sugars. In Peru, the research about the nectarivores diet is limited and does not exist data about the metabolomic profile of the Anophelines species by Ultra High Performance Liquid Chromatography Mass Spectrometry which can separate chemical compounds and identify metabolites with high sensitivity, resolution and accuracy. The aim of the study was to identify and create a metabolomic database of the mosquitoes Anopheles species' diet. The samples were mosquitoes' crop of An. pseudopunctipennis collected in the field, and crops of the bioassay's mosquitoes exposed in a cage to five plants which were Bidens alba, Ludwigia octovalvis, Ludwigia peploides, Bougainvillea spectabilis and Lonicera japónica collected in the field too. Other samples used to compare metabolomic profile and quality control were methanolic extracts of the five plants and internal standards of sugars; the metabolomic profile of the mosquito's crops were analyzed by UHPLC MS technique. The data analysis was performed with the software and libraries MZmine 2.51, Xcalibur 3.1, XCMS 3.7.1., Rstudio 4.2.0, and Metaboanalyst 5.0, HMDB, GNPS and Metlin database. The results obtained show that there is a relationship between the plants' compounds and those found in the mosquito´s crop. Some compounds found were sugars such as glucose, fructose, sucrose, trehalose, cerelose, D-manitol, 10 amino acids, 6 pesticides, 11 lipids, and other compounds. The results will contribute to better understand the feeding ecology of mosquitoes and on the future design more efficient traps based on the sugar preferences of the local mosquitoes' populations for vector control and the secondary metabolites will allow to study metabolism pathways and resistance to pesticides.

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DETERMINANTS OF AEDES AEGYPTI AND CULEX SPECIES LANDING RATES IN NORTHERN ESMERALDAS PROVINCE, ECUADOR: HUMAN LANDING CATCH STUDY JUNE 2021 - JULY 2022

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Mosquitoes vector several infectious diseases; ascertaining what contributes to their biting patterns in distinct contexts enables us to tailor public health interventions. The human landing catch method approximates per-person-time biting rates of mosquitoes and provides a low-cost method to quantify patterns in mosquito behaviour. We aimed to establish the human landing patterns of mosquitoes in a peridomestic context in northern Ecuador and to explore their variability across the year in two communities. Starting in June of 2021, mosquitoes were collected during three-hour periods, thrice daily for five consecutive days each month. Collections occurred in two communities - one smaller, riverine community with less infrastructure (Santa María), while the other had a larger population and

serves as a regional hub for commerce and travel (Borbón). Two collections (one in a semi-enclosed setting and another in an unenclosed setting) were done in each community simultaneously. The semi-enclosed setting used netting to simulate being within a dwelling, while the unenclosed setting was outside but still near a dwelling. We also assessed several environmental variables: temperature, humidity, wind speed, and rainfall. Of the total mosquitoes (n = 18,408), 17,525 (95%) were of the genus Culex, and 354 (2%) were Aedes aegypti. More total mosquitoes were found in Santa María (16,723 or 94%), which was driven by Cx. spp., with 16,691 Cx. mosquitoes collected there. Ae. aegypti preferred Borbón, with 91% (322) of all Ae. aegypti there. There were statistically significant temporal and environmental preferences for both Cx. and Ae. aegypti in Borbón, with Cx. being crepuscular and Ae. aegypti landing throughout the day, and both have distinguishable temperature and humidity variations. Temporal preferences for Cx. spp. do not differ by community; however, insufficient Ae. aegypti were captured in Santa Maria to compare. The differences in mosquito behaviour are relevant in the context of climate change and vector-control programming. Capturing the heterogeneity across diverse communities can inform site-specific interventions.

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MALARIA VECTOR BIONOMICS AND PHENOTYPIC RESISTANCE STATUS TO INSECTICIDES USED IN VECTOR CONTROL IN NDOLA DISTRICT, ZAMBIA

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Malaria is one of the main causes of morbidity and mortality in Zambia contributing to 1.4% of the global burden. LLINs and and IRS are the main malaria elimination strategy. However, the success of vector control is dependent on a good understanding of the bionomics and susceptibility status of the local vectors. Thus, this study aimed at assessing the bionomics and susceptibility status of the local malaria vectors. This study was conducted in Ndola district from July 2021 to October 2021. Mosquito collection was done using CDC - light traps, PSC, Aspiration and Larval Collection. Anopheline mosquitoes collected were morphologically identified and confirmation of malaria vectors was done using PCR. Data analysis was done using Williams's mean for mosquito densities; Kruskall Wallis H test used to compare the distribution of mosquitoes. A negative binomial was used to determine predictors affecting mosquito counts; insecticide resistance testing was done was done using WHO tube and CDC bottle bioassay. The malaria vectors identified were Anopheles funestus s.s and An. gambiae s.s. Anopheles funestus was the predominant malaria vector and exhibited a homogeneous distribution (X2 = 4.717, P>0.05). An. gambiae was found to be highly endophilic and anthrophilic. An. funestus s.s and An. gambiae s.s seeking a blood meal in the urban areas was at least 2.24 and 9 times more respectively in the urban sites than in the rural sites. Indoor resting density of An. funestus s.s in rural site was 1.67 times more than in the urban sites and the indoor resting density of An. gambiae s.s in the urban site was 262 times more than in the rural site. Main breeding sites identified were irrigation trenches (4.67 larvae/dip) and garden ponds (2.72 larvae/dip). Sprayed houses were significantly associated with reduced mosquito numbers (B = -0.956, IRR = 0.384, P < 0.05. An. gambiae s.s was fully susceptible to organophosphates and neonicotinoids but highly resistant to pyrethroids, carbamates and organochlorines. Lastly, the two main vectors in Ndola vary in bionomics and insecticide susceptibility and recommend that control measures must be tailored to these findings.

