resistance to traditional chemical insecticides is confirmed in adults. Understanding historical surveillance and control approaches is essential to the advancement of invasive *An. stephensi* mitigation efforts in Africa and the reduction of impacts on malaria morbidity and mortality.

7000

ASSESSMENT OF TWENTY-FOUR HOURS BITING PATTERNS AND HUMAN EXPOSURE RISK TO BITES OF *ANOPHELES* MOSQUITOES IN SOUTH-EASTERN TANZANIA

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Over the past two decades, Tanzania has made remarkable progress in reducing the malaria burden, instilling hope for its elimination by 2030. This success is attributed to the large-scale implementation of core vector control interventions such as LLINs and IRS. However, persistent transmissions from 24 hour exposure to infective mosquito bites remain a challenge to current elimination efforts. This study aimed to assess the 24-hour biting patterns and human exposure risk to bites of *Anopheles* mosquitoes in Ulanga district South-eastern Tanzania to inform strategies for addressing persistent transmissions. Hostseeking mosquitoes were collected hourly using a miniaturized double net trap over 24 hours both indoors and outdoors. Pooled hourly collections were morphologically and stored as dried samples for subsequent laboratory analyses Data analysis was done using R statistical software and all tables charts and graphs were generated using grammar for graphics R package. *An. arabiensis* and *An. funestus* were found to be the major vectors in the study area, accounting for 94% and 4% of the entire collections respectively. Interestingly, both species exhibited a shift towards day-biting behavior and their aggressiveness was not just limited to morning and evening hours but widely distributed across the entire daytime period. There was no difference between indoor and outdoor biting rates of the two species except only during daytime for the case of *An. arabiensis*. More than half of the mosquitoes collected during the daytime were unfed, a probable indicator of daytime host-seeking behavior. More than 65 percent of the dissected mosquitoes were parous potentially indicative of an older population with high malaria transmission potential. The suddenness of the day-biting behavior of malaria vectors may potentially increase the risk of malaria transmission This highlights the need for novel tools to supplement the existing interventions and intensive community engagement to increase awareness regarding day-biting mosquitoes and their associated malaria transmission risk.

7001

CHARACTERIZATION OF THE SPECIFIC COMPOSITION, TROPHIC AND RESTING PREFERENCES AS WELL AS THE LEVEL OF INFECTION OF MALARIA VECTORS IN THE CITY OF OUAGADOUGO, BURKINO FASO

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Malaria in urban areas is a scourge whose importance is increasing with the increase in immigration to urban areas. Urban malaria remains a public health problem whose fight relies on better knowledge of vector biology. The objective of this research was characterize the specific composition, trophic and resting preferences as well as the level of infection of malaria vectors in the city of Ouagadougo. Adult mosquitoes were collected during the rainy season from July to October 2023 in the city of Ouagadougou. A total of 31 neighborhoods across three health districts (Baskuy, Bogodogo and Nongremassom) were visited. The choice of neighbourhoods in the three districts was 10 neighborhoods per district and was done randomly. Mosquitoes were collected outside and inside houses. The distance between the houses is 100 meters. Collections were made using electric vacuum cleaners. Collections were carried out in the morning between 6 a.m. and 9 a.m. and in the evening between 4 p.m. and 5 p.m. to increase the chances of collecting resting mosquitoes. PCR was used to identify the members of Anopheles gambiae complex, as well as the origin of the blood meals. The ELISA method was used to determine the infection of mosquitoes by *P. falciparum*. Approximately thirty-nine thousand seven hundred and twenty-seven (39,727) mosquitoes including 1,304 *Anopheles gambiae* s.l females were collected. After molecular identification, 1261 (96.7%) was *Anopheles arabiensis* and 43 (0.03%) from *Anopheles coluzzii*. Five hosts were identified as the source of blood meals, 108 (43.37%) human blood meals, 93 (37.65%) blood meals in cattle, 24 (9.71%) in pigs, 18 (7. 28%) on dogs and 04 (1.61%) on goats. The majority, 66.41% of *Anopheles gambiae* s.l were collected outside homes. A total of 10 mosquitoes infected with *P. falciparum* sporozites were identified, representing an infection rate of 0.7%. Anopheles represent 5.6% of the number of mosquitoes collected in the different areas. Despite this relatively low infection rate, the exophilic behavior of these mosquitoes, associated with rapid urbanization, deserves specific attention in the fight against malaria.

7002

DEVELOPMENT OF ENVIRONMENTAL DNA (EDNA) SAMPLING FOR ARBOVIRUS VECTOR SURVEILLANCE IN SOUTHERN NEVADA

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Accurate, rapid, and cost-effective surveillance of arbovirus mosquito vectors is critical for monitoring species distribution and infection prevalence and ultimately mitigating transmission risk. Vector surveys conducted by the Southern Nevada Health District (SNHD) are limited to a few productive sentinel sites, with considerable infrastructure and logistical requirements. New vector surveillance methods that are simple and unbiased at the sampling stage are needed. One potential method to increase efficient vector sampling capacity may be to exploit detection of environmental DNA (eDNA), shed by vectors breeding in aquatic environments. In this study, we first designed and optimized a novel multiplex TaqMan qPCR assay, based on SNPs in COXI, for simultaneous detection of the three major regionally important arbovirus vector species: *Culex* (*Cx.*) *quinquefasciatus*, *Cx. tarsalis,* and *Aedes* (*Ae.*) *aegypti*. 50ml water samples were collected from across Clark County using sterile plastic syringes and 0.22µm filters. Collection sites included water bodies that were adjacent to overnight gravid traps and BG sentinel traps, set by the SNHD, to compare vector species composition between sampling methods and additional aquatic environments in local public parks, golf courses, and drainage ditches. eDNA was extracted from filter membranes and screened for vector species presence using our qPCR assay. eDNA deposited by co-occupying *Cx. quinquefasciatus* and *Ae. aegypti* was detected in water samples, without observable larvae breeding, from multiple drainage ditches. *Cx. tarsalis* was identified in water samples from stormwater runoff and drainage channels in a public park. eDNA surveillance has the potential to be implemented as a field-friendly, arbovirus vector surveillance tool for expanded entomological monitoring capacity in southern Nevada, to detect changes in dispersal patterns of arbovirus vector species as well as the spread of new invasive vector species. eDNA amplicon-seq is ongoing to characterise vector population dynamics and insecticide resistance mechanisms to inform potential regional control initiatives.

7003

UNDERSTUDIED MALARIA VECTORS MAY DRIVE RESIDUAL MALARIA TRANSMISSION IN CHOMA DISTRICT, AN AREA OF LOW MALARIA TRANSMISSION

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Choma District in southern Zambia continues to measure low rates of malaria transmission despite very low counts of f what have been recognized as the primary vectors, *Anopheles funestus* and *An. arabiensis.* This altered vector landscape may create opportunities for understudied secondary vectors to subsequently act as sources of residual malaria as demonstrated by the recent presence of *Plasmodium falciparum* sporozoites in *An. squamosus, An. coustani* and *An. rufipes*. This study investigated understudied malaria vectors; species composition, relative abundance, and sporozoite infectivity as measures of potential malaria transmission. The study was conducted in three catchment areas of Choma district; Macha, Simaubi and Mapanza, which together recorded a parasite prevalence of less than 1% from October 2022 to February 2024. Forty-eight sentinel households in historical malaria hotspots were recruited. Monthly, Center for Disease Control and Prevention Light Traps were set indoors (sleeping area), the peri domestic area (outdoor kitchens) and near animal shelters (goat pens and/or cattle kraal). In 1,991 trap night-traps, 11,114 *Anopheles* mosquitoes were collected. *Anopheles squamous* was the dominant species (*n*=5,190; 58.6%). Other species were *An. gambiae* s.l., *An. coustani* s.l., *An. rufipes*, *An. pretoriensis*, *An. funestus* group, *An. Pharoensis* and most mosquitoes were collected from goat pens (n=8,112; 73.0%). There was a statistically significant higher mean count of anopheline mosquitoes outdoors in the peri domestic area (mean=1.44, 95% CI 1.22-1.65) and outdoors near goat pens (mean=23.8, CI 22.7-24.9) than indoors (mean= 0.78, CI 0.68-0.89) (t-test, $t_{(1483)} = 8.38$, $P > 0.001$ and $t_{(1483)} = 4.88$, $P > 0.001$ respectively). Sporozoite infectivity rates in *An. coustani, An. squamosus* and *An. rufipes* were 0.52%, 0.58% and 0.10% respectively. High outdoor counts of understudied malaria vectors present a potential risk to sustaining residual malaria transmission.

7004

THE ESCALATING BIOLOGICAL THREAT: OBSERVATIONS FROM TEN YEARS OF MAPPING INSECTICIDE RESISTANCE IN MALARIA VECTORS.

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Insecticide resistance remains a key biological threat recognized by World Health Organization (WHO) as a key biological threat to the stagnating gains in malaria control and elimination. Insecticide Resistance Management (IRM) is important to identify areas where resistance has been reported and understand the associated resistance mechanisms. IR Mapper has offered insecticide resistance mapping support since 2012. IR Mapper collates insecticide resistance information reported in peer reviewed, published literature, with monthly updates. These are loaded onto a cloud database, then visualized on the mapping platform developed using ArcGIS API. Partnerships and collaborations have been focal in the IR Mapper process. Growing from a platform that maps phenotypic resistance and resistance mechanisms, to addition of malaria endemicity layers and modelled surfaces that predict the probability of resistance to cover scarcity of resistance data due to monitoring constrains. This analysis gives a view of pyrethroid resistance trends between the years 2000-2015, when pyrethroid LLINs offered the greatest impact against malaria, and 2016-2023 when gains stagnated, focusing on sub-Saharan Africa which holds more than 90% of global malaria cases and deaths. By the main vector species, pyrethroid resistance in *Anopheles gambiae* s.l., increased 1.3-fold, from a median mortality of 59 (IQR: 30-78) between 2000-2015 to a median mortality of 45 (IQR: 16-72) between 2016-2023. In *An. funestus*, pyrethroid resistance has grown from a median mortality of 54 (IQR:23-74) in 2000-2015 to a median mortality of 60 (IQR: 40) in 2016-2023. The most reported resistance mechanism are knock-down resistance gene mutations and over expression of mixed function monooxygenases. Regions with the highest malaria burden also show high levels of pyrethroid resistance. IR Mapper continues to be a valuable tool in aiding vector control decisions by being a point of reference for up-to-date insecticide resistance data. With ever changing needs, IR Mapper is getting an update to encompass additional molecular resistance mechanisms such as the P450 gene family data.

7005

QUANTIFYING FEW, FIXED, AND FINDABLE: A DIGITAL, STRATIFIED SURVEILLANCE APPROACH TO ASSESS LARVAL SOURCE MANAGEMENT FEASIBILITY IN MOZAMBIQUE'S CAPITAL CITIES

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Malaria remains a major health challenge in Mozambique. Insecticide-treated nets and indoor residual spraying face issues such as rising insecticide resistance and outdoor biting, and depend on community compliance. Larval source management (LSM) offers a supplementary method, especially in urban and semi-urban areas. To evaluate the feasibility of Larval Source Management (LSM) and its alignment with the "few, fixed, and findable" criteria set by the WHO, we assessed the density, types, positivity, and permanency of water bodies in the 11 provincial capital cities of Mozambique. To ensure unbiased sampling, we combined stratified and random sampling methods, enhancing the representativeness of our data. All areas of the cities were stratified based on factors such as population density, topography, and proximity to rivers. Sectors were randomly selected for surveillance from each strata. Field officers were assigned to walk through the selected sectors and report water bodies using the Zzapp mobile app. Water bodies were reported, categorized (e.g., swamp, agricultural), and sampled for larvae. In all cities, the density of water bodies was below 200 per square kilometers, making LSM feasible. With over 50 houses per water body, the cost per person for LSM is projected to be low ("Few"). Most water bodies were classified as permanent or semi-permanent ("Fixed"). Field workers thoroughly mapped the area, and we report related quantitative measures for area coverage and community acceptance ("findable"). In total, an area of 34.3 sq km was scanned, revealing 3,168 water bodies. Among all sampled water bodies across 11 cities, positivity rates for Anopheles and non-Anopheles larvae were 3% and 11%, respectively, with regional variations for Anopheles between 2-5%. Water bodies hosting Anopheles larvae included ponds (8%), swamps (4%), and other sites like puddles, agricultural, and construction sites (~2%), while pools and tires were not conducive to Anopheles larvae. The study provides a quantitative evaluation of the "few, fixed, and findable" criteria and suggests that all cities included in the study meet the WHO standards for LSM.

7006

HOW DOES BEDNET USE AFFECT FEMALE *ANOPHELES* EXPOSURE IN COTE D'IVOIRE: ASSESSING VECTOR-HUMAN INTERACTION USING ENTOMOLOGICAL SURVEILLANCE AND ACCELEROMETER-BASED BEDNET MONITORING

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The timing of bednet use may not correspond with the timing of vector exposure in malaria-prone households leading to continued transmission of malaria despite wide-scale distribution of long-lasting insecticide treated bednets. Surveys about bednet use provide only a snapshot of bednet use the previous night, whereas remote monitors can provide objective measurements of whether a bednet is in use over longer time periods. This observational study deployed accelerometer-based bednet monitors in Cote d'Ivoire to assess how exposure to female *Anopheles* mosquitoes overlapped with patterns in bednet use. Bednet use monitors were attached to the side of one bednet in each of 50 households from 3 regions representing different malaria transmission settings: urban Yamoussoukro (20 households), peri-urban Tiassalé (20) and rural Korhogo (10). Accelerometer data was classified using a previously trained random-forest machine learning algorithm (Koudou et al. 2022). Entomological surveillance was performed using window traps. Mixed-effects regression models were employed to account for multiple measures per household. Negative binomial regressions were used to assess the biting rate, defined as the number of fed *Anopheles* mosquitoes retrieved from the window traps per night. Fifty households were followed for a mean of 115 nights each (5,749 total nights), and mean bednet use was 10.3 hours per night (95% CI: 9.8 - 10.9). Each additional hour of bednet use per night was associated with a 4.0% decrease in the nightly biting rate (95% CI: 0.0% to 7.5%; p=0.03), which is equivalent to 29.4% decreased rate of mosquito biting for each hour of additional bednet use averaged over a month. There were differences between regions, with peri-urban Tiassalé (+83%; p=0.05) and urban Zatta (+94%; p=0.07) having higher rates of fed mosquitoes compared to Korhogo. These findings suggest that bednets provide variable protection between regions based on differences in vector and human behaviors. Further work characterizing these differences by vector species and the timing of biting could shed light on better ways to prevent malaria in the future.

7007

ADVANCES IN ARTIFICIAL INTELLIGENCE FOR VECTOR IDENTIFICATION AND MONITORING

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Recent advances in artificial intelligence and machine learning, such as the use of convolutional neural networks (CNNs) for image recognition, have emerged as a promising modality with the capability to visually differentiate between mosquito species. Here we present the first performance metrics of IDX, Vectech's system for AI mosquito identification, as part of Maryland's mosquito control program in the USA. Specimens were collected over 14 weeks in 2023 from 12 CDC gravid trap collection sites in Anne Arundel county, identified morphologically by an entomologist, and imaged using the IDX system. By comparing entomologist identification to the algorithm output by IDX, we are able to calculate the accuracy of the system across species. Over the study period, 2,591 specimens were collected and imaged representing 14 species, 10 of which were available in the identification algorithm on the device during the study period. The micro average accuracy was 94.9%. Of these 10 species, seven consisted of fewer than 30 samples. The macro average accuracy when including these species was 79%, while the macro average when excluding these species was 93%. In the next iteration of this technology, Vectech is optimizing the vector identification capabilities of IDX to handle high-accuracy identification of both primary and secondary malaria vectors including *Anopheles gambiae s.l., An. funestus, An. stephensi, An. coustani, An. pharoensis* and others that will allow public health organizations in malaria endemic countries to increase entomological surveillance capability. These advances demonstrate the utility of artificial intelligence in contemporary entomological practice and its potential to support current vector surveillance and control programs around the world.

7008

DOES DOMESTIC USE OF INSECTICIDAL SPRAYS UNDERMINE PUBLIC HEALTH CONTROL STRATEGIES?

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Despite the ongoing threat of evolving insecticide resistance to anti-mosquito campaigns worldwide, insecticide-based intervention remains the primary strategy for preventing vector-borne disease (VBD) transmission. Untangling the drivers of mosquitoes' evolving resistance to insecticides is critical for resistance management and interventions' effectiveness. Meanwhile, public health and agriculture-related insecticide use have been suggested as primary drivers of increased mosquito resistance, although the role of household insecticide use for self-protection remains an unappreciated contributing factor. Herein, we aimed to assess the level of household insecticide usage in VBD-endemic countries through a literature review and determine mosquito resistance to pyrethroid-based domestic insecticides. Our findings indicate that using household insecticides for self-protection has been commonplace over the past decade in all 19 studied countries across the Americas, Africa and Asia, with ≈60% of homeowners surveyed using insecticide-based products. Our results also suggest that the widespread use of domestic insecticides may impose heterogeneous insecticidal selection pressure, driven by a vast spectrum of pyrethroid blends identified worldwide within 67 distinct insecticidal aerosol products. Aerosolized household formulations may vary in effectiveness - our susceptibility results for 10 *Aedes aegypti* populations from three Brazilian Northeastern states (PB, PE, RN) revealed mortality rates from 30% to 100%, which aligns with susceptibility profiling against public health pyrethroid insecticides. Furthermore, genotypic-phenotypic inferences indicate that ≈100% of surviving *Ae. aegypti* mosquitoes exposed to two aerosolized insecticides were triple-resistant homozygotes (*Kdr* - 410Leu/016Ile/1534Cys), which are also known to impact public health insecticides efficacy. Together, this evidence highlights the need to re-scrutinise the impact of private use of domestic insecticides on public health programmes to ensure the sustainability of current and novel vector control interventions.

7009

APPLICATION OF PREDICTIVE MODELLING OF DENGUE CASE NUMBERS USING METEOROLOGICAL DATA IN PERU

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Climate change is anticipated to increase the frequency and magnitude of extreme weather events during the El Niño Southern Oscillation (ENSO), intensifying meteorological determinants that compound mosquito-borne diseases. In 2023, Peru experienced its highest-ever dengue burden after surpassing 270,000 cases, and the situation is expected to worsen with ENSO continuing from June 2023 into 2024. The objective of this study is to assess the accuracy and applicability of a meteorological predictive model for dengue cases in Peru amidst varying scenarios during ENSO, with potential adaptability to other ENSO-affected countries. Weekly dengue cases for Peru and meteorological data from January 2014 to July 2023 were aggregated monthly. Using a linear model with a five-month lag

applied to meteorological variables, we forecasted dengue cases from July 2023 to July 2024. Forecast accuracy was assessed by the percentage error between forecasted and actual case counts. ENSO projection scenarios of an increase in the ten-year monthly precipitation average of 10%, 20%, and 50% were evaluated. Monthly dengue cases correlated with precipitation, but not temperature. Forecasting projected 292,337 cases (CI: 213,256-400,742) by the end of 2023 and 188,455 (CI: 135,815-261,497) dengue cases for the first half of 2024. Forecasts were accurate to +/- 7% difference for the last half of 2023 and February 2024, while a difference of -52.7% was observed for January 2024, likely exaggerated by small numbers due to reporting year recalibration. ENSO projections for increases in the ten-year monthly precipitation average for the first half of 2024 ranged from 223,530 (CI: 160,164-311,967) to 442,437 (CI: 308,735-634,039). The forecasting success demonstrates the potential of this methodology as an early warning system for dengue-endemic countries increasingly affected by weather events brought on by climate change. Projection scenarios can be used to better target existing vector control interventions as dengue vaccination capacity is further developed.

7010

SEMI-FIELD EVALUATION OF AQUATIC PREDATORS FOR THE CONTROL OF *ANOPHELES FUNESTUS* IN RURAL SOUTHEASTERN TANZANIA

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Biological control is a promising alternative or complementary approach for controlling vector populations in response to the spread of insecticide resistance in malaria vectors. This study evaluated the efficacy of three selected potential predators on the density and fitness parameters of *Anopheles funestus* larvae in rural Tanzania. Common predator families (Aeshnidae, Coenagriondae, and Notonectidae) and *An. funestus* group larvae were collected from natural aquatic habitats in rural south-eastern Tanzania. Predators were starved for 12hours while *An. funestus* larvae were given fish food before starting the experiment. *Anopheles funestus* larvae were placed into artificial habitats containing predators, exposing them to potential predation. The number of surviving *An. funestus* larvae was counted every 24hours. An emergence trap was placed at the top of artificial habitats to capture emerging mosquitoes. Emerged mosquitoes were monitored until they died. Female wings were measured and used as a proxy for body size. Generalized linear mixed models (GLMM) with binomial variates at 95% CI and Cox proportional hazard models were used to assess the proportion of dead mosquitoes and the daily survival determined. There were significant differences in the number of emerged mosquitoes between the treatment and control groups ($p<0.001$). Thus, all predator species played a significant role in reducing the density of *An. funestus* mosquitoes ($P<0.001$). Furthermore, these predators had notable effects on the fitness parameters and survival of emerged mosquitoes ($P<0.001$). Among the three predators studied, Coenagrionidae were most efficient followed by Notonectidae, with Aeshnidae being the least efficient. Selected aquatic predators have the potential to reduce the survival and density of *Anopheles funestus* larvae. They might eventually be included within an integrated malaria vector control strategy, ultimately leading to a reduction in malaria transmission.

7011

NAVIGATING THE EVALUATION OF NOVEL IRS PRODUCTS: LESSONS LEARNED FROM ASSESSING RESIDUAL EFFICACY WITHOUT SUSCEPTIBLE MOSQUITO COLONIES

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Novel, longer-lasting insecticidal products are now on the market that can help countries extend IRS protection and combat resistant mosquitoes. However, residual efficacy varies widely from setting to setting. While the need to measure the residual efficacy of such products prior to their implementation is paramount to appropriately targeting them, justifying their higher price point, and sometimes even for registering the product, many countries lack the susceptible mosquito colonies required to do so. One such example, Honduras, was in search for a longer-lasting product capable of addressing resistant vector populations, yet did not have a susceptible colony to measure its local residual efficacy. With support from CHAI and Envu, the country embarked on a study to evaluate the residual efficacy of Fludora® Fusion on local surfaces using local wild mosquitoes. This session presents the findings of the study conducted in Honduras, highlighting the challenges encountered in the absence of a susceptible mosquito colony and because of the specific post-exposure holding times required for assessing this innovative product. The lessons learned will support other countries that, like Honduras, are interested in introducing novel IRS products and need practical solutions to overcome a lack of susceptible mosquito colonies to measure their residual efficacy.

7012

DEVELOPMENT AND EVALUATION OF A NOVEL, MULTI-ACTIVE INGREDIENT ATTRACTIVE TOXIC SUGAR BAIT FOR MOSQUITO CONTROL

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The continuingly high burden of disease caused by mosquito-borne pathogens highlights the need to develop novel tools to suppress mosquito populations. Attractive toxic sugar baits seek to exploit mosquito nectar-feeding behavior through a lure-and-kill approach, coaxing mosquitoes to feed on baits containing a lethal products. To be viable, these products must retain their efficacy for weeks or even months after their initial deployment. Declines in activity over time could potentially mediate resistance amongst exposed mosquitoes. To address this issue, we have developed a novel attractive toxic sugar bait that contains several different chemical and microbial active ingredients. Each active ingredient mediates adult mosquito mortality through a distinct mechanism, potentially mitigating issues of insecticide resistance. Our data demonstrate high efficacy of this bait as an attractant. We observed rapid, and significant mortality amongst pyrethroid-susceptible and -resistant, adult *Aedes aegypti* and *Culex quinquefasciatus* mosquitoes after feeding on the bait under laboratory conditions. We also demonstrate synergistic mortality effects accrued when the different active ingredients were tested in combination. Semi-field trials highlight that the bait retains high mosquitocidal activity under environmental heterogeneity. Further testing of the bait is ongoing, but these initial findings highlight a promising new tool for mosquito control.

7013

HOW FREQUENTLY DO WE NEED TO TREAT BREEDING SITES WITH *BACILLUS THURINGIENSIS ISRAELENSIS* (*BTI*)? EVIDENCE FROM LARGE-SCALE LARVAL SOURCE MANAGEMENT ON BIOKO ISLAND

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Larval source management (LSM) is one of the few vector control interventions available to target indoor and outdoor biting mosquitoes. In 2023, due to increasing evidence of residual biting both indoors and outdoors, the Bioko Island Malaria Elimination Project (BIMEP) expanded LSM in urban Malabo as a complement to indoor household interventions. The larvicide *Bacillus thuringiensis israelensis* (*Bti*) in granular form was used due to it being available, affordable and easy to apply. A critical aspect of the product is the required frequency of treatment of breeding sites to maximize impact. The manufacturer recommends a 7-to-14-day frequency of application, however there is limited field evidence about the effect size of different frequencies. Here, we investigate the effect of treatment frequency over four months (85 field days) in urban Malabo. At varied frequency bins, daily data on prospective breeding sites detected, verified positive sites, and sites treated were utilized to estimate positivity rate (sites positive/sites found/day). The median frequency of field teams visiting target areas was 10 days. Initial findings reveal a 7-day revisit frequency considerably lowers positivity rates than longer intervals. Visit frequency bins of 8-10, 11-14, and 15-20 days had similar effects on positivity, while frequencies longer than 20 days did not significantly reduce positivity relative to baseline. These findings may be context specific, and suggest that on Bioko, shorter than longer intervals did maximize the impact of LSM. This represents an operational challenge as shorter revisit intervals demand more resources. Moreover, the fact that medium intervals (between 8-20 days) appear to provide similar results in positivity that remain significantly below baseline levels gives some implementation flexibility. As part of the BIMEP's approach to adaptive malaria control, this information will prove useful to inform LSM targeting strategies whereby places with higher larval densities could be revisited at the highest operationally feasible frequency while others can be visited at the longer intervals resulting in impact.

7014

ASSESSING THE SUSCEPTIBILITY AND EFFICACY OF TRADITIONAL NEUROTOXIC (PYRETHROID) AND NEW GENERATION INSECTICIDES (CHLORFENAPYR, CLOTHIANIDIN, AND PYRIPROXYFEN), ON WILD PYRETHROID RESISTANT POPULATIONS OF *ANOPHELES GAMBIAE* FROM SOUTHERN BENIN

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This study aimed to determine the susceptibility of wild *Anopheles gambiae* sensu lato (s.l.), the main malaria vector in southern Benin, to chlorfenapyr (CFP), pyriproxyfen (PPF), clothianidin (CTD), and three pyrethroids insecticides (alpha cypermethrin, deltamethrin, and permethrin). Additionally, the efficacy of ITNs containing CFP, PPF and alpha-cypermethrin (ACM) was assessed with wild *An. gambiae* s.l. reared to adults from larvae and the susceptible laboratory strain, *An. gambiae* sensu stricto (Kisumu). Wild *An. gambiae* from the communes of Allada, Ifangni, Akpro Missérété, and Porto-Novo were tested for susceptibility to CFP and PPF using the WHO bottle test and to the pyrethroids and CTD using the WHO tube test. WHO ITN efficacy tests using standard plastic cones were used to evaluate the efficacy of ACM only, (CFP, ACM), and (PPF, ACM) nets. The ovaries of blood fed *An. gambiae* from Ifangni and the susceptible laboratory strain, *An. gambiae* (Kisumu) exposed to a PPF treated net were dissected, and egg development status was examined using Christopher's stages to determine the fertility status. Using a standardized protocol, the oviposition rate and oviposition inhibition rate were calculated from live blood fed *An. gambiae* placed in oviposition chambers after exposure to PPF. In resistance bioassays, the mosquito populations from the four communities, pyrethroid mortality ranged from 5% to 80%, while CFP and CTD mortality ranged from 98% to 100%. At Ifangni, all mosquitoes exposed to nets with (PPF, ACM) were infertile while most (74.9%) of mosquitoes exposed to nets with ACM only had fully developed their eggs to Christopher's stage five. The oviposition inhibition rate after exposure of the mosquitoes to the PPF was 99% for the wild population of *An. gambiae* s.l. and *An. gambiae* (Kisumu). Pyrethroid-resistant *An. gambiae* from the selected communes in southern Benin were susceptible to CFP, CTD, and PPF. Furthermore, nets with (PPF, ACM) and (CTD, ACM) insecticides were effective against pyrethroid resistant mosquitoes from Ifangni. Continued monitoring for insecticide resistant *An. gambiae* is needed in Benin.

7015

SPECIES-SPECIFIC SALIVARY ANTIGEN ELISAS AS BIOMARKERS OF EXPOSURE TO LA CROSSE VIRUS VECTORS IN NORTH CAROLINA

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La Crosse virus (LACV) is the leading cause of pediatric arboviral neuroinvasive disease in the United States. Three mosquito species are likely responsible for the majority of LACV transmission – *Aedes triseriatus*, the primary, endemic vector and two invasive, secondary vector species: *Ae. albopictus* and *Ae. japonicus*. The risk of LACV disease is geographically persistent in North Carolina; however, current estimates of disease risk do not accurately reflect exposure risk or the genuine burden of disease. Furthermore, low incidence and poor detection rates grossly limit the evaluation of potential public health interventions. We seek to use mosquito salivary gland ELISAs to measure LACV vector exposure as a proxy for exposure/disease risk. Here we share the development of salivary gland (crude extract) IgG ELISAs for *Ae. triseriatus*, *Ae. albopictus* and *Ae. japonicus*. Using convenience human sera (n=41 individuals) from North Carolina, we compared optical density (OD) values for all three species. Pairwise comparisons (ANOVA, Tukey's HSD comparisons) detected higher mean OD values for *Ae. albopictus* as compared to *Ae. triseriatus* ($P = 0.013$). This is consistent with prior knowledge that *Ae. albopictus* is the more common peridomestic container *Aedes* in the areas where the human samples were obtained (Piedmont NC). Field and colony OD values of *Ae. triseriatus* were highly correlated ($r=0.88$) suggesting homologous immunogenic proteins are present in divergent species strains. The results of ongoing western blot and peptide sequence analyses will be shared. The application of these novel methods will be further demonstrated using field collected human sera from ongoing epidemiological studies in western NC (Summer 2024).

7016

IMPACT OF INDOOR RESIDUAL SPRAYING WITH SUMISHIELD® 50WG ON ENTOMOLOGICAL DRIVERS OF TRANSMISSION IN KIGOMA REGION NORTHWEST TANZANIA

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Despite the deployment of insecticide-treated nets (ITNs), indoor residual spraying (IRS), and artemisinin-based combination therapy (ACT), the population in Tanzania's Lake Zone remains at high risk of malaria transmission. PMI VectorLink Tanzania has supported IRS implementation in the region since 2015. The impact of IRS on transmission drivers was assessed through routine entomological surveillance. The IRS campaign with SumiShield® 50WG took place from October 5th to November 4th, 2022, in Kasulu and Kibondo districts. Monthly entomological surveillance, using various methods, was conducted before and after spraying in three sentinel sites: Kagerankanda and Minyinya (sprayed) and Murufiti (unsprayed). *Anopheles* species collected included *An. gambiae* (25.1%), *An. funestus* (29.8%), *An. arabiensis* (44.9%), and *An. parensis* (0.2%) in sprayed sites, with *An. funestus* predominating (75.1%) in unsprayed sites. Indoor resting densities were generally higher in Minyinya and Murufiti than in Kagerankanda. IRS led to reduced human biting rates in sprayed sites compared to unsprayed ones. Annual Entomological Inoculation Rates (EIR) varied, with the lowest in Kagerankanda (0 i/b/p) and the highest in Minyinya (39 i/b/p) and Murufiti (19.5 i/b/p). IRS with SumiShield® 50WG reduced human biting rates in sprayed areas, suggesting its effectiveness. However, varied impacts on indoor resting densities and EIR were observed, with reduced transmission noted in one sprayed site.

7017

COMPARISON OF UNTREATED AND TREATED INSECTICIDE-TREATED NETS TO DETERMINE THE VALIDITY OF WHO TUNNEL ASSAYS

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The WHO has established guidelines that provide specific, standardized procedures for testing Insecticide-Treated Nets (ITNs) for personal protection and malaria vector control. In these guidelines, the tunnel test is recommended for the evaluation of bio-efficacy of Insecticide treated nets against malaria transmitting mosquitoes. The laboratory bioassays results are an indicator of the bioavailability of the active ingredient of the tested product samples. In standard tunnel test a restrained bait (guinea pig or rabbit) is exposed to 50-100 mosquitoes for 12-15h overnight. According to animal welfare regulations, restraining laboratory animals for prolonged periods should be avoided unless it is not possible to achieve research objectives by other means. Here, three tunnel assays: 3-hours daytime, 6-hours daytime with sedated guinea pigs and 15h overnight with un-sedated bait were conducted. Firstly, untreated net was used to determine the feeding success. Then treated net material (unwashed Olyset) was evaluated and the main outcome measure was mortality and blood feeding success (BFS) which are determinants of a WHO tunnel assay validity. Both pyrethroid resistant and susceptible mosquito strains were used in the assay. The control experiments all replicate of both Kisumu and Muleba KisKis strains passed the WHO criteria of blood feeding success > 50%. In the treatment arm using susceptible Kisumu strain the % mean mortality at 24 hours was 90%, 84% and 98% for 3h day, 6h day and 15h overnight respectively while blood feeding inhibition was 87%, 73%, 92% for 3h day, 6h day and 15h overnight respectively. For the resistant strain Muleba Kis the %mean mortality at 24 hours was 8%, 35% and 23% for 3h day, 6h day and 15h overnight respectively, the blood feeding inhibition was 51%,30% and 27% for 3h day, 6h day and 15h overnight respectively. The results suggest that it is possible to avoid restraining laboratory animals for prolonged period of time by replacing the traditional method with the modified tunnel and achieve the recommended WHO research objectives.

7018

LATE MORNING BITING BEHAVIOUR OF *ANOPHELES FUNESTUS* IS A RISK FACTOR FOR MALARIA TRANSMISSION IN SCHOOLS IN SIAYA, WESTERN KENYA

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Children in Kenya spend a substantial amount of time at school, including at dawn and dusk when mosquitoes are often active. With changing vector behaviour towards early morning biting, it is important to determine whether there is an additional risk of transmission in schools. This study sought to understand whether late morning biting by *Anopheles funestus* previously documented in households in western Kenya was replicated in schools. From the 4th to the 6th of August 2023, human landing collections were conducted hourly in four schools in Alego Usonga Sub-County, Siaya County. The collections were conducted inside and outside five classrooms in each school and ran for 17 hours, starting at 18:00 until 11:00 hours the next morning. *Anopheles funestus* was the predominant species collected, accounting for 93.2% of the 980 mosquitoes collected, with peak landing between 06:00 and 07:00 hours and continuing until 11:00 hours. All *An. funestus* were identified as *An. funestus* sensu stricto by PCR. More than half of the collected *An. funestus* were either fed or gravid, potentially indicative of multiple bloodmeals within each gonotrophic cycle, and had a sporozoite rate of 2.05%. Other species collected included *An. gambiae* sensu lato (n=49; 6.3%), *An. coustani* (n=2, 0.26%), and *An. ziemanni* (n=2, 0.26%). Of the 49 *An. gambiae* s.l., 48 were identified by PCR as *An. arabiensis*. None of the *An. gambiae* s.l. tested positive for sporozoite infection. School children spend up to 10 hours per day at school, reporting between 06:00 and 07:00 hours and often staying in school until 17:00 hours, meaning that they are potentially exposed to infectious mosquito bites while at school. Targeting vector control approaches to schools and other peridomestic spaces in the morning hours when *An. funestus* is active may help control malaria in school-aged children.

7019

KNOCKING OUT TO KNOCK IN: IMPACT OF LOSS OF END JOINING FACTORS ON HOMOLOGY DIRECTED REPAIR INCIDENCE IN THE DISEASE VECTOR MOSQUITO, *AEDES AEGYPTI*.

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Aedes aegypti mosquitoes are vectors for a number of viruses of public health concern. Homing-based gene drives offer an intriguing tool to combat these disease vectors. Many homing-based gene drives leverage the Double Strand Break (DSB) repair pathway, Homology Directed Repair (HDR), to convert wild type genes to the engineered drive gene. However, another DSB repair pathway, Non-Homologous End Joining (NHEJ), is antagonistic to HDR and can even result in resistance alleles that prevent further super-Mendelian inheritance from the gene drive. Here, we utilize

previously generated *Aedes aegypti* strains with key NHEJ factors knocked out to evaluate the impact of loss of NHEJ efficiency on the incidence of HDR. The key NHEJ factors and associated knockout strains are *Ku80* (Ku80$^{-/-}$ strain), *DNA-PKcs* (DNA-PKcs$^{-/-}$ strain), and *Ligase IV* (Lig4$^{-/-}$ strain). We initiated site-specific DSBs utilizing CRISPR/Cas9 and guide RNA targeting a locus in the *kmo* gene (which is involved in eye pigmentation to allow for facile phenotype screening of results). Our data suggest that a loss of NHEJ efficiency in the germline cells of *Aedes aegypti* is compensated for by an increase in the incidence of HDR. Knockout of *DNA-PKcs* and *Ligase IV*, but not *Ku80* elevates the rate of HDR over that observed in the NHEJ wild type strain. Therefore, gene drive approaches that rely on HDR could potentially be made more efficient by incorporating some method of NHEJ down-regulation into the overall strategy. Such approaches could prove useful in vector control.

7020

ANTIBODIES TO *AEDES AEGYPTI* D7L SALIVARY PROTEINS AS A NEW SEROLOGICAL TOOL TO ESTIMATE HUMAN EXPOSURE TO *AEDES* MOSQUITOES

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Aedes spp. are the most prolific mosquito vectors in the world. Found on every continent, they can effectively transmit various arboviruses, including the dengue virus which continues to cause outbreaks worldwide and is spreading into previously non-endemic areas. The lack of widely available dengue vaccines accentuates the importance of targeted vector control strategies to reduce the dengue burden. High-throughput tools to estimate human-mosquito contact and evaluate vector control interventions are lacking. We propose a novel serological tool that allows rapid screening of human cohorts for exposure to potentially infectious mosquitoes. We tested 563 serum samples from a longitudinal pediatric cohort study previously conducted in Cambodia. Children enrolled in the study were dengue-naive at baseline and were followed biannually for dengue incidence for two years. We used Western blotting and enzyme-linked immunosorbent assays to identify immunogenic *Aedes aegypti* salivary proteins and measure total anti-*Ae. aegypti* IgG. We found a correlation (r_s=0.86) between IgG responses against AeD7L1 and AeD7L2 recombinant proteins and those to whole salivary gland homogenate. We observed seasonal fluctuations of AeD7L1+2 IgG responses and no cross-reactivity with *Culex quinquefasciatus* and *Anopheles dirus* mosquitoes. The baseline median AeD7L1+2 IgG responses for young children were higher in those who developed asymptomatic versus symptomatic dengue. The IgG response against AeD7L1+2 recombinant proteins is a highly sensitive and *Aedes* specific marker of human exposure to *Aedes* bites that can facilitate standardization of future serosurveys and epidemiological studies by its ability to provide a robust estimation of human-mosquito contact in a high-throughput fashion.

7021

THREE YEARS OF ENTOMOLOGICAL SURVEILLANCE IN HOUSES RECEIVING TARGETED INDOOR RESIDUAL SPRAYING (TIRS) AGAINST *AEDES AEGYPTI* IN MEXICO

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Targeted indoor residual spraying (TIRS) is a novel approach for *Aedes aegypti* control that uses adult female mosquito resting behavior to target insecticide applications and has the advantage of being deployed preventively (before the peak transmission season). We report the preliminary entomological findings of the TIRS trial, a two-arm, parallel, cluster randomized controlled trial conducted in Merida, Mexico. The protocol involves one preventive application of TIRS during each of three consecutive years (May-June 2021-2023) on a total ~27,900 houses. Indoor adult *Ae. aegypti* collections using Prokopack aspirators on a sub-sample of 1,500 houses were monitored monthly for a period of 6 months post-TIRS application, covering the peak arbovirus transmission season. Before TIRS, house infestation rates and female mosquito abundance were similar for both study arms. After TIRS, the strongest impact was observed during the first three months for both infestation (OR=0.18-0.41, P<0.05) and mosquito abundance (IRR=0.08-0.37, P<0.05). Significant reductions were maintained throughout the 6 months post-intervention in Year 1. Average treatment coverage increased from 60.2% in 2021 to 74.9% of target households per cluster in 2023. Intervention clusters (central and external blocks) were categorized according to TIRS coverage: 1= >75% of coverage in both central and external blocks; 2= <75% central/external blocks (n=10); 3= >75% central/<75% external blocks; 4= <75% central/>75% external blocks. Significant reduction in *Ae. aegypti* abundance was observed between houses in clusters with higher than 75% versus below 75% TIRS coverage (IRR=0.55, P<0.005); we observed significant increases in density (IRR=3.14 and 2.11, P<0.005) and positivity (OR=2.4 and 2.6, P<0.005) in the central vs external blocks when external blocks had <75% TIRS coverage. These promising results on entomological impact emphasize the importance of maintaining broad coverage to ensure better effectiveness of TIRS in the real world setting.

7022

TESTING A COMBINED IIT-SIT APPROACH TO CONTROL *AEDES AEGYPTI* AND URBAN ARBOVIRUS TRANSMISSION IN YUCATAN, MEXICO

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Due to the successful implementation of the sterile insect technique (SIT) in area-wide control of several insect pests of agricultural and

veterinary importance, significant efforts have been made to develop analogous techniques for mosquito control. One of them is Incompatible Insect Technique (IIT), in which males carrying the maternally inherited endosymbiotic bacteria *Wolbachia* are released to induce incompatible mating with target females who either do not carry *Wolbachia* or carry different *Wolbachia* strains. We present baseline and preliminary results from a two-arm cluster randomized controlled trial to evaluate the entomological and epidemiological impact of *Aedes aegypti* population suppression via IIT-SIT on arbovirus transmission in urban neighborhoods of the city of Mérida, Mexico. The intervention includes integrated control activities structured in two phases: 1) an Attack phase (~1-2 months prior to the transmission season) with area-wide ULV adulticide spraying to control Aedes adults in four weekly applications followed by 2) Male *Aedes aegypti* releases (2,000 male mosquitoes per hectare twice a week). We present information of the overall study design, baseline epidemiological and entomological data, and preliminary results of entomological impact. Findings from this study will allow establishing a link between epidemiologic, entomo-virological, and entomological indicators to determine the effectiveness of IIT-SIT in real world conditions. Built on the successful field trial and existing mosquito mass rearing capacity established in Merida, scaling-up this innovation is not only logical but also feasible. Successful findings from this study will pave the way for future expansions of the technology to the entire city and nationwide using a rolling-carpet strategy, which has been successfully demonstrated for area-wide control of screwworm and medfly in Latin America.

7023

NON-HOUSEHOLD ENVIRONMENTS PROMOTE DENGUE TRANSMISSION: IMPLICATIONS FOR VECTOR CONTROL

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Aedes-borne pathogens have been increasing in incidence despite vector control activities implemented in endemic settings. Vector control for *Aedes*-transmitted arboviruses typically focuses on households because vectors breed in household containers and bite indoors. Yet, our recent work shows a high abundance of *Aedes* vectors in public spaces. We used field-collected data on the distribution of vectors in different urban environments in Kenyan cities of Kisumu and Ukunda along with movement data to create an agent-based model. The model quantified the number of infections happening in both household (HH) and non-household (NH) environments. We additionally modeled the outcome of vector control activities implemented in different environments in preventive (before an outbreak) and reactive (after an outbreak commences) scenarios. We estimated that more than half of infections take place in NH environments, where the main spaces for transmission are workplaces and markets. Accordingly, a greater reduction of cases was estimated when control activities targeted only NH as opposed to when targeting only HH. As expected, greater control effectiveness is achieved when activities are implemented earlier and at higher levels of coverage. Additionally, we included spatial variables to study how the movement of individuals affects the dengue burden of both environments under three different urban conformations of NH: randomly distributed, centered, or clustered. According to the model, the number of cases is slightly higher when NH are randomly distributed, suggesting a role as spreaders of disease toward nearby HHs. Also, we discovered that the number of people visiting NH is an important factor determining dengue burden. At very low movement of people, transmission decreases and the number of infections in both environments becomes roughly even. Together, these results lead us to rethink the way urban transmission is understood, which is often placing HH as the main transmission environment. Accordingly, new control guidelines and risk factors estimation methods should be developed to render control and prevention truly effective.

7024

VERTICAL AND HORIZONTAL TRANSMISSION OF *MICROSPORIDIA MB*: A *PLASMODIUM* INHIBITING NATURAL SYMBIONT OF *ANOPHELES*

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Microsporidia MB, a naturally occurring symbiont in *Anopheles arabiensis* inhibits *Plasmodium* development and is avirulent. *Microsporidia MB* is transmitted vertically, from mother to offspring, and horizontally through mating. Transmission is expected to promote its spread through mosquito populations, enhancing the potential of *Microsporidia MB* as a candidate for the development of a symbiont-mediated malaria transmission-blocking strategy. In-depth understanding of *Microsporidia MB* transmission patterns is required for mass production of mosquitoes, a pre-requisite for mosquito release, and robust estimates from theoretical models on *Microsporidia MB* spread in the natural populations following release. Iso-female lines originating from field-collected *Microsporidia MB*-infected and uninfected females were compared for various life history traits from the egg to adult stage. Bioassays were conducted on first filial-generation mosquitoes to determine effect of diet type and quantity on *Microsporidia MB* prevalence and density. *Microsporidia MB* -infected and uninfected males were compared individually and in groups for mating competitiveness. Larval development time of *Microsporidia MB* -infected *An. arabiensis* is shorter compared to uninfected mosquitoes. Diet type and quantity influence density of *Microsporidia MB*. *Microsporidia MB* -infected adults have a higher mating rate compared to uninfected mosquitoes. In general, *Microsporidia MB* -infection has a positive effect on the development of *An. arabiensis* mosquitoes. *Microsporidia MB*-infection is influenced by diet type and quantity, therefore, diet can be manipulated to rear highly infected mosquitoes. *Microsporidia MB* is inherently able to spread in mosquito populations due to higher mating rate making it a promising candidate for malaria transmission-blocking strategy.

7025

DATA-DRIVEN TARGETING OF MALARIA AT-RISK POPULATIONS FOR DISTRIBUTION OF TOPICAL REPELLENTS IN ZIMBABWE

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Reported annual malaria incidence in Zimbabwe ranged from 9 to 32 cases per 1,000 population over the past five years, with 14 cases per 1,000 population reported nationally in 2023. Over 75% of malaria cases nationally are reported from three of the country's ten provinces. Despite consistently reporting indoor residual spraying (IRS) coverage of >85% of the population, prevention gaps remain, particularly among farmers whose livelihoods require outdoor nighttime activities and time away from home-based vector control strategies. To address residual transmission resulting from protection gaps among these farmers, we explored criteria for topical repellents as a supplementary protective intervention. Wards (administrative unit 3) considered eligible for a topical repellent-based intervention included those with a reported annual parasite incidence >100 cases per 1,000 population, an IRS population coverage >85%, and a large population of agricultural workers engaged in outdoor nighttime activities during peak malaria season. Of the country's 396 wards, we identified seven (1.8%) meeting these criteria using descriptive and spatial analyses of routine surveillance, and malaria programmatic, socioeconomic, and 2022 census data. A bottom-up approach through stakeholder engagement was used to target communities and healthcare authorities at the sub-national and national-levels to gather insights on priority populations to be covered by topical repellents. A ward with approximately 6,000 people will be prioritized for distribution and monitoring of topical repellents commencing in July 2024. This data-driven approach with key informant input was essential to tailor malaria interventions at the subnational level and address these unique drivers of malaria transmission.

7026

TWO MOSQUITO SALIVARY ANTIGENS DEMONSTRATE PROMISE AS BIOMARKERS OF RECENT EXPOSURE TO *PLASMODIUM FALCIPARUM* INFECTED MOSQUITO BITES

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Measuring malaria transmission intensity using the traditional entomological inoculation rate is difficult. Antibody responses to mosquito salivary proteins such as SG6 have previously been used as biomarkers of exposure to *Anopheles* mosquito bites. Here, we investigate four mosquito salivary proteins as potential biomarkers of human exposure to mosquitoes infected with *P. falciparum*: mosGILT, SAMPSP1, AgSAP, and AgTRIO. AgSAP and AgTRIO are transcriptionally upregulated in *P. falciparum*-infected mosquitoes, and all four proteins have either a prior reported association with sporozoites or could be secreted into *An.* saliva. We tested population-level human immune responses to these proteins in longitudinal and cross-sectional plasma samples from individuals with known *P. falciparum* infection from low and moderate transmission areas in Senegal using a multiplexed magnetic bead-based assay. AgSAP and AgTRIO were the most closely associated with recent exposure to infected mosquitoes. Antibody responses to AgSAP, in a moderate endemic area, and to AgTRIO, in both low and moderate endemic areas, were significantly higher than responses in a healthy non-endemic control cohort ($p = 0.0245$, 0.0064, and <0.0001 respectively). Antibody responses did not significantly differ between the low and moderate transmission area for any of the four proteins, or between equivalent groups during and outside the malaria transmission seasons. For AgSAP and AgTRIO, reactivity peaked 2-4 weeks after clinical *P. falciparum* infection and declined 3 months after infection. Since reactivity to both AgSAP and AgTRIO peaked after infection and did not differ seasonally, nor between areas of low and moderate transmission, the data suggest reactivity is likely reflective of exposure to infectious mosquitos or recent biting rather than to general mosquito exposure. Kinetics suggest reactivity is relatively short-lived. AgSAP and AgTRIO are promising candidates to incorporate into multiplexed assays for serosurveillance of population-level changes in *P. falciparum*-infected mosquito exposure.

7027

DEPLOYMENT OF ATTRACTIVE TARGETED SUGAR BAITS IN WESTERN ZAMBIA: INSTALLATION, MONITORING, REMOVAL, AND DISPOSAL PROCEDURES DURING A PHASE III CLUSTER RANDOMIZED CONTROL TRIAL

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Attractive Targeted Sugar Baits (ATSBs) offer a complementary vector control strategy to interventions targeting blood feeding or larval control by attacking the sugar feeding behavior of adult mosquitoes. Western Zambia was the first location to receive and deploy ATSB Sarabi v1.2 stations, in a Phase III cluster randomized control trial (cRCT). The cRCT was implemented in 70 study clusters (35 intervention and 35 control) across three districts, representing a population of 23,466 households at baseline. The trial measured epidemiological and entomological outcomes during a two-year seasonal deployment of ATSB stations (November 2021-June 2022; November 2022-June 2023). Two ATSB stations were installed on eligible structures in intervention clusters through planned installation campaigns. During deployment, ATSB monitoring was conducted to maintain high coverage of ATSBs and to assess their condition. Damaged ATSBs required replacement per pre-defined criteria for holes, leaks, mold, depletion, and dirt. Annual cross-sectional household surveys measured ATSB coverage. ATSBs were removed from all structures at the end of each transmission season and transported to Lusaka for incineration. A total of 67,945 ATSBs were installed in Year 1 (41,695 initially + 26,250 during monitoring) and 69,494 ATSBs were installed in Year 2 (41,982 initially + 27,512 during monitoring). The primary reasons for ATSB replacement were holes and mold. Cross-sectional surveys documented high coverage of ATSB stations across both years with 93.1% of eligible structures having ≥2 ATSB stations in any condition; however, only 71.5% of eligible structures had ≥2 ATSB stations not meeting the replacement criteria, demonstrating the high volume of ATSB damage. Additional research is needed to better understand the impact of damage on ATSB effectiveness, including the thresholds below which holes and mold are associated with reduced product efficacy. This presentation will describe the Zambia trial ATSB station installation, monitoring, removal, and disposal methods, quantify ATSB station coverage, and report reasons for ATSB station replacement.

7028

MATRIX-ASSISTED LASER DESORPTION/IONIZATION TIME-OF-FLIGHT (MALDI-TOF) MASS SPECTROMETRY AS A RELIABLE APPROACH FOR THE SURVEILLANCE OF CHIKUNGUNYA VIRUS IN MOSQUITO VECTORS

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Since its first outbreak in Africa, Chikungunya virus has spread to South Asia, the Indian Ocean islands, and the Americas, affecting over 100 countries. Quick identification of vector species and determination of infection status is critical for accurate vector-borne disease surveillance. Mosquito identification is often performed through morphological criteria and/or molecular methods, which can be time-consuming and expensive. Here, we use MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight) mass spectrometry to simultaneously identify mosquito species and infection status with CHIKV, which is more accessible, quicker, and cheaper than the current methods. Experimentally infected and non-infected *Aedes aegypti* and *Aedes albopictus* were dissected to obtain either legs or combined head and thoraxes for spectra generation. Spectra were grouped according to body part, species, and infection status. Spectra were assessed for quality using FlexAnalysis software and for reproducibility and specificity using pseudo-gel and PCA analyses with ClinProTools software. Leg spectra from infected and non-infected mosquitoes clustered separately in PCA analyses, while significant overlap was observed with cephalothorax spectra, indicating leg data were more suitable for differentiation. A database was created with high-quality reference spectra for each species. Samples were queried against this database, and all were correctly identified to the species level. Additionally, all non-infected mosquitoes were recognized as such while 97% of infected mosquitoes were correctly detected as infected. MALDI-TOF MS has been a critical development in the clinical and surveillance field for rapid and sensitive testing of microbial and arthropod samples. The present study

demonstrates the use of MALDI-TOF MS in the concurrent identification of mosquito species and infection status with CHIKV. The continual addition of quality spectra to the database and modifications to the current protocol will aid in the quick and accurate identification necessary for the surveillance of this spreading arboviral disease.

7029

LANDSCAPE PREDICTORS OF *AEDES AEGYPTI* ABUNDANCE IN A DENGUE-ENDEMIC LOCALITY IN MANAGUA, NICARAGUA

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Dengue has been traditionally recognized as an urban disease where urban centers are thought to provide ample habitat for *Aedes aegypti* reproduction and susceptible human hosts to drive dengue virus (DENV) transmission. Increasing evidence of DENV infections in rural populations challenges this narrative. DENV transmission is driven by various spatial, environmental, and anthropogenic factors, often summarized by a dichotomous urban-rural variable. However, this urban-rural dichotomy overlooks underlying drivers of spatial spread, many of which can be captured by landscape features. As such, this study proposes to quantify the landscape structure and composition of two characteristically urban and peri-urban neighborhoods in Managua, Nicaragua, a dengue endemic locality. Elucidating differences in landscape composition between peri-urban and urban sites will facilitate a more nuanced analysis of DENV epidemiology among heterogeneous spatial patches. We approached this analysis using remote sensing and landscape structure characterization techniques and household level *Ae. aegypti* abundance data that were systematically collected within 500 households across both neighborhoods using manual aspiration and container inspection. We employed high resolution multispectral WorldView 3 imagery and a machine learning Random Forests model to classify land types of the two study sites. Using FRAGSTATS software, we computed landscape metrics to spatially assess patch connectivity, geometry, and aggregation for each land type across the two study sites. To assess the relationship between landscape metrics and *Ae. aegypti* abundance we will also integrate ancillary environmental and climatic data and generate DENV transmission risk estimates using spatial regression and spatial clustering techniques. This landscape scale analytic framework provides a more mechanistic understanding of spatial risk patterns and moves beyond the urban-rural dichotomy concept for risk mapping and will allow us to delineate specific urban features and typologies that sustain dengue transmission within urban- or rural-like landscapes.

7030

THE POTENTIAL USE OF DIGITAL TOOLS FOR LARVAL SURVEYS IN VECTOR CONTROL: EXPERIENCE FROM ANAMBRA AND ONDO STATES OF NIGERIA

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Malaria Consortium is conducting studies to assess the entomological and epidemiological impacts of insecticide-treated net (ITN) campaigns in 2021 and 2022 in Ondo and Anambra states respectively. These studies involved the use of a digital questionnaire completed alongside the collection of mosquito larvae for resistance tests. We report observations from using the digital tool, and explore its potential use for mapping larval habitats to inform the targeting of vector control interventions. The digital tool was developed using SurveyCTO, a customisable application, and deployed on mobile devices. The tool facilitated the collection of data on breeding sites capturing various attributes of the habitats. *Anopheles* larvae were collected alongside images of the sites and their geocoordinates, type and characteristics, and the timestamps of collection. Data were submitted in real time which allowed research staff to monitor field activities in progress and immediately map survey sites. Although the primary use of the digital data was to locate the sources of mosquitoes used in resistance tests, the findings indicated the potential use of the tool to link species- after rearing and identification of adult mosquitoes - with the collection sites to deploy larval source management (LSM) and other measures. Digitization of larval surveys for resistance monitoring or other entomological studies could allow mapping of important breeding sites for vector control, beyond the primary purposes of the sample collections. Insecticide resistance monitoring activities in several African countries are based on larval collection and rearing. If during such activities information is gathered on larval habitats employing similar digital tools, this could allow real-time monitoring of transmission foci by integrating into the surveillance system. A similar approach could also be used at community levels for mapping of breeding sites for wider geographic coverage of LSM measures.

7031

STRATEGIES FOR ALTERING THE FREQUENCY AND COVERAGE OF INSECTICIDE-TREATED NET MASS CAMPAIGNS WITH DIFFERENT NET TYPES TO MAXIMIZE CASES AVERTED UNDER FIXED BUDGETS

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Mass campaigns of insecticide-treated nets (ITNs) are recommended every three years to control malaria. However, evidence indicates most nets do not last this long, and those that do may have impaired effectiveness in areas of pyrethroid resistance. The availability of pyrethroid-only, pyrethroid-PBO and dual-active ingredient (AI) ITNs with differing costs and durability means it is unclear whether biennial distribution of a cheaper net may be more cost-effective than triennial distribution of other more costly but more effective ITNs. It is also unclear whether distributing fewer but better pyrethroid-PBO and dual-AI nets through mass campaigns will be more cost-effective than larger quantities of pyrethroid-only nets under fixed budget constraints. Here we fit retention curves to Demographic and Health Survey data to estimate sub-national mean net retention times in Burkina Faso, Ghana, Malawi, Mali, Mozambique and Senegal. Central estimates of mean retention times were less than 2 years for 68.8% of regions investigated. Models indicate considerable sub-national heterogeneity, with mean retention ranging from 0.95 years (95% CrI: 0.92-0.97) in urban Maputo, Mozambique, to 3.04 years (95% CrI: 2.84-3.23) in urban Est, Burkina Faso. By accounting for sub-national heterogeneity in net retention, in addition to transmission intensity and pyrethroid resistance, we generate projections of cases averted for biennial vs triennial mass campaigns for pyrethroid-only, pyrethroid-PBO and dual-AI nets under different costed strategies using a transmission-dynamics model. Results highlight distribution strategies for administrative-one level regions investigated where biennial distribution with pyrethroid-pyrrole nets could be more cost-effective than triennial pyrethroid-only campaigns under fixed budget constraints. As policymakers look to move towards distributing pyrethroid-pyrrole nets in the face of increasing pyrethroid resistance, our findings highlight increased distribution frequencies could also be considered concurrently in some regions for optimal cost-effectiveness.

7032

MODELLING THE POTENTIAL OF GENE DRIVE MOSQUITOES FOR MALARIA CONTROL IN SETTINGS WITH MULTIPLE VECTOR SPECIES IN MAINLAND TANZANIA

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Malaria persists as a significant global health challenge especially in regions such as mainland Tanzania where multiple vector species mediate transmission dynamics. This study aims at evaluating the potential of gene drive (GD) modified mosquitoes to combat malaria with such complex eco-epidemiological settings. Focusing on the Kilombero Valley – a well-documented site for malaria endemicity with predominant *Anopheles funestus* and *Anopheles arabiensis* mosquito populations, we propose a multifaceted approach to understanding the impact of deploying GD mosquitoes as part of an integrated vector management (IVM) strategy. Through mathematical modelling and scenario analysis, we will simulate the release of GD mosquitoes into local vector population and assess the efficacy of replacement drive strategies in diminishing the rate of malaria transmission. The study will determine the necessary scale of GD mosquito releases required for substantial reduction, factoring in the variation in epidemiological conditions specific to Kilombero Valley. We will also investigate the integration of GD mosquitoes with current control measures, such as insecticide treated nets (ITNs) to discern potential synergistic or antagonistic outcomes on malaria control. A critical component of our research includes the identification of thresholds for escaped GD mosquitoes that could present ecological or health concerns. In here, we aim to develop a comprehensive monitoring plan to address the risks associated with escape and unintended establishment, contemplating both full-drive (super-mendelian inheritance) and effector-only (mendelian inheritance) constructs to enable robust risk management strategies. The study's results will provide strategic insights into the operational feasibility of incorporating GD mosquitoes within broader malaria elimination initiatives, paving the way for novel, sustainable approach to vector control in settings challenged by the presence of multiple vector species.

7033

VALIDATION USING ATTRACTIVE SUGAR BAITS (ASBS) CONTAINING A FLUORESCENT DYE IN SIAYA, WESTERN KENYA: AN EVALUATION OF ANOPHELES FEEDING RATES

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Vector control is an essential component of malaria prevention. Additional mosquito control tools like Attractive targeted sugar baits (ATSBs) are urgently needed to further suppress malaria transmission worldwide. Prior to epidemiological trials on ATSBs, validation studies were conducted to assess the levels of mosquito feeding on attractive sugar baits (ASBs) with uranine fluorescent dye and to evaluate whether the deployment of two versus three bait stations per building structure led to a significantly different daily feeding rate in local malaria vectors as a proxy for ATSBs. The study followed a cross-over design in twelve clusters of Siaya western Kenya. Either two or three ASBs were deployed to all structures and switched over at two months' time point so that clusters which initially received two ASBs were given three and vice versa. ASB monitoring was done for four months from initial deployment then an additional four months for extended monitoring of ASBs. Mosquitoes were collected using UV light traps and Prokopack aspiration indoors and outdoors then screened for morphological characteristics and fluorescence due to the uranine dye. Samples of mosquitoes collected were processed by PCR and sporozoite infectivity. Data analysis was performed using R statistical software. *An. funestus* s.s. was the dominant malaria vector with overall dye feeding of 11.2% followed by *An. gambiae* s.l. at 3.5%, translating to daily feeding rates of 4.8% in *An. funestus* and 1.2% in *An. Gambiae*. No significant difference was detected between two or three ASB stations. *An. funestus* s.l. comprised 82% *An. funestus* s.s. and 6.3% *An. leesoni* while *An. gambiae* s.l. constituted 68% *An. arabiensis* and 21% *An. gambiae* s.s. Sporozoite positivity rate was 2.28% and1.00%. in *An. funestus* s.l. and *An. gambiae* s.l. respectively. *Anopheles funestus* s.s. demonstrated higher rates of feeding on ASBs compared to *An. gambiae* s.l. No significant difference was detected between deploying two or three bait stations per structure. The study provided important information utilized in the subsequent deployment of ATSBs in epidemiological trials.

7034

COMPARISON OF SEASONAL MOSQUITO POPULATIONS ACROSS A DIVERSIFYING SEMI-PASTORAL LANDSCAPE IN LOITOKITOK SUB-COUNTY, KENYA

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Ecological variables have a profound impact on mosquito populations and micro-environments suitable for proliferation of certain species can result in disease transmission hotspots. Rift Valley fever virus (RVFV), a priority zoonotic arbovirus, is transmitted by a wide range of mosquito species, and endemic transmission is poorly understood. A subset of randomly sampled households in different ecozones and land use types (cropland, grassland, and shrubland) were used to capture outdoor mosquitos associated with livestock using Biosentinel (BG) traps baited with CO_2 set for 48-96 hours. We trapped in three seasons, the August 2023 dry period, the rains at the end of November into December 2023, and in February 2024 after the El Niño phenomenon prolonged the short rains. Total mosquitos were adjusted for trapping time and transformed for analysis. We caught 323 mosquitos over 30 trapping events, lasting on average 54.5 hours. The majority, 94%, of mosquitos were *Culex spp.* We caught *Anopheles spp*. at one trapping event in a cropland household at 1,497 meters elevation, and eight of the ten total *Aedes spp.* were captured in shrubland. We had similar mosquito totals in shrubland and grassland landcover (β=1.01, SE=0.06, *p=0.89*) and caught more mosquitos in cropland households (β=1.10, SE=0.05 *p=0.10*) but did not identify a significant association with the elevation or ecozone. The greatest impact was seasonality, with significantly fewer mosquitos in the August dry period (β=*0.84,* SE=0.06, p=0.005), and catches were only slightly higher in February (β=1.04, SE= 1.04, *p=0.41*) compared to December. Furthermore, in December, we repeated trapping at three households and caught significantly more mosquitos six weeks after our weather station recorded the first major rainfall event compared to three weeks after (β =1.12, SE=0.03, *p=0.01*). We captured very few mosquitos during the dry season and demonstrated that following the first major rainfall event after a dry period, mosquito abundance continues to increase significantly. We also caught more in cropland and, as this land use type continues to expand, could increase total mosquito abundance.

7035

THE USE OF INSECTICIDE TREATED EAVE RIBBONS AS A PROTECTION TOOL AGAINST POPULATIONS OF MOSQUITOES THAT TRANSMIT MALARIA AND DENGUE

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Mosquito-borne diseases such as malaria and dengue continue to pose a significant public health challenge in disease-endemic communities worldwide. While insecticide-treated nets and indoor residual spraying have been successful in preventing these diseases, they face challenges such as insecticide resistance, high costs, logistical difficulties, and limited durability. Therefore, there is a need for simpler and affordable interventions that can be used on a large scale in endemic communities to supplement current approaches. This study evaluated the efficacy of insecticide-treated eave ribbons as a potential tool for complementing the current vector control methods. Eave ribbons are pieces of hessian fabric placed around the eave spaces of houses to kill or repel mosquitoes. Laboratory cone bioassays were conducted to assess the efficacy of eave ribbons treated with the organophosphate, pirimiphos-methyl, for killing the malaria vectors, *Anopheles funestus* and *Anopheles arabiensis*, and the dengue vector, *Aedes aegypti*, under varying exposure durations and insecticide doses. A semi-field experiment was done to assess the efficacy of eave ribbons treated with pirimiphos-methyl against the malaria vectors. The findings revealed that treated eave ribbons resulted in higher mosquito mortality than the untreated ribbons, but the impact increased with increased exposure duration or dose. The semi-field study indicated moderate levels of bite prevention and mortality of the mosquitoes. At the doses of 1g a.i./m^2 and 2g a.i./m^2 pirimiphos-methyl, there was no significant protection against *An. arabiensis*, but at the dose of 4g a.i./m^2 pirimiphos-methyl, there was a significant protection in outdoor biting *An. arabiensis* (RR = 0.80, 95% CI: 0.71-0.91, $p < 0.001$), but not *An. funestus*. In conclusion, while insecticide-treated eave ribbons may have potential for controlling malaria and dengue vectors, further research is needed to validate their efficacy in field settings and to identify suitable insecticides or insecticide combinations that are highly effective, particularly against pyrethroid-resistant vectors.

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MALARIA TRANSMISSION RISK IN THE CITY OF ACCRA, GHANA

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Unplanned urbanization in sub-Saharan Africa is altering urban malaria transmission dynamics, challenging existing control methods such as indoor residual spraying (IRS) and long-lasting insecticide-treated nets (LLINs). Therefore, understanding these dynamics is crucial for tailored control strategies. This study investigated the vector densities, bloodmeal sources and infectivity rate of malaria vectors in Accra, Ghana. Biting and resting mosquitoes were collected in ten sites within the city of Accra, Ghana using human landing catches (HLC) and Prokopack aspirators (PPA) during the dry and rainy seasons in 2023. Sites were selected and categorized into five sectors (two sites per sector): Irrigated Urban Farming (IUF), Lower (LS), Middle (MS) and High (HS) socioeconomic status, and Peri-urban (PU) sites. Vector speciation, sporozoite infection and blood meal analysis were determined using PCR. Overall, a total of 42,331 mosquitoes were collected over the entire sampling period; Culicine = 17,820 [HLC = 16,742, PPA = 1,078], Anopheline = 21,520 [HLC = 20,931, PPA =589], Aedine = 1,708[HLC = 1491, PPA = 217]. Significantly high biting activity was observed in the late evening (LE) for both seasons [Dry (69.93%, 2,925/4,183); Rainy (70.44%, 8,367/11,878)] [F (2, 27) = 6.03, $P = 0.019$, 95% CL 135.2691 - 1388.731]. High biting activity (HBR = 352.9) and entomological inoculation rate (EIR) 0.409 (ib/m/n) were observed in IUF site categories compared to other sectors. Vectors preferred to feed on humans (HBI = 86.30%, 359/416). Higher sporozoite infection rate (Tuba = 77.27%) was found in indoor resting mosquitoes. The L1014F mutations were detected at higher frequencies (0.98 - 1) in all sites, followed by G119S (0.86 – 0.89). L1014S was detected at very low frequencies (0.15 – 0.5). The study highlights the importance of adopting novel approaches to complement existing strategies in controlling urban malaria vectors.

7037

UNDERSTANDING THE ECO-EPIDEMIOLOGY OF MOSQUITOES IN HOUSTON, TEXAS: INFORMING PUBLIC HEALTH STRATEGIES

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Mosquito-borne diseases present a significant challenge to public health, particularly in regions like Harris County, Texas, characterized by a humid subtropical climate and dense population. Effective disease surveillance and control strategies necessitate a comprehensive understanding of mosquito community dynamics, including species composition, abundance, and distribution. To address this need, we extensively analyzed routine mosquito surveillance data collected from 2018 to 2022, comprising nearly 4 million female mosquitoes collected over 55,000 trap nights using three trap types. Our analysis revealed *Culex quinquefasciatus* (the primary vector for West Nile virus in the southern United States) as the predominant species (88%), alongside *Aedes albopictus, Culex salinarius, Aedes taeniorhynchus,* and *Aedes aegypti.* Biodiversity analysis indicated variations in species richness and diversity among trap types and years, with BG-sentinel traps capturing the highest diversity in 2018. To investigate variation in female *Culex quinquefasciatus* abundance, global and local spatial autocorrelation analyses were performed to identify high-abundance neighborhoods surrounded by similar high-abundance neighborhoods (hotspots) for 2020 to 2022. Interestingly, we observed the highest abundance of female *Culex quinquefasciatus* in some of the oldest communities in Harris County, characterized by a higher median home age. Our findings underscore the importance of understanding population dynamics and species composition for targeted disease surveillance and control efforts. Furthermore, these results emphasize the interconnectedness of humans, mosquitoes, and the built environment in a large metropolitan region. Continued monitoring and research efforts are essential for effectively implementing public health interventions, safeguarding both human and animal populations against vector-borne illnesses.

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URBAN VECTORIAL TRANSMISSION OF MALARIA IN KOULIKORO DISTRICT, MALI

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The rapid but unplanned urbanization occurring in several African countries and the global warming could lead to an increase in malaria burden through the proliferation of mosquitoes breeding sites in specific areas of the cities. The study aimed to determine the species composition of malaria vector population during the transmission season from August to November

2021 in an urban area of Mali, Koulikoro. Mosquitoes were collected each month in 60 randomly selected rooms using Pyrethrum spray catches. Specification of vectors was done using molecular techniques while other entomological indicators such as blood meal sources and infection rates were determined by ELISA techniques. A total of 2106 Culicidae specimens were collected and among which 30.1% were *Anopheles gambiae s.l.* and 69.9% were Culex sp. Three species composed of the *Anopheles gambiae s.l.* population: *Anopheles coluzzii* (84.2%), *Anopheles arabiensis* (11.6%), and *An. gambiae sensu stricto* (4.2 %). The mean density of *An. gambiae s.l.* was 2.7 individuals per room. The mean human blood index was 98.1% and the infection rate was 0.50%, with 0.1 infected bites per person per month. This study not only reported the presence of the three main vector species in the Koulikoro urban area but also a significant human and vector contact enough to sustain malaria transmission. The observed adaptation of the main malaria vectors to the urban environment calls for more attention in terms of vector control specific to this environment. **Keywords :** Malaria, Anopheles; Urban, Mali.

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THE IMPACT OF CLIMATE CHANGE ON MOSQUITO ENTOMOLOGY AND SPATIOTEMPORAL DENGUE TRANSMISSION

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Dengue disease is caused by four serotypes (DENV- 1-4). Infection confers lifelong immunity to a homologous serotype, but only temporary immunity against a heterologous serotype. Secondary infection drastically increases the likelihood of disease. Dengue's primary vectors, *Aedes aegypti* mosquitoes, display high sensitivity to climate. Therefore, climate change has the potential to markedly affect the spatiotemporal dynamics and disease burden of dengue, by increasing disease incidence (and the frequency of secondary infections) in traditionally low transmission settings. Here we infer the relationship between temperature and rainfall and dengue transmission intensity. We then use these inferred relationships to investigate the impact of projected climate change-driven shifts in temperature and rainfall on dengue transmission. We developed an age-structured, stochastic transmission model that captures human infection history. Where possible, the model further represents mosquito entomology parameters (e.g. fecundity, carrying capacity, extrinsic incubation period, mortality and biting rate) mechanistically as functions of temperature and rainfall. UNWPP population data is used to model non-stationary demography. Previously estimated laboratory-derived relationships between temperature and mosquito parameters are used as model prior distributions. Using approximate Bayesian computation, we calibrate our model against multiple epidemiological data streams, including large, historical and spatiotemporally resolved incidence, prevalence and seroprevalence datasets. We reproduce climate-driven seasonal and inter-annual dengue disease incidence, and our analysis shows that the majority of inter-annual variation in dengue incidence is climate-driven. Together with the World Climate Research Programme (WCRP) Coupled Model Intercomparison Project Phase 6 (CMIP6) high resolution climate projections, we project potential changes in dengue transmission. Our work will inform ongoing dengue vaccination and control policies.

7040

TRENDS IN ORGANOPHOSPHATE RESISTANCE AMONG *AEDES AEGYPTI* IN TAPACHULA: IMPLICATIONS FOR VECTOR CONTROL FROM 2018 TO 2021

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In Tapachula, Mexico, the exclusive deployment of pyrethroids (PYRs) for 15 years in *Aedes aegypti* control programs resulted in substantial PYR resistance and subsequent failures in dengue prevention. In response, PYRs were phased out in 2013 in favor of organophosphates (OPs), which have a different mechanism of action. However, the extensive application of OPs since then has raised the risk of developing resistance mechanisms in field populations of *Ae. aegypti*. Therefore, ongoing surveillance of mosquito susceptibility to OPs is crucial to mitigate resistance development. This study used the bottle bioassay to track changes in susceptibility from 2018 to 2021, determining the lethal concentration 50 (LC_{50}) for two OPs—malathion and chlorpyrifos—at 24 collection sites throughout Tapachula. The results showed a slight but significant increase in resistance to both insecticides over time. Mosquito populations showed moderate to high resistance to chlorpyrifos and low resistance to malathion. Given that OPs and PYRs constitute two of the three insecticide classes used in public health, it is essential to develop more sensitive bioassays and molecular markers to detect early signs of OP resistance.

7041

INNOVATIONS RESULTING FROM THE USE OF CULTURED *ANOPHELES* CELL LINES

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Research involving *Anopheles* cell culture systems represents an accessible, cost-effective, versatile approach to support *in vivo* experiments. Molecular biology approaches that can both inform, or themselves constitute, novel interventions to block pathogen transmission can be first elucidated in cell culture. Our particular focus is cellular secretion mechanisms. We first provide a summary of available *Anopheles* cultured cell lines, then describe past successes resulting from work in these lines. Cellular secretory pathways may hold key information about the contributions of mosquito secretions to pathogen infectivity in human hosts immediately following a transmission event, as was shown previously for ticks. We then offer a comprehensive approach to molecular characterization of *Anopheles* cellular secretion, including an efficient cDNA-based method for determining the sex of an Anopheles cell line, and provide preliminary data. In summary, we hope to leverage cellular secretion to develop new methods of preventing the spread of mosquito-borne diseases. This work highlights the importance of molecular processes, including cellular secretion, in the transmission of mosquito-borne diseases.

7042

HYBRIDIZATION BETWEEN *AEDES AEGYPTI* AND *AE. MASCARENSIS* MOSQUITOES LEADS TO DISRUPTION OF MALE SEX DETERMINATION

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Understanding the sex determination pathway and its disruptions in mosquitoes is critical for the effective control of disease vectors through genetic manipulations based on sex separation. When male hybrids of *Aedes aegypti* females and *Ae. mascarensis* males are backcrossed to *Ae. aegypti* females, a portion of the backcross progeny manifests as males with abnormal sexual differentiation. We discovered a significant correlation between the abnormality of pupae and the feminization of subsequent adults exemplified by the relative abundance of ovarian and testicular tissues. All intersex individuals were genetic males as they expressed a male determining factor, *Nix*. Further, our analysis of the sex-specific splicing of *doublesex* and *fruitless* transcripts demonstrated the presence of both male and female splice variants indicating that sex determination is disrupted. A comparative transcriptomic analysis revealed similar expression levels of the majority of female-associated genes in reproductive organs and carcasses between intersexual males and normal females. Moreover, intersexes had largely normal gene expression in testes but significant gene downregulation in male accessory glands when compared with normal males. We conclude that evolving hybrid incompatibilities between *Ae.*

aegypti and *Ae. mascarensis* is due to the disruption of sex determination and is accompanied by changes in gene expression associated with sexual differentiation.

7043

CHROMATIN ARCHITECTURE OF THE MALARIA VECTOR, *ANOPHELES COLUZZII*

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Transcriptional enhancers are non-coding regulatory elements that are responsible for most gene expression above basal levels in eukaryotes. Through their regulation of gene expression, enhancers likely play a role in natural *Anopheles* vector susceptibility phenotypes such as behavior, ecological adaptation, insecticide resistance, and an intrinsic resistance to *Plasmodium falciparum* infection. To better characterize the chromatin architecture of a major African malaria vector, Micro-C approaches were used on an *An. coluzzii* hemocyte cell line to comprehensively identify enhancer-promoter physical interactions. Downstream analyses were performed on the high-resolution enhancer-promoter contact matrices to identify open/closed chromatin domains (A/B compartments), topologically associating domain (TAD) boundaries, and chromatin loop interactions. Results will be presented on chromatin architecture data coupled with gene expression data focused on the previously characterized *Plasmodium* resistance island (PRI) and well characterized immune genes, such as LRIMs, TEPs, and APLs. A molecular understanding of endogenous gene regulation is crucial for a functional understanding of mosquito immune biology and for use in the generation of genetically modified mosquitoes.

7044

HEAD-SPECIFIC TRANSCRIPTOMIC STUDY REVEALS KEY REGULATORY PATHWAYS FOR WINTER DIAPAUSE IN MOSQUITO *CULEX PIPIENS*

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The primary vector of West Nile virus, *Culex pipiens*, undergoes reproductive dormancy during the adverse winter season. Although there is much documentation on the correlation between phenotypic shifts and global transcriptome modifications, there is still a lack of information concerning tissue-specific transcriptomic changes. This knowledge gap is a major challenge in interpreting the regulatory mechanisms at the tissue level. To examine the transcriptome dynamics particular to different tissues that contribute to the diapause phenotype, the present work used RNA-seq technology to analyze the regulatory mechanisms of head-specific genes. RNA samples were obtained from the heads of diapausing and nondiapausing female mosquitoes at two specific time intervals, namely ZT0 and ZT16, and then subjected to sequencing. The findings revealed significant variations in the number of differentially expressed genes between ZT0 and ZT16 under diapause (912) and non-diapause (767) conditions. Additionally, there were differences in the number of differentially expressed genes between diapause and non-diapause at ZT0 (499) and ZT16 (1106) periods, indicating the presence of circadian and seasonal variations in gene expression. In addition, eleven genes associated with the diapause phenotype were chosen, and the abundance of transcripts at six different periods for 24 hours was determined. qRT-PCR analysis showed similar up- and down-regulation of transcripts between the diapause and nondiapause phenotype thus validating the results of RNA-seq. In summary, our findings reveal crucial genes and their corresponding regulatory pathways that play a vital role in the diapause phenotype and are regulated by the circadian clock. The newly presented information here will significantly enhance our comprehension of insect diapause and may provide novel opportunities for vector control strategies

7045

SUPPRESSION OF H3K27ME2 DEMETHYLASE DISRUPTED DIAPAUSE FORMATION IN MOSQUITO *CULEX PIPIENS*

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The northern house mosquito, *Culex pipiens*, undergoes diapause to endure the harsh winter environment. Diapause triggers a cascade of transcriptional and physiological changes, enhancing stress resistance, promoting fat storage, arresting ovarian development, and prolonging lifespan. Understanding of the basis of diapause can help in uncovering potential targets for genetic or biological control methods. Epigenetic regulation, known to influence developmental and behavioral traits in some mosquito species, has attracted attention to researchers. Our previous study revealed a significant reduction in H3K27me2 levels in the fat body of diapausing female *Cx. pipiens* upon diapause onset, suggesting a link between histone methylation and diapause initiation. However, the exact mechanism of the regulatory pathways remains elusive. Here, we inhibited histone demethylases responsible for H3K27 methylations using the histone demethylase inhibitor GSK-J4. Mosquitoes injected with GSK-J4 exhibited elevated H3K27me2 levels, accompanied by reduced lipid conservation and shortened lifespan, ultimately disrupting diapause. Our findings highlight the involvement of H3K27me2 in diapause formation, suggesting potential for targeting histone methylation in novel mosquito control strategies.

7046

MOLECULAR DIVERSITY OF *ANOPHELES* SPECIES OVER THREE YEARS OF INSECTICIDE-TREATED DURABILITY MONITORING IN KAYES, WESTERN MALI.

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Local Anopheles species' composition and bionomic characteristics are drivers of insecticide-treated nets (ITN) effectiveness. This study aims to investigate the diversity of Anopheles mosquitoes during understudied low-density periods towards evaluating species-specific drivers of residual transmission after universal coverage of ITNs. From 2018 to 2020, adult Anopheles were collected in Western Mali using indoor and outdoor CDC light traps, outdoor BG-Pro traps, and indoor Prokopak aspirator collection methods. Morphological identification was performed using taxonomic keys. Molecular identification was performed using specific PCR protocols, and the phylogenetic analysis of rDNA-ITS2 was conducted to identify specimens that could not be identified. Circumsporozoite enzyme-linked immunosorbent assay was used to estimate mosquitoes' *Plasmodium falciparum* infection rate. Of 308 adult female Anopheles sampled, five species were identified morphologically, including *An. gambiae* s.l. (53.6%), *An. rufipes* (15.2%), *An. funestus* s.l. (3.9%), and non-identified specimens (22%). With molecular identification, eight species were identified *An. gambiae* ss (45.8%), *An. coluzzii* (15.6%), *An. arabiensis* (1.3%), *An. funestus*, *An. rufipes* (16.9%), *An. pretoriensis* (2.9%), *An. ziemannii* (4.2%), *An. pharoensis* (1%) and non-identified specimens (6.8%). *An. gambiae* sl was the predominant species with endophilic behavior. Only *An. gambiae* ss was infected with *P. falciparum* sporozoites (0.7%; n = 141). Consensus ITS2 sequences were aligned to construct a phylogenetic tree. The sequence of the novel species clustered within Series Myzomyia. This study highlights the complexity of Anopheles mosquitoes. Detecting a novel and unidentified species suggests potential underreported Anopheles diversity and a potential vector of malaria transmission during the low transmission season. This points to the importance of continuous surveillance and

advanced molecular identification techniques to understand the drivers of malaria towards reducing residual malaria transmission effectively on the road to malaria eradication.

7047

MOLECULAR SURVEILLANCE OF ANOPHELINE VECTORS TO SUPPORT MALARIA ELIMINATION IN BRAZIL

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In 2022, the Brazilian Ministry of Health launched a Malaria Elimination Plan for Brazil. To support malaria elimination, rapid and cost-effective monitoring of the country's main malaria vectors is fundamental for understanding mosquito dynamics and planning timely vector control actions. The primary objective of this project is to establish a practical protocol for molecular analysis of *Anopheles* mosquitoes. This protocol will be used to develop a large-scale implementation strategy for entomological surveillance, specifically for identifying *Anopheles* species in various water collections. In this study, we will analyze the changes in mosquitoes, both spatially and temporally, before and after the application of the VectoMax biolarvicide in fish farming ponds in a malaria-endemic area in Juruá Valley, Acre State, Amazon region, Brazil. Our approach involves the use of metabarcoding of the D2 rDNA marker. Sampling and molecular pipelines were used to verify the species that were using the fishponds as habitats using mass identification of *Anopheles* species. Preliminary results showed that in the pre-intervention period, 2,016 monthly collections of *Anopheles* immature forms were carried out in 170 fishponds, with the presence of approximately 32,210 different larval stages (L1 to L4). The average density of larvae before the fishpond intervention was 0.467 (95% CI, 0.444 to 0.490) anopheline larvae per dip. There was a decrease in the density of larvae to an average of 0.046 (95% CI, 0.041 to 0.051) larvae per dip after implementing larvicide. For analyses and sequence processing, we used MOTHUR v.1.36.1 to analyze the sequence data obtained from the Illumina MiSeq platform. Metabarcoding of immature stages could confirm the temporal and spatial distribution of *Anopheles* species in different water collections in a malaria endemic area. It is expected to translate scientific evidence into a practical metabarcoding protocol to apply at state and municipal level to support entomological surveillance of Anopheline vectors.

7048

POPULATION STRUCTURE OF THE *AEDES ALBOPICTUS* VIROME IN SUFFOLK COUNTY, LONG ISLAND, NY

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Aedes albopictus is an invasive mosquito species known to vector several arboviruses worldwide and was recently detected in Suffolk County, Long Island, NY. Advances in next-generation sequencing have fundamentally shifted our understanding of viruses worldwide and revealed a variety of symbiotic viruses with no known pathogenicity that infect a range of hosts, including *Ae. albopictus*. However, little is known about the distribution of these viruses, their ecology, and how they interact with each other and their hosts. Additionally, given that many of these viruses are likely species-specific, viral phylogenetic structure likely reflects their host's population dynamics and structure. Using georeferenced individual *Aedes albopictus* sampled across Suffolk County, between May 2022 and October 2023, we describe how virome composition varies between individuals and how diversity shifts across seasons and environments. We additionally use phylogeographic models based on whole genomes of select viruses to estimate *Ae. albopictus* population structure in the region. By comparing these results to those predicted by models, we test for the relative impact of active (flight) and passive (human-mediated) dispersal on *Ae. albopictus* population structure. This work will not only help inform future vector control in the area by identifying possible source and sink populations and routes of invasion, but also serve as a proof-of-concept that can be applied to other vector species.

7049

RADIATION EXPOSURE INDUCES GENOME-WIDE ALTERNATIVE SPLICING EVENTS IN *AEDES AEGYPTI* MOSQUITOES

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The sterile insect technique (SIT) is a radiation-based method to control arthropod pest populations. Ionizing radiation, used to sterilize the pests, affects gene transcription patterns, including alternative splicing events in irradiated cells. In this study, we investigated the effect of radiation on alternative splicing in male *Aedes aegypti* mosquitoes. *Ae. agypti* is a major vector of dengue, Zika, and other arboviral diseases. Analyzing RNA sequencing data, we found that radiation altered the splicing of genes involved in a variety of biological processes, including signal transduction, phosphorylation, and metabolism. Specifically, we observed changes in the expression of splicing factors and alternative splicing events in transcript-coding genes. Our results suggest that radiation damage produced by ionizing radiation can alter the splicing of genes involved in important biological functions in male *Ae. aegypti* mosquitoes. Understanding the impact of radiation on alternative splicing may prove critical for improving mosquito Sterile-Insect-Technique and to prevent the transmission of mosquito-borne diseases.