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A DIGITAL QUESTION-BASED ENTOMOLOGICAL SURVEILLANCE PLANNING TOOL INCREASES KNOWLEDGE ACQUISITION AND SELF-EFFICACY IN USERS

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Stalled progress in malaria control across Africa underscores the need to focus on gaps in protection so that programs can tailor vector control to local drivers of transmission. A paper-based Entomological Surveillance Planning Tool (ESPT) was developed in 2018 to distil normative guidance into an operational decision-support tool to enable cost effective, locally tailored, and evidence-based vector control. Currently, an electronic version of the ESPT (known as eSPT) is being developed to improve access, uptake and use of the paper-based ESPT. To inform its further development, the eSPT's contribution towards question-based entomological surveillance planning was evaluated through exploring knowledge acquisition and retention, and technology acceptability. The evaluation workshops were conducted with target users in Ethiopia and Malawi, with further evaluations currently underway in Mozambique. These users included entomologists and decision-makers from government, and partner institutions in vector-borne disease control. A mixed-methods, uncontrolled, before and after study investigated the impact of the eSPT on knowledge, attitudes, and work practices related to entomological surveillance planning. The evaluation workshops in Ethiopia and Malawi showed that the eSPT significantly increased participants' entomological knowledge acquisition (p = 0.044), and self-efficacy to develop entomological surveillance plans (p = 0.001). These results reveal that the eSPT improves users' entomological knowledge acquisition and self-efficacy to develop entomological surveillance plans.

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FIRST DETECTION OF ANOPHELES STEPHENSI IN ACCRA, GHANA, USING MOLECULAR SURVEILLANCE

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The invasive Anopheles stephensi is rapidly expanding its range in Africa. It was first detected in the horn of Africa but has now spread to many countries in east Africa and subsequently detected in West Africa in Nigeria. Through ongoing studies on urban malaria transmission in Accra, where Anopheles mosquitoes were seen breeding in polluted and unfamiliar habitats including car tyres in sympatry with Aedes mosquitoes, we set up surveillance for An. stephensi in the city of Accra, Ghana. Larval collections were done in and around human habitations in 17 urban and 3 peri-urban sites. Urban sites included sites that were closer to the Kotoka International Airport and the Tema seaport. Larvae were raised into adults and identified morphologically. PCR was done on suspected An. stephensi samples that could not be fully morphologically identified. PCR unamplified samples were sent for sequencing of the ITS2 region. Sequencing revealed some of the unamplified samples from two different areas of Accra to be An. stephensi. The other samples turned out to be An. coluzzii and An. pretoriensis. More

samples are being screened by PCR and subsequently by sequencing. The malaria situation in the areas with An. stephensi will be discussed. This study confirms the rapid expansion of the invasive An. stephensi in Africa. Increased surveillance to understand the extent of the spread of this vector is important to inform vector control measures for An. stephensi.

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ANOPHELES STEPHENSI - SIGNIFICANCE OF ITS UBIQUITOUS PRESENCE IN URBAN AND RURAL SETTINGS; IMPACT ON VECTOR CONTROL AND MALARIA ELIMINATION IN INDIA

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Anopheles stephensi is the primary vector of urban malaria and has been widely incriminated in metropolitan cities in India with the detection of gland and gut infections. The vector breeds in clear water habitats such as overhead tanks, wells, cisterns, barrels/drums, sumps (underground tanks), roof gutters, curing pits in construction sites, fountains, ornamental tanks and also in lesser examined rain-fed habitats. An. stephensi breeds and co-exists with other disease vectors like Aedes aegypti in water storage containers and is a risk if vector control operations are targeted disease-specific. The increasing urban agglomeration of human populations and inadequacy in protected piped water supplies necessitates an increase in water storage containers, consequently increasing the breeding potential of An. stephensi which has a longer flight range and maintains a high degree of contact with the human population. So even at low densities, it can transmit infection and with high population density in urban areas, the chances of being bitten are comparatively high. The adult vectors in urban areas predominantly rest in cattle sheds with close proximity to human dwellings. In recent years, the vector has been observed predominantly in rural areas in India owing to the increase in water storage containers and have outnumbered the earlier known malaria vectors. Hence, An. stephensi is not only a problem to urban areas but also a threat to rural settings. Considering the invasive nature of the vector in African countries and WHO cautioning to many other countries, its presence in rural settings in India along with the existing vectors would delay the progress of elimination and warrants effective surveillance mechanism to control the spread of the vector.

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FOREST COVER AND THE DYNAMICS OF PEAK BITING TIME OF INFECTED NYSSORHYNCHUS DARLINGI IN RURAL COMMUNITIES OF THE BRAZILIAN AMAZON

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Deforestation, changes in land use, availability of blood-meal hosts, and human mobility are major drivers of malaria risk. Environmental changes can influence the peak biting time of Nyssorhynchus darlingi. This study aimed to test the effect of forest cover percentage on the peak biting time of infected Ny. darlingi females in Amazonian rural communities where malaria transmission is continuous with API (> 30). Human landing catch (HLC) was performed outdoors from 18:00 to 00:00 h, in the peridomestic environment of 78 houses, and Shannon traps with HLC in the forest fringe, in 12 municipalities of Acre, Amazonas, Pará, and Rondônia states, amounting to 942 collections hours. Deforestation was measured as the percentage of forest cover, the sum of forest edges, and the distance of each house from the drainage network in each location sampled. A generalized linear mixed (GLM) model was employed to examine the association between forest cover and peak biting time of infected Ny. darlingi. In total, 11,810 Ny. darlingi females were tested for Plasmodium, 110 were infected in peridomestic and 3 in forest fringe (81 with P. vivax and 32 with P. falciparum). The GLM model showed a significant positive association between infected females and landscapes with 25% ¬ 45% forest cover percentage at 21:00-22:00 h and 22:00-23:00 h, whereas in those with forest cover percentage > 75% the peak occurred at 18:00-19:00 and 19:00-20:00 h. We showed that deforestation can affect the peak biting time of Ny. darlingi females infected with P. vivax and P. falciparum. These results provide new insights into the variation observed in the peak biting time of Ny. darlingi across multiple anthropogenic landscapes in the Brazilian Amazon.

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IMPACT OF NEW GENERATION INSECTICIDE TREATED NETS AND INDOOR RESIDUAL SPRAYING ON ENTOMOLOGICAL INDICATORS OF MALARIA TRANSMISSION IN RWANDA

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Insecticide treated nets (ITNs) and indoor residual spraying (IRS) are the core malaria control interventions in Rwanda. However, since 2013, widespread resistance to insecticides has been reported threatening the effectiveness of these vector control interventions in Rwanda. As part of the insecticide resistant management strategy, Rwanda introduced the use of non-pyrethroid insecticides in 2017 for IRS and new generation nets in 2020, following a stratified map of interventions, endemicity of malaria and insecticide resistance. IRS with Actellic 300CS was implemented in Ngoma district, Karongi district received interceptor G2 (IG2) nets and Kicukiro district received piperonyl butoxide (PBO). Entomological indicators of malaria transmission that included sporozoite infection rate (SIR), entomological inoculation rate (EIR) and vector composition was monitored, one year before (2019) and two years after (2020-2021) the deployment of these interventions. The SIR before and after the deployment of interventions were 0.2% vs 0% in Ngoma district (IRS),1.2% vs 0.7% in Karongi district (IG2 nets), 1.05% vs 0.1% in Kicukiro (PBO nets), respectively. The EIR per person per year before and after the deployment of intervention was 5.47 vs 0 in Ngoma (IRS), 3.94 vs 2.04 in Karongi (IG2 net) and 19.16 vs 1.97 in Kicukiro district (PBO net), respectively. Prior to the interventions the predominant species was An. gambiae sensu stricto (s.s.), making up to 75.4%, 90.4%, and 94.8% of the An. gambiae complex, in Ngoma, Karongi and Kicukiro districts, respectively. After the interventions, the proportion of An. gambiae s.s. dropped drastically to 3.9%, 56.9%, and 58.8% in Ngoma, Karongi and Kicukiro, respectively. The deployment of IRS and new nets decreased the SIR and EIR in all sites. These changes were also accompanied by a shift in vector species composition from An. gambiae s.s. to An. arabiensis, with the highest shift occurring in Ngoma (IRS).

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ASSOCIATION BETWEEN LANDCOVER CHARACTERISTICS AND AQUATIC HABITATS OF THE MALARIA VECTORS, ANOPHELES FUNESTUS DURING THE DRY SEASON

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Anopheles funestus can sustain malaria transmission during the dry season due to its use of larger and more permanent aquatic habitats. Ability to predict where An. funestus larval are most likely to occur during the dry season would facilitate their targeting by larval control. Here we investigated the land use and environmental factors associated with An.

funestus breeding in the dry season and used results to develop a habitat suitability models for predicting the distribution of An. funestus habitats in southern Tanzania. A systematic survey was conducted in 19 villages in the dry season to identify all water bodies and test for An. funestus larvae. Water bodies were characterized based on type, size, and the presence of emergent vegetation. Multiple logistic models were used to associate the proportion of different landcover types within 300m, physical characteristics of habitats and the presence of An. funestus. Significant predictors of An. funestus habitats were used to develop a habitat suitability model for this species in the dry season. Thirty percent of 1466 aquatic habitats surveyed had An. funestus larvae: majority being streams (73%), large ponds (15%), and human created habitats (5.5%). Anopheles funestus habitats were characterized by permanent clear water, slow moving with emergent vegetation. The proportion of forest within 300m buffer was the most important land use predictor of An. funestus occurrence (positive association). Conversely, the proportion of built area within 300m was negatively associated with An. funestus presence. Other terrain variables including elevation and slope were retained in the model but had lower relative importance. The suitability of An. funestus aquatic habitats across the study area was predicted to vary between 0.22-0.82 with the accuracy of 83%. The results suggest that in the dry season, An. funestus larvae are most likely to be found in aquatic habitats, often under trees, and permanent clear water. The habitat suitability map generated from these criteria could be useful to prioritize where larval control should be targeted in the dry season of southern Tanzania.

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THE IMPACT OF POLARIZED LIGHT AND PHYSICAL-CHEMICAL WATER BODIES PARAMETERS ON OVIPOSITION SITE SELECTION IN ANOPHELINE MOSQUITOES

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It is vital to comprehend oviposition site selection to strengthen vector control strategies, such as larval source management. The detection of water during the oviposition still needs to be better understood. Although some aquatic mosquitoes use horizontally polarized light and chemical cues to detect potential breeding sites to lay their eggs, their roles in Anophelines mosquitoes remain unclear. This study aims to better understand Anopheline oviposition behavior and the environment by analyzing chemical-physical properties and light polarization in water surfaces. We sampled 115 breeding sites across Lima, Peru, between 2020 and 2021. We used an in vivo and in vitro quantitative analysis of the physical-chemical parameters of water samples from breeding sites. In the field, we used a camera with a lens multiple wavelength polarized filter to recreate the mosquito vision. We then run a statistical analysis for the statistics of water physical-chemical parameters and polarized light patterns.Our findings align with recent studies that suggest the spread of mosquitoes in uninhabited areas and the survival of larvae in polluted breeding sites. According to the results, some chemicals, such as total dissolved solids, pH, alkalinity, phosphate, and nitrate, significantly impacted larval abundance. While there was not enough evidence to imply the positive role of the polarization effect on oviposition site selection, larval density and pH showed significance when captured by the circularly polarized light. These findings suggest a constrained polarotaxis, which could critically affect mosquito egg-laying and repellent studies.