7050

HYBRID ASSEMBLY AND ANNOTATION OF TWO GEOGRAPHICALLY DISTINCT STRAINS OF THE MALARIA VECTOR *ANOPHELES ALBIMANUS* REVEALS LOW INTRA-SPECIFIC DIVERGENCE

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Anopheles albimanus is one of the principal malaria vectors in the Americas and exhibits phenotypic variation across its geographic distribution. High-quality reference genomes from geographically distant populations are essential to deepen our understanding of the biology, evolution and genetic variation of this important malaria vector. In this study, we applied long-read PacBio and short-read Illumina sequencing technologies to assemble the complete genomes of two reference strains of *An. albimanus*, Stecla (originating from El Salvador), and Cartagena (originating from Colombia); and investigated the structural features of these genomes, including gene content, transposable elements (TE) genetic variations, and structural rearrangements. Our hybrid assembly approach generated reference-quality genomes for each strain and recovered ~96% of the expected genome size. The genome assemblies of Stecla and Cartagena consisted of 109 and 149 scaffolds, respectively, with estimated genome sizes of 167.5 Mbp (N_{50}=88 Mbp) and 167.1 Mbp (N_{50}=87 Mbp), respectively. They exhibited a high level of completeness and contained a smaller number of gaps and

ambiguous bases than either of the two previously published reference genomes for this species, suggesting a considerable improvement in the quality and completeness of the assemblies. A total of 12,082 and 12,120 protein-coding genes were predicted in Stecla and Cartagena, respectively. TE analyses indicated more repetitive content was captured in the long-read assemblies. The assembled genomes shared 98.12% pairwise identity and synteny analyses suggested that gene position was primarily conserved between both strains. These genome assemblies will serve as an important resource for future research in comparative genomics, proteomics, epigenetics, transcriptomics, and functional analysis of this important malaria vector

7051

PHOSPHOPROTEOMICS ANALYSES OF *AEDES AEGYPTI* FAT BODY REVEAL BLOOD MEAL-INDUCED SIGNALING AND METABOLIC PATHWAYS

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The mosquito fat body is the principal source of yolk protein precursors (YPP) during mosquito egg development in female *Aedes aegypti*. To better understand the metabolic and signaling pathways involved in mosquito reproduction, we investigated changes in the mosquito fat body phosphoproteome at multiple time points after a blood meal. Using LC/MS, we identified 3,570 phosphorylated proteins containing 14,551 individual phosphorylation sites. We observed protein phosphorylation changes in cellular pathways required for vitellogenesis, as well as proteins involved in primary cellular functions. Specifically, after a blood meal, proteins involved in ribosome synthesis, transcription, translation, and autophagy showed dynamic changes in their phosphorylation patterns. Our results provide new insight into blood meal-induced fat body dynamics and reveal potential proteins that can be targeted for interference with mosquito reproduction. Considering the devastating impact of mosquitoes on human health, worldwide, new approaches to control mosquitoes are urgently needed.

7052

PREVALENCE OF MALARIA AND LONG-COVID AMONG INDIVIDUALS PREVIOUSLY INFECTED WITH THE SARS-COV-2 VIRUS IN ETHIOPIA AND UGANDA: A CASE CONTROL STUDY

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By 15th April 2024, more than 12 million patients had recovered from SARS-CoV-2 infection across Africa. Although most patients fully recover after acute infection, a proportion experience long-term complications and symptoms referred to as long COVID. The potential interplay between any such post-COVID syndromes and the risk of other infectious diseases like malaria is largely unknown. We determined the prevalence of malaria and long COVID among individuals with previous SARS-CoV-2 infection in a case-control study in Uganda and Ethiopia. Detailed clinical evaluation was conducted using a standardized clinical tool and malaria was diagnosed using rapid diagnostic tests, microcopy and molecular methods. Previous *Plasmodium falciparum* exposure was assessed using serologic responses to a panel of *P. falciparum* antigens using a multiplex bead assay. Additional evaluations including radiological investigations were carried out as needed. Of 3,251 individuals enrolled between 15th September 2022 and 30th March 2024, 1700 (52%) were female and median age (SD) was 35 (15.3) years. Preliminary findings show an overall prevalence of malaria infection was 9.5% (197/2076, 95% CI 8.3 to 10.8), with a higher prevalence among controls (16.7%, 150/898) compared to cases (4.0%, 47/1178), 95% CI 10.1% to 14.5%, p<0.0001. Overall, the prevalence of long COVID was 62.2% (1119/1800, 95% CI 59.9 to 64.4). The commonest manifestations of long COVID included mental health issues, headache, memory loss, brain fog, muscle/joint/bone pains, chest pain/dyspnea and suicidality. Some symptoms persisted up to 24 months post-acute illness. No clear healthcare pathways for the management of these long-term complications were reported. Additional findings will be presented. The burden of long COVID in these settings is significant and defining treatment strategies and recommendations for African patients with long COVID is critical.

7053

EMERGENCE OF CRIMEAN CONGO HEMORRHAGIC FEVER VIRUS IN EASTERN SENEGAL IN 2022

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Crimean-Congo hemorrhagic fever (CCHF), the most widespread tick-borne viral human infection, poses a threat to global health. In this study, clinical samples collected through national surveillance systems were screened for acute CCHF virus (CCHFV) infection using RT-PCR and for exposure using ELISA. For any CCHF-positive sample, livestock and tick samples were also collected in the neighborhood of the confirmed case and tested using ELISA and RT-PCR, respectively. Genome sequencing and phylogenetic analyses were also performed on samples with positive RT-PCR results. In Eastern Senegal, two human cases and one *Hyalomma* tick positive for CCHF were identified and a seroprevalence in livestock ranging from 9.33% to 45.26% was detected. Phylogenetic analyses revealed that the human strain belonged to genotype I based on the available L segment. However, the tick strain showed a reassortant profile, with the L and M segments belonging to genotype I and the S segment belonging to genotype III. Our data also showed that our strains clustered with strains isolated in different countries, including Mauritania. Therefore, our findings confirmed the high genetic variability inside the CCHF genotypes and their introduction to Senegal from other countries. They also indicate an increasing CCHF threat in Senegal and emphasize the need to reinforce surveillance using a one-health approach.

7054

INVESTIGATING THE EMERGING BURDEN OF DENGUE IN THE KATHMANDU VALLEY, NEPAL THROUGH A LONGITUDINAL POPULATION-BASED SEROSURVEY

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Dengue, an arthropod-borne infection by *Aedes aegypti* and *Ae. albopictus*, is intensifying globally due to climate change. In Nepal, dengue was previously limited to lower elevations, but recent clinical reports indicate transmission is now occurring at higher altitudes. This study aimed to characterize the population-level risk of dengue in the Kathmandu Valley, Nepal's densely populated region. We enrolled a geographically representative, stratified random sample of individuals between the ages of 1 and 25 residing in Kathmandu and Kavrepalanchok districts. We collected dried blood spot (DBS) samples from participants between 2019-2021 and collected a follow-up sample in 2023. We tested samples for IgG responses against dengue-derived recombinant antigens using commercial ELISA kits. We determined seropositivity cut-offs using Gaussian mixture models, then calculated seroincidence as the number of individuals who seroconverted

from negative to positive divided by their person-time. We enrolled 843 participants (352 in Kathmandu and 491 in Kavre) and analyzed 2091 blood samples. The median age at baseline was 11 years (IQR: 6-17); 47% (396/843) were female. Dengue seropositivity rose from 1.9% (15/792) in 2019 to 12.4% (44/354) in 2023 and was highest in Kathmandu, where it rose from 4.1% (11/271) to 34.0% (36/106). Seroincidence was highest in Kathmandu (99.2 per 1000 person-years, 95% CI: 69.8-136.7). In Kavre, seroincidence ranged from 0 in Panauti to 31.0 (95% CI: 8.5-79.5) in Panchkal. Across all regions, seroincidence increased with age, peaking among 15-25-year-olds at 47.7 infections per 1000 person-years (95%CI: 31.2-70.0). In conclusion, this study reveals a significant rise in dengue incidence in Kathmandu Valley between 2019 and 2023, which may be linked to warming temperatures. The findings indicate an urgent need for interventions to mitigate dengue's rise in Nepal's higher altitudes and contribute to the broader understanding of climate change on vector-borne diseases worldwide.

7055

DETECTION OF ANTIBODIES TO POSSIBLE FILOVIRUS-LIKE PATHOGENS IN RURAL COMMUNITIES IN SARAWAK, MALAYSIA

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Ebolaviruses (EBOV) are zoonotic pathogens that have the potential to cause severe morbidity and mortality. They are deemed to be viruses with high pandemic potential. During our analysis of samples from rural communities in Sarawak, Malaysia, we note the presence of antibody signatures against EBOV in the high throughput serological platform, Phage Immunoprecipitation Sequencing VirScan. We followed up these results using commercially available ELISA for verification. Here, we present preliminary data that shows detection of EBOV glycoprotein (GP) antibodies in several communities in the rural forests of Sarawak, Malaysia.Samples from the rural communities and urban controls were ran on commercially available ELISA with a variety of EBOV GP (Bundibugyo, Tai Forest, Reston, Sudan and Zaire GP) as antigens. Manufacturer recommended cutoff determination was used to interpret the results and the individuals' ELISA results to different EBOV GP was then assessed. Antibody responses were primarily detected against Bundibugyo, Reston, Sudan and Zaire EBOV GP, with a cross-reactive pattern noted in individuals with positive results. Of the EBOVs studied, Sudan and Reston responses are predominant. We observed that individuals residing in the rural community yielded higher ELISA ZEBOV results compared to their urban counterparts.
While known to be lethal and highly pathogenic in most cases, there are certain EBOV (e.g., Reston) that causes asymptotic infections in humans. Given that there were no reports of unidentified illness and there have been no known Filoviruses circulating in the locale, it is possible that a novel zoonotic Filovirus-like pathogen may be the cause of these antibody signatures. Further work - such as neutralization tests - are required and are being conducted to verify our results.

7056

RE-EMERGENCE OF RIFT VALLEY FEVER VIRUS LINEAGE H IN SENEGAL IN 2022: *IN VITRO* CHARACTERIZATION AND IMPACT ON ITS GLOBAL EMERGENCE IN WEST AFRICA

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Rift Valley Fever (RVF) is an re-emerging vector-borne zoonosis causing major epidemics and huge losses in livestock production. In West African countries, the lineages A, C and N were previously detected but since 2020, mainly the lineage H from South Africa were detected in Senegal. In this study, clinical samples collected through national surveillance system were screened for RVF virus (RVFV) acute infection by RT-PCR and exposure by ELISA. Molecular and *in vitro* phenotypic characterization were also performed on RT-PCR positive samples. Four human cases were detected RVFV positive by RT-PCR (2) and ELISA (2) in four regions in Senegal. Phylogenetic analyses revealed that these strains belonged to lineage H and clustered with West African strains, specifically found in Senegal and Mauritania in 2020. The *in vitro* characterization showed that the lineage H had significant higher replication than lineage C. Our findings showed a re-emergence of the lineage H in Senegal in 2022 and showed its higher replication compared to previous lineage C identified in West Africa. This study gives new insights on the biological properties of the lineage H and will be useful for the implementation of control strategies of RVF in Senegal and neighboring countries.

7057

MPOX VIRUS SEROPREVALENCE AMONG INDIVIDUALS VULNERABLE TO INFECTION IN EAST AFRICA

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Endemic in Central and West Africa as a zoonotic infection, mpox has recently been associated with human-human transmission in many non-endemic countries. No mpox cases have been reported in East Africa, but asymptomatic or mild cases in conjunction with limited mpox testing capacity could underestimate disease spread. Results from a mpox seroprevalence study among individuals in East Africa vulnerable to infection during the 2022-23 global outbreak are presented. The African Cohort Study (AFRICOS) is a prospective cohort of adults and adolescents living with, or vulnerable to HIV in four African countries. Cohort participants in Kenya, Tanzania, and Uganda were identified as vulnerable to mpox by meeting one of the following criteria per their study enrollment questionnaire: men or transgender women who have sex with men, HIV pre-exposure prophylaxis use, alcohol/recreational drug use during sex, four or more sex partners in the past six months, sexually-transmitted infection in the past month, or transactional sex. A participant's most recently collected plasma/

serum was tested for anti-clade IIb mpox antibodies using the Meso-Scale Discovery (MSD) Orthopoxvirus panel 1 MULTI-SPOT kit. Mpox seropositive participants' most recent demographic and social behavior data were described. Of the 618 participants identified as vulnerable to mpox, 50 (8.1%) were seropositive. Median age was 53 (interquartile range: 44-63) and 13 (26%) were female. Ten reported recent behaviors associated with mpox vulnerability (eight men who have sex with men and two reporting transactional sex). The high seroprevalence observed in these participants with relatively low mpox vulnerability per their recent behavior data suggests prior infection with other orthopoxviruses or cross-reacting immune responses to Vaccinia virus vaccination may be contributing. However, these results may also indicate previously unrecognized human mpox in East Africa and highlight the need for expanded seroprevalence studies and prospective surveillance to address the persistent knowledge gap in mpox epidemiology in Africa.

7058

FOLLOWING A 50-YEAR HIATUS TAMANA BAT VIRUS (TABV) IS DETECTED AGAIN IN IQUITOS, PERU

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Tamana Bat Virus (TABV) is a putative flavivirus first identified and isolated in 1973, from the salivary glands, saliva and spleen of *Pteronotus parnellii*, an insectivorous bat collected in the Tamana bat caves of Trinidad, in South America. At the time, the authors showed serological evidence of TABV infection in bats (72/850, 8.5%) of several species (15), as well as in humans (21/172, 12%), suggesting this novel flavivirus could potentially be a pathogen of concern. The complete TABV genome of the original isolate was sequenced 30 years later, in 2002, but in the 50 years since its original discovery in Trinidad there have been no further reports of TABV anywhere, until now. As part of ongoing metagenomic investigations of the virome of various bat species residing at the human-animal interphase in the Amazonian Region of Peru, we used unbiassed NGS to identify partial genomic sequences matching TABV in a feces sample from a pale spear-nosed bat (*Phyllostomus discolor*) collected within the city of Iquitos. Given that the genomic sequences initially identified covered only ~46% (4,587 of 10,053 total bp) of the complete TABV genome, we used this information in combination with the previously published TABV whole genome to design TABV-specific primers for tiling amplification, and we further supplemented 5'- and 3'-UTR sequences using 5'- and 3'-RACE. With this approach we have generated a complete TABV genome from Peru, which in turn has enabled other downstream analyses, including a basic phylogeny. Here, we report complete genomic characterization of TABV from a sample collected from a city-dwelling omnivorous bat known to feed on insects, fruit, pollen, nectar and flowers. Further, we report on ongoing efforts to test additional samples for this relatively novel flavivirus to further characterize its little-known epidemiology.

7059

METABOLOMIC BIOMARKERS IN DENGUE VIRUS INFECTION FOR PREDICTING SEVERE DISEASE

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Dengue virus (DENV) infection results in a range of clinical outcomes, spanning from self-limited febrile disease known as dengue fever (DF) to severe disease characterized by hemorrhage and vascular leakage called dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). While diagnostic tools aid in identifying infections, the triage of those at risk of progression to DHF/DSS relies on clinical and hematological parameters. Here, we aimed to identify prognostic biomarkers by analyzing the metabolome of DENV-infected children early after infection (≤3 days post-symptom onset). Using liquid chromatography/mass spectrometry, we analyzed the serum metabolome of children from the prospective Pediatric Dengue Hospital-based Study and the Pediatric Dengue Cohort Study in Nicaragua. To control for potential confounders, children who progressed to DHF/DSS (n=14) were matched with DF cases (n=81) using propensity score full matching. We used a multivariate regression with regularization to identify discriminant features between both clinical groups. The dataset (n=95) was split into training/testing subsets (50:50) for parameter estimation of the model via cross-validation (n=10). The median age was 10.6 years (interquartile range 7.9-12.6, female 52.6%). From a total of 3850 metabolomic features that were extracted, filtered, and normalized, only 56 were discriminant between children who developed DHF/DSS vs. DF during follow-up. Fifty-four were enriched in DF, while only two were enriched in DHF/DSS. Interestingly, a molecular feature with mass to charge 780.5538 was associated with DHF/DSS in primary and secondary infections (OR 3.66, 95%CI 1.39 to 14.42 and OR 3.59, 95%CI 1.38 to 13.89, respectively), while a molecular feature with mass to charge 777.695 was associated with DF in both primary and secondary infections (OR 0.07, 95%CI 0.01 to 0.42). Further analysis will identify metabolites associated with DF vs DHF and will explore metabolic pathways during the acute, critical and recovery phases of disease. Our results suggest that specific metabolomic markers may serve as early prognostic indicators during DENV infection.

7060

PREVALENCE AND PREDICTORS OF PERSISTENT SYMPTOMS POST-ACUTE COVID-19 INFECTION AMONG A COHORT OF FRONTLINE HEALTHCARE WORKERS IN BANGLADESH

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Despite evidence of a wide range of persistent symptoms among COVID-19 survivors, commonly known as long COVID, their frequency, clinical spectrum and risk factors are not well characterized. We assessed the prevalence and predictors of long COVID among healthcare workers (HCWs) in Bangladesh. Between July 2021-December 2023, we enrolled a cohort of HCWs from purposively selected 10 hospitals across Bangladesh to prospectively record COVID-19 illness. At enrolment, we captured data on HCWs' demographics, co-morbid conditions and COVID-19 illness. The study physician followed the participants biweekly to record any new and persistent symptoms following acute illness. We used the WHO case definition for long COVID (symptoms occurring 3 months from the acute COVID-19 infection and persisting for at least2 months). We performed a multivariable logistic regression to identify the predictors of long COVID. The analysis included 875 HCWs with lab-confirmed SARS-CoV-2 infection: 30% (261) doctors, 53% (468) nurses, and 17% (146) support staff. Themedian age of the HCWs was 35 (IQR, 29-44), and 69% (601) were female. Of the 875 HCWs, 462 (53%) reported persistent symptoms, with fatigue being the most common (83%), followed by brain fog (14%), cough (5%), breathing difficulties (4%),and joint pain (4%). HCWs with co-

morbidities (aOR 3.39, 95% CI 2.32-4.95; p=0.0001), breathing difficulty during the acute phase (aOR 2.84, 95% CI 1.77-4.55; p=0.0001), and those who required hospitalization during acute infection (aOR 2.25, 95% CI 1.53-3.04; p=0.0001) were more likely to develop persistent symptoms than HCWs without a history of co-morbidities, respiratory symptoms, or hospitalization. Nurses (aOR 1.36, 95% CI 1.01-1.85; p=0.04) were more likely to develop persistent symptoms than doctors. More than half of the HCWs in our cohort experienced long-term symptoms of COVID-19, with a greater risk observed among nurses and those with the co-morbid condition. These findings underscore the pressing need for long-term care and rehabilitation strategies with a standardized guideline to enhance the post-acute recovery of COVID-19 patients.

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VIRAL CLEARANCE IN COVID-19 PATIENTS WITH AND WITHOUT COMORBIDITIES IN BAMAKO, MALI.

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Coronavirus Disease 2019 (COVID-19) rapidly spreading to the rest of the world afteridentification. Comorbidities have increased morbidity and mortality rates and have been linkedto more hospitalization and intensive care unit (ICU) admissions. Thus, the aim of our study wasto determine the duration of the positivity of SARS-CoV-2 in COVID-19 patients with and withoutcomorbidities at the University Teaching Hospital (UTH) of Point-G, Bamako, Mali. A Crosssectional study was conducted between March 2020 and December 2022 enrolling SARS-CoV-2 RT-PCR positive patients in IRB approved protocol after written consent. Treatment was donein accordance with the national protocol combining Chloroquine, azithromycin, and vitamin C for7 days. Clearance was defined as anyone with two consecutive negative RT-PCR results within24 hours on nasopharyngeal swabs. One hundred and twenty-eight patients were included, andthe sex ratio was 1.6. While most patients had no symptoms, some had a wide range of symptomsfrom mild complaints to hospitalization at ICU. Among the 128 patients, 91 had comorbidities ofwhich 13.3% had critical symptoms. The average duration of viral clearance was 11.76days±4.48. The difference between age groups (years) was not statistically different, 14 days±0for [8-17], 11.5±3.54 for [18-60], and 12.6 ±6.39 for those aged greater than 60 years respectively(p= 0.24). In addition, we didn't find a difference on gender based with 12.3±5.31 for women and11.4±3.85 for men respectively (p=0.43). On the other hand, the average time to clearance ofpatients without comorbidities was higher than those with comorbidities, 13 days±3 vs. 11.30days±3.85 respectively (p = 0.007). The most common comorbidities identified were high bloodpressure (N=61), diabetes (N=36), sickle cell disease (N=8) and HIV (N=5). Viral RNA frompatients without comorbidities persists for a somewhat long period than those on patients withcomorbidities. A complete monitoring of these patients including the check for long COVID-19together with some immunological factors will determine the impact of COVID-19 on Human hostfactors.

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CLINICAL AND RISK FACTOR PROFILE OF OROPOUCHE VIRUS DISEASE DURING AN ONGOING OUTBREAK IN THE PERUVIAN AMAZON: FINDINGS FROM THE RIVERA ACUTE FEBRILE ILLNESS SURVEILLANCE STUDY.

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Oropouche fever is an emerging arthropod-borne zoonotic disease caused by the Oropouche virus (OROV) and leads to undifferentiated acute febrile illness (AFI) symptoms. OROV transmission is endemic among wild animal hosts in the forests and jungles of Central and South America, with occasional spillover to humans in the bites of midges and mosquitoes resulting in sporadic outbreaks. Incidence is increasing with over 500,000 cases and >30 outbreaks reported in the Americas, likely underestimated due to surveillance limitations. An outbreak of OROV is currently underway in Amazonian Brazil and Peru. RIVERA is an ongoing surveillance study of AFI etiology with a case-control design. AFI patients and matched controls are enrolled at urban and rural health facilities in and around Iquitos, in the Peruvian Amazon. Blood samples are tested for 32 locally relevant endemic and emerging pathogens using multiplex PCR. Using a nested case-control approach, OROV-positive AFI patients from the parent study were identified, and symptomatic AFI cases negative for all pathogens (unattributed AFI) were treated as controls. Relevant risk factors, signs and symptoms were compared, and logistic regression models fitted to the OROV positive/unattributed AFI binary outcome. From 8/25/2021, through 3/31/2024, 24 cases of OROV attributable AFI were identified, with 18 (75%) occurring in 2024. 1,012 unattributed AFI controls were recruited in the same period. The odds ratio for joint pain in the prior two weeks in cases compared to controls was a statistically significant 12.4 (2.89, 53.33). 16.7% (4) of OROV cases reported having traveled in the preceding 15 days compared with 7.2% of controls, giving a statistically significant odds ratio of 3.11 (1.12, 8.60). As the outbreak plays out, we will prospectively add new cases of OROV attributable AFI to the analysis, eventually giving large enough numbers for confounder matching and adjustment. OROV disease is characterized by muscle and joint pain, malaise, and headache in this study population in the Peruvian Amazon. Those contemplating travel within Amazonia, should take precautions against OROV insect vectors.

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THE GLOBAL HEALTH BURDEN OF CHIKUNGUNYA FROM 2011 TO 2020: A MODEL-DRIVEN ANALYSIS ON THE IMPACT OF AN EMERGING VECTOR-BORNE DISEASE

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Chikungunya is a mosquito-borne arboviral disease posing an emerging global public health threat. Understanding the global burden of chikungunya is critical for designing effective prevention and control strategies. However, current health estimates caused by chikungunya remain limited and are potentially underestimated. Considering the increasing risk of large-scale outbreaks driven by climate change and globalization, it is crucial to have a thorough understanding of the health burden of chikungunya. Therefore, we aimed to estimate the global and regional burden of chikungunya from 2011 to 2020 based on a data-driven simulation model. Based on worldwide case numbers from several publicly available sources, we estimated the disability-adjusted life years (DALYs) for the acute and chronic phase of chikungunya per country, super-region, and globally over a ten-year time period. Because the true burden of chikungunya is likely underreported due to misdiagnosis amongst others, we included an underreporting

factor for the reported case numbers. DALYs were calculated using the GBD methodology and represent the sum of the years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs). Our model revealed 17.5 million chikungunya cases in 110 countries between 2011 and 2020, causing 1.8 million DALYs lost in this ten-year timeframe. The majority was driven by long-term chronic illness, accounting for 1.4 million DALYs lost. YLDs take up most of the total DALYs, with 77%. YLLs in the acute phase were 426,000. In 2014, the highest DALY burden was recorded, with 640,000 DALYs. This aligns with the significant case numbers reported in the Latin American and Caribbean super-region that year. These results show that the burden of chikungunya should not be neglected. The disease's unpredictable nature in combination with the emerging spread due to climate change poses a significant threat to public health and can cause a substantial health burden for individuals affected.

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RAPID ALTERNATIVE DETECTION ASSAY OF SARS-COV2 RNA USING A ONE-STEP RT-FAST-MULTIPLEX PCR AND LATERAL FLOW IMMUNOASSAY

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COVID-19 pandemic has put emphasis on diagnosis and surveillance, and the subsequent shortage of diagnostics reagents and kits. It is strategic for the countries to be able to access, expand diagnosis, and acquire capacity to deploy alternative rapid accurate nucleic acid tests that are at lower costs. Here, we propose a visual SARS-CoV-2 detection using a one-step RT-fast-multiplex PCR amplification coupled to lateral flow immunoassay detection on a generic PCRD dipstick. Simplex fast-PCRs were developed by screening 17 primer pairs. They include 12 designed primer pairs targeting genes encoding the S protein (N=6 pairs), the N protein (N=2 pairs), the E protein (N=2 pairs), and the Open Reading Frame ORF1ab (N=2 pairs), and 5 other primer pairs selected from the published and validated WHO quantitative (q) RT-PCR protocols. For PCRD detection, labelled primers with Fam/Biotin or Dig/Biotin were used in fast RT-PCR protocols using RNA isolated from patients' nasopharyngeal swabs. Two primer pairs were selected based on their specificity, sensitivity, stability and absence of background to noise in the PCRD, and were used to set up a multiplex assay targeting two different viral genomic regions, N and E genes. The selected assay was then evaluated on 98 samples including 46 SARS-CoV+ with Ct values varying from 15 to 38, and 48 SARS-CoV-, comparing the performances to those of the RT-qPCR used to diagnose the patients by the virology lab of IPT. Our one step RT-fast-multiplex PCR coupled to PCRD showed a sensitivity of 86,96% (40/46) and a specificity of 97,75% (47/48). All patients presenting Ct values lower than 33 were positive with our assay. Patients with Ct values higher than 33 showed negative results. Our results brought proof of principle on the usefulness of the one step RT-fast-multiplex PCR assay coupled to PCRD for specific, sensitive, and rapid detection of SARS-COV-2 without requiring costly laboratory equipment, and thus at reduced costs and prone to be deployed when resources are limited. This new method of SARS- CoV2 detection appears as a good alternative for Covid19 diagnosis or screening at points of need.

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FIELD EVALUATION OF VALIDITY AND FEASIBILITY OF PAN LASSA RAPID DIAGNOSTIC TESTS FOR LASSA FEVER IN ABAKALIKI, NIGERIA: A PROSPECTIVE DIAGNOSTIC ACCURACY STUDY

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Background Lassa fever is a viral haemorrhagic fever with few options for diagnosis and treatment. A point-of-care bedside test diagnosing Lassa fever,adhering to REASSURED criteria, is not currently available but is urgently needed in west African regions with high Lassa fever burden. We aimed to assess the validity and feasibility of a rapid diagnostic test (RDT) to confirmLassa fever in people in Nigeria.Methods We estimated the diagnostic performance of the ReLASV Pan-Lassa RDT (Zalgen Labs, Frederick, MD, USA) as a research-use-only test, compared to RT-PCR as a reference standard, in 217 participants at a federal tertiary hospital in Abakaliki, Nigeria. We recruited participants between 2022 and 2023. The RDT was performed using capillary blood at the patient bedside and using plasma at the laboratory. The performance of the test, based on REASSURED criteria, was assessed for user friendliness, rapidity and robustness, sensitivity, and specificity.ResultsParticipants were aged between 0 and 85 years, with a median age of 33 years (IQR 22·0-44·3), and 24 participants were younger than 18 years. 107 (50%) participants were women and 109 (50%) were men. Although the specificity of the Pan-Lassa RDT washigh (>90%), sensitivity at bedside using capillary blood was estimated as 4% (95% CI 1-14) at 15 min and 10% (3-22) at 25 min, far below the target of 90%. The laboratory-based RDT using plasma showed better sensitivity (46% [32-61] at 15 min and 50% [36-64] at 25 min) but did not reach the target sensitivity. Among the PCR-positive participants with Lassa fever, positive RDT results were associated with lower cycle threshold values. Personnel conducting the bedside test procedure reported being hindered by the inconvenient use of full personal protective equipment and long waiting procedures before a result could be read.ConclusionThe Pan-Lassa RDT is not currently recommended as a diagnostic or screening tool for suspected Lassa fever cases. Marked improvement in sensitivity and user friendliness is needed for the RDT to be adopted clinically. There remains an urgent need for better Lassa fever diagnostics in low-resource settings.

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COMPARATIVE ANALYSIS OF NS1/IGM RAPID DIAGNOSTIC TESTS WITH NS1 AND IGM ELISA FOR DENGUE CASES AND ITS POSSIBLE CORRELATION WITH UNDER-REPORTING OF DENGUE CASES IN INDIA.

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According to the guideline of National Center for Vector Borne Diseases Control (NCVBDC), Government of India, IgM Antibody Capture ELISA kit (MAC ELISA) is provided for definitive diagnosis of dengue infection in the network of sentinel surveillance laboratories, established across the country. Therefore, a negative IgM ELISA result concludes to a dengue negative result. However, most patients with dengue infection get tested by Rapid Diagnostic Kit (RDT) during the first 4 days of the febrile illness

when IgM are not usually formed. This could be a possible factor behind under-reporting of Dengue cases in India. Our study aims to compare the results of the rapid test for dengue with NS1 and IgM ELISA and find the possible correlation that IgM negative NS-1 Antigen (NS1Ag) positive cases have with under-reporting of Dengue cases and to formulat an efficient combination of serological tests which could bring the "missed-out" Dengue cases in the fold of reported cases. Blood samples (n=264) from patients diagnosed with dengue with RDT in CCI Lab, SSL Hospital, BHU were used in our study from September 2023 to November 2023. We performed NS-1 ELISA and IgM ELISA by DENV NS-1 ELISA kit and IgM Antibody Capture MAC ELISA kit, respectively in all the samples. RDT of 264 samples, showed NS1 Ag positive in 251 sample out of which 239 were NS-1 positive and 12 were NS-1/IgM co-positive while 13 were IgM positive. Out of the 239 samples solely positive for NS-1Ag by RDT, we detected 237 sample to be positive through NS-1 ELISA and from the co-positive samples, we found 10 to be positive from NS-1 ELISA. Similarly, IgM positive samples via RDT were 25 in which 13 were solely positive for IgM out of which 12 were found positive by IgM ELISA while all 12 positive for both NS-1/IgM by RDT was positive by IgM ELISA. Overall, out of 264 samples, 257 (97.34%) were found positive for NS-1Ag via NS-1 ELISA and only 54 (20.45%) were positive for IgM via IgM ELISA. This shows almost 80% of the cases will be missed if only IgM ELISA is used for definitive diagnosis of Dengue. Our study suggests revision of guidelines, recommending NS1-ELISA alongside IgM for accurate dengue case reporting in India.

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DETECTION OF ANTI-MARBURG VIRUS IGG ANTIBODIES IN WATSA, DEMOCRATIC REPUBLIC OF THE CONGO: 25 YEARS AFTER OUTBREAK

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Marburg virus (MARV) is a rare, but potentially fatal, zoonotic pathogen responsible for Marburg virus disease (MVD) among humans and non-human primates. As a member of the *filoviridae* family of viruses, and close relative of *Ebolavirus*, historic outbreaks of MARV have almost been exclusively in Sub-Saharan Africa, with six alone reported between Uganda and the Democratic Republic of the Congo (DRC). The most recent MARV outbreak in DRC was reported in the Watsa/Durba region of Haut Uele province from 1998-2000-near recent reported MARV outbreaks in Uganda in 2022. With limited outbreaks of MARV and no available clinically approved MARV vaccines, this study sought to elucidate the prevalence of anti-MARV antibodies (Ab) among a mixed cohort of Watsa/Durba residents enrolled in 2023. This cohort (n = 370) included known MVD survivors of the 1998 outbreak (n = 6), close contacts (n = 29) and healthcare workers (n=318). Among this group, 6.8% of respondents reported recent travel to Uganda, and 9.5% were under 24 years of age - thus, born after the 1998 outbreak. Additionally, a small sample of the cohort (n = 3) indicated that their primary occupation was gold-panning - an activity shown to be a significant risk factor for MARV exposure. Using a multiplex bead-based immunoassay, the seroreactivity to MARV antigens was compared among the Watsa/Durba cohort with the cut-off for seroreactivity calculated at 6711 Median Fluorescence Intensity (MFI) for MARV glycoprotein (GP) and 11491 MFI for viral matrix protein 40 (VP40). In this comparison, the seroreactivity to MARV GP was 3.5% and 1.2% to MARV VP40. Interestingly, none of the seroreactive individuals were known survivors of the 1998 outbreaks. There were no associations between travel to Uganda and seroreactivity, nor employment as a goldminer. When using a less stringent cut-off to determine seroreactivity, all known survivors were classified as reactive for both MARV GP and VP40 - with 42.9% and 39.4% seroreactivity among the entire Watsa cohort. This high seroprevalence may indicate exposure to MARV or MARV-like antigens despite no active outbreak declared in the area.

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DETECTION AND PARTIAL GENOMIC CHARACTERIZATION OF ROTAVIRUS A STRAINS CIRCULATING IN DIARRHEAL OUTBREAKS IN LLAMA AND ALPACA FLOCKS FROM BOLIVIA

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In marginal agricultural areas of the Bolivian highlands, South American camelids (SAC) often constitute the indigenous farmer's only resource for food, clothing, and extra income. Acute diarrheal diseases affecting llama and alpaca newborns constitute major annual financial losses for farmers due to high levels of mortality. The objective of this study was to report the preliminary genomic analysis of two RVA strains affecting llama and alpaca flocks with diarrhea during March–June 2018 using an NGS-based approach. For this purpose, seven fecal samples were selected out of twenty five from animals with diarrhea in two highland regions. Following viral RNA extraction, cDNA library construction, and sequencing on an Iseq100 platform (Illumina), the genotype of each RVA gene was determined using the RotaC v2.0 tool. Sequences were compared to those of RVA strains obtained from GenBank. For each gene, multiple alignments were carried out using MAFFT 7.0, and phylogenetic trees were constructed using neighbor-joining in MEGA-X. Two samples isolated from alpaca and llama revealed the presence of two different genotypes: G8-P[14] and G3-P[14] that were partially classified as: G8-P [14]-I2-Rx-C2-M2-A11-N2-Tx-E3-H3 and G3-P [14]-I2-R2-C2-M2-A17-N2-T6-E3-H3, respectively. The isolated segment genotypes G8, P[14], I2, C2, M2, A17, E3, and T6 were closely associated with RVA strains isolated from vicuñas, guanacos, and alpacas, while R2, N2, and H3 were related to bovine-RVA strains, and G3 and A11 to strains identified in humans. This data suggests complex reassortment events among rotaviruses from diverse host species, which may have contributed to the genetic constellation of llama and alpaca RVA strains, highlighting the need for monitoring the potential emergence of novel rotavirus strains in the region.

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COMORBIDITIES AND HOSPITALIZATION RISK FROM DENGUE, CHIKUNGUNYA, AND ZIKA, PUERTO RICO, 2012-2023

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Previous research has established links between comorbidities and severe arbovirus infections, but there is limited research on how specific comorbidities impact hospitalization risk for each arbovirus. We analyzed data from 2012–2023 from the ongoing Sentinel Enhanced Dengue Surveillance System in Puerto Rico, focusing on adults aged ≥18 years diagnosed with dengue, chikungunya, or Zika virus infection via RT-PCR or serology. Mixed-effects logistic regression was used to evaluate associations between each comorbidity and arbovirus, adjusting for age group, sex, days post onset, previous dengue infection, respiratory viral coinfection, pregnancy, other comorbidities, and hospital site. To account for potential confounding by disease management practices, including admission for dengue warning signs, we additionally adjusted the dengue analyses for severe dengue status. Of 18,941 adults with acute febrile

illnesses, median age was 40 years [IQR: 26-57] and 52.6% were female. From these, 1,359 (7.2%) had Zika, 1,250 (6.6%) had chikungunya, and 594 (3.1%) had dengue. The most frequent comorbidities were obesity (Zika: 39.5%, chikungunya: 20.0%, dengue: 22.7%) and hypertension (Zika: 26.6%, chikungunya: 29.4%, dengue: 22.1%). Logistic regression showed increased odds of hospitalization among adults with hypertension and Zika (OR: 2.28, 95% CI: 1.21–4.28), diabetes and chikungunya (OR: 2.11, 95% CI: 1.28–3.48), and cancer and chikungunya (OR: 2.97, 95% CI: 1.27–6.95) compared with patients without those comorbidities. No associations were found between any comorbidity and hospitalization for dengue. No associations were found between asthma, congenital heart disease, high cholesterol, obesity, thyroid disease, or hospitalization for any arbovirus. While null findings for dengue may reflect the lower case count compared with Zika and chikungunya, future analyses leveraging the ongoing PR dengue epidemic could strengthen this investigation. These findings underscore the importance of understanding comorbidities for arbovirus management.

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TRANSMISSION DYNAMICS OF RIFT VALLEY FEVER AND CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUSES IN THREE DIFFERENT ECOLOGICAL REGIONS IN SENEGAL

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Rift Valley Fever (RVF) and Crimean Congo Hemorrhagic Fever (CCHF) are 2 emerging diseases with great economic, medical and veterinary impact. Humans can be infected through arthropod bites or contact with fluids or tissues from infected animals. As a result, livestock workers are at high risk of contracting these diseases. In the absence of specific treatment and licenced vaccines for humans, their epidemiology needs to be better understand for the implementation of preventive measures. Here we sampled humans, animals and arthropods in Kedougou (South) Barkedji (Center), and Podor (North) to analyze the circulation dynamics of RVF and CCHF. Indeed, at-risk and low risk healthy humans as well as cattles, sheep and goats from transhumant and sentinel herds were sampled. Ticks were collected by extirpation while mosquitoes were collected using different traps. Animal and human samples were tested by IgM and IgG ELISA while arthopod samples were tested by RT-PCR and virus isolation. In humans as in animals, the seroprevalence rates varied by virus, sex, locality, age and exposure level to animals for humans. RVF and CCHF were not detected in arthropods but a North-South gradient of relative abundance of their main vectors has been found. The data showed different transmission modes for these two viruses according to the area. Indeed, in the North and Center, RVF is circulating in at-risk and low risk populations, while CCHF is mainly detected in at-risk populations. However, in the South, a different transmission pattern has been observed with RVF circulating only in at-risk populations while CCHFV is circulating in both at-risk and low risk populations. These data suggest the enzootic and regular circulation of these viruses in Senegal with different transmission modes. This emphasize the need to reinforce surveillance and to consolidate data to identify risk factors in order to better prevent and control the spread of these viral infections.

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UNRAVELING THE TRANSMISSION DYNAMICS OF RIFT VALLEY FEVER : INSIGHTS FROM EAST AND CENTRAL AFRICA

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In East Africa, outbreaks of Rift Valley Fever (RVF), a vector-borne viral zoonosis, follow a 5-10-year cycle, with periods of quiescence in between. Although RVF outbreaks in animals are known to precede human cases, some human outbreaks may go unnoticed and are difficult to predict. A multi-country initiative of the Center for Research on Emerging Infectious Diseases-Eastern and Central Africa (CREID-ECA), undertook surveillance of acute febrile illness (AFI) and community human-animal linked seroprevalence studies to unravel the dynamics of cryptic RVF transmission. In Kenya, the Democratic Republic of the Congo (DRC) and Uganda, a 2-year longitudinal health facility-based study enrolled AFI cases while the human-animal serosurveys is assessing RVF burden in communities in direct contact with animals. Human and animal sera are analyzed for anti-RVF virus antibodies (ELISA) and viral RNA (PCR). Demographic, behavioral and environmental factors and RVF knowledge were assessed by questionnaires. In the health facility-based study, 4,755 subjects (median age 31 years, IQR 22-44, female 57.4%) were enrolled. In Uganda, 77 (4%) participants tested positive for IgM/PCR, documenting unusual sustained cases, in contrast to Kenya and DRC where no acute cases were detected. A total of 232 (4.9%) participants tested positive for total RVF antibodies: DRC 1.5%, Kenya 2.0%, and Uganda 9.5% ($p< 0.001$). At multivariable analysis, male participants (OR: 1.73; 95% CI 1.29, 2.32), age ≥50 years (OR: 1.64; 95% CI 1.16, 2.27), low schooling (OR: 1.49; 95% CI 1.05, 2.16) and sheep contact (OR: 1.6; 95% CI 1.00, 2.52) were significantly associated with RVF seropositivity. No significant association was found between RVF knowledge and previous RVF exposure. The community serosurvey in Kenya detected 1.8% (5/282) RVF IgG in humans and 4.4% (31/706) in livestock with goats significantly less affected than cattle (OR = 0.29 CI 0.12, 0.65). A substantial exposure to RVF was identified in the three countries with significant differences among them. Complete findings from this study will provide important insights for understanding the epidemiology of RVF in ECA.

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DENGUE VIREMIA AMONG FEBRILE PERSONS IN GRENADA, WEST INDIES

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Dengue virus (DENV) is endemic in Grenada, a small island developing state in the Caribbean, and circulates at low levels causing sporadic outbreaks during rainy seasons. However, the incidence of DENV is likely underestimated, as the gold-standard diagnostic test, reverse transcription polymerase chain reaction (RT-PCR), is not routinely available on the island. To more accurately determine the incidence of DENV infection in Granada, we performed febrile illness surveillance among adults and children in Grenada using serum RT-PCR for DENV, Zika virus (ZIKV) and chikungunya virus (CHIKV). Participants also provided demographic, symptom and mosquito behavioral data to evaluate factors associated with infection. Enrollment is ongoing, but to date 214 participants have been enrolled and tested from June 2023 through February 2024. Most participants are female (66%), with median age of 32 years (IQR 24-44) and were enrolled from private clinics throughout the country (66%). To date we have identified 27 positive DENV cases, an incidence of 12.6%, and one case of CHIKV, an incidence of 0.5%. No cases of ZIKV have been identified. The peak DENV incidence rate occurred in July 2023 (21.7% of samples tested positive). In interim univariate analysis comparing DENV positive and negative persons, those with DENV were less likely to live in a house (56 vs 85%, $p<0.01$), more likely to report use of window screens (63 vs 36%, $p=0.02$), and more likely to endorse controlling mosquito breeding sites around the home (100 vs 81%, $p=0.03$). We do not currently observe statistically significant differences between age, sex, education, income, subjective reporting of mosquitoes or reported symptoms. Our results show a relatively high incidence of DENV among febrile persons in Grenada. Possible epidemiologic risk factors are observed, but analyses will be ongoing as we continue to enroll additional participants.