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EFFECTS OF INSEMINATION AND BLOOD-FEEDING ON LOCOMOTOR ACTIVITY OF WILD-DERIVED FEMALES OF THE MALARIA MOSQUITO ANOPHELES COLUZZII

Behavioural shifts in the canonical location and timing of biting have been reported in natural populations of anopheline malaria vectors following the implementation of insecticide-based indoor vector control interventions. These modifications increase the likelihood of human-vector contact and allow mosquitoes to avoidinsecticides, both conditions being favourable to residual transmission of the malarial parasites. The biting behaviour of mosquitoes follows rhythms that are under the control of biological clocks and environmental conditions, modulated by physiological states. In this work we explore modifications of spontaneous locomotor activity expressed by mosquitoes in different physiological states to highlight phenotypic variability associated to circadian control that may contribute to explain residual transmission in the field. The F10 generation progeny of field-collected Anopheles coluzzii from southwestern Burkina Faso was tested using an automated recording apparatus (Locomotor Activity Monitor, TriKinetics Inc.) under LD 12:12 or DD light regimens in laboratory-controlled conditions. Activity recordings of each test were carried out for a week with 6-day-old females belonging to four experimental treatments, representing factorial combinations of two physiological variables: insemination status (virgin vs inseminated) and gonotrophic status (glucose fed vs blood fed). Chronobiological features of rhythmicity in locomotor activity were explored using periodograms, diversity indices, andgeneralized linear mixed modelling. The average strength of activity, onset of activity, and acrophase were modulated by both nutritional and insemination status as well as by the light regimen. Inseminated females showed a significant excess of arrhythmic activity under DD. When rhythmicity was observed in DD, females displayed sustained activity also during the subjective day. Insemination and gonotrophic status influence the underlying light and circadian control of chronobiological features of locomotor activity. Overrepresentation of arrhythmic chronotypes as well as the sustained activity of inseminated females during the subjective day under DD conditions suggests potential activity of natural populations of A. coluzzii during daytime under dim conditions, with implications for residual transmission of malarial parasites.

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EXPOSURE TO MALARIA VECTOR BITES IN RELATION TO HUMAN SLEEPING PATTERNS IN RURAL MALAWI

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Many primary malaria vector species commonly bite people indoors at night. Insecticide-treated bednets (ITNs) exploit this behavior to protect individuals while asleep. However, mosquito behaviors such as increased outdoor biting may result in gaps in protection for ITN users. Likewise, human outdoor activity during late evening or early morning can result in exposure to mosquito bites and malaria risk. We assessed people's sleeping and waking up time and location in relation to mosquito biting profiles to quantify exposure to malaria vectors and malaria risk. Human host-seeking mosquitoes were sampled using the human landing catch technique. From September 2020 through February 2021, mosquitoes were collected every hour from 6pm to 10am both indoors and outdoors at study sites in two rural districts of southern Malawi. A questionnaire was also administered to household heads to record self-reported sleeping and waking up times. A total of 1,501 Anopheles mosquitoes were collected consisting of 80% An. gambiae s.l. (13% indoors and 67% outdoors), 14% An. funestus s.l. (10% indoors and 4% outdoors) and 6% other anopheline species (6 indoors and 80 outdoors). The majority of participants (84%, n=26,672) reported going to sleep within an hour or two after sunset, between 6-8PM. In contrast, 16% of participants reported being awake during the same period during which 4% of vectors were caught biting. Likewise, 49% (n=26,674) of respondents woke up at sunrise or within an hour after sunrise (5-6AM), followed by 44% (n=26,674) who woke up one to three hours after sunrise (6-8AM). During the same periods, 21% of vectors were caught biting. We conclude that while a good proportion of study participants reported being indoors when 75% (n=1126) of mosquito bites took place, 25% (n=375) of bites occurred when nearly 93% of people

were already awake and thus potentially exposed to bites. The results suggest that many people were either outdoors, or not under an ITN while Anopheles vectors were biting. Thus, risk of malaria could be lowered by using personal protection while outdoors or indoors outside an ITN, particularly in the evening and early morning hours.

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NON-RESIDENTIAL SPACES AROUND HOUSES ARE IMPORTANT SOURCES OF AEDES AEGYPTI MOSQUITO VECTORS IN WESTERN AND COASTAL KENYA

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Aedes aegypti is an important vector of dengue, Zika and chikungunya and other arboviruses. Non-residential spaces close to human dwellings are rarely targeted during vector control activities due to the endophilic and anthropophilic behavior of this vector. The current study assessed the importance of non-residential spaces in production of Ae. aegypti in two cities in Kenya: Ukunda (coastal Kenya) and Kisumu (Western Kenya). The two study sites were divided into eight 200x200 meter zones. Mosquitos were collected in each of the zones using BG traps and Prokopack aspirators from October 2020 through January 2022. Trapping by BG traps was done once every two months in each of the 8 zones per study site. Prokopack was done monthly in each of the 8 zones per study site. In total, 2,887 and 4,148 Ae. aegypti mosquitoes were collected by BG traps and Prokopack, respectively. BG traps collected significantly more Ae. aegypti mosquitoes in non-residential spaces (P<0.0001) compared to residential spaces. Prokopack collected significantly more mosquitoes in residential spaces (P<0.0007) compared to non-residential spaces. In residential spaces and for both traps, abundance of Ae. aegypti mosquitoes was positively associated with houses with higher number of rooms (>8) and negatively with houses with surrounding vegetation. The number of Ae. aegypti mosquitoes trapped by Prokopack were negatively associated with having a cemented floor and absence of domestic animals. BG traps placed in yard shops and gardens trapped significantly more mosquitoes compared to uninhabited houses. In Prokopack traps, presence of trees was positively associated with abundance of Ae. aegypti mosquitoes while presence of short grass and wet drainage channel were negatively associated mosquitoes in the non-residential spaces. Our results indicate substantial contribution of non-residential spaces to Ae. aegypti mosquito abundance. Presence of vegetation and the type of non-residential spaces influences mosquito abundance. Non-residential spaces near human dwellings are important targets for vector suppression interventions.