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SURVEILLANCE OF CORONAVIRUS IN WILD MAMMALS SEIZED AND RESCUED BY THE NATIONAL FOREST AND WILDLIFE SERVICE OF LIMA, PERU

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Coronaviruses are pathogens that cause respiratory or enteric diseases in humans and animals. They exhibit high genome plasticity and replication errors, allowing them to change host range. The illegal trafficking of wildlife is a key factor in the emergence of infectious diseases, as it can lead to long-distance circulation and outbreaks of viruses in areas other than their usual environment. The aim of this study was to detect coronaviruses in mammals seized and rescued by the National Forestry and Wildlife Service from tracheal and rectal swabs using a pancoronavirus PCR assay that amplifies the RNA-dependent RNA polymerase (RdRp) gene. Ninety mammals were collected, of which 11.11% (10/90) tested positive by molecular analysis of the collected tracheal swabs. The species that tested positive were *Aotus* sp. (n=1), *Sapajus apella* (n=3), *Saimiri sciureus* (n=2), *Procyon cancrivorus* (n=1), and *Otaria flavescens* (n=3). Sequencing analysis of the ten positive PCR products indicated that nine of them shared 98% similarity with porcine epidemic diarrhea virus (PEDV) from GenBank. In addition, all of them were 100% identical to each other. The remaining sample showed a 95.52% similarity to feline coronavirus (FCoV). Both belonged to the genus Alphacoronavirus. We constructed a phylogenetic tree using sequences from this study and a large set available from GenBank. The maximum likelihood phylogenetic tree supports the hypothesis that PEDV sequences form a monophyletic clade, and FCoV sequence was found to be closely related to other FCoV from different countries. Notably, we only detected the viral RNA in the respiratory tract, despite the enteric nature of these viruses. This discovery confirms airborne transmission, a recently proposed alternative pathway. This study represents the first report of PEDV and FCoV in animals other than their natural hosts, highlighting the importance of epidemiologic surveillance.

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ASSESSING CORRELATIONS IN SEROLOGICAL STATUS TO MULTIPLE VACCINE-PREVENTABLE DISEASES: A CASE-CONTROL STUDY IN ZAMBIA, 2016

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Novel methods for assessing immunization system performance could provide additional insights on opportunities for improvements to reach unvaccinated children. One method to examine gaps in vaccination programs or assess the likelihood of recent infection history is to conduct serologic analyses measuring antibody responses to multiple vaccine-preventable diseases (VPDs), such as measles, diphtheria and tetanus. This study aimed to assess correlations in serological status across VPDs by testing whether individuals who are measles seronegative were more likely to have also missed diphtheria and tetanus vaccination. Nationally-representative samples stored in a biorepository collected during the 2016 ZAMPHIA study were previously tested for measles and rubella IgG serostatus. Paired measles seronegative and seropositive samples from this biorepository among children aged 2-to-10-years-old were identified by exact matching on gender, age, province (i.e., first-administrative unit) and HIV status and proximity matching for district (i.e., second-administrative unit), such that samples from districts closer together were more likely to be matched. Additional paired samples were identified by exact matching on gender, province and HIV status with proximity matching for age, such that samples with similar ages were more likely to be matched. For all selected samples (n = 1298), plasma sera were tested for diphtheria and tetanus IgG antibodies using enzyme-linked immunosorbent assays. Antibody concentrations were standardized using a four-point logistic regression and seropositivity was determined using internationally recognized thresholds. Serologic results for diphtheria and tetanus were analyzed based on underlying measles serostatus using conditional logistic regressions controlling for age and province. Results suggest differential titers over age and varying associations across measles serostatus. More broadly, this study illustrates a key use case of serological data on VPDs to identify the geographic and demographic reach of vaccination programs.

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A SYSTEMATIC LITERATURE REVIEW OF COMMUNITY ACUTE RESPIRATORY INFECTIONS (ARI) AND ACUTE GASTROENTERITIS (AGE) INCIDENCE RATES: A SYSTEMATIC LITERATURE REVIEW OF COMMUNITY-BASED OBSERVATIONAL STUDIES

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Acute respiratory infections (ARI) and acute gastroenteritis (AGE) are major causes of global morbidity and mortality. Most estimates of ARI and AGE incidence emphasize medically attended disease. Such data can severely underestimate true disease burden, especially in low- and middle-income countries (LMIC) where access to healthcare is limited. A systematic literature review of community-based observational studies was conducted to estimate community incidence rates of ARI and AGE. A PubMed search conducted in January 2024 identified 205 studies published between 1965-2017. Studies were included if sampling was performed at the community level with prospective monitoring for ARI or AGE. Studies of single pathogens, and those with follow-up of <12 months or insufficient data to calculate incidence were excluded. Weighted averages of incidence (cases per 1000 person-years (PY)) were calculated by age group from studies using similar case definitions. Meta-regression methods were conducted to identify differences in ARI/AGE incidence by study design characteristics. Eighteen studies of ARI incidence including 26,504 participants were identified, with 13 conducted in LMIC. Eleven studies of AGE incidence among 8,812 participants were identified, all from LMIC. The average all-age incidence rate was 1701 per 1000 PY (95% CI 1680-1723) for ARI and 320 per 1000 PY (95% CI 312-328) for AGE. Children under 5 had the highest incidence of both ARI (3188 per 1000 PY; 95% CI 3150-3227) and AGE (1349 per 1000 PY; 95% CI 1302-1398). ARI incidence was also elevated among adults ≥60 years (2405 per 1000 PY; 95% CI 2359-2453). ARI incidence rates were lower when symptom screening was performed virtually versus through in-person interviews (aIRR=0.30, 95% CI=0.13-0.68). In summary, this systematic literature review of community-based observational studies estimated a high incidence of ARI and AGE, particularly among young children and older adults. Accurate measurement of these conditions is vital to understand their burden and impact, and to help inform proper design, evaluation and implementation of related interventions.

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MARBURG VIRUS DISEASE OUTBREAK PREPAREDNESS AND RESPONSE IN THE SOUTH REGION OF CAMEROON, FEBRUARY - APRIL 2023

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Since the declaration of the first Marburg Virus Disease (MVD) outbreak in Equatorial Guinea on February 13, 2023, several neighboring countries have been implementing preparedness efforts to prevent MVD cross-border transmission and respond in case of confirmation. We described the experience of the South region, Cameroon, bordering Equatorial Guinea, in MVD preparedness activities. We conducted a descriptive study of preparedness from February to April 2023. We collected data from activity reports and from the regional staff involved in MVD preparedness. Preparedness activities were organized into 7 key pillars: coordination, epidemiological surveillance, specimen transportation and biologic diagnostic, case management and infection prevention and control, risk communication, emergency supply, continuity of essential care and services. The regional Incident Management System (IMS) was activated on February 13, 2023 with the Regional Delegate of Public Health as incident manager. Case definitions were developed and disseminated in the community and health facilities. We defined a suspected case as any resident or visitor in the region with sudden fever (T°≥38°c) or anyone with unexplained bleeding or any unexplained death since January 18, 2023. A total of 120 community health workers were recruited to strengthen rapid detection. At the 6 points of entry, 4272 passengers were screened to detect suspected MVD cases. A total of 159 alerts were investigated with 7 validated as suspected case and samples, collected and transported to Centre Pasteur Cameroon; all came negative. About 62283 persons were sensitized on MVD and prevention methods through radio spots and communications in gathering places. Three isolation and treatment units were established in the districts and protective equipment, disinfection and decontamination provided. A total of 14 biweekly meetings were organized and 11 situation reports developed. No MVD case was confirmed while the Region activated its IMS. The aim was to strengthen MVD preparedness activities. It is important to sustain preparedness efforts, not only for MVD but also for other epidemics.

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INVESTIGATING THE EPIDEMIOLOGY AND RISK FACTORS FOR DENGUE VIRUS AND CHIKUNGUNYA VIRUS INFECTIONS IN KARACHI, PAKISTAN

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Dengue virus (DENV) and chikungunya virus (CHIKV) are spread by *Aedes* species mosquitos that can thrive in pooled fresh water and have recently caused outbreaks across south Asia. Pakistan has endured recent outbreaks of DENV in addition to CHIKV, which can present similarly. Concurrently, Pakistan has also suffered repeated periods of severe flooding with some of the worst floods in history occurring in 2022, when approximately one-third of the country was under water. Given the ongoing climate crisis, this trend is likely to continue and worsen. With this reported re-emergence of infection we hypothesize there is a substantial burden of DENV and CHIKV in Karachi that can be linked to the built environment, human behavior, and other elements like surrounding litter. With shifting of vector proliferation to newer communities it is critical to better understand the epidemiology and transmission of these arboviruses in the region and the links to climate, especially in densely populated cities like Karachi. Through this cross-sectional pilot study of children we evaluated risk factors for dengue and chikungunya infection in the peri-urban setting in Karachi, in relation to the environmental impact, behavior, and demographics associated with infection. We recruited 500 children from two demographic and health survey program sites Karachi, Pakistan. In a single visit, participants are undergoing phlebotomy and survey administration to identify risk factors for exposure to these pathogens. All serum samples will be tested for DENV IgG and CHIKV IgG by enzyme-linked immunosorbent assay (ELISA) to determine seroprevalence. Within the cohort, 100 children had prior serum collected two years prior and will be evaluated for interval DENV/CHIKV seroconversions. This study is ongoing with active data collection and will be completed by mid-2024. Initial preliminary data suggests a high burden of DENV compared to CHIKV with majority of participants testing positive for DENV. With active data collection ongoing, we anticipate to continue to delineate the burden of DENV exposure in this cohort and will link to potential risk factors for the community.

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CLINICAL CHARACTERISTICS ASSOCIATED WITH DENGUE SEROTYPES IN AMAZONAS, PERU

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Dengue represents a major public health challenge worldwide. In Peru, a significant rise in dengue cases has particularly impacted the region of Amazonas, reporting a total of 24 981 cases and 28 deaths until the epidemiological week 7th of 2024, almost double the amount reported in 2023. In this study, we analyzed the clinical and epidemiological characteristics associated with the circulating serotypes in Amazonas by using 591 serum samples from dengue-confirmed patients collected in five provinces between 2021 and 2024. Serotype detection was conducted with a multiplex reverse transcription polymerase chain reaction (RT-PCR) assay. Statistical analysis was performed using R software v.4.3.1. Results revealed that 250 patients were infected by DENV-1 and 341 by DENV-2. According to our results, these serotypes have co-circulated across all affected provinces. For instance, DENV-1 caused the majority of infections in Bagua (13.6%) and Bongará (24.8%), while DENV-2, in Chachapoyas (9.4%), Condorcanqui (18.5%) and Utcubamba (59.8%) ($p < 0.001$). Additionally, dengue infections with warning signs were more frequent in patients with DENV-2 compared to DENV-1 ($p = 0.005$), and severe cases were exclusively reported in DENV-2 infections, highlighting its association with the severe form of the disease. Fever (DENV-1: 93.20% and DENV-2: 91.50%) and headache (DENV-1: 88.80% and DENV-2: 87.68%) were the most prevalent symptoms. Nausea (prevalence rate: 1.28, 95% CI: 1.02-1.62), conjunctivitis (prevalence rate: 1.78, 95% CI: 1.04-3.03), and abdominal pain (prevalence rate: 2.71, 95% CI: 1.35-5.45) showed a significant association with DENV-2. Its enhanced pathogenicity could be due to its faster replication, resulting in a higher viral load that could lead to severe cases. In conclusion, this study emphasizes the widespread circulation of DENV-1 and DENV-2 in Amazonas, highlighting the necessity to understand its transmission dynamics. Furthermore, it underscores the importance of real-time molecular surveillance that could provide an early prognosis of the disease severity.

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SEROPREVALENCE OF CHIKUNGUNYA VIRUS INFECTION IN SURAT THANI PROVINCE, THAILAND

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Chikungunya virus (CHIKV) infection is characterized by an abrupt onset of high fever, profound joint pain, and although low mortality, often lasting morbidity due to joint pain. Although globally distributed, there are multiple gaps in our understanding of CHIKV epidemiology, which pose challenges for the evaluation of CHIKV vaccines and countermeasures. CHIKV epidemics are frequently explosive, emerging unpredictably and waning to low levels after high levels of population immunity achieved. In 2008-2009 a large-scale outbreak of CHIKV occurred in 47 of 76 provinces in Thailand including Surat Thani province in southern Thailand. Despite a second outbreak in 2018-2019, little is known about the distribution of disease in the area. This study examined the seroprevalence and patterns of CHIKV transmission and persistence in communities within Surat Thani stratified by age. Investigators enrolled 1,700 participants aged 2 years and older to collect the blood for CHIKV serological testing in 10 rural, semi-urban and urban communities of Surat Thani province. Seropositivity was determined by CHIKV IgM/IgG (positive ≥40 EIA units) and CHIKV PRNT80 (NT80). The median age of enrollees was 25.0 years (IQR 9.3-39.9) with 62.5% of female gender. The primary occupation was student (49.6%). Overall, the seropositive rate for CHIKV IgM and IgG was 0.12% and 16.06%, respectively. Female had significantly higher levels of CHIKV IgM ($p=0.034$) and IgG ($p=0.007$) than male participants. Seropositive data by age group indicated that subjects between 18-50 years old had significantly higher IgM ($p=0.053$) and IgG ($p<0.0001$) levels than other groups. CHIKV IgG seropositive rate increased in an age dependent manner (from 4.6 years to 88 years old). The CHIKV NT 80 showed good correlation with all positive CHIKV IgG. The 2 urban community sites showed significantly higher seropositivity by CHIKV IgG than rural and semi urban sites ($p=0.048$ and 0.006 respectively) but was not significant based on CHIKV NT80 level. This data identifies CHIKV seroprevalence in the study area and will be crucial for future vaccine and countermeasure studies.

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FACTORS ASSOCIATED WITH DEATH IN PATIENTS ADMITTED WITH EBOLA VIRUS DISEASE TO EBOLA TREATMENT UNITS IN GUINEA, SIERRA LEONE, AND LIBERIA DECEMBER 2013 TO MARCH 2016

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The 2013-2016 West African Ebola Virus Disease (EVD) outbreak resulted in 28,600 cases and 11,300 deaths officially reported to the World Health Organization. Previous studies investigating factors associated with death had conflicting findings, interventions showing promising outcomes had small sample sizes, studies were often single- or dual-country based and most focused on laboratory-confirmed EVD and not on clinically-suspected EVD. We used the Ebola data platform of the Infectious Disease Data Observatory (IDDO) to review individual patient records to assess factors associated with death, and particularly whether there were differences between laboratory-confirmed and clinically-suspected cases. This was a cohort study involving analysis of secondary data in the IDDO database. The study population included all patients classified as having either clinically-suspected or laboratory-confirmed EVD, admitted to 22 Ebola Treatment Units (ETU) in Guinea, Liberia and Sierra Leone between December 2013 and March 2016. Baseline characteristics and treatments were documented along with ETU exit outcomes. Factors associated with death were investigated by multivariable modified Poisson regression. There were 14,163 patients, of whom 6,208 (43.8%) were laboratory-confirmed and 7,955 (56.2%) were clinically-suspected. Outcomes were not recorded in 2,889 (20.4%) patients. Of the 11,274 patients with known outcomes, 4,090 (36.3%) died: 2,956 (43.6%) with laboratory-confirmed EVD and 1,134 (18.8%) with clinically-suspected EVD. The strongest risk factor for death was confirmed disease status. Patients with laboratory-confirmed disease had 2.9 times higher risk of death compared to clinically-suspected patients. Other factors significantly associated with death included a higher risk for patients aged ≥60 years and a lower risk for patients in Sierra Leone. Although laboratory-confirmed patients admitted to ETUs fared worse than clinically-suspected patients, the latter still had a substantial risk of death and more attention needs to be paid to this group in future EVD outbreaks.

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MODELING DENGUE FORCE OF INFECTION AMONG EXPATRIATES LIVING IN THAILAND

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Dengue fever virus (DENV) is a mosquito-borne illness that causes as many as 96 million cases of dengue fever annually. Two dengue vaccines are now licensed for use in several countries, but a vaccine that confers sustained tetravalent protection in DENV-naive individuals remains aspirational. Travelers from non-endemic regions have unique viral exposure histories and associated immunological profiles. The WHO recommends Takeda's Qdenga® vaccine for populations with at least 60% DENV seroprevalence but does not make specific recommendations for travelers. Models of dengue force of infection in children suggest that most people born in dengue endemic areas (DEA) will be DENV seropositive by age 6; whether non-locals share this exposure profile is a critical epidemiological question in the recommendation of novel dengue vaccines for travelers. In this analysis, we use catalytic models of force of infection (FOI) to estimate time to 60% DENV seropositivity for a cross-section of expatriates in Thailand. Demographic and risk history data was collected using a short survey. Blood specimens were tested for neutralizing antibody titers against all four DENV serotypes, Japanese encephalitis, and Zika, using plaque reduction neutralization tests. Our full model adjusted for average daily time outside, years not exposed to DENV, gender, living setting, and four mosquito prevention strategies: repellent, nets, long sleeves, and air conditioning. We estimated an adjusted average FOI of 0.016 (95% CI: 0.004-0.069) per year spent in DEA (approx. 55.7 years to 60% seropositivity). Urban living setting was significantly associated with DENV seropositivity (OR = 2.66; 95% CI: 1.18-6.00) in the adjusted model. These findings suggest that expatriates have a dengue exposure profile unique from locals, which is characterized by a lower force of infection. With the current need to deprioritize vaccination of dengue-naive individuals, this suggests that even long-term travelers will require separate vaccine recommendations.

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TRENDS IN MORTALITY CAUSED BY VIRAL HEPATITIS IN THE UNITED STATES POPULATION: A RETROSPECTIVE CROSS-SECTIONAL STUDY USING THE CDC WONDER DATABASE.

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In this retrospective cross-sectional study, spanning from 1999 to 2023, we examined mortality trends using national mortality datasets among individuals infected with hepatitis virus. Our aim was to analyze these trends in mortality among US residents by demographic characteristics including age, gender, race/ethnicity, and geographic characteristics like urbanization and census region. The national mortality data from the multiple causes of death files in the CDC WONDER Database were queried by applying the ICD-10 codes as B15-B19 for viral hepatitis to identify deaths among the US population from 1999 to 2023. Trends in age-adjusted mortality rate (AAMR) were assessed for age groups, gender, race/ethnicity, urbanization, and census region using state-level data. Results were expressed as annual percentage changes (APC), average annual percentage changes (AAPC), and 95% confidence intervals (CI). The data was analyzed on statistical software i.e., the Joinpoint regression by National Institutes of Health (NIH version 5.0.2). The county-level data was analyzed according to the National Center for Health Statistics [NCHS] urbanization classification scheme 2013. The crude mortality rate for viral hepatitis from 1999-2023 was found to be 4.4 per 100,000 US population and AAMR was 3.4 per 100,000 US population. Mortality rates for viral hepatitis were found to be highest for the male gender, age group 55-74 years, American Indians or Alaskan Natives, Census Region West, and metropolitan suburban areas (although rural areas showed the highest upgoing trends with AAPC: +2.64). Geographically, states in the top 90th percentile for viral hepatitis-associated mortality included the District of Columbia, Oklahoma, Oregon, California, New Mexico, and Washington. These findings provide valuable insights into age-adjusted mortality patterns among the United States population with these diseases. Mortality rates among the US population with viral hepatitis were noted to slightly decrease overall from 1999 to 2023 (AAPC -0.61, p=0.002), and certain subgroups with specific demographic and geographic characteristics had high AAMR.

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DENGUE SEROPREVALENCE AND FORCE OF INFECTION IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Introduction: There is limited knowledge on dengue transmission in the Democratic Republic of Congo (DRC). However, recent publications highlight an increasing dengue prevalence among individuals presenting with febrile symptoms in Kinshasa, the capital of DRC. The extent of dengue circulation in the country is unknown, which poses questions around the burden of dengue infection and the potential impact of new interventions. The objective of our analysis was to assess the age-stratified dengue seroprevalence and estimate the force of infection (FOI, per-capita risk of dengue infection for a susceptible subject) in Kinshasa and Matadi. Methods: By leveraging samples collected from individuals aged 0 to 94 years in a SARS-CoV-2 serosurvey, we assessed the age-stratified dengue seroprevalence using a combination of two Enzyme-Linked Immunosorbent Assay (ELISA) IgG antibody tests, respectively a purified dengue particles test (ELISA-1) and a recombinant non-structural protein 1 (NS1) (ELISA-2) assay and a serotype-specific Plaque Reduction Neutralization Test (PRNT) for all 4 dengue serotypes. We employed a Bayesian framework to estimate the FOI for each location and reconstruct the results obtained across each testResults: Overall, 3580 plasma samples were tested by IgG ELISA-1 and a subset of 202 samples was also tested by IgG ELISA-2 of which 70 were also tested by PRNT. Our findings reveal endemic dengue circulation in DRC, with an average FOI of 2.9% (95% CrI: 2.2-3.9) in Kinshasa and 1.4% (95% CrI: 0.9-2.0) in Matadi and an overall population seroprevalence of 41% (95% CrI: 34-48) in Kinshasa and 23% (95% CrI: 17, 32) in Matadi respectively. Conclusion: These results confirm endemic dengue transmission in different regions of DRC and highlight the dengue transmission differences between the two cities. These findings underscore the importance of establishing dengue surveillance in the country, to monitor prevalence and changes in transmission in a changing climate.
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A MULTICENTER STUDY TO ASSESS THE EFFECTIVENESS OF AN INACTIVATED COVID-19 VACCINE AGAINST HOSPITALIZED COVID-19 IN THE PHILIPPINES

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There is limited information on the protection conferred by Coronavac (Sinovac, China), an inactivated COVID-19. We conducted a multi-center, hospital-based test-negative case control study to determine the vaccine effectiveness of a complete CoronaVac regimen with or without a homologous or heterelogous booster dose against hospitalized and critical COVID-19.

Between 9 November 2022 and November 2023, we enrolled adult patients experiencing acute respiratory illness (ARI) admitted to three government referral hospitals. We collected clinical and socio-demographic data, vaccination histories, and oro/nasopharyngeal swabs for SARS-CoV-2 RT-PCR testing from eligible patients who consented to participate. Patients testing positive in at least one SARS-CoV-2 RT-PCR test were classified as cases while those testing negative served as controls. Critical COVID-19 was defined as having either respiratory failure, acute respiratory distress syndrome, sepsis/shock or multi-organ failure. We enrolled 2,365 participants, and 165 (7.0%) were SARS-CoV-2 positive. More than a year after the last vaccine dose, unmatched analysis showed that full vaccination of CoronaVac did not protect against hospitalized and critical COVID-19 (VE:0.69%,CI: -23.7%-20.3%, p=0.9511 and VE:5.4%, CI:17.8%-24.0%, p=0.6201 respectively), but conferred 31.3% (CI: 9.5 - 47.9, p=0.0077) protection against death. The protection against death increased to 45.8%(CI:18.6%-63.8%, p=0.0031) with a booster dose. Cases were significantly older than the controls (mean age±SD: 58.12±20.15 vs. 53.41±17.60, p=0.001). An age-matched analysis showed that a full regimen of CoronaVac provided 61.3% (CI:5.3% - 84.2%,p=0.0376) protection against critical COVID-19, and 27.1% (CI:-25.3%-57.6%, p=0.2528) against death, which increased significantly to 91.2% (CI: 30.7% - 98.9%, p=0.0210) and 60.1% (CI:16.4%-81.0%, p=0.0150) with a booster dose, respectively. Our findings show that a primary series of inactivated COVID-19 vaccination provided protection against critical outcomes over time, which was enhanced by booster vaccination.

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MOLECULAR EPIDEMIOLOGY IMMUNOLOGICAL RESPONSES TO SARS-COV-2 OTHER RESPIRATORY VIRUSES IN SELECTED URBAN RURAL AREAS OF GHANA

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Ghana implemented non-pharmaceutical interventions and vaccination campaigns to mitigate the impact of COVID-19. However, the effectiveness of these interventions has not been fully evaluated. Understanding the prevailing levels of exposure and immunity in different sociodemographic settings offers an important overview of the epidemiology of respiratory viruses in these populations. This study seeks to determine the prevalence of SARS-CoV-2 and other respiratory viruses (RVs) in selected areas in Ghana, using Kumasi Metropolis as a case study. Nasopharyngeal swabs and blood (serum) samples of 109 participants above 10 years in Kumasi were collected with consent. Their socio-demographic data, clinical symptoms, and vaccination status were taken with structured questionnaires. Viral RNA was extracted and tested with multiplex real-time RT-PCR detecting respiratory viruses including SARS-CoV-2, Influenza A, Human Rhinovirus (HRV), Adenovirus, Picornaviruses, and common cold coronaviruses. Samples with Ct ≤ 30 will be sequenced and analysed. Results from 109 participants from Kumasi who were aged 10-55 years, mostly females (62.4%) showed an RNA positivity rate of 1.0% for both SARS-CoV-2 (n =1) and HRV (n = 1). Both positive cases were females aged 35 and 37 with headache and fever as common symptoms, traders, not living alone, married and both cases were detected in the Manhyia study site. None of these characteristics was found to have a statistically significant association to respiratory virus positivity as determined by a Fisher's exact test (P < 0.05). We observed a low circulation of RVs in Kumasi. The collected serum samples will be tested for SARS-CoV-2 antibodies, their longevity and new seroconversions by ELISA. Further sampling will be done in urban and rural areas represented by Tamale, Buoyem, Forikrom, and Obuasi to estimate the prevalence of SARS-CoV-2 and other respiratory viruses circulating in Ghana. The mean IgG levels will be analyzed using R to determine the difference in seroprevalence for rural and urban areas. Individuals with a positive ELISA result will be sampled again after one year.

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BEYOND RAINFALL: ENVIRONMENTAL DRIVERS OF HISTORIC RIFT VALLEY FEVER OUTBREAKS IN KENYA

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Rift Valley fever (RVF) is a viral vector-borne zoonosis of the *Phlebovirus* genus, causing widespread abortion in livestock with potential to cause severe disease in humans. RVF was first identified in Kenya in 1931 and has since led to numerous outbreaks that have resulted in loss of life and livelihoods. Several environmental variables have been linked to cases in some areas, but these efforts have not considered ecologically relevant spatial heterogeneity on a national scale. Here, we collated a database of historic cases in Kenya by expanding methods described in previous systematic reviews. To account for underreporting, we transformed RVF as a binary outcome variable for a specific year and geographic regions divided according to existing Agro-Ecological Zones (AEZ) in all models. We selected scaled temperature, precipitation, potential evapotranspiration, Palmers Drought Severity Index (PDSI) and soil moisture as environmental predictors. Linear relationships were tested using Linear Mixed Models (LMM), with AEZ and species as random effects. Non-linear relationships were tested using General Additive Models (GAM), fit to datasets subset by AEZ. The best fit LMM included precipitation and PDSI which showed precipitation to have a strong positive effect and PDSI a slightly negative effect on RVF occurrence in Kenya, with AEZ significant as a random effect. Including AEZ as a random effect produced the top 17 LMM models and the non-linear relationships (in the GAMs) varied in magnitude and shape depending on AEZ, suggesting the relationships between the environment and RVF are distinct among regions. These findings support the hypothesis that heavy rainfall after drought, which decreases soil permeability, is an environmental risk factor for RVF transmission, and this effect is more significant in some AEZs potentially due to varying soil types. The results of this study will contribute to ongoing national efforts to map the risk of RVF in Kenya. We conclude the drivers of historic RVF outbreaks extend beyond solely rainfall and further climate extremes, such as drought and flooding, may lead to more frequent outbreaks.

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CAN'T START A FIRE WITHOUT A SPARK: HIGHLY VARIABLE VIRUS IMPORTATION RATES UNDERLIE THE UNPREDICTABLE TIMING OF CHIKUNGUNYA OUTBREAKS

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The epidemiology of chikungunya virus (CHIKV) is notoriously sporadic. Outbreaks of this mosquito-borne pathogen are often intense and short-lived and, in many populations, are not repeated for years, or even decades. This unpredictability presents a major challenge to public health preparedness and intervention trial planning. Epidemiological theory suggests three primary drivers of the frequency of outbreaks of a pathogen such as CHIKV. Two of those drivers, the basic reproduction number (R_0) and population immunity, are commonly estimated. The third—the importation rate of the pathogen itself—remains elusive and poorly quantified, although for CHIKV this importation is believed to occur mainly through the movement of infected humans. To address this gap, we performed a model-based analysis of age-stratified serological data that yielded joint estimates of R_0, population immunity, and the importation rate of CHIKV infections for each of 35 populations affected by CHIKV between 1950 and 2020. Our approach leverages the fact that some imported infections may not have resulted in chikungunya outbreaks due to population immunity or stochastic fade-out. Estimated annual CHIKV importation rates spanned orders of magnitude across the populations considered, with posterior means ranging from one imported infection per 4.5 to 80 million residents. Combining these values with R_0, immunity, and growth rate estimates for each population results in highly variable expected inter-epidemic periods for chikungunya, ranging from as few as eight years between outbreaks or as many as 100. This variability highlights the significance of the CHIKV importation rate as a driver of chikungunya's sporadic epidemiology. More broadly, these results demonstrate the value of better understanding pathogen importation rates for enhancing public health preparedness.

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RISK FACTORS FOR LASSA FEVER VIRUS INFECTION IN A POPULATION-BASED COHORT STUDY IN SIERRA LEONE

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An improved understanding of Lassa fever virus (LASV) epidemiology is needed to inform efficacy trials for LF vaccines. Investigators at Kenema Government Hospital (KGH) in Sierra Leone, Tulane University, and IAVI implemented a prospective study (X100) to characterize risk factors for incident LASV exposure. Participant data and blood was collected using finger sticks and dried blood spots (DBS) at two time points (baseline and 18-24 months later). DBS were tested by pan-LASV-NP IgG ELISA (Zalgen Labs, MD, USA). Re-exposures were defined as seropositive at baseline, with a ≥4x antibody titre at follow up. Independent predictors of incident exposure were characterized with a mixed effects model to control for cases clustering within households. Between April 2021 and May 2022, 8,237 residents aged ≥2 years were enrolled; baseline and follow-up data were available for analysis for 6,447 (78.3%) participants, our analysis set for this abstract. Of the 6,447 participants, 655 (10.2%) had evidence of incident exposure to LASV. While controlling for other covariates, we found that residing in Kenema district, a traditionally "higher risk" geographic area, was associated with incidence (incidence rate ratio IRR 1.73, 95% CI: 1.41-2.11) as was being seronegative at baseline (IRR 2.26, 95% CI: 1.82-2.78). Children ages 2-10 were less likely to become LASV positive compared to other ages (IRR 0.72, 95% CI: 0.59-0.88). Efforts to store food securely from rodents, perhaps as a proxy for known rodent infestations, was associated with incidence (IRR 1.74, 95% CI: 1.26-2.39) as was having cleared all bush within 5 meters of the dwelling, suggesting rodents moved into the house rather than into foliage that was >5 meters from a home (IRR: 1.55, 95% CI: 1.27-1.89). We observed multiple individual and household characteristics associated with high rates of LASV seroincidence in this rural, population-based cohort of Sierra Leonians at risk of LASV infection. These data improve our understanding of LASV epidemiology and will inform clinical trial design, recruitment, and conduct.

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MOLECULAR DIAGNOSIS AND CLINICAL CHARACTERISTICS OF CHIKUNGUNYA VIRUS INFECTIONS IN THE PERUVIAN JUNGLE, 2020-2023

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Chikungunya virus (CHIKV) infections cause acute febrile illness associated with unspecific symptoms that can progress to joint pain and arthritis over time. In 2015, Peru reported its first autochthonous case, followed by an outbreak nationwide. Peruvian Andean and jungle regions report prevalence rates ranging between 2.4% and 9.4%, sometimes surpassing dengue as the primary cause of AFI. In high-risk areas, it is important to differentiate CHIKV infection from other arboviruses due to its concurrent circulation. To evaluate the prevalence and clinical manifestations of CHIKV in Peruvian patients, we conducted a study in the Peruvian jungle. AFI patients were enrolled if they had a 38°C axillary temperature and a source of infection that was unknown. Infection signs and symptoms were recorded using a standardized format after they were evaluated. Blood samples were collected for the detection of CHIKV infection by qRT-PCR and/or IgM detection using ELISA assays. During the study period (2020 through 2023), a total of 4413 patients with AFI were enrolled. 256 (5.80%) CHIKV cases were identified by qRT-PCR, and 472 (10.69%) were identified by IgM detection. Most infected patients were adults aged between 18-39 years (52.73% for qRT-PCR positive and 49.15% for IgM positive), with females being the predominant affected gender (54.69% for qRT-PCR positive and 62.92% for IgM positive). The most common clinical symptoms in CHIKV qRT-PCR and IgM positive patients were headaches (87.85% and 90.16%), myalgias (77.33% and 74.14%), and arthralgias (74.90% and 78.95%). The highest number of positive cases occurred in July 2021 (10.45%). In conclusion, our study underscores the substantial burden of Chikungunya virus (CHIKV) in the Peruvian jungle, revealing notable prevalence rates among patients with acute febrile illness. In regions where CHIKV co-circulates with other arboviruses, robust surveillance and diagnostic efforts are particularly important. It is crucial to understand the epidemiology and clinical presentation of CHIKV infection in order to develop effective disease management and control strategies.

7090

UNVEILING THE PATH TO POLIO ERADICATION: INSIGHTS FROM CONSECUTIVE SEROPREVALENCE SURVEYS AMONG PAKISTANI CHILDREN

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After the cessation of the trivalent oral poliovirus vaccine (tOPV), Pakistan has maintained immunity to type 2 poliovirus by administering inactivated polio vaccine (IPV) in routine immunization alongside monovalent OPV

type 2 (mOPV2) and IPV in supplementary immunization activities (SIAs). This study assesses the poliovirus type 2 immunity change after tOPV cessation and due to SIAs with mOPV2 and IPV among children aged 6-11 months. Three cross-sectional sequential serological surveys were conducted in 12 polio high-risk areas of Pakistan. Twenty-five clusters from each geographical stratum were selected using probability proportional to size. Seroprevalence of type 2 poliovirus was 49%, with significant variation observed among surveyed areas; <30% in Pishin, >80% in Killa Abdullah, Mardan & Swabi, and Rawalpindi. SIAs with IPV improved immunity from 38% to 57% in Karachi and 60% to 88% in Khyber. SIAs with IPV following mOPV2 improved immunity from 62% to 65% in Killa Abdullah, and combined mOPV2 and IPV SIAs in Pishin improved immunity from 28% to 89%. Results also reflected that immunity rates for serotypes 1 and 3 were consistently above 90% during all three phases and across all geographical areas. The study findings highlight the importance of implementing effective vaccination strategies to prevent the re-emergence of poliovirus. Moreover, the results provide crucial information for policymakers working towards achieving global polio eradication.

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ADDRESSING CHALLENGES IN WASTEWATER EPIDEMIOLOGICAL SURVEILLANCE IN TROPICAL REGIONS: COSTA RICAN EXPERIENCE

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The increasing recognition of wastewater-based epidemiology (WBE) as an invaluable tool for public health surveillance has prompted the initiation of a comprehensive program in Costa Rica. This study focuses on a pivotal wastewater treatment plant (WWTP) in the Great Metropolitan Area, serving approximately 10% of the Costa Rican population. Commencing in June 2023 and concluding a year later, the program systematically monitors the presence of various viral pathogens, including hepatitis A, enterovirus, rotavirus A, norovirus G1 and G2, Influenza A, Monkeypox, and SARS-CoV-2. This monitoring involves a concentration step followed by RNA extraction, one-step reverse transcription, and quantitative polymerase chain reaction (RT-qPCR) amplification with TaqMan probes. Despite observing an increasing viral pathogen load in wastewater and reported cases, particularly during the rainiest months of October and November, we noticed a reduction in the pathogen viral load. This reduction was confirmed by values obtained for our internal controls: PMMoV and somatic coliphages, suggesting external factors such as rainfall that can affect detection efficiency. Nevertheless, the program successfully identified the presence of hepatitis A in wastewater, coinciding with a significant outbreak of Hepatitis A in the Great Metropolitan Area. Additionally, Influenza and SARS-CoV-2 were concurrently detected with a noticeable increase in reported cases of respiratory diseases. This approach enhances our understanding of the dynamics of infectious diseases and strengthens the overall public health surveillance system in Costa Rica.

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HIGH CIRCULATION OF AVIAN INFLUENZA H9N2 SUBTYPE IN LIVE BIRD MARKETS: A NEW EMERGING THREAT IN SENEGAL

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Avian influenza virus (AIV) of the H9N2 subtype has gained increasing attention in recent years due to its widespread circulation in poultry populations and sporadic zoonotic transmission to humans. In Senegal, only one human case of H9N2 infection has been reported so far, despite ongoing influenza surveillance since 1996. However, until now, this surveillance was only focused on humans and the country has never experienced documented H9N2 infection in poultry even though unusual poultry outbreaks associated with mortalities are occasionally reported. So here, we present results of an active influenza surveillance effort focusing on live-bird markets (LBM). The Senegalese National Influenza Center initiated in December 2023 an active influenza surveillance in two LBM in Dakar. Each week, fresh feces, water troughs, carcass washing water and cloacal swabs from birds are collected in each market. Samples are examined by RT-PCR for the presence of, among others, AIV H9, H7 and H5 subtypes, which are then characterized further by next-generation sequencing. In total, 205 samples have been collected so far. Overall, AIVs were detected in 100 of the 205 poultry samples analyzed (48.8%). AIVs were most frequently detected in birds drinking water (32%), carcass washing water (28%), fecal samples (28%), and less frequently in cloacal swabs (12%). All influenza A-positive isolates were H9N2 subtypes. Genome sequences were obtained for 22 isolates and the phylogenetic analysis revealed that Senegalese H9N2 viruses belong to the G1-like lineage and are closely related to H9N2 viruses identified in Burkina Faso, Niger and Tunisia. Furthermore, H9N2 viruses from Senegalese poultry clustered with the H9N2 human case detected through the national influenza surveillance, and possessed multiple molecular markers associated with an increased potential for zoonotic transmission and virulence. Results of this study contribute to our understanding of the epidemiology and genetic characteristics of H9N2 in Senegal and highlight the need to strengthen surveillance and control of AIV in live poultry markets to mitigate public health threats.

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THE PHAGE FACTOR IN ANTIBIOTIC RESISTANCE SPREAD IN THE HOSPITAL AND URBAN SEWAGE SYSTEMS IN GREATER ACCRA REGION, GHANA

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Phages, which are recognized for their endurance and resistance, play an important role in spreading antibiotic resistance genes (ARGs) throughout the environment. This study aimed to assess the prevalence of ARGs in viral fractions of hospital wastewater and urban wastewater sampled from various sites in Greater Accra, Ghana. Whole genome sequencing was performed on DNA isolated from the samples, which was then assembled using the MetaViral SPADES platform. Subsequently, ABRicate was utilized to identify ARGs from the viral contigs. The findings revealed a wide array of ARG classes such as cephalosporin, macrolide, Carbapenem, aminoglycoside, and tetracycline antibiotics prevalence across hospitals, with notable prevalence of the *bla* genes, *mcr-1* genes, and *mecA* genes. Remarkably, ARGs detected in hospital wastewater were concomitantly detected in raw urban wastewater, indicating potential contributions from multiple sources. The study emphasizes the significance of exploring the carriage of ARG genes in the viral fraction and the role of hospital

wastewater in ARG dissemination. These findings offer valuable insights into the dynamics of antibiotic resistance in wastewater systems, thereby guiding strategies to mitigate its spread and impact on public health.

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COMET: A DATABASE TO UNTANGLE VIRAL, MOSQUITO, AND ABIOTIC DRIVERS OF VECTOR COMPETENCE

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Many recent emerging pathogens are arthropod-borne (arbo-) viruses, with over one-third of the world's population at risk for infection. Responding to "the next Zika" and forecasting future risks of vector-borne disease requires laboratory-based studies of mosquito infection. These experiments are often the best way to measure vector competence, and are critical to understanding outbreak risk. While hundreds of these studies have been conducted in the last few decades, their data is rarely shared or readily available. Further, there are numerous challenges to interpreting and comparing different studies. These include inconsistent terminology, insufficient experimental/methodological detail, and differences in reported outcomes. In collaboration with arbovirology labs at several institutions, we therefore compiled, cleaned, and standardized data on the infection, dissemination and transmission of mosquito-borne viruses, from published experimental studies into a database called COMET (vector competence experimental testing). We have thus far compiled over 100,000 measurements of mosquito vector competence for human-infective viruses from over 100 published studies. Using these data we will perform meta-analyses and modeling to decompose and predict extrinsic (temperature, humidity, other unaccounted-for experimental variability) and intrinsic (mosquito-omics, viral-omics) drivers of vector competence. In addition to its role in supporting research on vector-virus interactions and arboviral evolution, we anticipate that COMET will be an invaluable resource for public health agencies interested in contextualizing risk from local vectors during future disease outbreaks.

7095

CO-OCCURRENCE OF VIRAL PATHOGENS IN CHILDREN: INVESTIGATING RESPIRATORY AND GASTROINTESTINAL SYMPTOMS IN SÃO PAULO, BRAZIL, 2021

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Pneumonia and diarrhea are leading causes of death in children under 5 worldwide. This study investigates viral agents causing respiratory illness in ≤ 3 years old patients with diarrhea in São Paulo, Brazil, during spring 2021. Twenty paired samples (oropharyngeal swab and feces) were screened for viruses including HBoV, HAdV, RVA, EV, PeV-A, NoV, SARS-CoV-2, Influenza A/B, RSV and HAstV. Positive samples for HAdV, HBoV, EV, NoV and PeV-A underwent sequencing and phylogenetic analysis. HBoV and NoV were detected in 75% (15/20) of cases, with co-infections in 65% (13/20), suggesting their involvement in respiratory illness with gastrointestinal symptoms in children. HAdV, EV, PeV-A and RSV were each found in two cases (10%; 2/20), with Flu A identified in one case (5%; 1/20). A substantial number of co-infections involving respiratory and enteric viruses were observed (75%; 15/20), notably HBoV+NoV (40%; 8/20) and NoV+PeV-A (5%; 1/20). Triple infections occurred in 7 cases: HBoV+NoV+RSV (10%; 2/20), HBoV+NoV+HAdV (10%; 2/20), HBoV+NoV+EV (5%; 1/20), and NoV+EV+PeV-A (5%; 1/20). All samples tested negative for RVA, HAstV and SARS-CoV-2. Among the NoV samples, GII.4 Sydney[P16] predominated (69.2%; 9/13), followed by GII.2[P16] (27.1%; 3/13) and one GII.4 Sydney[P31] strain (7.7%; 1/13). HBoV was identified as HBoV-1, EV as Coxsackievirus A6 (CVA6), HAdV as type 6 (HAdV-C6) and PeV-A as PeV-A1. Phylogenetic analysis revealed no evidence of a community outbreak, with HBoV-1 strains forming distinct clusters and NoV strains showing diverse genotypes, indicating independent origins. Similarly, molecular analysis of HAdV-C6, CVA6 and PeV-A1 strains suggested distinct genetic sources. Our findings underscore the co-occurrence of respiratory and enteric diseases, an often-neglected epidemiological scenario, and despite the small sample size, highlight local viral diversity and significant exposure to enteric viruses. These results underscore the complexity of conducting differential diagnoses when symptoms overlap and emphasize the crucial role of syndromic surveillance.

7096

CO-CIRCULATION OF TWO LINEAGES OF OROPOUCHE VIRUS IN THE AMAZON BASIN, COLOMBIA, 2024

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Oropouche virus (OROV) is a reemerging vector-borne orthobunyavirus with a three-segmented genome that causes acute fever and has spread silently across Latin America since its identification in 1955 in Trinidad and Tobago. In February 2024, the PAHO/WHO began to issue epidemiological alerts because of the dramatic increase in OROV cases in the Amazonian states of Brazil that have more recently extended to bordering Peru and Bolivia. A pre-publication showed that the OROV strain causing the large-scale outbreak in Brazil is a new viral lineage with reassorted genome segments (OROV BR-2009-2018). We have previously established surveillance programs for acute fever illness in several clinics across Colombia and collect blood samples to screen for arboviruses and other pathogens at our One Health Center located in Medellin, Colombia. This center is a consortium established between the Global Health Institute at the University of Wisconsin-Madison and the National University of Colombia-Medellin and is also a member of the Abbott Pandemic Defense Coalition (APDC). Our newly designed OROV RT-qPCR assay and NGS sequencing enabled the confirmation of OROV infection in 22 febrile individuals from the Leticia municipality, Colombian Amazonas department, from January to March 2024. Nine of these individuals were infected with the new reassortant, BR-2009-2018 OROV, while 13 cases were infected with PE-CO-EC/2008-2021 OROV identified previously by our group in Colombia (Ciuoderis et al, Emerg Microbes Infect. 2022). No medical complications or hospitalizations have been reported in the OROV-infected patients during this outbreak. The co-circulation of different OROV strains in this Colombian arboviral hotspot raises concerns about new reassortments and the emergence of new lineages with more severe clinical phenotypes and enhanced vector competence. This ongoing investigation highlights the complex arbovirus dynamics in South America and is a demonstration of the challenges of preventing and controlling the reemergence of arboviruses in the Americas.

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SEROPREVALENCE OF DENGUE VIRUS IN THE TAMPA BAY REGION OF FLORIDA AMONG HOSPITALIZED PATIENTS WITH RESPIRATORY SYMPTOMS IN 2020 AND 2021

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Dengue Virus (DENV) is a flavivirus vectored by Aedes mosquitoes that is suspected to cause over 400 million human infections and 40,000

estimated deaths annually. Since 2010, the United States has seen over 45,000 reported cases, 34,000 of which were locally acquired. Florida has the highest number of DENV cases in the nation with 3,182 reported infections as of 2023. The state has seen multiple DENV outbreaks due to imported cases from the Caribbean and being home to two major competent vectors, *Aedes aegypti* and *Aedes albopictus.* All four serotypes of DENV have been found within the state, although serotype 4 has only been found in mosquitoes pools. The Tampa Bay region is particularly at risk due to having a large tourism industry and immigrant population. Hillsborough county, where Tampa Bay resides, does not have passive surveillance measures for DENV and the main form of mosquito management is through nontargeted air and ground adulticide spraying. To test prevalence of DENV in the Tampa Bay region of Florida, our study utilized enzyme linked immunosorbent assays (ELISAs) for IgG antibodies to test 334 serum and plasma samples collected at Tampa General Hospital during 2020 and 2021. As we tested for IgG antibodies to indicate a previous exposure, current respiratory status of patients would not impact DENV status. We found that over forty percent of samples were positive for serotypes 1/3 and over sixty percent of samples were positive for serotypes 2/4 by ELISA. DENV serotypes were separated into two groups, 1/3 and 2/4, for ELISAs as they are serologically similar to one another. Plaque reduction neutralization tests (PRNTs) were performed to confirm positive results with each serotype being tested individually. While we cannot determine if the cases in this study are locally or travel acquired, we can say that seroprevalence of DENV is higher than reportable cases suggest.

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

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In 2015, a three-dose dengue vaccine (CYD-TDV,Dengvaxia) was licensed for those 9 years and older in dengue-endemic areas. The World Health Organization (WHO) recommended that CYD-TDV would be used in settings with at least 70% seroprevalence. The Philippines Department of Health (DOH) implemented a three-dose dengue vaccination program in high dengue burden regions targeting children aged 9 to 14 years old. In June 2017, the program was expanded to Cebu province. A follow-up analysis of the CYD-TDV Phase 3 trials showed that vaccination conferred protection among dengue-seropositive but increased risk for severe dengue among dengue-seronegative participants, the dengue vaccination program was halted with children in Cebu offered only one dose. We conducted a prospective community-based cohort study in Cebu to evaluate the effect of baseline dengue serostatus and a single dose of CYD-TDV on the subsequent risk of virologically-confirmed dengue (VCD). We enrolled 2,996 healthy children 9 to 14 years of age in May 2017. Baseline sera were collected and batch tested by indirect IgG ELISA and focus reduction neutralization test (FRNT). Out of 2,996 sera, 320 (10.7%) was dengue naïve, 292 (9.7%) had one previous dengue infection (monotypic profile) and 2,384 (79.6%) had >2 previous dengue infections (multitypic profile). From June to August 2017, 1,790/2,996 (59.7%) children received a single dose of CYD-TDV. Active surveillance for an acute febrile illness (AFI) was conducted from November 2017 to October 2023. Those who developed AFI were identified, data were collected, and blood drawn for confirmation of dengue by RT-PCR. Cumulative incidence for VCD was 1.02 cases per 100 person-years and the incidence varied by baseline DENV serostatus. Crude and adjusted analyses showed that a single dose of CYD-TDV did not confer protection against VCD in children who were dengue naïve or had a monotypic profile at baseline. One dose conferred significant protection against hospitalized VCD among participants who had a multitypic profile at baseline: at first 3 years, 70% (95% CI 20-88; p=0.017), 5-year follow-up period, 67% (95% CI 19-87; p=0.016).

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MORPHOLOGICAL AND MOLECULAR IDENTIFICATION OF *AEDES* MOSQUITO POTENTIAL VECTOR OF ARBOVIRUS IN KATI FALADIE, MALI

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In Mali *Aedes* vectors and arbovirus coexist, several patients have been seropositive for these five arboviruses. However, given the *Aedes* vector species diversity across various ecoclimatic settings, which *Aedes* species is specific vector for which arbovirus remains to be determined. Precise identification of Aedes mosquitoes will help to differentiate between vectors and non-vectors. In addition, understanding the repertoire of *Aedes* mosquito species that are responsible for sustaining any specific arbovirus transmission at any specific ecoclimatic setting would target vectors fighting. We hypothesize that the new distribution of *Aedes* mosquitoes could contribute to the emergence of arboviruses in Mali. This project aims to identify the *Aedes* mosquito potential vector of arbovirus in Kati-Faladie rural aera from Mali using molecular tool. This study carried out in Faladie, a rural village in Kati, 80 kilometers from Bamako in Mali. Mosquitoes were captured by aspiration and biogents sentinel in Faladie. Collected specimens were identified using morphological dichotomies keys of Culicidae, PCR and sequencing. Circulating arbovirus was characterized from captured mosquitoes by RT-PCR for non-structural protein 5 NS5 gene and sequencing. 287 *Aedes* mosquitoes collected were morphologically identified as: *Aedes aegypti* 82,22% (N=287), *Aedes aedimorphus* 1,74% (N=287), *Aedes mucidus* 0,35% (N=287), *Aedes Aedimorphus hirsutus* 0,35% (N=287) and *Aedes* spp. 15,33% (N=287). With sequencing *Aedes* mosquitoes were identified as: *Aedes aegypti 73,87% (*N=287*), Aedes Aedimorphus hirsutus* 0,35% *(*N=287*), Aedes furcifer* 0,70% *(*N=287*), Aedes albopictus* 0,70% *(*N=287*), Aedes vitattus* 0,70% *(*N=287*) and Aedes spp 23,70% (*N=287*).* 56.44% (n=162) of our samples tested by RT-PCR were positive for arbovirus and 43.55% (n=125) negative. Sequencing of the positive arbovirus samples (n=162) and *Aedes spp* (68). This study will shed light on the *Aedes* species that transmits arboviruses in Mali.

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PRELIMINARY EVIDENCE OF SILENT CIRCULATION OF *ORTHOFLAVIVIRUS NILENSE* IN EQUIDAE POPULATION IN PIAUI STATE, NORTHEAST BRAZIL

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The West Nile virus (WNV; *Orthoflavivirus nilense*) is an arbovirus that belongs to the *Flaviviridae* family, *Orthoflavivirus* genus. Considered an emerging pathogen in South America, WNV can cause encephalitis in animals and humans. Until recently, Piaui state was the only Brazilian state reporting West Nile fever in humans and one of the few states reporting WNV infections in animals that could be used as sentinel animals. Aiming at detection of WNV circulation in animals of the Equidae family from Piaui state, a cross-sectional epidemiological study was conducted from 2019 to 2021, in eight municipalities with confirmed cases of West Nile fever in humans. Three-hundred seventy-seven whole blood samples collected

in the field were centrifuged and frozen in liquid nitrogen until tested. Epidemiological data collection was obtained by interviewing animal owners using a personalized questionnaire. Antibodies to several arboviruses were detected by the Hemagglutination Inhibition test in 75.86% (286/377) of the samples and 63.92% (241/377) were specific for the *Orthoflavivirus* genus. Until now, Plaque Reduction Neutralization Test (PRNT) was performed in 30 samples and, in a preliminary analysis, the presence of neutralizing antibodies to WNV ($PRNT_{50}$) was detected in 66.66% (20/30) of the samples. These preliminary results indicate that, in this northeastern Brazilian state, WNV has infected animals of the Equidae family even though there have been no reports of epizootic events by the public health officials of this state, despite the need for a compulsory reporting of any epizootic event to the Ministry of Health. To our knowledge, this is the first report of detection of neutralizing antibodies to WNV in the Equidae population in Brazil, and these results evidenced a high seroprevalence of neutralizing antibodies to WNV in animals that could serve as sentinel animals to an early detection of a WNV outbreak. Although only a small fraction of the samples was tested, these preliminary results detected the silent circulation of WNV leading to an underestimated prevalence and underreporting of a virus with zoonotic and encephalitogenic potential.

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CHARACTERIZATION OF KOUTANGO VIRUS FROM PHLEBOTOMINE SANDFLIES COLLECTED IN ISIOLO AND BARINGO COUNTIES OF KENYA.

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Koutango virus (KOUTV), a lineage of West Nile Virus, is highly neuroinvasive in animal models and has been associated with human disease. Recent studies in parts of Africa, including Kenya, have identified KOUTV among phlebotomine sandfly populations. However, our understanding of this virus remains limited. The present study aimed to characterize KOUTV from Kenyan phlebotomine sandflies. Sandflies were sampled from selected sites in different geographical regions of Kenya between 2021 and 2023 using CDC light traps. Female sandflies were taxonomically identified and pooled based on genus. Virus isolation was performed in Vero cells. The viral genome was determined using next-generation sequencing on illumina Iseq 100. Phylogenetic and molecular clock analyses were done to decipher the virus's evolutionary relationships. Comparative analyses of amino acid sequences were performed to determine variations. Protein modeling in Pymol was conducted to elucidate variations in key protein regions. Evolutionary pressure analysis was used to investigate both point and episodic selection pressure. In vitro cell growth experiments were used for virus growth kinetics in vero-E6 and C6/36 cells. We report two KOUTV isolates one each from Baringo and Isiolo counties in Kenya. The current KOUTV isolates clustered in a single clade with previously identified KOUTV from Kenya. Comparative analysis revealed alanine amino acid at NS5 653. Diversifying pressure was acting on NS3 267 of the KOUTV lineage. There was no significant difference in the growth rates of KOUTV in Vero-E6 and C636 cells when compared to West Nile virus Lineage 1a. The isolation of KOUTV in two disparate sites in sandflies suggest circulation of the virus amongst sandfly population. The growth of the virus in Vero-E6 may point to the ability of the virus to infect primates. Similarly, growth in C6/36 cells points to amenability of the virus to mosquitoes, hence potential vectors. The close genetic relationship of KOUTV strains between East and West Africa may be enabled by the bird migratory route between the two regions.

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DISSECTING ANTIGEN-SPECIFIC T CELL RESPONSES TO MPOX IN VACCINATION AND INFECTION BY GENOME-WIDE ANTIGEN SCREENING

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The mpox epidemic in July 2022 caused by Monkeypox virus (MPXV) prompted a public health emergency. Even after the epidemic peak, cases of mpox are still being reported both within and outside traditional endemic areas. The smallpox vaccine, Dryvax®, which successfully eradicated smallpox, comprises a live replicating vaccinia virus (VACV) and provides robust protection against MPXV, but poses safety concerns for immunocompromised individuals. In response, a non-replicating modified vaccinia Ankara (MVA) vaccine, JYNNEOS, was developed for smallpox and mpox, which is associated with the deletion of numerous open reading frames (ORFs). Recent data obtained during the 2022 mpox epidemic indicate that JYNNEOS may induce less immunogenicity and protection than Dryvax®. T cells play a pivotal role in controlling and terminating pox-virus infections, yet there is limited information on the antigen targets recognized by T cells following VACV vaccinations (Dryvax® and JYNNEOS) and/or MPXV infection. To fill this gap of knowledge, our study focuses on identifying the antigens and epitopes recognized by T cells in donors who have been vaccinated and/or infected. First, we classified the ORFs present in the two VACV vaccine strains and MPXV by their ortholog determination. We then measured T cell responses induced after JYNNEOS vaccination with pools of predicted peptides spanning the entire MVA proteome. Employing our deconvolution strategy, 113 CD4 and 83 CD8 MVA-derived epitopes were identified, exhibiting an unbiased recognition between structural and non-structural proteins. Among the recognized antigens, we identified the top 10 immunodominant antigens for CD4+ and CD8+ T cells with five antigens recognized by both populations of T cells. This comprehensive antigen identification provides a valuable understanding of T cell responses following JYNNEOS vaccination during the mpox epidemics, enabling comparison with responses post-Dryvax® vaccination and MPXV infection. Ultimately, these insights into potential protective antigen targets contribute to the development of next-generation pox vaccines with enhanced efficacy.

7103

PRIOR ZIKA VIRUS INFECTION RESTRICTS DIVERSITY OF SUBSEQUENT ACUTE-PHASE PLASMABLAST RESPONSE TO DENGUE VIRUS SEROTYPE 2 AND PREFERENTIALLY SELECTS A SINGLE CLONE

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Zika virus (ZIKV) and dengue virus serotypes 1-4 (DENV 1-4) co-circulate in the tropics, such that people are exposed to multiple viruses. DENV causes febrile illness ranging from mild to severe disease with vascular leak. We have shown that prior ZIKV infection is associated with increased the risk of subsequent severe DENV2 infection. Plasmablasts rapidly peak in the acute response to DENV infection and secrete antibodies. We hypothesized that prior ZIKV vs DENV1 infection selects for different antibody specificities in the acute immune response to subsequent DENV2 infection. Using single-cell transcriptomics and antibody variable heavy (VH) and light (VL) chain gene annotation, we compared the acute plasmablast (PB) response to DENV2 infection in peripheral blood mononuclear cells (PBMCs) from children with primary DENV2 (n=1), secondary DENV1-DENV2 (n=2), or

secondary ZIKV-DENV2 (n=3). A mean of 1,383 B cells were analyzed per child. The acute ZIKV-DENV2 PB clonal diversity (Shannon Diversity Index, H=5.6) was lower than that of DENV1-DENV2 (H=6.63), suggesting more selection pressure in ZIKV-DENV2 PBs. Surprisingly, a single clonotype of VH3-23_VK1-39, with a 17- or 18-amino acid VH hypervariable region, predominated (33-50%) in ZIKV-DENV2 PBs of all 3 children. We did not find this clone in acute DENV2 or DENV1-DENV2 PBs. In contrast, the most frequent clone in the DENV1-DENV2 group was only present in 1.7-6% of PBs. Monoclonal antibodies (mAbs) representing the VH3-23_VK1-39 clone potently neutralized ZIKV (Neutralizing titer; NT_{50}=0.012µg/mL) but not DENV1-4 (NT_{50}>10 µg/mL). In contrast, most mAbs (6-7) of a set of 8 representative clones from the DENV2 and DENV1-DENV2 PBs neutralized DENV1-4 (NT_{50} in µg/mL: DENV1=0.4-40, DENV2=0.4-20, DENV3=0.6-7, DENV4=0.3-20) but not ZIKV (NT_{50}>10 µg/mL). Thus, the acute PB response to ZIKV-DENV2 demonstrates less diversity and a preference for a single clone that does not neutralize DENV2. This supports that prior ZIKV immunity may not elicit effective immunity in the acute phase of a subsequent DENV2 infection and may partly explain increased risk associated with this infection history.

7104

BLOOD BIOMARKERS THAT PROSPECTIVELY PREDICT HIV-1 INFECTION IN HIGH RISK ADULTS.

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High heterogeneity in HIV-1 transmission is observed with individuals in sub-Saharan Africa exhibiting a nearly 4-fold elevated risk of male-to-female HIV-1 transmission per sexual contact compared to higher income countries. It is possible that environmental exposures may predestine one to becoming more susceptible to HIV-1 acquisition, for example by affecting host constitutive defence mechanism. We recently explored potential blood biomarkers predictive of HIV-1 acquisition using a retrospective case-control study nested in an HIV-1 high-risk longitudinal cohort. Plasma samples taken 3 months prior to HIV-1 infection were used for transcriptional analysis of the RNA encapsulated in small extracellular vesicles (sEVs) circulating in plasma. Preliminary data of the host and pathogen transcripts revealed distinct gene expression patterns 3 months prior to HIV acquisition, in individuals who 3 months later acquire HIV (cases) compared to those who remain HIV negative (controls). Notably, dampening of immunological pathways important for inducing antiviral immunity were associated with HIV-1 acquisition. Interestingly, significantly higher Pegivirus C RNA was observed in those who became HIV-1 positive compared to those who remained negative. Although this was contrary to the protective role of Pegivirus C in slowing HIV-1 disease progression to AIDS, our results suggest that Pegivirus C infection might dampen the immune system and predispose high risk adults to HIV-1 acquistion.

7105

SURVEILLANCE OF ACUTE FEBRILE ILLNESSES IN THE COUNTRY OF GEORGIA: INSIGHTS FROM A HOSPITAL-BASED STUDY

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Understanding the pathogens causing acute febrile illness (AFI) is crucial to address global and militarily health challenges. AFI-related morbidity and mortality remain significant concerns in Georgia. The service members operating in the country are at high risk of exposure to AFI agents. We initiated a hospital-based surveillance study in Georgia to determine infectious causes of undifferentiated febrile illnesses. The study enrolled patients aged 4 years and older who exhibited persistent fever (≥38°C for ≥48 hours) without definitive diagnoses and collected samples for testing. We utilized an enzyme-linked immunosorbent assay (ELISA), serum agglutination test and immunoblotting to detect antibodies against regionally relevant pathogens, including *Leishmania* spp., *Leptospira* spp., Crimean-Congo Hemorrhagic Fever Virus, *F. tularensis*, West Nile Virus, *R. typhi*, Spotted Fever, *Brucella* spp., *C. burnetii*, Tick-borne Encephalitis virus, *Borrelia* spp., and Hantavirus. From February 2023 to March 2024, we enrolled 196 outpatient subjects with a mean age of 46 years (range 13-81 years) of which 60% were female and 40% were male. Testing results indicated *R. typhi* as the predominant pathogen, with IgM positives in 60% of the samples followed by *Leptospira* spp. (29%), *F. tularensis* (15%), *Brucella spp*. (14%), *Borrelia spp.* (11%) and Spotted Fever (9%). In addition, 43% of the samples demonstrated the presence of IgM antibodies against 2 or more pathogens. In attempt to identify the agent causing the illness, samples were also subjected to polymerase chain reaction-based assay using the BioFire Global Fiver Panel. However, no positive AFI pathogens were obtained. The results of our study indicate presence of various AFI agents in the country and highlights the need of continued surveillance and research to develop region-specific diagnostic methods and analyses. The latter is essential to control and mitigate the spread of these infectious agents in the region.

7106

HUMAN *IN VITRO* MODELING CHARACTERIZES MECHANISM OF ACTION OF ADJUVANTATION SYSTEMS DEFINING SCALABLE AND AFFORDABLE PRECISION VACCINE FORMULATIONS FOR EARLY CHILDHOOD

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Children demonstrate distinct immunity in early life including diminished Th1-polarizing cytokine production contributing to high susceptibility to infections caused by intracellular pathogens such as respiratory viruses. This challenge also pertains to pediatric vaccine discovery and development, and could be overcome by developing precision adjuvantation systems with well characterized mechanisms of action (MOA) tailored to enhance age-specific immunogenicity. To this end, we employed novel age-specific human *in vitro* assays to characterize cellular and molecular activities of a selection of adjuvants in children aged between 2-4 years in soluble, oil-in-water and liposomal formulations, including several developed for global open access. In a whole blood assay, which predicts the reactogenicity potential of adjuvants, formulations containing the TLR4 agonist, monophosphoryl lipid A (MPLA), potently induced an innate immune response with primary activation of monocytes, and liposomal formulations were more selective in inducing cytokine production compared to soluble and oil-in-water formulations in children as well as adults. In a monocyte-derived dendritic cell (MoDC) assay, which dissects the mechanism by which adjuvants activate differentiation of T helper (Th) cell subsets, liposomal formulations activated MoDCs to produce Th1-polarizing cytokine response, which is important for anti-viral host defense, with more robust TNF induction observed in children than adults. In a DC-T cell interface assay that demonstrates antigen processing and presentation, activation of influenza-specific $CD4^+$ T cells was driven by MPLA-containing formulations and that of $CD8^+$ T cells was induced by the adjuvant QS-21 with greater variability observed in children than in adults. Insight into the MOA of adjuvanted vaccine formulations via age-specific human *in vitro* modeling may advance global health by accelerating and de-risking development of affordable and scalable precision-adjuvanted vaccines.

7107

SEROLOGICAL PROFILING OF RESPONSES TO VACCINATION AND/OR INFECTIONS CRITICAL TO UNLOCK IMMUNE CORRELATES OF PROTECTION

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Pathogen-specific antibodies are commonly used to assess immunity to various pathogens. Serological readouts often rely on measuring antibodies to a single antigen and, in many cases, inform on disease exposure rather than immunity to the respecting pathogen. Attempting to correlate protection with a single point serological measurement, have shown that depending on the study population, pre-existing immunity and vaccine-induced immunity, such direct relationship between antibodies and protection is highly variable. This has led to the increasing reluctance of conducting serological analysis as they may fail to expand our knowledge in immune mechanisms conferring protection.In this study we showcase the power of serological profiling, specifically, establishing the antibody profiles to SARS-CoV2 and mapping the functional activity (isotype, neutralization) of various study populations. The study populations include male and female donors with/without mRNA vaccination, pregnant women, and neonatal cord blood. The results have led to several conclusions that the single assessment of antibody titers to just SARS-CoV2 spike or nucleocapsid would not have revealed: (1) antibodies to SARS-CoV2 nucleocapsid waned in our study populations over time thus increase the uncertainty on determining immune individuals; (2) distinct antibody profiles in neonatal cord blood vs. maternal blood; (3) distinct functional antibody profiles between the study populations; and (4) vaccination compared to disease induces a distinct functional profile and cross-reactivity with other SARS-CoV2 variants than the original strain. Our results show a clear need to advocate for enabling a full assessment of immunity by profiling both fine specificity and function, to potentially identify immune correlates of protection.

7108

CYTOKINE PROFILING REVEALS DISTINCTIVE IMMUNE RESPONSES IN DENGUE, ZIKA, CHIKUNGUNYA AND MAYARO VIRUS INFECTIONS

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Arboviruses, including Dengue virus (DENV), Chikungunya virus (CHIKV), Zika virus (ZIKV), and Mayaro virus (MAYV) are important causes of acute febrile illness (AFI) in high-risk regions in Peru. Differential diagnosis based on clinical manifestations is challenging due to overlapping symptoms. We conducted a pioneering study to compare cytokine profiles among these arboviruses, aiming to elucidate distinct immunological features for diagnostic and therapeutic insights. We conducted a cross-sectional study in patients with acute febrile illness from Cajamarca, Peru. Blood samples were collected for the diagnosis of arboviruses and the quantification of cytokines. Diagnosis of Dengue, Zika, Chikungunya, and Mayaro virus infections relied on specific IgM antibody detection via enzyme-linked immunosorbent assays (ELISA). Cytokine quantification was carried out by ELISA assays for IL-2, IL-6, IL-10, TNF-α, and IFN-γ. Comparative analysis of cytokine levels was performed between all viruses and controls. A total of 20 patients were recruited for each arbovirus and control group. Our study revealed similarities in clinical symptoms across arboviral infections, with headaches, myalgias, and arthralgias as the predominant symptoms. IL-2 levels were similar across the arboviruses; however, DENV and ZIKV patients had higher levels compared to controls. Elevated IL-6 levels were associated with CHIKV and ZIKV, while IL-10 levels were highest in DENV as compared to other arboviruses. TNF-α and IFN-γ were significantly elevated in DENV and ZIKV, and they were significantly higher in DENV compared to MAYV. Our findings provide valuable insights into the unique cytokine profiles of arboviral infections. We found similar levels of IL-2 across the arboviral groups, IL-6 was predominantly elevated in CHIKV and ZIKV, while IL-10 showed the highest levels in DENV. TNF-α and IFN-γ showed a similar pattern, with DENV and ZIKV patients expressing the highest levels. Understanding the distinct immunological signatures of these arboviruses is crucial for effective diagnostic and therapeutic approaches in high-risk regions.

7109

SERUM INTERLEUKIN-6 AND ZINC LEVELS ARE ASSOCIATED WITH SEVERITY IN COVID-19 PATIENTS FROM LIMA, PERU

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The individual's immune system can determine the progress of SARS-CoV2 infection and lethality. The modulation of the inflammatory response through various molecules, such as cytokines and trace elements, is crucial during the disease. In this context, the objective of the present study was to determine the serum levels of IL-6 and zinc and their association with the severity of the disease in patients with COVID-19 from Lima, Peru. Four groups of patients were analyzed. Hospitalized patients were divided into two groups: 26 admitted to ICU and 26 who did not require ICU. The other two groups included 36 patients who did not require hospitalization, 24 of which belonged to the outpatient group and 12 to the control group. Sixty-four and eight percent (64.8%) of the patients were male. The lowest IL-6 values were obtained in the outpatient group (2pg/mL) and the highest values in the ICU group (168.5 pg/mL). On the other hand, the highest zinc values were also obtained in the UCI group (3402.5 µg/dL).

7110

SERUM SPIKE SPECIFIC IGG3 SERVES AS A DISTINGUISHING IMMUNOLOGICAL MARKER BETWEEN SARS-COV-2 INFECTION AND VACCINATION

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Both SARS-CoV-2 infections and COVID-19 vaccines elicit immunological responses. However, it is difficult to distinguish the responses generated either from vaccination or infection. Here we have investigated SARS-CoV-2 spike receptor-binding domain (RBD)-specific IgG subclasses (IgG1, IgG2, IgG3 and IgG4) responses using ELISA in four different groups; (1) COVID-19 patients (n=39) with varying disease severity and (2) COVID-19 vaccinated individuals (n=30, adenovirus/mRNA based) (3) vaccinated after infection (n=39) (4) patients experiences breakthrough infection (n=19), in Bangladesh. We observed distinct IgG subclass responses in COVID-19 patients compared to COVID-19-vaccinated individuals. Specifically, COVID-19 patients exhibited elevated levels of both IgG1 and IgG3, with IgG3 dominating in the early phase (days 1-7) followed by a subsequent increase in IgG1. Conversely, COVID-19 vaccination predominantly induced IgG1 responses without a concurrent rise in IgG3. This effect was more evident when a significant rise of IgG1 but not IgG3 was observed

in patients who received COVID-19 vaccines after 90 days of infection. However, following breakthrough infection, we observed an increase in both IgG1 and IgG3. All of these findings collectively indicate that COVID-19 vaccination predominantly induces IgG1, whereas natural infection can elicit both IgG1 and IgG3 subclasses. These findings identify the importance of serum spike-specific IgG3 as an important distinguishing marker that can differentiate individuals based on their vaccination and natural infection history. More studies with larger sample size might be needed to establish this marker. This marker can be used as an important tool for longitudinal monitoring of vaccinations and for establishing SARS-CoV-2 correlates of protection.

7111

NO DISTINCT CYTOKINE, CHEMOKINE AND GROWTH FACTOR (CCG) BLOOD PROFILE ASSOCIATED WITH MONKEYPOX VIRUS CLADE IIB INFECTED PATIENTS

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Previous literature, in particular on related orthopoxviruses, suggested a cytokine storm association with overt mpox disease. To date, only a handful of studies have investigated the modulation of circulating cytokine, chemokine and growth factor (CCG) profiles in monkeypox virus (MPXV)-infected patients with limited panels. The sole study on CCGs in clade I MPXV infections in 19 mpox patients showed that cytokine modulation correlated with disease severity. It remains unknown if a similar CCG profile is associated with clade II infections, as patients exhibit different clinical manifestations to both clades. We used a 65-plex CCG panel to analyze serum samples of 100 acute mpox patients from the 2022 outbreak and 26 pre-outbreak healthy controls. All 100 patients were men, median age 40 years (interquartile range: 33-46). Cluster analyses indicated no strong CCG profiles in mpox patients compared to healthy controls, but a trend towards certain cytokine modulations. Individual CCG analyses showed MIF, CXCL10, CCL8, CD30, IL2R, CXCL13, IL18, APRIL, CCL4, TNFRII, VEGFA, CXCL12, CXCL9, and CXCL11 to be significantly elevated in mpox patients, while TWEAK, CCL11, CCL2, CXCL5, and SCF were significantly suppressed. We did not detect significant differences in the expression of key pro-inflammatory cytokines such as IL-1α, IL-1 β, IL-6, IL-8 or anti-inflammatory cytokines such as IL-4, IL-10 and IL-13. Comparing with pre-outbreak samples of 10 mpox patients living with HIV before mpox infection, confirmed an increase in BLC, IL18, and MIF during mpox disease. A higher number of lesions correlated positively with BLC and TSLP expression, and negatively with CCL2. Presence of proctitis was associated with an increase in CD30 and LIF. Presence of systemic symptoms or ongoing fever were associated with an overexpression of IL2R, LIF, and CXCL11 and suppression of CCL24. In addition to well-known differences in clinical manifestations, clade I and clade IIb MPXV infections evoke marked differences in blood CCG profiles. The absence of discriminatory CCG profiles in mpox patients suggests limited clinical applications.

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MODULATION OF THE SPP1 GENE BY CHIKUNGUNYA VIRUS INFECTION *IN VITRO* AND ITS POSSIBLE IMPLICATION IN INFLAMMATION AND DISEASE SEVERITY

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The SPP1 gene is responsible for encoding the osteopontin protein, which has several natural functions in our body, such as bone remodeling, angiogenesis, and tumor migration, in addition to play a role in chronic inflammatory and autoimmune diseases. Furthermore, this protein may also act as a Th1 cytokine on the regulation of the immune response by T cells, contributing as an inhibitor of the anti-inflammatory cytokine IL-10 and increasing the Th1-mediated (pro-inflammatory) response. In this study, expression of the SPP1 gene in monocytes that were infected *in vitro* with the Chikungunya virus (CHIKV) was compared to CHIKV infection of another co-circulating alphavirus in Brazil, Mayaro virus. Although the diseases caused by these viruses bear a strong resemblance, Mayaro disease typically results in a milder clinical presentation than Chikungunya, with less frequent recurrence of joint inflammation. Our transcript analysis revealed that the expression of the SPP1 gene was approximately 12-fold higher at early times after Chikungunya virus infection when compared either to the Mayaro virus and uninfected cells. Later in the infection, SSP1 gene was also observed to be positively modulated, although the expression showed a progressive decrease at later hours post-infection. In the case of Mayaro virus infection there was no significant difference in the SPP1 expression when compared to uninfected cells. This increased gene expression correlated positively with the levels of inflammatory cytokines and chemokines, such as IL-6, IL-15, and eotaxin. Our findings suggest that interventions in the production and secretion of osteopontin could attenuate the inflammatory effects induced by the Chikungunya virus, thereby presenting a potential target for development of drugs that counteract osteopontin functions. Also, therapy strategies for the Chikungunya disease, such as CRISPR-Cas9 and RNAi methodologies, may target the SSP1 gene to reduce the severe chronic manifestations of this disease.

7113

INFLUENCE OF COUNSELLING ON POSITIVE STATUS DISCLOSURE AND VIRAL SUPPRESSION AMONG PEOPLE LIVING WITH HIV IN GHANA

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Counselling is a key gateway to major HIV/AIDS services. Silence on HIV positivity non-disclosure remains dire, encouraging increase disease transmission and death. This study assessed the influence of counselling on HIV positive status disclosure and antiretroviral therapy (ART) adherence among people living with HIV (PLWHIV) at the Korle Bu Teaching Hospital (KBTH) in Ghana. The mixed-methods study design involved 423 participants. A semi-structured questionnaire with both close and open-ended questions was used to collect data from PLWHIV presenting at the Fevers Unit of KBTH. STATA 15.1 was used for data analysis. For open ended questions, thematic data analyses in Nvivo software were used to explore transcripts and appropriate themes generated. HIV positive status disclosure among the 49.3 ± 12.2years mean-aged population was 92.4%. Majority (61.5%) disclosed their status in the symptomatic phase of disease and disclosure to sexual partner was only 51.8%. Prevalence of HIV viral suppression (target not detected) was 52.2% with 68.4% high medication adherence. Having HIV pre-test counselling [aOR = 2.18, 95% CI 1.05 - 4.55, p=0.04] and age on ART (aOR = 0.94, 95% CI 0.89 - 1.00, p = 0.04) were associated with status disclosure. Not having HIV pre-test counselling (aOR = 2.17, 95% CI 1.28 - 3.67, p = 0.004), having enhancement counselling, rural residence, not having a partner/spouse as social support and not having assistance in taking medication were associated with increased odds of not having viral suppression. Qualitatively, counselling "educated", "encouraged", and "supported" ART adherence and status disclosure among PLWHIV, and gave them "hope" to cope with life. Status disclosure served as avenue for "financial assistance", "emotional support" and "reminders to take one's medication" towards attaining viral suppression. We found enough evidence to support the influence of counselling on HIV positive status disclosure, and the duo leading to ART and medication adherence - a call for their enhancement towards reduction of the disease transmission, and improving the quality of life of PLWHIV.

7114

PERSISTENCE OF ANTI-YELLOW FEVER VIRUS IMMUNOGLOBULIN M ANTIBODIES POST-VACCINATION AND ITS REACTIVITY TO THE ENVELOPE DOMAIN III ANTIGEN OF THE YELLOW FEVER VIRUS

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Yellow fever (YF) is a vaccine-preventable, mosquito-borne viral infection endemic to tropical and subtropical parts of South America and Africa. In these parts, a live attenuated YF vaccine is routinely administered to children at 9-12months of age. If an infant vaccinee develops fever and jaundice years post-vaccination and anti-YF IgM antibodies are detected in their serum, it becomes unclear what these results represent. Does the IgM detection suggest a recent natural YF virus infection indicating vaccine failure or does it suggest the persistence of YF-IgM antibodies years post-vaccination? To better understand YF IgM sero-positivity post-vaccination, we tested archived sera from the ANRS 12225/12140-PEDIACAM study- a prospective observational cohort study of infants born alive to HIV+ and HIV- mothers enrolled from 3 hospitals in Cameroon. The infants were followed from birth to present and received the YF vaccine at 9-12months. To determine the presence and persistence of anti-YF IgM antibodies, we tested samples collected pre-vaccination, at 2-6months and 1-2years post-YF vaccination using the CDC YF IgM antibody capture 72hrs ELISA. We found that at 2-6months post-YF vaccination, 18/352(5.1%) of infants had anti-YF IgM antibodies while, 10/433(2.3%) of infants still had anti-YF IgM antibodies by 1-2years post-vaccination. Our results indicate that, YF IgM is rare by 6 months post-vaccination in infants who receive the YF vaccine at 9-12months. However, IgM persistence years post-YF vaccination could be observed in a minute proportion of infants. To further maximize the insight we could obtain from these samples, we assessed and compared the reactivity of YF IgM-positive vaccinee sera and YF natural infection sera to 3 recombinant YF antigens (Envelope protein, Envelope Domain III protein (EDIII), non-structural protein 1) using the multiplex immunoassay which makes use of antigen-coupled beads. The IgM antibodies from both sera groups exhibited stronger reactions to the YFV DIII envelope protein compared to other proteins, hence could serve as a more specific and sensitive marker for detecting IgM in both cases.

7115

AEDES AEGYPTI MOSQUITO SALIVA INHIBITS HUMAN T CELL PROLIFERATION: IMPLICATIONS FOR ARBOVIRAL DISEASE OUTCOME?

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Dengue fever is one of the most rapidly spreading mosquito-borne viral diseases in the world and is caused by the bite of an infectious *Aedes* mosquito. To facilitate the blood feeding process, the mosquito salivates into the host skin, releasing several compounds known to limit host vasoconstriction, inhibit coagulation processes, and suppress pain receptors. Previous murine studies showed saliva of *Ae. aegypti* to be implicated in enhanced viral dissemination and increased pathogenesis of viral infections, while epidemiological studies have suggested a protective role for anti-*Ae. aegypti* saliva antibodies against symptomatic dengue. Here, we investigate the response of human peripheral blood mononuclear cells (PBMCs) to *Aedes* saliva, to better understand how anti-saliva immune responses influence dengue disease outcome. Preincubation of human PBMCs with salivary proteins of *Aedes* for three hours prior to being stimulated with Concanavalin A, a lymphocyte mitogen, inhibited CD3+ T cell proliferation by 30.8% and reduced IFN-γ and IL-2 secretion by 42.5% and 93.4%, respectively. Repeating this experiment with either denatured (30min at 70ºC) or digested (proteinase K) salivary proteins, abrogated the phenotype (7.1 and 3.6% inhibition of proliferation; 2.95% and 0% reduced IFN-γ secretion; and 41.6% and 14.2% reduced IL-2 secretion, respectively), supporting the hypothesis that saliva has a direct effect on T cell proliferation. Ongoing experiments using a SARS-CoV-2 peptide pool as stimulus on PBMCs of individuals with confirmed high neutralization titers against SARS-CoV-2, will elucidate whether saliva inhibits antigen-specific T cell proliferation. This is the first time that *Aedes* saliva is shown to have an inhibitory effect on human lymphocytes. Future mechanistic studies will uncover the implicated salivary components and potential differences between highly *Aedes* exposed vs. unexposed individuals. We aim to test if anti-saliva antibodies neutralize this saliva-induced inhibition, which will help characterize whether host differences in immune inhibition are associated with dengue disease outcome.

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HUMORAL IMMUNITY FOLLOWING VACCINATION IS SUFFICIENT TO PROTECT AGAINST RIFT VALLEY FEVER VIRUS ENCEPHALITIS

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Prevalent in Africa and the Arabian Peninsula, Rift Valley fever virus (RVFV) is a mosquito-borne virus that infects humans and livestock. In humans, RVFV infection typically presents as a self-limiting febrile illness. However, in a subset of individuals severe complications such as hepatitis, retinitis, encephalitis, or death can occur. While there are no RVFV vaccines currently licensed for human use, previous work using promising live attenuated vaccine candidates demonstrated that humoral immunity was sufficient to confer vaccine-mediated protection from lethal *hepatic* disease in C57/BL6 mice. Here, we investigated whether vaccination was effective in preventing lethal *central nervous system* (CNS) disease. Unlike traditional inbred mice such as C57BL6, CC057/Unc mice develop uniform late-onset encephalitis between 8 to 12 days post infection (dpi) when challenged with wild-type (WT) RVFV by foot pad injection. Attenuated RVFV vaccine candidates (DelNSsRVFV and DelNSs/DelNSmRVFV) were safe and immunogenic in CC057/Unc mice. Vaccinated mice also survived subsequent WT RVFV challenge and were fully protected from CNS disease. Furthermore, naïve mice that received passive transfer (PT) of serum from vaccinated animals 2 days post WT challenge were also protected against late-onset encephalitis, indicating that humoral immunity is sufficient for protection against RVFV encephalitis. Notably, protection through humoral immunity was dependent on PT dose and timing of PT administration. A decline in animal survival was observed when PT was administered 2 dpi at lower doses or when PT was given on days 3 to 6 post WT challenge. Overall, these data demonstrate that humoral immunity following vaccination is sufficient to protect against RVFV encephalitis and highlight the utility of attenuated RVFV vaccines in preventing diverse disease manifestations.

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DEFINING INNATE IMMUNE MEDIATORS REQUIRED FOR THE EFFECTIVE RIFT VALLEY FEVER VIRUS ANTIVIRAL RESPONSE

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Rift Valley fever virus (RVFV) is an arthropod-transmitted virus affecting humans and ruminants. RVFV infection most frequently manifests as an acute self-limiting disease, but in a subset of cases involves severe manifestations including hepatitis, encephalitis, and/or hemorrhagic fever. The determinants of infection severity are largely unknown. The NSs protein of RVFV is a critical mediator of virulence and is thought to exert its effects through antagonizing the host interferon response, suggesting a key role for innate immunity in controlling RVFV infection. When mice are infected with strains of RVFV that are deleted for the NSs protein they do not develop clinical illness; in contrast, 100% lethal hepatitis is observed in mice infected with WT RVFV. To evaluate the role of specific innate immune sensors and signaling mediators in modulating in vivo RVFV pathogenesis, we infected various immune mediator knockout mice with strains of RVFV that are deleted for the NSs gene. These attenuated NSs-deleted strains

were lethal in MAVS, STAT1, and IFNAR knockout mice. No lethality was observed in TLR3, TLR7, MyD88, TRIF, NLRP3, or TNF knockout strains, suggesting unique functions of MAVS, STAT1, and IFNAR in the RVFV antiviral response. Future investigations will aim to elucidate the contribution of hematopoietic versus stromal compartments of these innate immune mediators in protection from RVFV hepatitis.

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IDENTIFICATION OF EPITOPE-SPECIFIC T CELL RESPONSES TO LASSA BY GENOME-WIDE ANTIGEN SCREENING AND CONSERVATION ACROSS ARENAVIRIDAE

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CD4 and CD8 T cells play a key role in clearing Arenaviridae infections, even before the appearance of neutralizing antibodies. Thus, while vaccine strategies that would generate a rapid and durable neutralizing antibody response are desirable, a vaccine also inducing a rapid and durable T cell response would be of significant interest, especially if the T cell response could broadly target different viral species and isolates. Studies performed on Lassa survivors also show a robust and durable T cell response able to cross-recognize different Lassa lineages. Human data is however limited, and most studies so far focused on specific domains or immunodominant epitopes for GPC and NP. We have initiated a systematic study of all Lassa proteins (including GPC, N and L proteins), in terms of which epitopes are immunogenic in humans using a de-novo in-vitro stimulation approach. This approach will also determine the degree of conservation of Lassa human epitopes in other viruses of the Arenaviridae family (Old World and New World arenaviruses alike) Our approach re-reidentified epitopes previously shown in convalescent Lassa human samples and greatly expand the immunogenic regions induced by this virus in GPC, N and L proteins and identify several immunogenic and conserved regions, thus allowing to assess the feasibility of a panArenaviridae vaccine approach.

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FILOVIRUS VIRUS GLYCOPROTEIN - EPITOPE MAPPING, AND PSEUDOTYPING

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Recent disease outbreaks highlight the need to characterize the immune response to filoviruses to develop vaccines and therapies. We have used extensive GP mutation libraries to map the epitopes for >200 monoclonal antibodies (MAbs) targeting the EBOV surface glycoprotein, GP. We have extended these studies to Marburg virus (MARV) by generating an Ala-scan library of MARV Δmucin GP (Uganda strain). Initial maps of anti-MARV MAbs include those of two non-neutralizing MAbs MR228 and MR235, targeting the wing region of MARV GP, that showed therapeutic protection in animal models (MR228) or that increased binding (MR235) by neutralizing MAbs. The variety of EBOV MAbs mapped, many from survivors of ebolavirus infection, include cross-neutralizing MAbs targeting the GP membrane-proximal external region (MPER); a broadly cross-reactive MAb that blocks GP interaction with its endosomal receptor Niemann-Pick C1; and MAbs who synergistically transform a non-neutralizing MAb into a potent neutralizer. The epitope maps have expanded our understanding of how the immune system recognizes EBOV GP, and allow correlation of epitopes with MAb neutralizing capabilities, to develop anti-EBOV therapeutics and vaccines. Mapping also identified mutations that increase the exposure of neutralizing epitopes, impacting future anti-ebolavirus vaccine strategies. To provide critical reagents for analyses of antibody or serum immune responses to ebolaviruses, we have developed a pseudotyped lentiviral reporter virus (RVP) system for EBOV and MARV, expressing bearing the appropriate viral GP. These replication-incompetent RVPs perform one round of infectivity and enable safe (BSL-2) and reproducible virus neutralization assays with luminescent or fluorescent readout.