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ENTOMOLOGICAL SURVEILLANCE AND COMMUNITY KNOWLEDGE ON MOSQUITOES AND DENGUE RISK IN THE GALAPAGOS ISLANDS, ECUADOR

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Spread by the Aedes aegypti mosquito, dengue presents an ongoing threat to community health, even in places like Ecuador's Galapagos Islands, located 1,000 km west of the mainland. Known for their unique biodiversity and Darwin´s theory of evolution, Galapagos has a population of over 30,000 people distributed in 5 islands, two of which (Santa Cruz and San Cristobal) are endemic for dengue fever. Dengue cases are reported almost every year with the first significant outbreak occurring in San Cristobal in 2010 and since then, smaller outbreaks approximately every five years. Here, we report results from a mixed-methods study with entomological surveillance and qualitative research through KAP related to the mosquito and dengue. BG-sentinel traps and Prokopack aspirators were used to collect mosquitoes in and around houses in 2017 and 2018. A total of 1,929 adult and immature mosquitoes were collected from 419 houses in Santa Cruz, San Cristobal, Isabela, and Floreana islands. Of these, 532 specimens (27.6%) were identified as Ae. aegypti which was found in all collection periods revealing its year-long presence and in 121 of 419 (28.9%) of surveyed residences. Although not found in Floreana, Ae. aegypti was confirmed on Isabela, indicating its recent expansion to this island; a subsequent first dengue outbreak on Isabela was reported in 2020. Five focus group discussions with a total of 41 participants revealed that residents know about dengue and understand its transmission by mosquitoes, but they did not consider it as an important health threat, despite 65 dengue cases were notified in the 2017-2018 period and increased to 205 cases between 2020-2021 during the COVID-19 pandemic. Vector control efforts by governmental agencies are sporadic and often ineffective. Abatization and mosquito control is done at blind and thus most likely increase insecticide resistance in local mosquito populations, which needs urgent investigation. Establishment of a year-long mosquito surveillance program with community involvement may help to prevent dengue or other vector-borne diseases in the Galapagos in the future.

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DEFINING THE CONTRIBUTION OF COMPLEMENTAL MALARIA VECTOR ANOPHELES COUSTANI S.L. TO PLASMODIUM FALCIPARUM SPOROZOITE INFECTION IN A HIGHLY ENDEMIC REGION IN UGANDA.

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Entomological surveillance and assessment of the impact of vector control interventions, targets primary malaria vectors; Anopheles gambiae s.s, An. arabiensis, An. funestus and an. coluzzii. Rarely is the contribution of secondary malaria vectors examined. This study aimed to underscore the role of An. coustani s.l. in Plasmodium falciparum sporozoite infection in Adjumani district, a highly endemic area. Mosquitoes were collected for 21 months (May 2021-January 2023) indoors using CDC light traps (CDC LT) and pyrethrum spray collections (PSC). Additionally, the human baited double net (HBDN) method was used for indoor and outdoor catches. Overall, 58,351 mosquitoes were collected. Of these, 21.8% (12,741/58351) were An. gambiae s.l; 69.2% (40,387/58351) were An. funestus s.l and 9% (5223/58351) were An. coustani s.l. CDC light traps, PSC and HBDN accounted for 74.5%, 23.8% and 1.6% of all collections respectively. Whilst, CDC LT collected significantly more An. funestus s.l (31,419 vs 8,773, CI: 0.006-0.0035, P=0.006) compared to PSC; An. coustani s.l. accounted for 61% of all HBDN collections with similar proportions to An. gambiae s.l in PSC (18.9% vs 18.1%). An. coustani constituted 72.4% (indoor) and 61.3% (outdoor) of HBDN collections. A subset of indoor catches including An. gambiae s.l. at 30% (1545/5085), An. funestus s.l. at 40% (2019/5085) and An. coustani s.l. at 30% (1521/5085) were examined for P. falciparum sporozoites. Overall, the sporozoite infection rates were 1.9% in An. gambiae s.l, 1.5% in An. funestus s.l and 0.1% in An. coustani. However, evaluation of monthly sporozoite rates showed that in December 2021, An. coustani s.l. sporozoite rate (0.18%) was higher (not significant) than that of An. funestus s.l (0.0%). In February 2022, the An. coustani sporozoite rate (0.2%) was higher than An. gambiae s.l (0%) though not statistically significant. Of note, the contribution of An. coustani as a malaria vector exhibiting both indoor and outdoor biting may be underestimated. The requisite for understanding the contribution of this species to outdoor malaria transmission remains relevant.

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CHARACTERIZATION OF MOSQUITO BITE EXPOSURE IN HUMAN USING NOVEL BITE DIARY APP AS A NEW PARADIGM LINKING SOCIO-ENVIRONMENT AND MOSQUITO-BORNE DISEASE TRANSMISSION