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INHIBITORY EFFECTS OF PLANT-DERIVED COMPOUNDS ON ROTAVIRUS PATHOGENESIS

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Acute diarrhea due to Rotaviruses remains a public health concern among newborns worldwide. Despite efforts to develop efficacious vaccines, the morbidity and mortality associated with rotavirus infections persist and this has necessitated the need for alternative therapeutic options. This study sought to investigate the inhibitory effects of specific terpenoids on rotavirus replication, with the goal of identifying potential candidates for antiviral therapy. Rotavirus infections manifest as acute gastroenteritis, characterized by symptoms such as fever, vomiting, abdominal pain, diarrhea, and dehydration, posing significant challenges to healthcare systems globally. Rotavirus infections represent a formidable challenge in pediatric healthcare, particularly in resource-limited settings where access to medical care and sanitation infrastructure may be limited. The burden of rotavirus-associated morbidity and mortality underscores the urgency of advancing strategies for prevention and treatment. Natural compounds such as Terpenoids provides a therapeutic alternative and presents an appealing avenue for the development of novel antiviral therapies. Fresh samples of avocado and guava leaves were assessed for their antiviral activity with crude extracts compared for their efficacy. Phytochemical analysis confirmed the presence of active compounds in both leaf extracts with the former exhibiting the highest inhibition percentage. This study provides compelling evidence for the potential utility of plant-derived phytochemicals as a source of pharmacologically active compounds. The superior inhibitory activity of Avocado leaf extract against rotavirus underscores its promise as a candidate for further investigation in the development of novel antiviral therapies.

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THE ARYL HYDROCARBON RECEPTOR/AXL PATHWAY AT THE CROSSROADS BETWEEN POLLUTION AND VIRAL INFECTIONS

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There is still a big gap in our knowledge regarding the molecular mechanism by which anthropogenic pollutants contribute to pathogenesis. Our laboratory has recently published data proving that the aryl hydrocarbon receptor (AHR), a ligand activated transcription factor that acts as an environmental sensor of xenobiotic chemicals, has a pro-viral role during infections with dengue (DENV), Zika (ZIKV), Junín (JUNV) and coronaviruses. AHR can regulate the expression of numerous genes, including some involved in the antiviral cellular response. In this work we aim to study the effect of AHR pharmacological modulation on Axl, a member of the TAM receptor family of proteins. Axl is a well-known entry co-receptor for different viruses and in vivo studies have shown that its expression is altered in rats exposed to secondhand smoke. We hypothesize that an AHR/Axl pathway plays a key role during viral infections. To study the effect of AHR modulation on Axl transcript and protein levels we pre-treated A549 cells with AHR endogenous agonist (L-Kynurenine) or with an AHR antagonist (CH223191) and then carried out the infection with DENV-2. We observed a 4-fold change increase and a 0.6-fold change decrease in Axl transcript levels respectively, measured by RT-qPCR. In concordance, we observed a 17% increase in Axl protein levels measured by flow cytometry in kynurenine-treated and infected cell cultures relative to the untreated

infected control. Finally, we carried out plaque forming unit assays to determine the effect of Axl modulation on the related arboviruses DENV-2 and ZIKV and the unrelated JUNV arenavirus replication. To do this, we pretreated A549 and Huh-7 cell cultures with a specific Axl inhibitor (R428) for 3 hours prior to infection. We observed a significant inhibition of viral replication, following a dose dependent response. Furthermore, we treated cell cultures with Gas-6, an Axl activating ligand, and observed a dose-dependent increase in viral titers. In conclusion, this work proposes an AHR/Axl pathway with a key role during viral replication and highlights the relevance of these pollutant receptors during viral infections.

7122

SARS-COV-2 MAIN PROTEASE: MOLECULAR DYNAMIC STIMULATION WITH COMPOUNDS FROM AFRICAN NATURAL PRODUCTS

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The fast growth of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is causing a major threat to global public health, requiring the most urgent research for potential therapeutic agents. New targeted drugs are necessary to address the problem of resistance. The use of molecular dynamics (MD) simulations allows us to investigate the conformational details of biological systems as well as the interactions between proteins and ligands. In this work, we use molecular dynamic stimulation to validate some compounds from African Natural Products databases which have shown high affinity score with the main protease of SARS-CoV-2 by virtual screening. **Results:**Gypsogenic acid and Maslinic acid have revealed to have a high affinity with the main protease of SARS-CoV-2 by molecular dynamic analysis. Among the seven compounds used, two were shown very strong affinity for the SARS-CoV-2 main protease and those compounds are more likely to have anti-SARS-CoV-2 activities.

7123

PROMISING EFFECT OF SILYMARIN IN AN ANIMAL MODEL OF ARTHRITIS AND MYOSITIS INDUCED BY ALPHAVIRUS MAYARO AND CHIKUNGUNYA VIRUSES

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Mayaro virus (MAYV) and Chikungunya virus (CHIKV) are both members of the *Togaviridae* family causing similar diseases such as severe joint/muscle pain and fever. Our research group is focused on investigating factors contributing to the pathogenesis of MAYV and CHIKV, as well as identifying natural substances with potential antiviral activity. In a recent study, we demonstrated that silymarin, a complex of antioxidants obtained from *Silybum marianum*, exhibited antiviral activity against MAYV in cells. Subsequently, in animal model, we observed that silymarin displayed outstanding hepatoprotective, antioxidant, anti-inflammatory, and antiviral properties in liver of infected animals. Given that joint and muscle pain are prominent symptoms in Mayaro and Chikungunya fevers and that literature shows a potent antiviral activity of silymarin against these viruses, this study aims to evaluate in an animal model of arthritis and myositis induced by MAYV and CHIKV whether silymarin can reverse the damage to joints and muscles post-infection. To achieve this, 6-week-old BALB/c mice were infected with MAYV or CHIKV in the right hind paw pad (10^6 PFU) and the treated groups received 100 mg/kg/day of silymarin every 12 hours by gavage. Preliminary results from infected animals showed paw edema and inflammation, both of which were reduced in animals treated with silymarin. Euthanasia was performed on 7- and 12-days post-infection (dpi), and various organs/tissues including liver, spleen, brain, footpad, quadriceps, tibial, soleus, and extensor digitorum muscles were collected. CHIKV presence was assessed by qRT-PCR; in the quadriceps, tibial, and extensor digitorum muscles, no virus was detected in any of the groups. However, in the infected group that received silymarin, viral load was reduced in the liver, spleen, brain, and footpad at 7dpi, and in the liver, spleen, brain and soleous at 12dpi. The qRT-PCR results for MAYV are currently undergoing processing by our study group. These findings support further investigation into the potential benefits of silymarin in treating MAYV and CHIKV infections.

7124

DISCOVERY OF NOVEL HENIPAVIRUS INHIBITORS

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The prototype species of henipaviruses, Hendra virus (HeV) and Nipah virus (NiV), are zoonotic, negative sense, single stranded RNA paramyxoviruses capable of infecting at least 18 species across seven orders of animals and are considered a serious pandemic risk by the CDC. Following an incubation period of 5-14 days, NiV infection in people will often present as a severe respiratory, vascular, and neurological disease. Outbreaks of NiV, in Bangladesh and Malaysia have led to high rates of human mortality (40->90%) with significant morbidity in survivors. Transmission of infection to people can be through contact with natural hosts (*Pteropus* fruit bats), excreta-contaminated food, or infected virus-shedding livestock or people. There are no currently approved vaccines or therapeutics to prevent or treat NiV or HeV infection for human use. Work with authentic NiV requires BSL-4 containment which represents a substantial challenge to drug discovery efforts. Here we report the successful application of recombinant Cedar henipavirus encoding nano-Luciferase (rCedV-nanoLuc), a BSL-2 approved surrogate system, to screen for compounds that inhibit NiV and HeV replication. We screened 1.7 million compounds and processed hits through a hit-finding flow chart which includes secondary assays such as a novel BSL-2 NiV minigenome reporter and a biochemical assay probing the polymerase activity of the NiV L-protein. Several counter-screens were also included to filter out hits that prevent viral replication through inhibition of host cell roles. Compounds that passed all filters were subsequently tested for inhibitory activity against authentic NiV. Finally, in order to further accelerate henipavirus antiviral drug discovery and enable structure-based approaches, we solved the cryo-EM structure of the L polymerase in complex with the P protein. Here, we present a comprehensive approach that uses a combination of cell-based NiV surrogate systems, high throughput biochemical assays and structural biology analyses to identify new direct-acting antiviral candidates for the treatment of highly pathogenic henipaviruses.

7125

ASSAY DEVELOPMENT OF FLAVIVIRUSES CELL-BASED LUCIFERASE REPORTER SYSTEM TO ENABLE HIGH THROUGHPUT DRUG DISCOVERY

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There is an urgent need for antiviral therapies against flaviviruses. More than 1 billion people are at risk and disease burden is rapidly rising due to climate change. To prepare for future pandemics, the flavivirus program within UTMB-Novartis Alliance for Pandemic Preparedness (UNAPP) was established to find broad spectrum inhibitors targeting RNA-dependent RNA polymerase (RdRp), protease and NS4B. We have developed and validated high throughput cell-based assay on an automation platform to screen and prioritize compounds for Structure Activity Relationship (SAR) optimization enabling novel drug discovery. Using various *in vitro* transcribed recombinant stable nanoluciferase flaviviruses (Dengue, Zika, YF and JEV), >1500 compounds were tested in duplicates. The protocol was optimized for MOI, signal window and robustness in 384-well format, with robust Z' score of >0.5 for all flaviviruses. Viral replication was measured at 3dpi via luminescence readout. A chain-terminator adenosine analogue, a potent RdRP inhibitor, was used as active control, showing consistent activity and robust correlation with historical high-content image-based data. We have optimized the assay on an integrated automated screening platform in a BSL2 enclosure with robotic arms enabling movement of 384-well plates between various pieces of equipment, improving assay quality, reproducibility and throughput. The transfer of compound into an infected assay plate was possible using an acoustic liquid handler. With the current capacity to test 90 compounds per week in concentration-response in all 4 dengue serotypes, we enabled compound optimization towards increased pan-serotype activity with minimal cytotoxicity for our second-generation dengue NS4B project. In addition, similar cellular nanoluciferase assays were developed for Zika, YF and JEV to enable broad spectrum flavivirus profiling of protease and RdRP inhibitors. These established assays provide a critical opportunity to identify a novel broad-spectrum lead candidates that can be developed into a promising therapy, thereby alleviating the disease burden in future outbreaks.

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ESTABLISHMENT OF A BSL-2 NIPAH MINIGENOME SYSTEM FOR ANTIVIRAL DRUG DISCOVERY.

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Nipah virus (NiV) is a deadly and highly contagious zoonotic virus that emerged first in Malaysia and has a high mortality rate of 40 to 75% with severe morbidity in survivors. Nipah virus consists of a negative sense RNA strand (18.2 kb) consisting of L protein, an RNA-dependent RNA polymerase which forms a complex with phosphoprotein P. This complex is encapsidated by nucleocapsid N proteins allowing for viral replication. Owing to its high pathogenicity, NiV is classified as a BSL-4 virus. To enable work in a BSL-2 set up, we developed a noninfectious Nipah minigenome system as a valuable tool to identify potential inhibitors of Nipah replication for drug development. Utilizing only the minimum essential genetic elements required for viral replication, our current transient system is a 5-plasmid system consisting of N, P and L proteins and a minigenome construct that contains the NiV specific leader and trailer sequences flanking a nanoluciferase reporter gene and a T7 promoter. A T7 polymerase-encoding plasmid is co-transfected to generate the negative strand RNA mini genome. We successfully established a 384 well-plate transient assay in human host cells measuring luciferase expression 48hrs post transfection along with a parallel cytotoxic assay. We observed an AC_{50} as reported in literature for the tool compound in our NiV minigenome assay. Using this assay, we assessed NiV specific activity of inhibitors that were identified in a recombinant Cedar virus high throughput screen. To enhance assay robustness and decrease variability, also we developed and characterized a novel cell line stably expressing NiV N, P and L proteins that can be used to screen for novel inhibitors and support structural activity relationship (SAR) studies for Nipah drug development.

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RAPID-RESPONSE RNA-FISH ASSAY PLATFORM FOR CORONAVIRUS ANTIVIRAL HIGH-THROUGHPUT SCREENING

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Over the past 25 years, the global community has faced the challenges posed by three distinct outbreaks of coronaviruses. The first of these outbreaks was the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic, which occurred from 2002 to 2004 and tragically resulted in over 700 deaths. Following this, the Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic emerged in 2012, causing over 2600 infections with a case-fatality rate of 36%. More recently, the world has become severely impacted by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of the COVID-19 pandemic, responsible for causing nearly 7 million deaths worldwide. It is crucial to note that the threat of further coronavirus outbreaks continues to be a significant concern, as evidenced by the recent identification of the novel canine coronavirus CCoV-HuPn-2018 in several patients with pneumonia in Malaysia. The threat of the ever-evolving nature of viral infections as well as the lingering health and socioeconomic effects of the recent SARS-CoV-2 pandemic emphasize the urgent need for advanced antiviral drug screening tools to strengthen preparedness and preventive measures against future outbreaks. Here, we present the development and validation of a novel RNA-fluorescence *in situ* hybridization (FISH) assay as a high-throughput rapid response platform for antiviral drug discovery. The flexibility of RNA-FISH probe sets allows for synthesis to for any RNA viral genome, enabling detection of any viral replication inhibition of compounds within cells. Screening of 170 antiviral compounds in concentration-response demonstrates a strong R^2 correlation between the results obtained from our RNA-FISH assay and an immunofluorescence assay (IFA) in both human coronaviruses OC43 and 229E. Additionally, we successfully applied this methodology in the context of CCoV 1-71, opening new avenues for the evaluation of antiviral drugs to future emerging threats.

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UNVEILING THE ANTIVIRAL POTENTIAL OF WEDELOLACTONE AGAINST THE OROPOUCHE VIRUS

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Oropouche virus (OROV), belonging to the *Orthobunyavirus oropoucheense* specie and *Peribunyaviridae* family, induces dengue-like febrile illness transmitted by the midge *Culicoides paraensis* and some mosquito species. Despite its typically mild symptoms, it can lead to severe complications such as neurological symptoms. With diagnostic challenges, particularly in impoverished endemic regions, OROV poses a potential threat for new epidemics, akin to other arboviruses like Dengue, Yellow Fever, and Zika virus. Exploring natural molecules for antiviral properties offers a promising avenue for therapies with minimal or no side effects. Wedelolactone (WDL) has shown significant inhibitory effects on viral proteins and replication,

positioning it as a promising candidate across various viruses. Our study delves into WDL's antiviral activity against OROV. In Vero cells, WDL exhibited an EC_{50} value of 18.92 ± 9.4 μM under post-infection treatment condition, showcasing its inhibitory effect against OROV infection. Additionally, *in silico* analyses shed light on WDL's potential inhibitory action on the N-terminal polymerase of OROV, suggesting its effectiveness at multiple stages of viral infection in mammalian cells. These findings underscore WDL's potential as a promising inhibitor against OROV infection.

7129

2-PYRIMIDONE COMPOUND SERIES PREVENTS ACUTE VIREMIA AND CHRONIC CHIKUNGUNYA VIRUS IN A MOUSE MODEL OF INFECTION

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Alphaviruses are arthropod-transmitted RNA viruses, including the NIAID Category B priority pathogens Eastern equine encephalitis (EEEV), Venezuelan equine encephalitis (VEEV) and chikungunya (CHIKV) viruses. In November of 2023, the first chikungunya virus vaccine became FDA approved for use in individuals 18 years of age and older who are at increased risk of exposure to CHIKV, although no FDA-licensed antiviral therapeutics are available to treat alphavirus infection or disease, thus demonstrating a need in the field of public health. We identified a small molecule antiviral hit using a screen against CHIKV. Derivatives of the hit were made by medicinal chemistry, and we identified a first-in-class, orally available, non-nucleoside small molecule (SRI-42718) that targets a conserved region in nsP4-RdRp. The SRI-42718 chemical series blocks both gRNA and sgmRNA synthesis as well as viral protein production. The compound has shown no adverse toxicity in mice as repeat dosing at 40 mg/kg, TID, is a well-tolerated treatment for up to 10 days. *In vivo* PK analysis indicates that the compound has good bioavailability by oral delivery in mice and nonhuman primates, and the compound was distributed to several mouse tissues including joints and muscles. Importantly, oral administration of the compound prevents viremia at a dose of 40 mg/kg three times per day (TID) in acutely infected mice. Viral tissue burden and virus-induced foot/ankle swelling (tissue disease) are also significantly reduced in treated animals compared to vehicle controls. A seven-day treatment of mice beginning at 28 days post infection during the persistent phase reduced the viral RNA level in joint-associated tissue. Combined, our data indicate that SRI-42718 is capable of blocking CHIKV replication *in vivo* during both the acute and persistent phases, which increases the therapeutic potential for this compound. SRI-42718 promises to be an important preclinical candidate and the compound has entered early drug development studies.

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IN VITRO ANTI-SARS-COV-2 ACTIVITY OF CPM01 HERBAL TINCTURE AND ITS FRACTIONS

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The recent COVID-19 pandemic posed a significant challenge to public health worldwide and continue to threaten many lives. While vaccines are instrumental in curbing the spread of the virus, the need for effective treatment remains crucial in managing severe cases and emerging variants. CPM01, an herbal tincture developed by the Centre for Plant Medicine Research in Ghana as an immunomodulatory agent has garnered attention for its clinical efficacy in alleviating COVID-19 symptoms and expediting patient recovery without complications. The study sought to evaluate the anti-SARS-CoV-2 activity of CPM01 and its partitioned fractions *in vitro* in Vero E6 TMPRSS2 cells. The effect of CPM01 and partitioned fractions on SARS-CoV-2-induced cytopathy and virus inhibition was determined by crystal violet staining and fluorescence assay targeting the ORF3a protein of the virus respectively. The phytochemical content of CPM01 and fractions were quantified by colorimetry. The findings indicate that CPM01 and its chloroform fraction exhibited remarkable efficacy in preventing virus-induced cytopathic effect with a minimum inhibitory concentration of 0.31 μg/ml. The hexane and ethyl acetate fractions displayed promising virus inhibition, with minimum concentrations of 1.20 and 20.00 μg/ml respectively. The effective concentrations required to inhibit 50% (EC_{50}) of viral ORF3a were 5.55, 5.20 and 6.22 μg/ml respectively for CPM01, chloroform and hexane fractions. The total phenolic content (TPC) of CPM01 was determined to be 9.006±1.075 mg/100 mg GAE, while the total flavonoid content (TFC) was found to be 16.741±1.386 mg/100 mg QE. Even though the ethyl acetate fraction showed the lowest inhibition, it had the highest TPC and TFC, implying the anti-SARS-CoV-2 activity of CPM01 may not be dependent on its phenolic content alone. The findings highlight CPM01 as a potent anti-SARS-CoV-2 candidate with promising therapeutic potentials against COVID-19. However, further research involving mechanistic investigations and clinical trials, is imperative to comprehensively understand its role in managing COVID-19 and its evolving variants.

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GENERATION OF ANTIVIRAL RECOMBINANT PROTEINS TO OVERCOME MOSQUITO-BORNE VIRUS INFECTION

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Mosquito-borne virus infections impact more than 400 million people annually. With limited therapeutics available, the main control mechanism is vector control, however mosquitoes have become resistant to some insecticides. Other mechanisms to control arbovirus transmission include transgenic mosquitoes; however, the current methods are virus-specific or mosquito population replacement with lethal genes. Both control methods are insufficient because they are not broadly active against multiple viruses or long-lasting due to the ability for mosquito populations to rebound. Thus, alternative strategies that are broadly acting against multiple arbovirus families are needed. Host restriction factors are a large category of antiviral immune proteins, some of which can inhibit multiple virus families. For example, PKR and RNase L antiviral pathways are both activated by double stranded RNA (dsRNA), which is produced during the replication cycle of most viruses. However, viruses have evolved multiple strategies to evade these pathways to promote productive infection. To obtain broad antiviral activity, we generated recombinant enhanced antiviral restrictor (REAVRs) proteins containing the virus-sensing domains of PKR fused with the effector domains of RNase L. REAVRs showed high antiviral activity against dengue, Zika, and chikungunya virus when stably expressed in mammalian cells. Transgenic REAVR-expressing mosquitoes showed strong resistance against Zika virus infection and reduced virus dissemination. To improve efficacy of REAVRs, we have constructed a second generation of REAVRs with different vertebrate RNase L sensor domains and replacing PKR double-stranded (ds) RNA-binding domain with other sensor domains to further increase the breadth of viral families inhibited by REAVRs. We are currently characterizing the antiviral activities of these new REAVRs against a panel of arboviruses.

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USE OF AN INSECT CELL EXPRESSION PLATFORM FOR THE PRODUCTION OF NIPAH AND CRIMEAN-CONGO HEMORRHAGIC FEVER VIRAL FUSION, GLYCO-, AND NUCLEOPROTEINS

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Development of recombinant production methods characteristic antigens of priority pathogens, such as Nipah Virus (NiV) and Crimean-Congo Hemorrhagic Fever Virus (CCHFV), are critical for public and global health research. Recombinant proteins have numerous research and biopharmaceutical applications including the use in surveillance of potential outbreaks, studying immunological responses to infection, and the development of vaccines and serological assays. NiV has caused over 600 human infections between 1998 and 2023 in Singapore, Malaysia, Bangladesh, and India with case fatality rates up to 70%. CCHFV has resulted in over 450 human cases since its identification in the mid 1900s, throughout Africa and Southeast Asia overlapping with NiV endemic countries, CCHFV has case fatality rates between 5% and 30%. Currently, it is suspected that cases of CCHFV are largely underreported with several epidemiological studies showing a seroprevalence around 11% in endemic countries. This underreporting can be due to the lack of affordable multianalyte assays available in these areas. There is an urgent need to develop more cost-effective multianalyte serological assays to assess human and animal seropositivity to NiV and CCHFV. High quality recombinant protein production using a scalable *Drosophila* S2 expression system and affinity purification offers an avenue for the development of affordable multiplex immunoassays in both high and low resource settings. Here we present first results of the production of NiV (pre)fusion (pf/F), attachment (G), and nucleocapsid (N) proteins as well as CCHFV receptor recognition glycoprotein (Gc and Gn) and nucleocapsid (N) proteins using our proprietary expression vector and *Drosophila* S2 cells. Recombinant proteins were purified using metal ion affinity chromatography. This research allows for production of antigens to be further used in the development of multiplex serological assays. These can then be used to better understand the prevalence of infection in humans and livestock in endemic and co-endemic areas of NiV and CCHFV, as well as other priority pathogens.

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INITIAL CLINICAL CHARACTERIZATION OF EGT710, A NOVEL CORONAVIRUS MPRO INHIBITOR, FOLLOWING ORAL ADMINISTRATION TO HEALTHY ADULTS

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EGT710 is a low molecular weight inhibitor of the coronavirus main protease (Mpro). It has activity against 8 coronavirus genera Mpro enzymes and potent cellular activity against SARS-CoV-2 variants. It has also shown efficacy in vivo in a mouse infection model. The safety, tolerability, and pharmacokinetics of EGT710 were investigated in a randomized (3:1), blinded, placebo-controlled study of healthy adults at a single center using a conventional single and multiple ascending dose design. Each cohort was 8 study participants (6 receiving EGT710; 2 receiving placebo). A relative bioavailability and food effect study were also included to evaluate the performance of a capsule and liquid (suspension) formulation in a separate cohort of 18 study participants using a Williams crossover design. A total of 70 received EGT710 and 18 received placebo across all parts of the study. Single doses up to 1100 mg and multiple doses up to 700 mg once daily for 7 days were safe and well tolerated. The most common adverse events involved general disorders and administration site conditions, none of which was considered related to the study treatment. There were no evident dose-dependent or dose-limiting adverse effects. Systemic exposure increased with dose. The two formulations showed comparable bioavailability. Administration of the suspension formulation with food modestly increased exposure to EGT710 and delayed the Cmax, suggesting EGT710 may be taken with or without food. The dose range investigated included therapeutic and supratherapeutic exposures, thus generating sufficient data to support dose and regimen selection for subsequent investigations of clinical efficacy in patients with acute coronavirus disease (using established antiviral PK/PD relationships). The data support once or twice daily administration of EGT710 without the need for a pharmacokinetic booster (e.g., ritonavir). The results support continued development of EGT710 as a treatment for coronavirus disease. The liquid formulation provides a unique option for patients who are unable to swallow or have difficulty swallowing.

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INVESTIGATION OF ANTIVIRAL ACTIVITY OF MEK INHIBITORS AGAINST YELLOW FEVER VIRUS USING IN VIVO MODEL

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Yellow fever virus (YFV) causes an acute viral hemorrhagic disease, varying from very mild infection to severe and life-threatening illness, with mortality rate of 20-50%. YFV is endemic in tropical areas of Africa, and Central and South America, with massive outbreaks causing thousands of deaths in recent years, showing that YFV is still a serious public health concern despite the vaccination. To date there is still no specific antiviral treatment for YF. Here, we established the lethal dose (LD) of wild type YFV_BR_2018, a new YFV lineage, in knockout mice for interferon type 1 receptor (IFNAR $1^{-/-}$), and evaluated the potential activity of Selumetinib and Trametinib using this in vivo model. Four-weeks-old male and female C57BL/6 IFNAR$1^{-/-}$ mice were infected with 1.6 x 10^3 to 5.75 x 10^3 PFU of YFV_BR_2018, and monitored for 14 days. Mice infected with the higher dose had survival rates of 60% (females) and 40% (males). They clinical signs, as piloerection, hunched back, conjunctivitis, edema, paralysis, tremors, or penis inflammation. Infectious particles were found in the testicles of convalescent males. The deaths occurred between 8 and 11 days post infection. Then, 4- weeks-old male and female C57BL/6 IFNAR$1^{-/-}$ mice were infected with YFV_BR_2018 and treated with Selumetinib (50 mg/kg/day) or Trametinib (3 mg/kg/day) for 8 days. Neither Selumetinib nor Trametinib showed protection against mortality. It was possible to establish an infection model for the wild YFV_BR_2018 strain, with a mortality rate close to 50%. Although, antiviral effect against orthoflaviviruses have been shown for Selumetinib and Trametinib preliminary results do not indicate antiviral effect of tested inhibitors against YFV, based on mortality rate. Further analyses will be performed to address the effect of treatment on experimentally infected mice.

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EX VIVO ANALYSIS OF AN IL2/ANTI-IL2 COMPLEX FOR THE TREATMENT OF CHRONIC CHIKUNGUNYA ARTHRITIS IN A COLOMBIAN COHORT

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Chikungunya virus (CHIKV) is an alphavirus that causes chronic arthritis in one-fourth of patients. No standard treatments exist for CHIKV chronic

arthritis. Our Colombian cohort is the largest longitudinally followed CHIKV patient cohort in the Americas. Immune analysis from this cohort revealed that low IL2 during acute infection predicted chronic joint pain. Chronic CHIKV arthritis is associated with altered gene pathways in regulatory T cell (Treg) function, decreased interleukin (IL)-2 production, and CD4+ effector T cell (Teff) synovial infiltration. Novel low-dose IL2 therapies preferentially activate Treg IL2 receptors with no apparent side effects reported in rheumatoid arthritis patients who received this treatment. Our previous studies in a CHIKV arthritis mouse model demonstrated that treatment with a complex containing low-dose IL2 and anti-IL2 monoclonal antibody (mAb) expanded and activated Tregs more than IL2 or the IL2 mAb alone, but also expanded Teffs and did not impact tarsal joint inflammation. The IL2 mAb alone amplified activated Tregs, increased expression of Treg suppression marker FoxP3, and improved histologic markers of inflammation, perhaps by augmenting the activity of endogenous IL2. To understand the mechanism of these IL2-related therapies in human CHIKV arthritis, PBMCs collected from our Colombian cohort of chronic CHIKV arthritis patients and a small group of healthy Colombian volunteers will be exposed to low doses of IL2 or the IL2/anti-IL2 mAb complex for 5 days. Flow cytometry of Treg populations, functional Treg suppression assays, and cytokine analysis will then be performed. This will be the first study to use an IL2/anti-IL2 mAb complex ex vivo using PBMCs from healthy donors or CHIKV arthritis patients. We hypothesize that IL2/anti-IL2 mAb complex treatment will significantly increase Treg immunosuppressive function via enhanced FoxP3-mediated CTLA4 suppression of Teff cells. This study is an important step toward determining the feasibility and safety of low-dose IL2-based treatments for CHIKV arthritis. This investigation is underway, and data will be available by August 2024.

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NOVEL IL2 FUSION PROTEIN FOR THE TREATMENT OF CHIKUNGUNYA VIRUS-INDUCED CHRONIC ARTHRITIS IN A MOUSE MODEL

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Chikungunya virus (CHIKV) is an alphavirus that causes persistent arthritis in one-fourth of patients. There are no standard treatments available for CHIKV chronic arthritis. Our preliminary data suggest that alteration of regulatory T cell (Treg) function and low IL2 levels play a role in CHIKV arthritis pathogenesis. Low-dose recombinant IL2 (rIL2) is an effective therapy for the treatment of autoimmune disease and may be of use in CHIKV arthritis flares. When rIL2 is complexed with an anti-IL2 monoclonal antibody (mAb), enhanced Treg differentiation is present in animal models. The mouse model for post-CHIKV arthritis involves footpad inoculation of wild-type C57BL/6 mice, which causes localized swelling and systemic infection. We previously treated CHIKV-infected mice with rIL2, anti-IL2 mAb, or rIL2/anti-IL2 complex. The complex increased peripheral IL2 and expanded and activated Tregs more than the other treatments, but also expanded effector T (Teff) cells and did not improve histological scores. We hypothesize that using a novel IL2 fusion protein in place of the complex will improve the outcomes by decreasing off-target Teff cell stimulation and improving histological inflammation markers. A fusion protein of IL2 and mouse IL-2Rα (CD25) joined by a non-cleavable linker extends the IL2 half-life and improves in vivo efficacy for Treg expansion and control of autoimmunity than rIL2. Mice infected with CHIKV or saline will be confirmed positive or negative by PCR. After the virus is cleared, mice will be treated with saline, rIL2, or the fusion protein for 5 days, at which time blood will be collected for cytokine analysis, spleen tissue harvested for flow cytometry analysis of T cell populations, and synovial tissue fixed for histology. This research provides a pre-clinical evaluation of fusion protein therapy for CHIKV arthritis and insights into using this novel therapeutic for alphavirus arthritis. This investigation is scheduled to begin in May 2024, and data will be available by September 2024.

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SYNTHESIS OF NOVEL QUINONES WITH ANTIVIRAL ACTIVITY AGAINST IMPORTANT HUMAN FLAVIVIRUSES

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Flaviviruses such as the dengue serotypes (DENV 1 to 4), and Zika (ZIKV) viruses pose a significant global burden to human public health worldwide. Despite advances in drug development, there are no effective antivirals or vaccines available for the treatment of these rapidly spreading viruses. Natural products (e.g. flowers, leaves, herbal plants) are a potential source of chemical compounds from which it has been documented antiviral activities with good tolerability and minimal side effects. Quinones are abundant natural substances, mainly characterized by intramolecular unsaturated cyclic diketone structures, and includes benzoquinones, naphthoquinones, and anthraquinones. Quinones are known to contribute to various biological activities, including pharmacological effects such as anticancer, anti-inflammatory and antiviral properties. As quinones have different biological activities for different receptors, it is considered a privileged structure. Here, we enhanced the structural complexity of quinones by alkylation and/or acylation reactions increasing their Fsp^3, and evaluate their antiviral activity against DENV (1 to 4) and ZIKV *in vitro*. A library of 21 natural compounds were initially tested for their ability to cause cytotoxicity (μM) on mammalian cells *in vitro*. Then, concentrations that maintained a cell viability higher than 90% were used to inhibit the infection with DENV (1 to 4) and ZIKV using a cell-based neutralization assay. Preliminary results indicate that carminic acid, together with aloemodin and their derivatives A2, A3, A4, A8 and A9 were able to reduce the infection of mammalian cells with all DENV serotypes and ZIKV. Further experiments will help to elucidate the magnitude of their antiviral activity (EC_{50}) as well as the antiviral mechanisms by which viral inhibition occurs in mammalian cells. These results are promising as natural products must play an important role in contributing to antiviral drug development as alternatives to combat the increasing burden of mosquito-borne diseases worldwide.

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BIASES IN ATTRIBUTION METHODS FOR NOROVIRUS ACUTE GASTROENTERITIS

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The estimated global burden of acute gastroenteritis (AGE) attributable to norovirus varies by the method used to estimate the pathogen-specific burden of disease. One method ("detection-as-etiology" [DE]) considers any norovirus detection to be etiologic, such that the population attributable fraction (PAF) of AGE is norovirus prevalence; but many coinfections are often observed among AGE cases, so not all detection is etiologic, causing overestimation. Another method ("odds-ratio" [OR]) considers the PAF to be function of the odds ratio comparing detection of norovirus among AGE cases and healthy controls, but this method may be confounded by natural immunity acquired from prior norovirus infection, causing underestimation. To assess the biases in these attribution methods and develop an alternative method, we developed a norovirus transmission model accounting for repeated infection and natural immunity to estimate the incidence of symptomatic norovirus infection, from which a model-based (MB) PAF was calculated. We fit the model to the country-specific norovirus prevalence in AGE cases and controls in the multinational MAL-ED cohort study, understanding relationships between enteric infections and a variety of health outcomes, to estimate the transmission rates of

norovirus and other pathogens and solve for the endemic equilibrium. We used the equilibrium states to calculate country-specific PAFs for the DE and OR methods. We characterized the bias as the difference between the MB PAF and the other PAFs. The MB norovirus prevalence in the AGE cases and controls was generally consistent with the observed. The PAF of the DE method expectedly exceeded the others, while the OR PAF was unexpectedly larger than the MB. The biases in the DE and OR methods are similar across most countries, with average relative differences of +290% and +92%, respectively, compared to the MB. Modifications of the model to reflect the variations in natural history by country that were observed in MAL-ED may further refine the attribution bias estimates.

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TOSCANA VIRUS - FINDING THE NEW VECTORS

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Arbovirus *Phlebovirus toscanaense* (TOSV) is an emerging but still neglected human pathogen that circulates in countries around the Mediterranean Sea. The manifestation of the disease varies from non-symptomatic forms through febrile illness to central nervous system disease. Although, it is one of the leading causes of meningitis and encephalitis, information about TOSV biology and epidemiology is limited. Based on the nucleotide sequences, TOSV is currently divided into 3 genetic lineages A, B and C; but the latter was only described based on partial sequences and virus isolate has never been obtained. Currently, there are only two species of sand flies (Diptera: Phlebotominae), *Phlebotomus perniciosus* and *P. perfiliewi*, considered as a proven TOSV vectors. However, the spread of TOSV to the new areas as well as the TOSV detection in several sand fly species suggested that the vector spectrum could be much broader. Here we aim to study in detail the vector competence of four sand fly species (*P. tobbi*, *P. sergenti*, *P. papatasi,* and *Sergentomyia schwetzi*) to two TOSV strains: 1500590 (TOSV A) and MRS20104319501 (TOSV B). Sand flies were infected by artificial feeding system with blood containing virus and fed females were collected and dissected at days 4, 8 and 14 after infection for virus quantification by infectious viral particles titration and RT-qPCR assay. First, we show that TOSV B appears to be more successful in development in sand flies than TOSV A. Moreover, *P. tobbi* with an infection rate of 66% and 53% at D4 and D8, respectively, seems to be the most susceptible species with a weak gut barrier to infection. In contrary, *P. sergenti* seems to be less susceptible to TOSV B with an infection rate of 5.5%, even though the virus disseminated in the head of all infected females. Additionally, *P. papatasi* and *S. schwetzi* appear to be refractory to TOSV B strain infection. In conclusion, our data suggest that two more sand fly species (*P. tobbi* and *P. sergenti*) are potential vectors of TOSV. In the context of climate changes and human activities, this information is crucial as sand flies are expected to expand to new areas, together with pathogens they carry.

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THE IMPACT OF CHRONIC SCHISTOSOMIASIS ON CO-INFECTIONS WITH DENGUE VIRUS IN MADAGASCAR

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Chronic schistosomiasis is highly prevalent in the tropics and can cause high morbidity. Research on the impact of this disease on morbidity caused by viruses circulating in the same areas, such as dengue virus (DENV), is scarce. Madagascar is a country highly endemic for schistosomiasis with only sporadic outbreaks of DENV. Our hypothesis is that chronic schistosomiasis might confer protection against DENV infections or dengue fever progression. A total of 990 serum samples, collected through a cross sectional study in schistosomiasis and DENV endemic regions of Madagascar have been collected and analyzed for Schistosome infection (59,5 %) and DENV/*Flaviviridae* seroprevalence (3,3 %/16,9 %) through an in-house PCR and pan-DENV IgG ELISA, respectively. Among them, 822 samples were used in a plaque reduction neutralization test (PRNT) to assess their potential to alter DENV infectivity. A significant reduction of the median plaque number in Schistosome-infected participants was observed and this effect remained significant when adjusting for other biological variables such as age and sex. In our Malagasy study population, we observed a low seroprevalence of DENV in a highly endemic schistosomiasis area. Our preliminary results corroborate our initial hypothesis of schistosomiasis interfering with DENV infections with the underlying molecular mechanisms remaining to be further investigated.

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MONITORING SURFACE CONTAMINATION WITH SARS-COV-2 AND INFLUENZA IN AN ADVANCED RESEARCH LABORATORY SETTING IN GHANA: A PROPOSAL FOR EFFECTIVE PREVENTIVE MEASURES

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The emergence of respiratory viruses such as SARS-CoV-2 and influenza presents significant challenges to public health. Understanding surface contamination and transmission dynamics within laboratory settings is crucial for implementing effective preventive measures. The aim of this study was to monitor laboratory surfaces contamination with SARS-CoV-2 and influenza viruses in an advanced research laboratory. We pre-moistened swabs with Virus Transport Medium and swabbed common shared surface areas in the laboratory environment, and its surroundings. Swabs were tested for the presence of SARS-CoV-2 and influenza viruses using real time RT-PCR with primers/probes and assays described by the CDC,USA . A total of 674 samples were collected from these surfaces between June 2023-April 2024 and tested. Out of this, 52% (352/674) were collected before commencement of work day and 48% (322/674) close of work. The distribution of swabbed surfaces were as follows: 16% (106/674) from lab benches, 8% (53/674) from biosafety cabinet used for RNA extraction, 8% (53/674) from biosafety cabinets used to prepare master mix only, 8% (53/674) from biosafety cabinets for template and positive controls addition only, 16% (106/674) from freezer door handles, 8% (53/674) from centrifuges and vortexes, 16% (108/674) from lab door handles and 5% (36/674) from a shared table used by all staff. Of the samples tested, 0.30% (2/674) SARS-CoV-2 RNA was detected from lab door handles before start of work day. The rest of the samples tested negative for SARS-CoV-2 and influenza. SARS-CoV-2 RNA was detected in the samples. Though not significant (p value = 0.397), the resultsshows the importance of such an attempt as it has implications for contamination and health of staff. Again, the fact that all other surfaces were negative for SARS-COV-2 shows strict adherence to decontamination procedures and good laboratory practices. This proactive approach will not only safeguard the health of research staff and limit contamination, but also provide valuable insights for similar settings globally. It is recommended that staff wash their hands prior to exiting laboratories.

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MULTIFACTORIAL CHARACTERIZATION OF DENGUE TRANSMISSION DYNAMICS IN THE FRENCH CARIBBEAN ISLANDS TO BETTER PREPARE FOR FUTURE EPIDEMICS

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Dengue is now the most widespread arboviral disease with incidence increasing more than 10-fold over the past 20 years, reaching a peak of 5.2 million cases in 2019, according to World Health Organization (WHO). The Americas are currently facing an unprecedented crisis, with more than 4 million cases of dengue recorded since the outbreak began in 2023, according to the Pan American Health Organization (PAHO). While it is endemic in all tropical and subtropical areas of the world, the Caribbean is one of the most affected regions, especially since the reintroduction of the *Aedes aegypti* vector in the 1970s. Since 2006, all four serotypes of dengue virus (DENV) have been detected during differents epidemics, with heterogeneous circulation in the French Caribbean islands (Guadeloupe and Martinique). During the recent outbreak in 2019-2021, three DENV serotypes were detected (DENV-1, DENV-2 and DENV-3), but curiously, their circulation was not homogeneous, with DENV-2 predominating in Guadeloupe, while DENV-3 was the main serotype circulating in Martinique. To investigate if genomic features of serotypes circulating in both islands were different, full genome sequencing was carried out on strains collected during the recent 2019-2021 outbreak in Guadeloupe and Martinique. Phylogenetic data revealed the homogeneous presence of genotype V for DENV-1, cosmopolitan genotype for DENV-2 and genotype III for DENV-3 in both French departments. To determine whether these differences in circulation of these viral strains are linked to a difference in vector transmission capacity, recent evaluations of vector competence of the 3 serotypes circulated during the 2019-2021 outbreak, as well as the current epidemic (DENV-2 only), were carried out on 6 populations (3 in Guadeloupe and 3 in Martinique) of *Aedes aegypti*, the local mosquito vector. Overall, these results confirm the active circulation of DENV in these regions, will help identify the factors inducing the epidemiological differences observed between the two islands and contribute to a better preparedness to cope with DENV emergences in the French Caribbean islands.

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A COMPREHENSIVE ANALYSIS OF COINFECTION DYNAMICS MODULATING MOSQUITO VECTOR COMPETENCE

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Arboviruses constitute a significant global health burden in part due to their complex ecologies and transmission dynamics. A growing area of interest towards controlling such pathogens are insect-specific-viruses (ISVs), as arbovirus-ISV coinfection has been shown to modulate vector competence, decrease viral titer, and block dissemination of medically important viruses. The biological mechanisms through which ISVs can impact arboviruses are poorly understood, but may include superinfection exclusion, sequestration of host factors, or effects on mosquito physiology. Studying these interactions can shed light on virus-virus interactions and vector competence within mosquitoes. However, such experimental approaches can be complex, and lack of standardization in data reporting makes comparison of outcomes across studies difficult to interpret. Through a comprehensive literature search we will collect and standardize coinfection experimental outcomes highlighting infection, dissemination, and transmission of arboviruses into a database. This database will support modeling networks for known ISV-arbovirus interactions in mosquitoes, which will be applied towards predicting ISVs that can suppress arboviral transmission. We will then test these predictions using *Aedes* sp. cell lines that have either competent or dysfunctional RNAi responses. Further testing will include additional *in-vitro* and mosquito colony experiments to validate modeling predictions and better understand ISV-arbovirus-vector interactions.

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MIDGUT ESCAPE OF YELLOW FEVER 17D VACCINE IN *AEDES AEGYPTI* AT AUGMENTED TEMPERATURES

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Yellow fever virus (YFV) is spread to humans by *Aedes* mosquitoes and is endemic in tropical regions of Latin America and Africa. Climate change projections predict a range expansion of *Aedes aegypti* and an increased risk of transmission to humans. In endemic regions, YFV outbreaks are mitigated using the highly safe and efficacious live attenuated vaccine, YFV-17D. Previous studies have addressed the competence of *Ae. aegypti* for YFV-17D. While this vaccine replicates in the mosquito midgut, it does not disseminate efficiently compared to wild-type YFV strains. For many *Aedes*-arbovirus pairings, increased temperatures alter vector competence. However, the impact of temperature on *Ae aegypti* vector competence for YFV-17D is poorly understood. Therefore, we exposed *Ae. aegypti* to YFV-17D and held them at varying temperatures (29°C, 32°C, and 34°C). On days 7 and 14 post-infection, we collected midguts, and legs and wings, then measured viral RNA using qRT-PCR to determine midgut infection and escape. We found a temperature-dependent increase in YFV-17D midgut dissemination; 54% of mosquitoes at 34°C had YFV-17D in their legs and wings compared to 8% of mosquitoes at 29°C. While mosquitoes had increased rates of dissemination at 34°C, they also displayed increased levels of virus in their legs and wings at both time points. This suggests that higher temperatures lead to both increased midgut escape and YFV-17D replication in *Ae. aegypti*. Ongoing research will characterize mechanisms of enhanced midgut escape at increased temperatures and determine whether YFV-17D can infect and escape the salivary glands, allowing for transmission. Additionally, we will sequence the virus to determine whether YFV-17D attenuating mutations are maintained through midgut escape.

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A SPATIALLY RESOLVED AND ENVIRONMENTALLY INFORMED FORECAST MODEL OF WEST NILE VIRUS AND ST. LOUIS ENCEPHALITIS VIRUS IN COACHELLA VALLEY, CALIFORNIA

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St. Louis encephalitis virus (SLE) is endemic to California and was detected annually until 2003 when West Nile virus (WNV) was identified in California. SLE was not detected again in California until 2015, and has been endemic since the recent introduction.. WNV and SLE exist in a complex transmission cycle that uses the same amplifying host, i.e., birds, and mosquito vectors. WNV is known to be a faster replicating virus, achieving higher viremias in both birds and mosquitoes. SLE, while slower, appears to be able to reach detectable transmission levels during periods when WNV transmission is low in the system, but it is still unclear how infection with one disrupts the transmission of the other. Preliminary analyses suggest that since the reintroduction of SLE to California in 2015, WNV and SLE transmission have occurred simultaneously. Like the dominance of WNV after its introduction in 2003, SLE outcompeted WNV from late 2015 when introduced and in 2016, possibly due to bird naïveté. In-season dynamics between WNV and SLE in mosquitoes may be dependent on when each

virus emerges, as both have the potential to outcompete the other and spillover to humans. Thus, a better understanding of how interactions of SLE and WNV impact the transmission cycle may improve our ability to predict arboviral risk and spillover events. This study builds on our previously developed multi-model inference system of WNV in Coachella Valley, California, and aims to incorporate and mathematically explain the interplay between WNV and SLE. We developed and tested a spatially resolved ensemble model to understand how fluctuations in environmental conditions influence WNV mosquito infection rates in the Coachella Valley. Using 17 years of mosquito surveillance data, we will compare how environmental conditions associated with WNV amplification change related to the SLE observed infection rates. Accurate early season predictions of arboviral risk have the potential to allow local abatement districts and public health entities to implement early season interventions such as targeted adulticiding and public health messaging before human transmission occurs.

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A DOUBLE THREAT TO ARTEMISININ-BASED COMBINATION THERAPY (ACT). EFFICACY IN AFRICA: REDUCED SUSCEPTIBILITY OF *PLASMODIUM FALCIPARUM* TO BOTH ARTEMISININ AND LUMEFANTRINE

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Clinical management of uncomplicated malaria caused by Plasmodium falciparum is reliant on the effectiveness of artemisinin-based combination therapy (ACT). New parasite genotypes encoding variants of the pfk13 gene are now emerging in Africa, and these are less susceptible to the artemisinin component drugs of ACT. This then poses a risk of resistance-selection against ACT partner drugs. Parasites of Ugandan origin isolated from two ACT-treated UK travellers with documented treatment failure, adapted to long-term culture in 2022, were less susceptible to lumefantrine in vitro than parasites from successfully treated individuals. This suggests that changes in parasite susceptibility to lumefantrine may contribute to treatment failure in these patients. Thus, the major African ACT, artemether-lumefantrine (AL), may now be at risk. We present a comprehensive assessment of in vivo treatment outcomes, in vitro parasite susceptibility to artemisinin and lumefantrine, and genomic and genotyping data from UK travellers with imported P. falciparum infections presenting from 2022 to 2024. This series includes 16 cases that suffered a relapse of symptomatic parasitaemia within weeks of initial treatment with AL. Future drug strategies for more effective malaria chemotherapy in Africa will be proposed in the light of these findings. Finally, we will consider the wider public health implications of a potential emergence of reduced lumefantrine susceptibility among African populations of P. falciparum.

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COMBINATION OF REDOX MODIFIERS WITH ARTEMISININ RESULTS IN INCREASED PARASITE SUSCEPTIBILITY TO ARTEMISININS

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Resistance has been recorded for every class of antimalarial, including artemisinin combination therapies (ACTs), the current first line. Drug resistant parasites have been reported to have an increased ability to manage oxidative stress and maintain redox homeostasis following drug treatment, possibly due to an enhanced antioxidant system. We hypothesised that disrupting this redox balance by targeting the parasites' glutathione pathway will make parasites more susceptible to oxidative stress, and therefore re-sensitise them to existing antimalarials. This work aims to tackle resistance by identifying redox-modifying drugs that can be combined with artemisinin derivatives. Growth inhibitory studies and ring-stage survival assays were used to determine the antimalarial activity of different redox compounds and to identify compounds that could be synergistic with artemisinin in vitro. Real time analysis of parasite intracellular glutathione was observed using *P. falciparum* NF54*attB*$^{[hGrx1\text{-}\ roGFP2]}$ parasite line and a plate reader based redox assay. Untargeted and targeted thiol metabolomic were carried out to identify metabolic changes in drug treated parasites. We identified sulforaphane (SFN) to be a promising candidate, which alters parasite redox status and potentiates the activity of artemisinin. The combination of 15μM SFN with 700nM dihydroartemisin (DHA) in early ring-stage parasites resulted in a decrease in parasite survival compared to DHA alone (41% ± 7.3).15μM SFN resulted in an increased oxidative burden within parasites after 1 h incubation. Untargeted and targeted thiol metabolomics confirmed that SFN's antimalarial activity is entirely redox mediated and not as a result of major metabolic changes within the parasite The addition of SFN to existing antimalarial therapies would re-sensitise resistant parasites to existing antimalarials thereby extending their life span. Ongoing studies will elucidate the mechanism responsible for this synergistic activity and determine the safety and efficacy of this approach in drug-resistant in vivo models of malaria.

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VARIABILITY IN ANTIMALARIAL DRUG SUSCEPTIBILITY PATTERNS IN KISUMU AND MARIGAT DURING THE PERIOD OF INCREASING FREQUENCY OF ARTEMISININ RESISTANCE GENOTYPES

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Malaria remains a major public health threat globally affecting 241 million people annually. Persistent malaria burden has been attributed to rapid emergence and spread of parasite resistance to policy recommended drugs. Consequently, timeliness of detecting drug resistance in diverse transmission regions is critical. This established susceptibility of *Plasmodium falciparum* parasites from Kisumu and Marigat between 2018 and 2023 using in vitro testing, genomic analyses and passive monitoring of treatment outcomes. A total of 637 consenting individuals aged 6 months and over, presenting with uncomplicated malaria were treated with Coartem® according to weight band and monitored on Day 7 to assess treatment outcomes. Up to 5mL whole blood samples collected from each individual prior to start of medication were latter tested for in vitro susceptibility to 14 antimalarial drugs. Each sample was tested for species composition, single nucleotide polymorphisms (SNPs)in drug resistance genes, and presence of residual parasitemia on day seven using genomic analyses techniques. 475/ 637 individuals comprising 385 from Kombewa and 90 from Marigat tested positive for malaria by polymerase chain reaction (PCR) assay. In vitro susceptibility showed mean ±standard deviation values of 25.1±32.5ng/ml for chloroquine, 32.7±22.3 ng/ml for quinine, 2.9±2.3 ng/ml for artemether and 40.0±38.3 ng/ml for lumefantrine. 70% of the infections contained P. falciparum single species infection while 30 % were contained P. falciparum species alongside other nonfalciparum species as multiple species infections. SNPs analyses showed three nonsynonymous mutation Pfk13 gene V568G, T508N and N554S in two samples and 36% mutation in PfMDR1-Y184F. PfMDR1 N86Y and Pfcrt K76T were wild-type for the entire study period. None of the day 7 visit samples tested positive for malaria by molecular diagnosis suggesting that all infections resolved after treatment with coartem®. Continuous monitoring of changing parasite susceptibility by in vitro and molecular methods is essential for early detection of resistance.

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MALARIA DIAGNOSIS AND DRUG RESISTANCE IN A MILITARY HOSPITAL IN YAOUNDE, CAMEROON

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The burden of malaria remains high in Cameroon, with almost 35% overall mortality. We studied diagnosis and drug resistance genes (DRG) for malaria in Yaounde military hospital, Yaounde, Cameroon. Microscopy, HRP2 Rapid Diagnostic Test (RDT), qPCR, and sequencing for DRG were used in this study. From March 2021 to December 2023, we enrolled 3,000 acute febrile illness cases (median age 35 years, 49% males). Microscopy identified 1,267 (42.2%) cases and had a higher positive detection rate than RDT (762 cases, 25.4%). qPCR identified 557(32.4%) cases out of 1,698 tested. HRP2 RDT negative cases had a mean of 43.9% in microscopy and in qPCR positive cases, suggesting a high prevalence of *pfhrp2* gene deletion and evidence for shifting from RDTs based only on HRP2. Sequencing for *Pfcrt*, *Pfcytb*, *Pfk13*, *Pfdhfr*, *Pfdhps*, *Pfmdr1*, and *Pfatp6* antimalarial DRG was done on a random set of 250 microscopy positive samples. For *Pfk13*, no mutations were observed in the propeller region, however, multiple mutations including G112E (4%), L116I (1%), K189T (58%), K189N (4%), L258M (1%) and R225K (1%) were noticed outside this region. *Pfatp6* mutant alleles H243Y (9%), L402V (14%), E431K (18%) and D436Y (1%) were detected. Wild type allele *cytB* was present in all samples. *Pfdhfr* haplotype N51I/C59R/S108N was detected in 95% of the samples, whereas C59R/S108N was observed in an additional 3%. *Pfdhps* mutant alleles were I431V (14%), S436A (37%), A437G (79%), K540E (2%), A581G (11%) and A613S (12%). *Pfcrt* new mutation C44F was noticed in all samples, K49Q in 0.8%, the triple resistant genotype (M74I/N75E/K76T) in 1.6% and M74I/N75D/K76T in 0.8%. *Pfmrd1* resistant genotype (N86Y) was found in 11% and the mutant allele Y184F in 75% of the isolates. Mutations associated with artemisinin and atovaquone resistance were not detected, suggesting efficacy of these drugs in Yaounde, whereas mutations conferring sulfadoxine-pyrimethamine resistance predominate. Finally, we noticed a decline in the prevalence of mutant chloroquine resistance alleles compared to previous decade. This study indicates a high prevalence of antimalarial DRG polymorphisms.

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INVESTIGATING *PLASMODIUM FALCIPARUM EX-VIVO* DRUG RESPONSES TO ARTEMISININ-BASED COMBINATION THERAPIES (ACTS) PARTNER DRUGS IN GHANA

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Antimalarial drug resistance poses a threat to malaria control. While artemisinin-based combination therapies (ACTs) are presently the most effective frontline antimalarials, signs of resistance are emerging in Africa. This includes resistance to artemisinin driven by mutations in *Plasmodium falciparum kelch13* gene and reduced efficacy of ACT partner drugs, but the extent of resistance to partner drugs such as AQ and LUM is not well understood. We assessed the *ex-vivo* sensitivity of clinical isolates cultured from individuals attending LEKMA or University of Ghana hospitals with confirmed malarial fever. We also determined the prevalence of known antimalarial drug resistance markers in these isolates using ONT-based amplicon sequencing. Mean 50% inhibitory concentrations (IC_{50}) results were below standard thresholds for resistance to CQ, DHA and AS, except one isolate that had mean IC_{50} values of 26.20 nM and 38.30 nM, above cutoffs for DHA and AS respectively. This isolate did not carry any validated *kelch13* mutations. Two isolates (4.08 %) and seven isolates (14.29 %) showed reduced susceptibilities to LUM and PPQ, respectively. About 29.50 % and 45.50 % isolates carried the combined *dhfr:dhps* quintuple mutant (IRNI-AGKAA) and quadruple mutant (IRNI-SGKAA) respectively. These combined mutant haplotypes are known to confer increased resistance to SP. In conclusion, we demonstrated that parasites are still sensitive to CQ, DHA and AS. However, there is emerging tolerance to LUM and PPQ that needs further investigation.

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AMPLICON DEEP SEQUENCING OF *PFKELCH13* GENE IN PATIENTS WITH *PLASMODIUM FALCIPARUM* MALARIA DURING THE THERAPEUTIC EFFICACY STUDY TRIALS FROM 2020 TO 2022 IN SENEGAL

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Senegal has used artemisinin-based combination therapy (ACT) to treat uncomplicated *Plasmodium falciparum* infection since 2006. Artemisinin (ART) resistance is mediated by mutations in the *Pfkelch13* (*PfK13*) gene and parasite genomic background modulates this resistance. Therapeutic Efficacy Studies (TES) demonstrate that ACTs including artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ) remain efficacious in Senegal. The appearance of ART resistance in Africa increases the urgency for ART resistance surveillance in Senegal. We used TES samples from Senegal to identify *PfK13* mutations among *P. falciparum* infections detected after day 0 (D0) of ACT treatment. We used amplicon sequencing of 400 TES samples from Kédougou, Kolda, and Kaolack (2020 - 2022). Participants were treated with AL or ASAQ on D0 with 28 (AL) or 42 (ASAQ) day follow up. Samples came from individuals that were parasite positive after D0, with priority given to pairs of samples (D0 and day of failure or DF). The 400 samples include 34 from 2020 (17 D0 + 17 DF); 22 from 2021 (11 D0 + 11 DF); and 56 from 2022 (28 D0 + 28 DF). We included an additional 288 DF samples from 2022. Samples were subjected to targeted amplicon sequencing of pooled and indexed samples. Sequencing data were aligned to the reference (PF3D7_1343700) sequence and four mutations in the propeller domain were identified from among the 400 samples. These variants and their frequencies included: V566L (0.25%), A578S (0.74%), V589I (0.25%), V637I (0.5%). An additional four mutations were found outside the propeller domain: T149S (0.25%), K189T (15%), K189N (1%), R255 (0.25%). None of these mutations are validated as associated with ART resistance. While new *PfK13* mutations need to be phenotypically tested for partial ART resistance, the appearance of DF infections may also result from partner drug resistance. Ongoing molecular surveillance for known and emerging malaria drug resistance mutations is important for detection of emerging risk and to identify novel mutations that may contribute to ART resistance in different genomic backgrounds.

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DISSECTING THE ROLE OF *PLASMEPSIN II AND III* IN PIPERAQUINE RESISTANT *PLASMODIUM FALCIPARUM* LINES

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Artemisinin (ART) combination therapies (ATC) are the current first line anitimalarials used world-wide. Resistance to both ART and the partner drugs like piperaquine (PPQ) are occurring and spreading in South East Asia. Major genetic determinants associated with recrudescence attributed to the partner drug PPQ are increased copy numbers of *plasmepsin II* and *III* and as well as mutations in the *chloroquine resistance transporter* (*pfcrt*). While mutations in *crt* were shown to be protective in vitro, experimental data on the role of plasmepsins in PPQ resistance is sparse. We have previously presented a bimodal growth response to increasing PPQ concentrations in PPQ resistant *Plasmodium falciparum* isolates from Cambodia in the absence of *crt* mutations. We chose the area under the curve (AUC) instead of the conventional half-maximal effective concentration (EC_{50}) used in drug assays to quantify the bimodal response. To specifically determine the role of plasmepsins in the response to PPQ, we used a relevant Cambodian isolate with a duplication in *plasmepsin II* and *III* but no mutation in *pfcrt*. Using this clonal isolate, we generated *plasmepsin II*, *plasmepsin III* and *plasmepsin II/III* combination KO lines with the CRISPR/Cas9 system. Our data demonstrate that a reduction in in *plasmepsin II* or *III* decreases the AUC three or six fold, respectively, compared to the parental line indicating direct involvement of *plasmepsin II* and *III* in the PPQ response at high concentrations. We detected a three to six fold increase in free heme in parasites treated with PPQ but no major differences between hemoglobin catabolism in parasite lines with different *plasmepsin* copy numbers. In contrast, changing the homeostasis of the food vacuole with pH modulators (CCCP or concanamycin A) did reduce survival under high PPQ exposure up to 50%. We demonstrated that increased *plasmepsin* copy number enhances survival under high PPQ pressure in Cambodian parasites and likely contributes to the emergence of resistance.

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POPULATION PHARMACOKINETICS OF ARTEMETHER-LUMEFANTRINE PLUS AMODIAQUINE IN PATIENTS WITH UNCOMPLICATED *PLASMODIUM FALCIPARUM* MALARIA

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Uncomplicated falciparum malaria is commonly treated with an artemisinin-based combination therapy (ACT), which has contributed to the reduction of the worldwide burden of malaria. Resistance to the artemisinin component and to the partner drug in ACTs has been observed in Southeast Asia, and artemisinin resistance has recently also emerged in eastern Africa. 'Triple' ACTs, consisting of two partner drugs with different mechanisms of action and similar pharmacokinetic profiles, could help to counter the effects of artemisinin resistance and prolong the efficacy of partner drugs. When adding a new compound to a combination, assessments of potential drug-drug interactions are needed to verify that all components attain therapeutic levels while remaining safe. The analyses presented here used data from two randomized, controlled interventional trials conducted in 7 Asian and 1 African countries, in which artemether-lumefantrine was given with or without amodiaquine to patients with malaria. Both studies included a cohort with dense pharmacokinetic sampling, combined with sparse data from the rest of the patients. Concentration-time data of artemether, dihydroartemisinin, lumefantrine, desbutyl-lumefantrine, amodiaquine, and desethylamodiaquine were analysed using nonlinear mixed effect modelling, implemented in NONMEM. Pharmacokinetic models developed for all drugs showed that amodiaquine does not impact the pharmacokinetics of lumefantrine. The model demonstrated showed good predictive performance and goodness-of-fit. No clinically relevant drug-drug interactions were identified, indicating that dose adjustment is not necessary for the triple combination. Also, three different models describing the pharmacokinetics of artemether, lumefantrine, amodiaquine, and their respective metabolites were successfully developed. These models could be used to simulate the effects of altered dosing of this triple combination.

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MODEL-GUIDED STRATEGIES FOR MITIGATING ANTIMALARIAL DRUG RESISTANCE: BENEFITS OF EARLY ADOPTION OF TRIPLE ARTEMISININ-BASED COMBINATION THERAPIES IN UGANDA AND TANZANIA

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The emergence and spread of drug-resistance mutations in Plasmodium falciparum pose a significant threat to malaria control efforts worldwide. As resistance to artemisinin-based combination therapies (ACTs) continues to evolve, there is an urgent need to evaluate alternative treatment strategies to mitigate the impact of drug resistance. We used a mathematical model to simulate the spread of drug-resistant mutations, particularly the 561H, 469Y, and 675V mutations, associated with resistance to artemisinin, under different treatment scenarios. We compared the outcomes of continuing with artemether-lumefantrine (AL) as the first-line therapy, switching to the triple ACT artemether-lumefantrine-amodiaquine (ALAQ) at different timepoints, temporarily adopting artesunate-amodiaquine (ASAQ) as an interim measure, and other available drugs (e.g. DHAPPQ, extended doses for AL to 5 days) deployments in Uganda and Tanzania. Our model predicts that an immediate switch from AL to ALAQ would result in the lowest number of treatment failures over the next five years (2024-2029). Delaying the transition to ALAQ by four years could double or even triple the number of treatment failures. Furthermore, the earlier the adoption of ALAQ, the more effective it would be in delaying the spread of the kelch13 variants, with predicted frequencies of 0.35 (immediate deployment) and 0.5 to 0.65 (4-year delay) in Tanzania for 2029. For countries where ALAQ will not be available soon, temporarily switching to ASAQ (3-day treatment) emerged as a viable second-best option.

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INCREASING VALIDATED ARTEMISININ PARTIAL RESISTANCE MARKERS CONFIRMED IN ETHIOPIA DURING NATIONAL SENTINEL-BASED *PLASMODIUM FALCIPARUM* MOLECULAR SURVEILLANCE

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Ethiopia aims to overcome a recent resurgence of malaria cases and eliminate local malaria transmission by 2030. With the emergence of artemisinin partial resistance (ArtR) in Africa, molecular surveillance is critical to monitor the relevant drug resistance markers. This study reports the results of sentinel site-based molecular surveillance for antimalarial drug resistance mutations. Between 2020 and 2022, dried blood spots (DBS) were collected from febrile outpatients ≥6 months old with microscopically confirmed falciparum malaria at 12 sentinel sites across a range of transmission settings. Molecular inversion probe (MIP) sequencing was used to target mutations associated with artemisinin and partner drug resistance: *kelch13, pfmdr1, pfcrt, pfdhfr,* pfdhps genes, target genome-wide markers to assess complexity of infection (COI) and parasite relatedness. A total of 1,200 patients positive for *P. falciparum* was assessed. Median age was 20 years (IQR: 14-30), and 489 (40.8%) were female. In the Kelch 13 propeller, the R622I mutation is reported mutation reported at high prevalence (>16%, range (0-58.8%) with variability across regions. A 675V mutation (WHO-validated) was were reported for the first time in Ethiopia (<5%) in Gambella region. Additional validated (441L, 574L) and candidate markers (527H, 537A) were detected in low frequency. Moreover, several partner drug resistance markers were identified; mutations in *mdr1* (184F), *dhps*, *dhpr* and *crt* were nearly fixed across the country. Majority (87.2%) of genotyped samples carried monogenomic infections (COI=1) and were highly-related to evidence of genetic clustering at the health facility level. Principal component analysis showed evidence of parasite clustering at the regional clustering regional level with district clustering of Gambella parasites. These analyses confirm the high prevalence and expansion of 622I mutation and identify other validated markers (675V and 441L) that require further investigation. Detection of multiple ArtR suggest intensive monitoring of ACT efficacy in vivo for early identification of partner drug resistance and ACT failure.

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UNDERSTANDING THE BIPHASIC DOSE-RESPONSE CURVE ASSOCIATED WITH PIPERAQUINE RESISTANCE IN *PLASMODIUM FALCIPARUM*

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The recent failure of dihydroartemisinin plus piperaquine (DHA+PPQ) antimalarial combination therapy in Southeast Asia poses a significant threat to malaria control efforts. A unique *in vitro* characteristic of PPQ-resistant *P. falciparum* is a bimodal dose-response curve indicating increased parasite survival under high drug concentrations. Due to the unique shape of the dose- response curve, area under the curve (AUC) has replaced the traditional IC_{50} when assessing susceptibility to PPQ. Previous work identified that a combination of novel substitutions in the chloroquine transporter (PfCRT) paired with multiple copies *plasmepsin II/III* (*pm2/3*) are required to generate this bimodal curve, with additional copies of *pm2/3* associating with an increased AUC. To further investigate factors driving this novel phenotype, we modified the standard 72h drug exposure to adjust the stage at which parasites were initially exposed to PPQ (early ring, late ring, trophozoite, or schizont) as well as duration of drug exposure. We performed these experiments using the parents of a previously conducted genetic cross as well as several PPQ-resistant isolates which are unique both in PfCRT genotype as well as *pm2/3* copy number. Our results reveal that exposing late-stage parasites to PPQ eliminates the bimodal nature of the dose-response curve (AUC: $p < 0.001$) without any significant change in PPQ susceptibility (limited point IC_{50}: 22.4nM vs 23.5nM; $p = 0.235$). Furthermore, we paired additional phenotypes and measurements with the disappearance of the biphasic portion of the dose-response curve to further understand the biological factors which contribute to this novel phenotype.

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EX VIVO SUSCEPTIBILITY OF UGANDAN *PLASMODIUM FALCIPARUM* ISOLATES TO DIHYDROARTEMISININ AND THE NOVEL TRIOXOLANE LEAD RLA-4735

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Artemisinin partial resistance (ART-R) has emerged in eastern Africa and threatens the efficacy of artemisinin combination therapies. In an attempt to identify novel antimalarials with improved properties, we studied synthetic endoperoxides inspired by artemisinins, but potentially not subject to ART-R. We compared susceptibilities of *Plasmodium falciparum* isolates to dihydroartemisinin (DHA), the active metabolite of clinically relevant artemisinins, the synthetic trioxolane artefenomel, which has potent activity but formulation and PK challenges and RLA-4735, a trioxolane designed to address ART-R and solubility/formulation challenges. We collected 39 isolates from eastern Uganda in 2019 and 166 isolates from northern and eastern Uganda in 2023-24, all from subjects with symptomatic *P. falciparum* infection. Susceptibilities were determined using the *ex vivo* ring-stage survival assay (RSA: % survival, relative to controls, 66 h after a 6-hour 700 nM pulse of compound), and a 72 h growth inhibition assay (IC_{50}), with SYBR Green detection. For 2019, RSA median survival was 0% for DHA, artefenomel, and RLA-4735. Median IC_{50}s were 1.5 nM (range 0.5 - 3.3 nM) for DHA, 0.5 nM (0.04 - 3.3 nM) for artefenomel, and 2.6 nM (1.1- 7.4 nM) for RLA-4735. For 2023-24, RSA median survival was 5.3% (range 0.0%-39.1%) for DHA, 0.0% (0.0%-1.9%) for artefenomel, and 0.0% (0.0%-3.23%) for RLA-4735, and median IC_{50}s were 3.8 nM (0.4 - 12.8 nM) for DHA, 3.0 nM (0.01 - 31.7 nM) for artefenomel, and 3.6 nM (0.05 - 23.4 nM) for RLA-4735. RSA median survival was higher in 2023-24 than 2019 for DHA, consistent with spreading ART-R, but not for artefenomel or RLA-4735. Also, median IC_{50}s were higher in 2023-24 than in 2019 for DHA and artefenomel, but not for RLA-4735. In summary, RLA-4735 demonstrated potent activity with both the RSA and IC_{50} assays against Ugandan *P. falciparum* isolates over time, including against isolates with reduced DHA susceptibility. We speculate that reduced iron reactivity and prolonged parasite residence time due to exceptionally high protein binding explain the potent antimalarial activity and lack of susceptibility to ART-R of RLA-4735

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HIGH EFFICACY OF ARTEMETHER LUMEFANTRINE AND ARTESUNATE PYRONARIDINE WITH SINGLE LOW DOSE PRIMAQUINE IN ADULT PATIENTS WITH *PLASMODIUM FALCIPARUM* IN A SETTING WITH HIGH PREVALENCE OF MARKERS OF PARTIAL ARTEMISININ RESISTANCE AND *PFHRP2 OR 3* GENE DELETION IN ETHIOPIA: A SINGLE BLIND RANDOMIZED CONTROLLED TRIAL

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The emergence and expansion of *Plasmodium falciparum* (*Pf*) parasites with reduced sensitivity to artemisinins in East Africa threatens progress in malaria control. *Pf* parasites with *pfkelch13* 622I variant are uniquely reported in the Horn of Africa and may co-occur with deletions in *hrp2* and *hrp3* gene that allow parasites evade diagnosis by rapid diagnostic tests (RDT). In this study, *Pf* infected adult patients were followed for 42 days following the WHO therapeutic efficacy surveillance protocol, between December 2021 and July 2022, in a randomized two-arm prospective efficacy trial (Artemether-Lumefantrine [AL, n=101] or Pyronaridine-Artesunate [PA, n=98] plus primaquine [PQ]). Recurrent infections and paired samples were genotyped by targeting *Pfmsp2* and *Poly-α*, digital PCR was used to genotype *pfhrp2/3* gene deletion, and *pfkelch13* and *pfmdr1* genes were sequenced on Illumina iSeq100. No early treatment failures were observed in both arms. All but one patient in the AL arm cleared their microscopy detectable parasites by day 3 whilst late parasitological failure (LPF) was observed in 11 patients (day 21-42) of which 8 were confirmed recrudescences. PCR-adjusted treatment success were 97.8% (AL) and 98.9% (PA) on day 28 and 94.2% (PA) on day 42. The *pfkelch13* 622I variant was detected in 62.5% (5/8) of the paired recrudescent infections but not in confirmed reinfections. The *pfmdr1* NFD haplotype (86, 184, 1246) linked with lumefantrine failure was detected in all LPF samples. At recruitment, 41.6% (82/197) of infections were HRP2-based RDT negative of which 68.3% (56/82) were *pfhrp2* gene deleted. Although numbers were small, the *pfkelch13* 622I variant was detected more in *hrp2/3* gene deleted (71.4%, 5/7) than wild type (50%, 7/14) infections. Both AL and PA with PQ were efficacious for the treatment of uncomplicated *Pf* malaria in adults in a setting with rapid expansion and co-occurrence of parasites with *pfkelch13* 622I mutation and *hrp2/3* gene deletions. The findings in this study call for further detailed investigation to include children, assessing efficacy without adding PQ, and preparing for action such as multi-first line treatments.

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EXPLORING THE *IN VITRO* PHARMACOLOGY OF 8-AMINOQUINOLINE ANTIMALARIAL COMPOUNDS.

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The 8-aminoquinolines are the only licenced drug class for the treatment of relapsing malaria. Key members of the class include currently licenced primaquine and tafenoquine; as well as legacy compounds: pamaquine and pentaquine. The hypothesised mode of action for primaquine comprises a 2-step biochemical relay: (1) Cytochrome P450 (CYP)-mediated (predominantly CYP 2D6) metabolism into reactive intermediates; and (2) redox cycling of metabolites with CYP reductase (CPR) to form anti-parasitic levels of Reactive Oxygen Species (ROS). This work investigated whether this mechanism is class-wide; scrutinising CYP-mediated metabolism of, and subsequent ROS production from the 8-aminoquinolines. This study provides a thorough exploration into the physicochemical and pharmacological properties of 8-aminoquinolines and clinically relevant combination partners. Key DMPK analyses include hepatic metabolism with HμREL® co-culture clearance assay and investigations into CYP-specific metabolism, inhibition, and induction. Preliminary data into the pharmacodynamic mechanisms of 8-aminoquinoline action includes the measurement of CYP-mediated ROS using Pan-CYP and CYP-specific inhibitors and measures of cellular oxidative stress including Haem Oxygenase-1, as well as interrogation of *in vitro* efficacy using a *Plasmodium cynomolgi* liver stage assay. Evidence is presented in support of a divergent bioactivation step (1), and convergent ROS-mediated step (2) in the mechanism of action across the 8-aminoquinoline class, with tafenoquine not showing hepatic metabolism or CYP-mediated ROS production. Tafenoquine licencing now requires compulsory co-administration with chloroquine due to treatment failure with alternative regimen, piperaquine-dihydroartemisinin. This study suggests that these drug-drug interactions are unlikely to be CYP-mediated for both primaquine and tafenoquine. Ongoing research is underway to confirm the potentiating effect of chloroquine, and inhibitory effect of dihydroartemisinin on the redox-related efficacy of 8-aminoquinolines.

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THERAPEUTIC EFFICACY AND SAFETY OF ARTEMETHER LUMEFANTRINE (AL) AND ARTESUNATE AMODIAQUINE (ASAQ) FOR THE TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN KAGERA REGION, TANZANIA 2023

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The World Health Organization (WHO) recommends pre-emptive antimalarial diversification to limit drug pressure and, when drug efficacy falls below 90%, a change in national policy. Artemisinin partial resistance (APR) and low uncorrected artemether-lumefantrine (AL) efficacy, are each indicative of increased pressure on lumefantrine. In 2022, Tanzania confirmed APR in Kagera region, and <90% AL efficacy in Pwani region. Low uncorrected efficacies have also been reported in Kagera, Pwani, Tanga (2022); and Tabora (2023) regions. We conducted this TES to

assess APR in Kyerwa district, neighboring Karagwe district and Kayonza district, Rwanda, which reported APR in 2015 and 2018. Children aged 6 months to 10 years were recruited in Kyerwa, treated with AL or artesunate-amodiaquine (ASAQ), and followed for 28 days to assess drug efficacy as per the 2009 WHO protocol. The primary outcome measure was polymerase chain reaction (PCR)-corrected efficacy using a 3/3 *msp1/ msp2/glurp* approach with gel electrophoresis. Parasite clearance rate and day 7 lumefantrine concentration levels were assessed. From June 2023 to January 2024, 176 participants (88 AL, 88 ASAQ) were enrolled; 87 (98.8%) AL and 88 (100%) ASAQ reached an endpoint. Respective uncorrected and corrected Kaplan-Meier efficacies for AL were 73.6% and 96.6% and 100.0% and 100.0% for ASAQ. Day 3 parasitemia was observed in 27 (15%): 8 (9.2%) AL, 19 (21.6%) ASAQ. The median parasite clearance half-life was 3.19 hours for AL and 3.04 hours for ASAQ. There was no association between day 7 lumefantrine concentration and malaria reinfection risk (hazard ratio=1.25, p=0.614). Genotyping for *k13* is ongoing to confirm APR. With high day 3 parasitemia, low uncorrected efficacy, and regional findings of APR in neighboring Rwanda and Uganda, which both use AL as first-line, a switch from AL to an alternate first-line ACT (ASAQ, Dihydroartemisinin Piperaquine) in Tanzania treatment guidelines should be considered as per WHO guidance. ASAQ's 100% efficacy and antagonistic selective resistance mechanism make it a strong replacement candidate for AL.

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THE UTILITY OF QPCR ESTIMATION OF PARASITE DENSITY IN EVALUATING THE EFFECT OF SULFADOXINE-PYRIMETHAMINE AS PERENNIAL MALARIA CHEMOPREVENTION

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Perennial malaria chemoprevention (PMC) is a strategy recently updated by the World Health Organization to protect infants from malaria infections contributing to the overall reduction of disease burden. To evaluate these guidelines, the Plus Project investigates the effect of PMC with sulfadoxine-pyrimethamine (SP) in countries such as Cameroon and Côte d'Ivoire. qPCR is a more sensitive diagnostic method than point of care rapid diagnostic tests (RDT) and microscopy despite not readily operationalized for use in national programs. Thus, those can lead to false or missed diagnosis and underestimating the number of malaria cases. Therefore, this study aims to assess the sensitivity of qPCR and how programmatic tools compare with this molecular diagnostic method in measuring the impact of PMC. This study is nested within a larger study conducted in Côte d'Ivoire (regions Seguela and Cani) and Cameroon (regions Mbankomo and Soa) between July and August of 2023. A subset of samples from children aged aged between 10 weeks and 6 months (Côte d'Ivoire) or 6 and 9 months (Cameroon) were selected from 'cases' (children having the opportunity to take the expanded PMC-SP dosing) and controls (children who received standard of care). All children were tested for malaria using RDTs and microscopy, followed by blood spots collected on filterpaper. A highly sensitive qPCR method targeting *Plasmodium falciparum cytochrome ß* gene was employed to confirm and estimate parasite density. Additionally, conducted *Plasmodium* speciation to further explore the presence of non-Pf malaria cases. A total of 230 and 59 patients were positive by both RDT and microscopy in Côte d'Ivoire and Cameroon, respectively. Among those samples, 67.8% and 64.4% were positive by qPCR, with an estimated median parasite density of 401 (range: 6 - 110,256) and 501 parasites per microlitre (range 5 - 29,338), respectively. Further analysis will be conducted to evaluate the correlation between microscopy density and Ct values. The study will provide data on the diagnostic capacity of RDT and microscopy, and the utility of qPCR as an additional tool to evaluate the impact of interventions.

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COMPARATIVE EVALUATION OF ANTIMALARIAL DRUG EFFICACY IN THREE STUDY SITES IN MALI

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Malaria remains a significant public health threat in Africa. The increasingresistance of *Plasmodium falciparum* parasites to available antimalarial treatmentsunderscores the urgent need for new therapeutic strategies. Some drugs previouslywithdrawn due to observed resistance are now being reconsidered for their potential utilityin certain regions due to the dynamic landscape of parasite resistance. This study aims toassess the efficacy of 15 antimalarials, categorized into three groups: drugs withdrawn due toresistance, currently used drugs, and new drugs under investigation. The goal is to explore theevolving efficacy of these treatments in the face of changing resistance patterns andpotentially reintegrate withdrawn drugs into effective treatment regimens. *P. falciparum* parasites were collected from three sites in Mali (Kolle, Bougoula-Hameau, and Faladje) and analyzed in a laboratory in Bamako. Each drug was tested on freshlycollected parasites, followed by a staining process using SYBR Green and Mitotracker. Thedrugs' efficacy was assessed by measuring parasite viability with flow cytometry, whichprovided data to estimate each drug's 50% inhibitory concentrations (IC50). We anticipate significant variability in the efficacy of antimalarial drugsacross the study sites, reflecting the genetic diversity of *P. falciparum* strains and their levelsof resistance. New-generation medications are expected to show higher efficacy againstresistant strains, offering promising prospects for malaria treatment. This study will provide critical insights into the efficacy of antimalarial drugs indifferent study sites. It has the potential to inform on the current status of used antimalarialsand support the development of tailored strategies with new ones.

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MINIMUM INOCULUM OF RESISTANCE STUDIES TO SUPPORT ANTIMALARIAL DRUG DISCOVERY

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Malaria remains a significant global health burden with an estimated 249 million cases and 608,000 deaths as of 2022. The emergence and spread of *Plasmodium falciparum* parasites resistant to multiple first-line drugs makes it imperative to develop new therapeutics with novel modes of action. Minimum inoculum of resistance (MIR) studies applied to candidate drugs provide a powerful tool to quantitatively assess the risk of resistance and measure its phenotypic impact in vitro. These experiments often extend to the identification of resistance mediators, a subset of which are drug targets. Here, we present our MIR studies on five different targets: dihydroorotate dehydrogenase (PfDHODH), ATPase4 (PfATP4), translation elongation factor 2 (PfeEF2), acetyl CoA synthetase (PfACS),

and phosphatidylinositol-4 kinase (PfPI4K), targeted by the compounds DSM265, KAE609, M5717, MMV019721 and MMV390048, respectively. Data from these results can be used to predict whether resistance would be quickly selected in the field. Compounds with robust MIR data can be used as a positive control for studies to assess the resistance liabilities of candidate therapeutics.

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RISK OF SELECTION AND TIMELINES FOR THE CONTINUED SPREAD OF ARTEMISININ AND PARTNER DRUG RESISTANCE IN AFRICA

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The introduction of artemisinin combination therapies (ACTs) has significantly reduced the burden of *Plasmodium falciparum* malaria, yet the emergence of artemisinin resistance (ART-R) as well as partner drug resistance threatens these gains. Recent confirmations of *de novo* ART-R markers in Africa, in particular in Rwanda, Uganda and Ethiopia, underscore the urgency of addressing this issue in Africa. Our objective is to characterise this evolving resistance landscape and understand the speed with which ART-R will continue to spread in Africa. We use a mathematical modelling approach to evaluate the risk posed by ART-R and explore scenarios for how ART-R will continue to spread in Africa. We incorporate current best estimates of both ART-R and partner drug resistance by bringing together WHO, WWARN and MalariaGen Pf7k data on antimalarial resistance in combination with a literature review to estimate model parameters known to impact the selection of ART-R for each malaria-endemic country. We identify 12 malaria endemic countries in Africa to prioritise for surveillance and future deployment of alternative antimalarial strategies, based on quickly selecting for ART-R once established. In scenarios designed to explore the continued spread of deletions in Africa, we identify 9 high-threat countries (Djibouti, Ethiopia, Kenya, Malawi, Rwanda, Sudan, Tanzania, Uganda, Zambia) that are most at risk of ART-R both spreading to and subsequently being rapidly selected for. In these 9 countries, under a range of scenarios, we predict that ART-R will spread out from the current hotspot in Central Africa, and within 30 years will replace the majority of parasites (>50% frequency). Our results provide a refined and updated prediction model for the emergence of ART-R in an effort to help guide antimalarial policy and prioritise future surveillance efforts and innovation. These put into stark context the speed with which antimalarial resistance may spread in Africa if left unchecked, confirming the need for swift and decisive action in formulating antimalarial policies focused on containing ART-R in Africa.

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GENOMIC SURVEILLANCE OF *PLASMODIUM FALCIPARUM* IN GOLD MINING AREAS IN THE BRAZILIAN AMAZON BASIN

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There is an association between gold mining activities, deforestation and increase in the number of malaria cases, as observed in the Brazilian Amazon. In Brazil, about 140,000 cases of malaria were reported in 2023, and the state of Pará contributed 17% of this burden. In this state there was a 21% increase in gold mining areas and a concerning 132% increase in the number of *Plasmodium falciparum* cases. Difficulties in accessing diagnosis and low adherence to treatment increase vulnerability to malaria, contributing to resistance of parasites to antimalarials. Deletions in the *pfhrp2/3* genes can impact the performance of rapid diagnostic tests. These factors pose challenges to malaria control and elimination. We analyzed 49 blood samples from patients infected with *P. falciparum* in gold mines located in Pará, Brazil. After DNA extraction, the samples were analyzed through semi-nested PCR and the fragments obtained were resolved by gel electrophoresis. The prevalence of deletions in *pfhrp2/3* genes was 6.12%. We assessed the prevalence of drug resistance markers in *P. falciparum* by carrying out a targeted amplicon sequencing protocol using the MinION platform from Oxford Nanopore Technologies. Multiplex PCR with specific primers for each gene was followed by sequencing. Mutations associated with *P. falciparum* resistance were detected in all isolates, with mutations for chloroquine (*pfcrt* K76T, C72S, and *pfmdr1* Y184F), for pyrimethamine (*pfdhfr* N51I and S108N), and for sulfadoxine (79% with double mutations - *pfdhps* A437G and A581G and 21% with triple mutations - A437G, A581G and K540E). No mutations associated with artemisinin resistance (*pfkelch13*) were found. Although no mutations associated with resistance to artemisinin have been detected, the misuse of antimalarials or illegal medicines poses a threat to the emergence of resistance to this antimalarial or partner drugs. Furthermore, deletions in the *pfhrp2/3* genes significantly impact the use of rapid diagnostic tests, which are crucial for diagnosis, especially in remote areas. These findings highlight the importance of ongoing genomic surveillance in malaria-endemic regions.

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LEVERAGING A *PLASMODIUM FALCIPARUM* GENETIC CROSS TO IDENTIFY CANDIDATE DETERMINANTS OF MULTIGENIC RESISTANCE TO QUININE AND CHLOROQUINE

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The emergence of *Plasmodium falciparum* strains showing partial resistance to artemisinin (ART) in multiple countries in east Africa poses a substantial threat to malaria treatment. ART derivatives constitute the core component of first-line combination therapies to treat uncomplicated malaria and are used to treat severe disease. Should ART resistance spread, alternative drugs will be required, yet the options are limited. The WHO recommends quinine (QN) as an option for treating severe malaria when artesunate or artemether are not available or are contraindicated. Moderate *P. falciparum* resistance to QN has been reported, but its genetic basis has remained elusive. We conducted a genetic cross between the QN-resistant Cam3.II parasite and the drug-sensitive NF54 parasite, using human liver-chimeric FRG-NOD mice. This cross yielded 120 independent recombinant progeny. Phenotypic analysis of progeny, combined with whole-genome sequence data, enabled us to apply quantitative trait loci mapping to identify regions associated with QN resistance. Our results identified a segment on chromosome 7, which for both IC_{50} and IC_{90} analyses included *dmt1* that encodes a putative drug/metabolite transporter. IC_{50} (but not IC_{90}) analyses also associated the QN response with mutant *pfcrt*, located 200 kb upstream of *dmt1*. Genetic disruption of *dmt1* sensitized Cam3.II parasites to QN, and transport studies with proteoliposomes reconstituted with recombinant mutant DMT1 showed evidence of QN transport. These data implicate *dmt1* as a component of a multigenic basis of QN resistance. We also identified a peak on chromosome 12, whose genes include mutant *ftsh1* that is a potential resistance mediator. This chromosome 12 peak was also associated with CQ resistance in addition to the dominant *pfcrt* peak on chromosome 7. Our data reveal a multigenic basis of QN resistance and identify a potential new modulator of mutant *pfcrt*-mediated CQ resistance.