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Mosquito-borne diseases are an increasing threat to global public health. Despite the key role that human-mosquito contact rates lay in driving mosquito-borne disease transmission, disease risk has been primarily studied through the lens of mosquito abundance and overlooks human-mosquito contact dynamics. As a result, we continue to have a limited understanding on how human-mosquito contact rates are influenced by socio-environmental and human behavioral factors that drive mosquito-borne disease transmission. To fill this gap, we used a novel mobile-app based bite survey instrument (Bite Diary) to characterize and quantify human exposure to mosquito bites in Florida. Research participants initially participated in a workshop to learn about the research project, mosquitoes, and mosquito-borne diseases. They then monitored mosquito bites they may receive in their normal daily lives for a period of seven days, and entered any bite-associated data in the Bite Diary app in a real-time fashion. They also participated in an online survey at the end of the bite monitoring period to provide data related to demography, knowledge, attitude and practice. Our study showed that bite exposure was highly heterogeneity with a small portion of participants experienced relatively higher number of mosquito bites than others. The bite exposure rate was influenced by human behaviors such as outdoor activity level, as well as environmental factors such as weather conditions associated with season. We also investigated relationship among mosquito bite reaction, bite tolerance, protective behavior (e.g., repellent usage), and the reported bite exposure rate. We emphasize the practicality of using surveys to investigate human-mosquito contact rate in relation to human behaviors, and the importance of a model-driven study design that produces field-quantified parameters which can be readily applied in mathematical models. Our focus on human-mosquito contact dynamics contributes new insights into the mechanisms behind mosquito-borne disease spread and emergence, and guides future research directions to inform disease prevention and control.

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DEVELOPMENT OF SEMI-AUTOMATED SYSTEMS TO GENERATE MOSQUITOES FOR VECTOR-BORNE DISEASE RESEARCH

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Malaria is a global health burden that is caused by the Plasmodium parasite and is spread by Anopheles mosquitoes. In order to comprehensively study malaria, live mosquitoes are needed. Obtaining and handling mosquitoes precisely and safely using traditional methods is laborious and time consuming and does not meet current research needs. We have developed several devices that partially automate the rearing and handling of Anopheles stephensi mosquitoes, including separating pupae from larvae and aspirating female mosquitoes. Our insectary raises approximately 50,000 mosquitoes a week, which requires rearing in over 100 pans where the pupae are separated from larvae daily before the pupae emerge into adult mosquitoes. To streamline this process, we developed the Pupation Station, which is a semi-autonomous system that aids in the daily draining and separation of larvae and pupae. It consists of an array of 6 large aluminum pans with fixed electronically actuated values that aid in the draining and filling of the pans. It simplifies the larva rearing process, reduces physical taxation, increases consistency, and maximizes mosquito yields compared to manual methods, reducing the amount of time needed for the separation process by 66%. Once adult mosquitoes emerge, females need to be separated from males as only females blood feed and transmit the Plasmodium parasite. We have developed an Automatic Aspirator to transfer mosquitoes between cartons, replacing the need for a traditional mouth aspirator. Together, these systems have increased the robustness, reproducibility, and efficiency of mosquito rearing. We anticipate that they could be extended to other mosquito species and scaled to other laboratory or manufacturing settings to enhance vector-borne disease research.

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VECTOR PROFILES AND RISK FACTORS AMONG EARLY EVENING VERSUS OVERNIGHT MOSQUITO COLLECTIONS IN THE HIGH MALARIA TRANSMISSION SETTING OF NCHELENGE DISTRICT, ZAMBIA

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Communities in Nchelenge District, Zambia experience intense residual malaria transmission despite existing interventions such as indoor residual spraying (IRS), bed net distribution, and integrated community case management. To further understand exposure to vectors capable of transmitting malaria parasites, mosquitoes foraging in 24 households were captured between the hours of 16:00-22:00 and 22:00-06:00 during two weeks of August 2019, resulting in 1048 female anophelines captured indoors including Anopheles funestus (94%), An. gambiae (2%), and other understudied anophelines (4%). Differences in mosquito counts in the early evening (N=466) versus overnight hours (N=582) were not statistically significant, and a more diverse population of mosquitoes was captured in the early evening hours. DNA from mammalian hosts was detected and the human blood index (HBI) of blooded anophelines was 97.1%. Plasmodium falciparum-specific CSP proteins were detected within anopheline head/thoraxes, revealing almost 2% (N=18) of the collected An. funestus (N=17) and An. gambiae (N=1) harbored sporozoites. Data from household surveys including household structural characteristics and intervention coverage suggest greater anopheline abundances in homes made with natural materials rather than manufactured products or finished structures, and more mosquitoes were found in homes with less IRS and bed net coverage. These studies suggest exposure to vectors occurs in both the early evening hours, when residents are not protected by bed net barriers, and overnight, with some mosquitoes actively feeding on humans and harboring infectious parasites. Given these results, further investigation into the settings where malaria transmission may occur, the magnitude of indoor biting, and how to refine methods of prevention in Nchelenge is warranted.

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ANTIBODY RESPONSE TO AEDES SPP. MOSQUITO SALIVARY PROTEINS AS A MARKER FOR EXPOSURE: A SYSTEMATIC REVIEW AND POOLED ANALYSIS

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Arboviruses, especially those transmitted by Aedes spp. mosquitoes, are responsible for a massive global burden of disease in humans. Additionally, hypersensitive/allergic humans can suffer from debilitating symptoms upon bite exposure. As current methods can be costly and cumbersome, more efficient mosquito surveillance, which can accurately examine bite exposure (and possible arbovirus exposure), is needed. One such promising alternative is the use of ELISA technology to quantitatively measure exposure to mosquito bite. Using PRISMA guidelines, a systematic review

and pooled analysis were performed to assess the efficacy of detection of human antibody response to mosquito salivary proteins as presented in the literature. A total of 1353 studies were screened by two reviewers; 99 articles were included in the qualitative synthesis. The pooled analysis included 20 papers that met our inclusion criteria, provided individual level human IgG response to MSP via ELISA, and explicitly stated how OD scores were reported. We assessed how subject age, Aedes spp. mosquito, antigen type, collection season, population level of mosquito exposure, Köppen-Geiger climate, and OD reporting method impact OD values in separate univariate analyses as well as a multivariate analysis. Furthermore, five studies from the pooled analysis included individual level IgG response data to endemic and non-endemic Aedes spp.; these underwent receiver operator curve (ROC) analysis. We found that OD values correlated positively with antigen complexity, population level of mosquito exposure, and wherein climates permitted year-round mosquito activity. The area under the curves from the ROC analysis indicate that there is a distinct signature for human exposure to endemic versus non-endemic Aedes spp. While there is considerable variation between studies (ICC=0.12), using human IgG holds promise in complimenting more traditional mosquito surveillance methods as a proxy for individual and population exposure to Aedes spp. mosquitos.

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INVESTIGATION OF MEDICALLY IMPORTANT ARBOVIRUSES AND INSECT-SPECIFIC VIRUSES IN THE SYLVATIC AND URBAN VECTORS OF YELLOW FEVER VIRUS COLLECTED IN THE BRAZILIAN AMAZON

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Culicids are important vectors and viral reservoirs of arthropod-borne viruses and insect-specific viruses (ISVs), respectively. Mosquitoes of the genera Aedes, Sabethes, and Haemagogus comprise species of great epidemiological relevance since they are involved as vectors in transmission cycles of arboviruses, such as yellow fever. From May 2021 to June 2022, mosquito collections were carried out at the Adolpho Ducke Forest reserve bordering Manaus, Amazonas state, Brazil. Mosquitoes morphologically identified as species of Aedes, Sabethes, and Haemagogus genera are being investigated in this work. So far, 284 pools from the Haemagogus genus and 26 pools from the Aedes genus have been macerated, and the supernatant obtained was used for viral isolation in vitro and molecular investigation for flaviviruses, alphaviruses, and insect-specific viruses such as PCLV, HTV, GUAPV, CxFV, and AeFV. All pools tested for medically important arboviruses were negative. HTV was detected in 25 pools (8.8%) of Haemagogus (Hg. janthionomys, Hg. leucocelaenus, and Hg. baresi). PCLV was detected in 13 pools (4.5%) of Haemagogus (Hg. janthionomys, Hg. leucocelaenus, and Hg. baresi) and in six pools (23%) of Aedes (Ae. aegypti, Ae. albopictus, and Ae. scapularis). We also detected GUAPV in two pools (7.7%) of Aedes (Ae. albopictus, and Ae. argyrothorax). We sequenced the PCR products by the dideoxy method, confirming the presence of HTV and PCLV Haemagogus spp. In addition, we had 19 pools (6.7%) of Haemagogus and five pools (19.2%) of Aedes positive for flavivirus. The isolation of HTV and PCLV was confirmed in C6/36 cells by end-point PCR. Next, we aim to confirm our results by sequencing and for the positive samples: genomic characterization, biological characterization, and electron microscopy. This finding reinforces how little we know about ISVs circulation and the importance of entomological and viral surveillance in Brazilian mosquitoes, especially in the Amazon Rainforest, a hotspot of circulation and maintenance of arboviruses.

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HUMAN BEHAVIORAL DETERMINANTS OF RISK OF EXPOSURE TO ANOPHELES AMONG SEASONAL MIGRANT WORKERS AND RESIDENT POPULATIONS IN LOWLANDS AND THE GENERAL POPULATION IN THE HIGHLANDS, NORTHWEST ETHIOPIA

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In northern Ethiopia, regular population movement from highlands to malaria endemic lowlands may be a barrier to malaria elimination that calls for tailored vector control strategies. In this study, we assessed the entomological and human behavioral drivers of malaria exposure among seasonal migrant workers and resident populations in lowlands and the general population in the highlands. In each setting 4 sites were selected. During the high transmission season, October-December 2022, hourly CDC light trap (CDC LT) collections coupled with human behavior observations (HBOs) were conducted for 52 nights from 18.00 to 06.00 hrs. In the highlands, per site 4 houses with recent malaria cases and 4 controls were selected. In the lowlands, 8 households/farm structures were sampled per site. Vector and human behaviors were quantified and compared with and without bed nets. In the highlands, 4,127 mosquitoes belonging to 13 species with both indoor and outdoor biting behaviors were captured. Based on morphology, Anopheles gambiae sensu latu (s.l.) was dominant (41.8%, 1726) followed by An. demeilloni (24.7%, 1018) and An. cinereus (11.3%, 467). The Anopheline mean capture rate for highland sites was higher in indoors (14.0) than outdoors (5.8). In the lowland sites, 2,553 mosquitoes belonging to 18 species were captured with mean capture rate 6.0 for indoors, and 6.2 for outdoors. An. gambiae s.l. (36.2%), An. pretoriensis (24.3%) and An. demeilloni (20.2%) were the most abundant. Human behavior adjusted capture rates suggested that the highest risk of being bitten was early in the evening (18.00-20.00 hrs.) for both highland and lowland sites. In highlands, most exposure (88.4%) occurred indoors (awake or asleep without bed nets) but outdoors in lowland sites (70.0% among seasonal migrants and 70.7% among the residents). These gaps in protection call for tailored interventions: in the highlands, indoor residual spraying (IRS) and human behavioral communication may be useful in reducing man-vector contact. In the lowlands, high outdoor exposure will require alternative interventions to address these gaps.

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CLOSE-KIN MARK-RECAPTURE METHODS TO ESTIMATE DEMOGRAPHIC AND DISPERSAL PARAMETERS OF MOSQUITOES

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Close-kin mark-recapture (CKMR) methods have recently been used to infer demographic parameters such as census population size and survival for fish of interest to fisheries and conservation. These methods have advantages over traditional mark-recapture methods as the mark is genetic, removing the need for physical marking and recapturing that may interfere with parameter estimation. For mosquitoes, the spatial distribution of close-kin pairs has been used to estimate mean dispersal distance, of relevance to vector-borne disease transmission and novel biocontrol strategies. Here, we extend CKMR methods to the life history and population structure of mosquitoes. We derive spatial kinship probabilities for mother-offspring, father-offspring, full-sibling and half-sibling pairs, where an individual in each pair may be a larva, pupa or adult. A pseudo-likelihood approach is used to combine the marginal probabilities of all kinship pairs. To test the

effectiveness of this approach at estimating mosquito demographic and dispersal parameters, we develop an individual-based model of mosquito life history which labels each individual with a unique identification number. Using the dengue vector Aedes aegypti as a case study, we find the CKMR approach can provide unbiased estimates of adult census population size, adult mean dispersal distance, and adult and larval mortality rates for logistically feasible sampling schemes. Considering a simulated population of 3,000 adult mosquitoes, estimation of adult parameters is accurate when ca. 40 adult females are sampled biweekly over a three month period. Estimation of larval parameters is accurate when adult sampling is supplemented with ca. 120 larvae sampled biweekly over the same period. The methods are also effective at detecting intervention-induced increases in adult mortality and decreases in population size. As the cost of genome sequencing declines, CKMR holds great promise for characterizing the demography and dispersal of mosquitoes and other insect vectors of human diseases.

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ADVANCEMENTS OF ARTIFICIAL INTELLIGENCE (AI) IMAGE RECOGNITION FOR USE IN VECTOR SURVEILLANCE OPERATIONS

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Mosquito surveillance, the monitoring of vector abundance, distribution, and diversity, is a critical step to assess mosquito-borne disease risk. Despite its importance, few vector control organizations have access to expert taxonomists with the capacity to evaluate the significant quantities of specimens collected by routine vector surveillance programs. As a result, organizations must rely on seasonal staff with minimal taxonomic expertise to guide important downstream intervention strategies. Convolutional neural networks (CNNs) for image recognition, a deep learning method, have emerged as a promising modality with the capability to visually differentiate between species. The IDX is a system consisting of a controlled optical configuration integrated with algorithms that continue to evolve and improve based on representative specimen image data contributed by partners. In the most recent iteration, the system performed with an accuracy of 97.75±0.06% across 21 species in lab testing. In a test of the deployed algorithm performance on IDX, data from a California vector control district was analyzed, and achieved a macro averaged recall of 97.1% across the top five species. These advancements demonstrate translation of these algorithms from the lab to field practice. In the next phase of work, data collection and testing will be conducted with a wider range of partners in operational scenarios.

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EVALUATION OF MYRISTICA FRAGRANS ESSENTIAL OIL AS A POTENTIAL BIOPESTICIDE FOR THE CONTROL OF AEDES MOSQUITOES IN JAMAICA

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The use of synthetic insecticides to control Aedes mosquitoes continue to be a significant challenge in Jamaica's fight against arboviruses due to rising resistance in mosquito populations. As a result, novel control methods are urgently required. As the use of plant extracts as mosquitocidal agents is currently being investigated worldwide, we therefore sought to assess the potential efficacy of Myristica fragrans (nutmeg), as a natural biopesticide. The nutmeg essential oil was screened against different life stages of laboratory and field Ae. aegypti mosquitoes. We discovered that the oil had significant efficacy against the third larval stage, with LC50 values of 7.18 ppm for the Rockefeller laboratory strain and 15.82 ppm for the Jamaican field strain. Interestingly, the oil displayed modest activity against the less commonly targeted pupal stage, with LC50 values of 1090.00 ppm and 965.90 ppm for laboratory and field strains, respectively. Future studies will focus on further evaluations against the larval stage using additional laboratory and field strains as well as conducting adulticidal assays. Additionally, chemical analysis of the oil and mechanistic studies will be done to identify the constituent (s) responsible for the observed mosquitocidal activity and to determine how the oil is producing this activity. If the oil is found to be highly efficacious, then preliminary field studies will be performed, and formulations of the oil may be studied for prospective use as a biopesticide in Jamaica. Keywords: Biopesticides, Aedes mosquito, Jamaica

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INTERIM EFFICACY REPORT OF ECO BIOTRAPS IN DHARAVI, MUMBAI, INDIA

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We had previously presented an introductory note on the use of a green ovitrap device – Eco BioTrap for an innovative adjunct integrated vector management for vector control. This longitudinal cohort study was carried out in two areas Kumbharwada and Rajiv Ganghi Nagar covering approximately 100,000 population in 10,000 households of Asia's largest slum Dharavi, Mumbai, India. Dharavi is endemic for dengue for several years. A set one trial (with mosquito attractant and anti-larval IGR compound (Pyriproxyfen) and control was placed 10 to 15 meter apart in the study sites following the World Health Organization (WHO) guideline for mosquito larvicides. Two teams comprising of two trained health staff each conducted the study with a follow-up period on day 7, day 14, day 21 and day 28, respectively. Data were recorded on excel sheet and thus analysed. The three-month interim deployment study showed that Eco BioTraps are effective (93%) in attracting the gravid female mainly Aedes aegypti for ovipositing to lay eggs and is highly impactful in eliminating breeding as part of Source Reduction/Larval Source Management (LSM). This device can also be used for larval surveillance for evaluating of any intervention. Further study is underway to find out the long-term impact on the mosquito vector burden and dengue.

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EVALUATION OF THE SYSTEMIC INSECTICIDAL EFFECTS OF IVERMECTIN TREATED CATTLE ON AEDES AEGYPTI, VECTOR OF ARBOVIRUSES

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The burden of Aedes-borne viral pathogens has increased over the past two decades. In the absence of specific treatments against the virus, insecticide-based vector control tools remain the best way to decrease transmission. However, the selection and spread of insecticide resistance in Aedes vectors call for the development of complementary vector control tools. In the IMPACT project funded by Unitaid Agency, we evaluated the systemic insecticidal effects of ivermectin injected to calves on the survival and fertility of Ae. aegypti, one of the primary vectors of arboviruses. A total