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THE GULART STUDY: A CROSS-SECTIONAL SURVEY OF ARTEMISININ PARTIAL RESISTANCE AND SPECIES DIVERSITY IN FIVE NORTHERN UGANDAN DISTRICTS

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Partial resistance to artemisinin derivatives, vital drugs in the treatment of malaria, has emerged in multiple East African countries and is linked to mutations in the *Plasmodium falciparum* (*Pf*) Kelch 13 protein (*Pfk13*). Published studies in Uganda have relied on convenience sampling, which are unable to provide an estimation of community-level prevalence. We employed a GIS-based two-stage cluster randomized cross-sectional survey of n=598 asymptomatic children <5 years in five districts of Northern Uganda: Gulu (n=180), Amuru (n=113), Lamwo (n=101), Pader (n=90), and Omoro (n=114) from Aug 2022 to Jan 2023. In addition, we sampled n=102 patients presenting with uncomplicated malaria at the Gulu Regional Referral Hospital (GRRH). In the asymptomatic community cohort, 54.2% were male, and the mean age was 1.9 yrs (SD=1.4). 44.1% (n=263) were positive for *Pf* by PfHRP2-based RDT and 54.3% (n=325) were positive for any *Plasmodium spp.* infection by real-time PCR. While the majority (66.8%; n=217/325) were positive for *Pf*, we found a strikingly high burden of *P. ovale* species (*Po*): 31.4% (n=102) were *Po* mono-infections and 22.2% (n=72) were *Pf-Po* co-infections. An additional 4.0% were *Pm* (n=13) and 0.6% (n=2) were *Pv* infections. Of the n=102 diagnosed as uncomplicated malaria cases at GRRH, a surprising n=32 were *Po* mixed or mono-infections by RT-PCR. Apart from *Pf* and *Po*, no other species were detected among symptomatic patients. Our study reveals a striking community-based prevalence of *Po* in children sampled in all districts, including in individuals presenting for care with symptomatic disease at GRRH. In addition, *PfK13* was successfully amplified by PCR for n=158/217 of *Pf*+ community samples. Thus far, C469Y has been identified by high-resolution melting (HRM) in our community samples. Further work, namely HRM and NGS, is underway to complete characterization of circulating *PfK13* haplotypes in the community. Together, these data present a complex scenario in Northern Uganda which necessitate urgent changes in malaria diagnostic and treatment policies in the region.

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DIAGNOSIS OF *PLASMODIUM* SPECIES USING A.I. TECHNIQUES VERSUS STANDARD MICROSCOPY

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Malaria diagnosis using standard techniques is challenging and time-consuming, leading to discrepancies and delays. Innovative technologies utilizing advanced technologies are changing the diagnostic landscape. The miLab™MAL, an automated malaria diagnostic solution, was compared with standard microscopy at Labcorp® reference laboratories. 409 samples submitted for parasitic examination were prepared with thick and thin smears and Noul's malaria diagnostic solution, miLab™MAL, and evaluated for positivity, negativity, and speciation. 399/409 samples were manually negative, while 397/409 were negative by miLab™MAL. Two samples initially classified as negative manually were found positive by miLab™MAL. Upon re-examination of the peripheral smear, very rare trophozoites, constituting less than 0.1% of the erythrocytes, were identified in both samples. In nine out of ten cases, *Plasmodium falciparum* was identified by both methods. In one case, *Babesia sp.* was identified by microscopy, but miLab™MAL identified *Plasmodium falciparum*. Our studies show that miLab™MAL was accurate in identifying the presence or absence of *Plasmodium*. All positive samples detected by microscopy were also identified with miLab™MAL. The miLab™MAL also showed greater sensitivity than the manual method. All cases negative for *Plasmodium* by microscopy were also negative by the miLab™MAL method (100% specificity), indicating that intraerythrocytic inclusions were not confused with malarial parasites. The miLab™MAL correctly identified *Plasmodium falciparum* species in 11/12 cases compared to the 10/12 cases by standard microscopy. Because machine learning tools for Babesia were not programmed into the miLab™MAL, this led to the discrepancy. Based upon the study's findings, miLab™MAL can be used to screen out negative *Plasmodium* samples. Since the positivity rate for malaria in reference laboratory specimens is low, resources can be saved using this technology. Due to the limited number of positive samples (n=12), further studies in malaria-endemic areas are necessary to assess the reliability of *Plasmodium* speciation.

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GENOTYPING OF PLASMODIUM FALCIPARUM MEROZOITE SURFACE PROTEIN 2 (PFMASP-2) REVEALED DIFFERENT ALLELIC PROFILES IN BLOOD AND SALIVA SAMPLES FROM MFOU HEALTH DISTRICT IN CAMEROON

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Monitoring Genetic diversity of malaria parasites might help address constant emergence of resistance of *Plasmodium falciparum* to antimalarials. the usefulness of Pf*MSP2* to monitor *P. falciparum* polymorphism is hampered by the lack of non-invasive sample collection method. In the current study we sought to assess the suitability of saliva as a biological material to assess the diversity of *P. falciparum*. To this end, we collected total of 27 saliva and 50 blood specimens from malaria positive patients at Mfou health district, Cameroon. Genomic *Plasmodium* spp. DNA was extracted from blood and saliva samples, and used in nested-PCR to detect the presence of *P. falciparum* and the different alleles of *Pfmsp-2*. The presence of *P. falciparum* was confirmed by nested PCR with a positivity rate of 94% (47/50) and 88.88% (24/27) in blood and saliva samples respectively. Altogether, 14 different alleles of the *Pfmsp-2* gene with bands ranging between 279-1178bp were detected in blood. The genetic diversity and multiplicity of Infection (MOI) of *Pfmsp-2* was 10.61% and 2.81 respectively in blood samples. In contrast, only 6 alleles of the *Pfmsp-2* gene with bands ranging between 450-708pb were detected in saliva samples. Here, the genetic diversity of *Pfmsp-2* gene and the multiplicity of infection were 35.29% and 1.33 respectively. Quadruple allelic infections (4 types of alleles) were predominant (29,78%) in blood, while single allelic infections (1 allele) were predominant in saliva (86,67%). These results demonstrated the use of saliva as specimen for investigating genetic diversity endemic area. Furthermore, our findings depict an extensive genetic diversity of Pfmsp-2 observed in Mfou and it could herald the rise and spread of drug resistant strains of *P. falciparum* which could have implication in MSP2-based vaccines efficacy in this locality.

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POINT-OF-CARE TEST OF BLOOD *PLASMODIUM* RNA WITHIN A PASTEUR PIPETTE USING A NOVEL ISOTHERMAL AMPLIFICATION WITHOUT NUCLEIC ACID PURIFICATION

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We present Pasteur Pipette-assisted Isothermal Probe Amplification (pp-IPA), a novel molecular point-of-care test (POCT) for malaria detection in resource-limited settings. In this approach, specific, tailed probes capture released 18S rRNA of *Plasmodium* onto the inner wall of an oligo-conjugated Pasteur pipette through sandwich hybridization. After

washing off impurities and unbound probes, the bound tailed probes are ligated to form complete dumbbell-shaped templates for subsequent isothermal amplification using a pair of primers, bypassing nucleic acid extraction and reverse transcription. The entire assay takes 60 - 80 min to complete requiring only a Pasteur pipette and a water bath. Experimental results confirm pp-IPA's analytical sensitivity to be $1.28*10^{-4}$ parasites/µl, a sensitivity 3 - 4 orders of magnitude higher than existing molecular POCT methods for malaria, with 100% specificity against various blood-borne pathogens causing malaria-like symptoms. Additionally, pp-IPA needs only liquid-transfer skill for operation and the cost for per test is around $0.25. pp-IPA's simplicity, affordability, high sensitivity/specificity, and minimal equipment requirement make it a promising point-of-care pathogen identification tool in resource-constrained regions.

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MOLECULAR AND SEROLOGICAL ANALYSIS OF AFEBRILE *PLASMODIUM FALCIPARUM* INFECTION IN SOUTHERN MOZAMBIQUE: A PROSPECTIVE COHORT

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Afebrile *Plasmodium falciparum* (*Pf*) infections have a debilitating impact on health and represent a hidden source of transmission that can compromise malaria elimination efforts. Understanding the dynamics and biological factors that maintain parasite-host interactions at the subclinical level would contribute to the ongoing debate on the relevance of afebrile infections as a barrier to malaria elimination, and guide the use of interventions to reduce this silent reservoir. In this study, healthy Mozambican individuals were screened at household level using a rapid diagnostic test (RDT) to detect Pf infection. Positive cases were confirmed microscopically and followed up for 28 days (daily visits for the first 4 days and weekly visits until the 28th day) during the 2020-23 rainy season. Antimalarial treatment was administered either upon reaching the end of the follow-up period or in response to clinical symptoms occurred before day 28. Blood samples and basic clinical-demographic information were collected at every visit. Samples were analysed using a combination of genetic and serological tools. The longitudinal analysis used data from 146 of the 177 enrolled individuals, excluding individuals with less than 3 observations on days 7, 14, 21 and 28. Seventeen of the 146 participants (11.6%) spontaneously cleared the infection and 11 (7.5%) developed fever during the follow-up. In 34 participants (23.3%), parasite densities and HRP2/LDH levels decreased dramatically and stabilized at low levels (i.e. below the geometric mean of the clearance samples), whereas in 28 participants (19.2%) they increased and stabilized at high density levels (i.e. above the geometric mean of the fever samples). In 56 participants (38.4%), parasite densities and HRP2/LDH levels were maintained at intermediate levels. Thus, approximately half (57.6%) of the afebrile RDT-detected infections maintained densities with high transmission potential. Ongoing molecular and serological characterization will provide further insight into the parasitological and immunological factors linked to disease progression in areas of low malaria transmission.

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MALARIA PREVALENCE AMONG PATIENTS ATTENDING TWO HEALTH CENTRES IN IKWUANO L.G.A, ABIA STATE, NIGERIA USING BLOOD AND URINE SAMPLES

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Malaria, a life threatening disease caused by the protozoa of the genus Plasmodium is transmitted to man through the bites of infected female Anopheles mosquitoes. The study was done between July and December, 2023 to determine the prevalence of malaria among patients attending Amawom and Umudike health centres using the conventional microscopy and RDT kit methods. Two mls of venous blood and 200 ul of urine were collected from 200 patients who gave their consent using sterile syringes for blood and sterilized dry mouthed cork screwed plastic containers for urine. Blood was dispensed into EDTA bottles and gently mixed. Blood samples were examined using conventional microscopy for thin and thick blood smears and Carestart TM strip for blood while urine test was done with SD Bioline strip. The overall prevalence of malaria with microscopy was 24.0% while RDT for blood and urine were 12.0% and 10.5% prevalences respectively. More males (27.3%) than females (20.8%) were infected. The age group 20-30 years recorded more infection (32.6%). The need for development of new, simple, quick, accurate non invasive and cost-effective diagnostic tests for malaria can be complemented by the use of RDTs, especially RDT for urine for non-invasive approach, since the results of RDTs used in the study have shown their usefulness as a rapid and simple tool for malaria diagnosis. This also promises to be a useful diagnostic tool that can be deployed for use in poor resource settings where regular supply of electricity and absence of an expert microscopist can be challenges to the use of microscopy

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STRENGTHENING THE QUALITY OF MALARIA MICROSCOPY THROUGH A CASCADE TRAINING MODEL IN TANZANIA

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In 2023, >1 million malaria microscopy tests were conducted in high-burden Mainland Tanzania and 35,550 were conducted in Zanzibar, an elimination-targeted area. However, there were no certified expert microscopists, and only 70.1% of health facilities (HFs) performed satisfactorily on malaria microscopy during Malaria Service Delivery and Quality Improvement (MSDQI) evaluations. We assessed the impact of a cascade model to expand the cohort of certified microscopists at HFs. A cohort of 12 microscopists underwent WHO-External Competency Assessment of Malaria Microscopy (ECAMM) expert certification. This expert cohort was further expanded with those passing advanced malaria diagnostic refresher training (MDRT) and ultimately served as MSDQI supervisors, quality improvement mentors, and administrators of laboratory external quality assurance (EQA) proficiency testing (PT), and basic MDRT. We used EQA PT and MSDQI evaluations to assess microscopy performance improvement of those trained with the cascade model. The 12 expert microscopists conducted 9 MDRT trainings, resulting in a total of 177 trained microscopists, and expanding the expert cohort by 25. In Zanzibar, 85 PT rounds conducted by this expert cohort demonstrated significantly improved scores from 84% to 92% in parasite identification (PID), 18% to 54% in species identification (SID), and 32% to 45% in parasite counting (PC) ($p<0.001$ for all PT). In mainland, 11 PT rounds demonstrated improved scores from 93% to 100% in PID, 64% to 77% in SID, and 43% to 50% in PC, but did not reach significance. In the same period, microscopy performance in 14 Mainland HFs receiving supervision and mentorship from the expanded cohort significantly improved MSDQI scores from 40% to 92% in smear preparation and staining ($p<0.001$); 60%

to 100% in slide examination; 33% to 71% in PT enrollment ($p<0.001$); and 33% to 57% in internal quality control performance. This cascade training model rapidly established a cohort of expert microscopists who, in turn, significantly expanded the cohort of trained microscopists and contributed to significant improvements in HF PT nationwide.

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MALARIA MICROSCOPY EVALUATION AND QUALITY ASSURANCE IN RURAL CLINICS IN WESTERN KENYA

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While rapid diagnostic tests are widely used, they have several limitations, and blood smear (BS) examination by microscopy remains the gold standard for malaria diagnosis. However, poor quality reagents, limited technical capacity, and turnaround times all threaten the ability to reliably provide accurate results in public health facilities (HF) in malaria endemic areas of Kenya. To assess the quality of malaria microscopy, we evaluated the concordance of BS results at 28 HF with expert microscopy in Siaya County, western Kenya. At each HF, the quality of reagents, slide preparation, standard operating procedures availability, and infrastructure (electricity and microscope) were documented. Approximately 20 patients per HF assessed for malaria by microscopy between January and March 2024 were randomly selected to have their BS re-examined by an expert microscopist. Two expert examinations were conducted for each patient, one on-site re-examination of the routine HF-prepared slide using the HF microscope (slide 1), and the second off-site at the Kenya Medical Research Institute (KEMRI) malaria laboratory, where a second dried but unstained slide was stained and examined (slide 2) as the gold standard. Concordance between the routine HF results and expert re-examined HF slide at the HF (slide 1) and expert stained HF slide at KEMRI (slide 2) were evaluated, and sensitivity and specificity calculated. Overall BS positivity was 35% (166/480). There was 85% (405/480) concordance between the routine HF results and slide 1 expert re-reading, with a range of 50% (10/20) to 100% (20/20), by HF. There was 81% (336/411) concordance between the HF results and slide 2, with a range from 65% (7/13) to 100% (10/10). Compared to slide 2, the routine HF results had sensitivity and specificity of 72% and 87%, respectively. HF with the lowest concordance had poor BS quality 21% (6/28), contaminated reagents 7% (2/28), and low-quality microscopes with intermittent electricity 4% (1/28). While overall concordance was high, the variability in results and moderate sensitivity highlight the need for ongoing monitoring of malaria microscopy quality at public HF.

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AN EFFECTIVE CASCADING CLASSIFIER FOR PATIENT-LEVEL MALARIA DIAGNOSIS ON THE MILAB™ PLATFORM WITH FOCUS-STACKING TINY VISION TRANSFORMER

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Determining a proper diagnosis can take varying lengths of time and effort. In the case of malaria, inspecting a smeared blood slide through a microscope is the most common method of diagnosis. AI solutions, such as those conducted with the miLab™ platform, have been proposed to inspect the blood cells digitally, and cascading classifiers have shown great performance. However, clumped or blurry cells are still difficult for the AI to classify correctly. These hard samples require review by an expert to provide an accurate diagnosis; however, this comes at the cost of increased time and monetary cost to provide a diagnosis. This study introduces a new deep-learning model based on a pre-trained vision transformer; fine-tuned on hard samples. Reducing the workload of a human expert, TinyViT, a state-of-the-art but small model, can augment the workflow of the miLab™ platform and decrease the number of cells required to be reviewed. To circumvent the shallow depth of field limitations, focal stacking using multiple auto-focused images was used to generate the input image. Experts have extensive experience examining images prepared using different staining qualities. To mimic this experience, we apply realistic microscopy image augmentations to improve generalization when fine-tuning the pre-trained model. Adding additional steps to the existing pipeline introduces unnecessary overhead; therefore, this method is used only when there are few equivocal cells to review. We have internally validated that extending cascading classifiers improved malaria readout performance. The number of cells designated for user review decreased, reducing the time experts need to confirm cells, even if using a more accurate AI model takes extra operation time. Appending TinyViT to the end of the miLab™ process improved the overall performance to 97% and reduced the number of false positives and negatives while not significantly increasing processing time. As a result, 80% less resources can be spent confirming cells, and it can instead be spent by on-site experts helping more people, improving accessibility, and maintaining a good patient-provider experience.

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DETECTION OF *PLASMODIUM VIVAX* IN NORTHERN KENYA VIA MICROSCOPY CONFIRMED BY MOLECULAR SPECIATION

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In Kenya, *Plasmodium falciparum* is the predominant parasite responsible for malaria infections, mainly in western Kenya. Presence of *P. vivax* can complicate both diagnosis and treatment, posing a challenge for malaria control in endemic counties. We describe confirmed detection of *P. vivax* cases in northern Kenya in the aftermath of heavy rains, Sept-Dec 2023. We conducted a retrospective review of data from the Kenya Health Information Systems between December 2023-February 2024 in the five northern counties of Isiolo, Marsabit, Mandera, Samburu and Wajir to ascertain increase in malaria cases. In the peripheral clinics, blood smears with morphological features inconsistent with *P. falciparum* at time of diagnosis were encouraged to be sent for confirmation by expert microscopy and PCR at the National Malaria Reference Laboratory (NMRL). In the five northern counties, 7,860 confirmed cases of malaria were reported between Dec 2023-Feb 2024, up from 2881 cases—a 173% increase from the same period in the previous year. So far, NMRL has processed 9 samples sent for species confirmation—six were confirmed as *P. vivax*, and three as *P. falciparum.* Additional samples remain but NMRL has not processed them due to limited reagents. Detection of *P. vivax* in the northern counties that border Ethiopia is of great concern, suggestive of potential cross-border transmission. Strengthening diagnostic and speciation capacity by microscopy is critical, especially because rapid diagnostic tests used in Kenya do not detect *P. vivax*. Complementing microscopy with molecular diagnostics can also improve speciation in a timely manner. Recent malaria outbreak investigations in Wajir and Marsabit counties also found >40 cases of *P.* vivax. Ongoing malaria surveillance, particularly on *P. vivax*, through strengthened microscopy and molecular confirmation in the northern counties is critical to inform national malaria program decisions and improve response, especially as weather patterns change to become more conducive to malaria transmission.

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EVALUATION OF THE PERFORMANCES OF RAPID DIAGNOSTIC TESTS TO DETERMINE THE PREVALENCE OF *PLASMODIUM FALCIPARUM PFHRP2* GENE DELETIONS IN THE HEALTH DISTRICT OF NANORO, BUKINA FASO

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Malaria diagnostic methods rely essentially on rapid diagnostic tests (RDTs) based on histidine-rich protein 2 in peripheral health centers and microscopy only performed in reference centers. Nowadays, the reliability of RDT results would be threatened by the appearance of strains that do not secrete *pfhrp2* antigen, making these parasites undetectable by RDTs. The objective of this study was to evaluate the performances of RDTs and to determine the prevalence of *Plasmodium falciparum pfhrp2* gene deletions in the health district of Nanoro. The study population consisted of children under Seasonal Malaria Chemo Prevention (SMC) coverage and aged 6-59 months. At each visit for chemo-prevention, blood samples were taken for the preparation of thick drops and blood smears. A rapid diagnostic test was also done to assess malaria infection on site. Blood was spotted on a filter paper for the detection of *pfhrp2* gene deletions using PCR.A total of 1059 children with a mean age of 34 months (range 6-59) participated in this study. The analysis of RDT performance indicators allowed us to obtain a specificity of 84.00% and a sensitivity of 77.06%. False positives were estimated at 15.99% compared to 22.94% false negatives. On a total of two hundred (200) samples analyzed by PCR, we obtained a prevalence of 2.58% of *pfhrp2* gene deletion. This study is one of the first to reveal the presence of *pfhrp2* gene deletions in Burkina Faso. With approximately 2.6% prevalence, this value is below the threshold of 5% set by the WHO to consider a change in the type of RDT. Therefore, HRP2 RDTs are still indicated for the diagnosis of malaria in Burkina Faso. However, a large-scale study to monitor the temporal dynamics of these *Plasmodium falciparum* strains that do not produce the *pfhrp2* antigen is necessary in Burkina Faso.

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STRENGTHENING THE LABORATORY DIAGNOSIS OF MALARIA IN GUINEA: THE KEY ROLE PLAYED BY WHO-CERTIFIED LOCAL EXPERTS

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Malaria continues to represent a substantial health burden in Guinea. In 2021, USAID | Guinea StopPalu+ facilitated the WHO certification of 10 local malaria microscopists from referral hospitals supported by the project. Since then these experts have been used to oversee and lead malaria diagnosis training workshops for laboratory technicians, as well as conduct regular supportive supervisions to monitor the quality of malaria diagnosis at health facilities. Here we describe how the quality of malaria diagnosis in Guinea has been strengthened, including elaborating on best known practices and lessons learned. We describe observations and findings from two cycles of quarterly supportive supervision visits to 22 specialized microscopy laboratories in 19 of the country's 39 districts. Visits included direct observations by the supportive supervision team of technicians performing laboratory malaria diagnosis, key informant interviews, a review of laboratory registers, and an assessment of laboratory competence against WHO-provided reference microscopy slides. Substantial improvements were seen across various domains following two cycles of supportive supervision. In terms of the External Quality Assessment, the correct diagnosis of malaria improved from 89% to 98%, correct species identification improved from 65% to 83%, and correct parasite quantification improved from 49% to 55%. Microscope maintenance improved from 86% to 91%, and the specialized technical interventions improved from 0% to 27%; similarly, the availability of key commodities improved substantially (e.g., the availability of Giemsa and immersion oil improved from 77% to 100% and 91% to 100%, respectively). Facilities that conducted internal quality control efforts increased from 27% to 36%. Two cycles of supportive supervision by 10 WHO-certified local malaria microscopists led to substantial improvements in the malaria diagnostic capacity of laboratory technicians in 22 laboratories. Additionally, key improvements in quality service provision were made, including with regards to the availability of commodities and functional equipment.

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ECONOMIC EVALUATION OF MALARIA DIAGNOSTIC STRATEGIES FOR MALARIA CAMPS IN REMOTE VILLAGES OF ODISHA STATE, INDIA

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In India, malaria predominantly affects tribal populations in remote areas of Odisha state. The deployment of 'malaria camps' (MCs) with a mass screening-and-treatment (MSAT) intervention was shown to be effective in reducing PCR-positive Plasmodium infection prevalence. *Plasmodium falciparum* histidine-rich protein-2 (*pfhrp2*) gene deletions may, however, lead to false-negative RDT results, posing a challenge to MSAT's sensitivity to detect true malaria cases. We evaluated the incremental cost-effectiveness (ICER) of two alternative malaria detection strategies in the context of MSAT, following standard guidelines for cost-effectiveness analysis. A decision tree model was developed with three arms with arm 1 representing the comparator screening strategy which is the existing HRP-2-based RDT and arms 2 and 3 being the alternative screening strategies with an LDH-based RDT and an isothermal (LAMP-based) molecular diagnostic strategy, respectively. The number of DALYs averted and the associated incremental costs were estimated to calculate ICER from both a healthcare provider and a societal perspective. Deterministic and probabilistic sensitivity analyses were both conducted to ensure the robustness of the findings. The ICER of Arm 2 was estimated at $0.98/DALY averted (95% CrI=[$0.64/DALY averted, $2.04/DALY averted]) from the healthcare provider perspective, and at $0.40/DALY averted (95% CrI=[cost-saving, $3.00/DALY averted]) from the societal perspective. The ICER of Arm 3 was $114.05/DALY averted (95% CrI=[$65.03/DALY averted, $352.04/DALY averted]) from the healthcare provider perspective and was $113.43/DALY averted (95% CrI=[$64.37/DALY averted, $351.25/DALY averted]) from the societal perspective. Transitioning to either an LDH-based RDT or a LAMP-based molecular diagnostic represents a cost-effective alternative to the current HRP-2-based RDT utilized in the MSAT component of the MCs. Notably, the LDH-based RDT exhibited a significantly less incremental cost while averting more disease burden compared to the LAMP-based method.

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EFFICACY AND SAFETY OF ARTEMETHER + LUMEFANTRINE AND ARTESUNATE + AMODIAQUINE FOR UNCOMPLICATED MALARIA IN EQUATORIAL GUINEA

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Malaria remains a significant public health challenge in Equatorial Guinea, particularly among children and pregnant women. With the country's national malaria control program, endorsing Artemether + Lumefantrine (AL) as the first-line treatment since 2017, continuous surveillance is essential to monitor ongoing efficacy and detect early signs of drug resistance. This study aims to evaluate the therapeutic efficacy and safety of the national first-line (AL) and second-line (Artesunate + Amodiaquine, ASAQ) malaria treatments in young malaria patients in Equatorial Guinea. This prospective cohort study will be conducted from March 2024 to July 2024 in three sentinel sites: Malabo (Bioko Island), Bata, and Ebibeyin Districts (located on the mainland of Equatorial Guinea). After obtaining informed consent from parents and guardians, we will consecutively enroll febrile children aged 6 months to 10 years diagnosed with uncomplicated *Plasmodium falciparum* malaria. Each site will parallel-test AL and ASAQ[CD1] [PJBD2] , given orally for a complete 3-day treatment course. The study aims to recruit treatment cohorts of 88 patients each for AL and ASAQ, summing to a total of 528 participants across all sites. Treatment efficacy will be assessed through close monitoring of clinical and parasitological outcomes for a 28-day follow-up period. The study will employ thick and thin blood smear malaria microscopy, PCR and sequencing to understand successful treatment rates, and to distinguish recrudescence from newly acquired infections. Drug safety evaluations will focus on the incidence and nature of adverse events associated with these treatments. Results will provide an evidence base for malaria drug policy in EG, hopefully supporting AL as the first line treatment and evaluating the role of ASAQ as a second-line therapy, ensuring optimal care for malaria patients in Equatorial Guinea.

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EVALUATION OF FOR EFFICACY OF ARTEMISININ-BASED COMBINATION THERAPIES ON *PLASMODIUM FALCIPARUM*, PLASMODIUM MALARIAE AND PLASMODIUM OVALE INFECTIONS IN MALI

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Most cases of malaria are caused by *Plasmodium falciparum*. Non-falciparum species (*P. vivax*, *P. ovale*, *P. malariae…)* can cause malaria infections as well. Little work exists on the efficacy and clearance of non-falciparum species; andall strategies are oriented on the P. *falciparum* species. The purpose of this study was to clearance and efficacy of ACT on *P. malariae*, *P. ovale* and *P. falciparum* on data from the WANECAM1 network in Mali.The database of the WANECAM1 study was used to perform the analysis for this thesis. The 28-day WHO *in vivo* protocol was used for estimation of therapeutic responses. The WWARNParasite Clearance Estimator Software was used for the estimation of the parasite clearance half-life. The classic parasite clearance time was estimated by taking the median of the parasitaemianegativation time.Out of a total of 4172 volunteers. The median parasite clearance half-life times were 2.9 h, 4.79 hand 4.74 h respectively for *P. falciparum*, *P. malariae* and *P. ovale*. There was a significantdifference between the half-life times of *P. falciparum* compared to those of *P. malariae* and *P.ovale* ($p<0.001$) while there was no significant difference between the half-life times of non-falciparum species. The classical parasite clearance time was 24h and 36h. Adequate clinical andparasitological response (ACPR) was 79.81% for *P. falciparum*, while ACPR were 99.32% and98.18% for *P. malariae* and *P. ovale*, respectively, with a significant difference statistically ($p <0.05$).We conclude that the parasite clearance half-life of *P. falciparum* species was faster compared to*P. malariae* and *P. ovale* species.The ACTs used in the study were more effective on *non-falciparum* species than on *P. falciparum*.

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OPTIMIZATION OF MULTIPLE-STAGE ACTIVE ANTIMALARIAL PRODIGININES

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Over the past several decades, natural products have an extensive history as pioneering agents for drug development. In particular, many of the promising antimalarials know to date are the natural products and/or their derivatives. Recently, we have discovered and developed prodiginine chemotype as novel class of orally efficacious antimalarial agents. Our work has shown that a number of the prodiginine derivatives were equally effective against a panel of *Plasmodium falciparum* pan-sensitive and multi-drug resistance strains at low nanomolar concentrations, suggesting potential to discover a new drug target to combat malaria parasites. In addition, these compounds inhibited formation of hypnozoites and schizonts in both radical cure and prophylactic modes at low concentrations. Herein, we present the detailed optimization and structure-activity relationships of prodiginine chemotype with enhanced antiplasmodial activities against both the asexual blood and liver stage malaria parasites and improved metabolic and pharmacokinetic profiles. This material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. Research was conducted under an IACUC-approved animal use protocol in an AAALAC International-accredited facility with a Public Health Services Animal Welfare Assurance and in compliance with the Animal Welfare Act and other federal statutes and regulations relating to laboratory animals.

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PRECLINICAL DEVELOPMENT OF NOVEL DUAL-STAGE ACTIVE ANTIMALARIALS

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The global impact of malaria remains staggering despite extensive efforts to eradicate the disease. The challenges for a sustainable elimination include the failing effectiveness of front-line artemisinin-based combination therapy (ACT) due to emerging resistance and safety concerns associated with limited radical cure options for relapsing *Plasmodium vivax*. There is an urgent need for novel, effective, affordable and safe antimalarial drugs to overcome drug resistance, and ideally, such agents would be efficacious against both blood stage and liver stage malaria infections. We have developed a novel antimalarial acridone chemotype with dual stage efficacy against both liver stage and blood stage malaria, as well as single-dose cure ability and potential to prevent relapsing infection. Our novel acridone chemotype represents a broad-spectrum approach with potential to vanquish many challenges. Extensive and comprehensive preclinical evaluations of our late lead acridone candidate will be presented.

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DRUG INTERACTION BETWEEN DIHYDROARTEMISININ-PIPERAQUINE AND SULFADOXINE-PYRIMETHAMINE IN PREGNANT WOMEN RECEIVING MALARIA CHEMOPREVENTION

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Comparative trials of intermittent preventive treatment in pregnancy (IPTp) have shown that dihydroartemisinin-piperaquine (DP) is a more efficacious antimalarial, but sulfadoxine-pyrimethamine (SP) is associated with better fetal growth. We hypothesize that DP+SP for IPTp may be superior to either therapy alone. However, potential drug-drug interaction between DP and SP requires investigation. We completed pharmacokinetic (PK) studies nested in a placebo-controlled, double-blinded randomized trial of pregnant women living in Busia District, Uganda who were randomized to IPTp with SP, DP, or DP+SP every 4 weeks starting at 16- or 20- weeks gestation. For intensive PK, serial sampling from day 0-23 was performed after the 28th gestational week IPTp course in 87 participants (27 DP, 36 SP, 24 DP+SP). For sparse PK, paired day 28 (trough) samples were analyzed in 198 participants (98 SP, 98 DP+SP) after the 20th and 28th gestational week IPTp course. Sulfadoxine (SDX), pyrimethamine (PYR), and piperaquine (PPQ) levels were determined using liquid chromatography tandem mass spectrometry. Non-compartmental analyses were used to determine PK parameters. Intensive PK analyses demonstrated that coadministration of DP+SP significantly reduced geometric mean C_{max} and $AUC_{day0-23}$ of SDX (by 25% [90% CI: 13%–33%] and 25% [11%–33%]) and PYR (by 26% [17%–34%] and 34% [26%–42%]) (all $p<0.05$). Sparse PK analyses indicated that co-administration of DP+SP significantly reduced trough SDX levels after the 28th, but not the 20th gestational week IPTp course (31% [10%–47%] versus 6% [-19%–26%] reduction; p-interaction=0.025). PYR levels were reduced with coadministration of DP+SP at both the 20th and 28th gestational week IPTp course (reductions of 18% [5%–30%] and 33% [22%–43%]; p-interaction=0.027). Co-administration of DP+SP moderately reduced PPQ C_{max} and $AUC_{day0-23}$ by 13% [-11%–32%] (p=0.34) and 19% [4%-32%] (p=0.046). Thus, coadministration of DP+SP significantly reduced SP exposure with a greater magnitude during the 3rd vs. 2nd trimester. Further investigation is needed to define optimal dosing strategies for IPTp with DP+SP.

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MICROVOLUME ANALYSIS OF ANTIMALARIAL DRUGS FOR PEDIATRIC PHARMACOKINETIC-PHARMACODYNAMIC STUDIES

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It is desirable to quantify antimalarial drugs in microvolume samples to support pharmacokinetic studies in pediatric populations, due to the limited volume of blood. We used capillary tube sampling to obtain plasma or dried blood spots (DBS), which were processed with protein precipitation, liquid-liquid extraction, or solid phase extraction, and analyzed by liquid chromatography tandem mass spectrometry (LC-MS/MS). We have developed plasma methods to determine concentrations of artemether and dihydroartemisinin (50 µL), piperaquine (25 µL), hydroxychloroquine and its metabolites (20 µL), amodiaquine (AQ) and desethylamodiaquine (DEAQ, 10 µL), lumefantrine and desbutyl lumefantrine (5 µL), sulfadoxine (SDX), and pyrimethamine (PYR, 5 µL). We also explored methods to determine piperaquine, lumefantrine, AQ and DEAQ concentrations from DBS. Here we present a method for determination of AQ, DEAQ, SDX, and PYR concentrations from 10 µL plasma. The method was developed on a Waters Acquity UPLC system (I class) coupled with Sciex TripleQuad 6500^{+} tandem mass spectrometry (MS/MS) managed with the software Analyst® 1.6.3. Plasma samples (10 µL) were processed by solid-phase extraction with an HLB micro-elution plate. Chromatographic separation was achieved on an ACE® Excel C_{18} analytical column (50 x 2.1 mm, 1.7 µm) eluted with water (A) and acetonitrile (B), both containing 0.1% formic acid at a flow rate of 0.8mL/min in gradient mode. The injection volume was 5 µL for AQ and DEAQ and 1 µL for SDX and PYR. The instrument time per sample was ~2 min. The calibration ranges were 0.1 – 100 ng/mL for AQ, 0.2 – 200 ng/mL for DEAQ. 0.2 – 200 ng/mL for PYR, and 20 – 20,000 ng/mL for SDX. Precision and accuracy were within 15%. The recoveries were 93.4±0.5 %, 87.8±2.2 %, 97.9±4.8 %, and 95.1±3.2 %, respectively. Matrix effect was negligible. DEAQ was unstable in plasma, with ~50% degradation overnight. The method was used to analyze 366 clinical samples, among which 82% have quantifiable AQ/DEAQ and 83% have quantifiable SDX/PYR. In summary, LC-MS/MS enables microvolume sampling and subsequent drug analysis to support clinical studies in pediatric populations.

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PRIMAQUINE PHARMACOKINETICS AND RADICAL CURE EFFICACY IN *PLASMODIUM VIVAX*-INFECTED ADULTS IN THAILAND

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Clearing dormant *Plasmodium vivax* hypnozoites with the anti-malarial drug, primaquine (PQ), may be hampered by ineffective metabolism of the drug into its active metabolites, particularly in individuals with polymorphisms in the cytochrome P450 2D6 enzyme. We conducted a clinical trial in Thailand designed to both assess efficacy of radical cure PQ (15 mg/day for 2 weeks) and to identify biomarkers of *P. vivax* hypnozoites. *P. vivax*-infected adults were randomized to one of two arms: EARLY group receiving PQ with concomitant oral artesunate (AS) for five days and the DELAYED group receiving PQ alone, six weeks after AS treatment. Both arms stayed in study housing for the first 28 days both to minimize risk of re-infection and obtain samples for retrospective analyses of hypnozoite biomarkers.

Recurrences of *P. vivax* over the 6-month study period were diagnosed by blood smear, both at study-specific time points and if clinical symptoms developed, and then confirmed with 6-species polymerase chain reaction (PCR) testing. Relapses were treated with PQ and chloroquine (CQ). For all volunteers, urine PK samples were collected for 24 hours after the first dose of PQ and at scheduled timepoints throughout the 2-week course. Thirty *P. vivax* patients were enrolled, with 28 receiving radical cure PQ: 12 with AS+PQ, 10 with PQ alone and 6 who received only AS, relapsed before six weeks, then received CQ+PQ. One volunteer in PQ+AS group, none in PQ alone, and three in the PQ+CQ had *P. vivax* recurrences, giving efficacy of 92% (1 of 12), 100% (0 of 10) and 50% (3 of 6), respectively. Urine PQ PK parameters for each volunteer and per drug regimen will be presented. Methemoglobin (metHgb), generated during PQ administration and a suggested signal of efficacy, was highest in the PQ+AS group (peak 4.6%, range 0-11%) versus PQ alone (3.6%, range 0-8.3%) or PQ+CQ group (2.8%, range 0-4.9%). These results will contribute to our knowledge of PQ metabolism parameters as predictors of radical cure efficacy, particularly when able to be combined with future hypnozoite biomarker data.

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DISCOVERY OF NOVEL ANTIPLASMODIAL COMPOUNDS USING RING FUSION OF INDOLE ALKALOIDS

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To mitigate the threat of emerging resistance to available antimalarials, new screening libraries are needed to discover novel chemotypes. Compound collections of commercial or "in-house" origin are often limited in diversity and stereochemical complexity. To address the lack of chemical diversity in current drug discovery efforts, we have developed an innovative "Complexity to Diversity" ring distortion approach to rapidly generate a diverse and unique library of complex small molecules from stereochemically complex indole alkaloids. Through the process of ring distortion, the complex ring systems of natural products are re-engineered utilizing ring fusion, cleavage, and expansion using various chemical reactions. Previous work in our lab has shown success in generating antiplasmodial compounds through ring distortion of vincamine and yohimbine - taking inactive starting compounds to products with submicromolar EC_{50}s against the multidrug resistant Dd2 parasite line with excellent selectivity. Using the ring-distortion approach of reserpine, a library of 83 compounds were synthesized and tested for antiplasmodial activity and selectivity. From these efforts, a reserpine derivative, AB-2-81 with potent antiplasmodial activity (EC_{50} 131 ± 21 nM) with high selectivity (SI >191) was identified. This work validates the value of ring distortion in re-engineering of natural products to develop new class of antiplasmodials.

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IN SILICO, IN VIVO AND *IN VITRO* TOXICITY ASSESSMENT OF NOVEL HETEROCYCLICS WITH ANTIMALARIAL ACTIVITY

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The emergence of resistance against most frontline antimalarials underpins the need for novel drugs. However, toxicity is a bottleneck for the further development of many inhibitory molecules. Although many *in silico* and *in vitro* approaches are available, *in vivo* models tend to simulate the real conditions more closely. Combined strategies may improve the detection and selection of molecules worth of further testing lowering time and costs. The aim of this study was to test the potential of *Galleria mellonella* (Insecta: Lepidoptera) as a low-cost *in vivo* model combined with *in silico* and *in vitro* assays to assess the toxicity of compounds with potential antimalarial activity. A total of 20 heterocyclics from an in-house library, showing inhibitory effects on *Plasmodium falciparum* parasite cultures (IC_{50} <1 μM) were selected for toxicity testing. *In silico* analysis was performed using SwissADME (Brent alerts) and ProTox-II. *In vitro* toxicity for cell membranes was assessed by hemolytic activity in human red blood cells (RBC) and the half-lethal doses (LD_{50}) were determined using six-instar larvae of *G. mellonella*. The larvae were initially injected with 500mg/kg and if >60% survived after five days, the assay was performed using higher doses up to 2000 mg/kg. Ten compounds showed no Brent alerts, Protox analysis revealed that 8 (out of 10) compounds showed predicted hepatotoxicity, 3 immunotoxicity, 6 carcinogenicity and 4 mutagenesis. None of the compounds was cytotoxic. In most cases the predicted likelihood of toxicity was low (consensus score:< 0.7), 3 compounds with higher predicted immunotoxicity and predicted toxicity level 4 (1000mg/kg) showed to be less toxic in the *Galleria* model. Most active compounds showed not induction of RBC damage at >200 μM, however two diphenyl-pyrazolines induced RBC hemolysis at lower concentrations (>50 μM). LD_{50} in *G. mellonella* classified most compounds as low or no toxic whereas *in silico* predicted toxicity was higher. *Galleria* model provides a more accurate representation of *in vivo* toxicity as *in silico* accuracy relies on the structural similarity of the novel compounds with those in the database.

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PARASITE CLEARANCE AND PROTECTION FROM *PLASMODIUM FALCIPARUM* INFECTION: CLINICAL RESULTS FROM A THREE-ARM, PARALLEL, DOUBLE-BLINDED, PLACEBO-CONTROLLED, RANDOMIZED TRIAL OF PRESUMPTIVE SULFADOXINE-PYRIMETHAMINE VERSUS SULFADOXINE-PYRIMETHAMINE PLUS AMODIAQUINE VERSUS ARTESUNATE MONOTHERAPY AMONG ASYMPTOMATIC CHILDREN 3-5 YEARS OF AGE IN CAMEROON

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The World Health Organization's (WHO) 2022 malaria chemoprevention guidelines recommend providing sulfadoxine-pyrimethamine (SP) to asymptomatic children living in high-transmission malaria areas as a perennial malaria chemoprevention (PMC). We will present results from a three-arm, parallel, double-blind, placebo-controlled, randomized trial in Cameroon designed to measure the effect of parasite genotypes associated with SP resistance on the efficacy of SP and SPAQ among asymptomatic children between 3-5 years of age (NCT06173206). Our sample size has 80% power to detect a significant difference in duration of protection in the presence or absence of the I431V mutation, derived from 1000 simulations and these assumptions: 6 infections per person per year, 40% microscopy prevalence, 10% loss-to-follow up, 30% *Pfdhps* I431V frequency, 28-day protection against *Pfdhps* I431 parasites, 15-day protection against *Pfdhps* 431V parasites, 85% genotyping success at *Pfdhps* codon 431. Children are randomly assigned to one of three directly-observed treatment groups: (i) SP group (n=450) receive daily artesunate (AS) placebo on days -7 to -1, then active SP plus placebo amodiaquine (AQ) on day 0, and placebo AQ on days 1 and 2; (ii) SPAQ group (n=250) receive placebo AS on days -7 to -1, then active SPAQ on day 0, and active AQ on days 1 and 2; and (iii) AS group (n=200) receive active AS on days -7 to -1, then placebo SP on

day 0 and placebo AQ on days 0 to 2. On days 0, 2, 5, 7, and thereafter weekly until day 28, children provide blood for thick smear slides. For future qPCR, dried blood spots are collected on the same days and weekly thereafter to day 63. We will report unblinded results including: (i) time-to-parasite clearance among SP and SPAQ recipients who were positive on day 0 by qPCR and followed to day 63; (ii) mean duration of SP and SPAQ protection against infection, and (iii) mean duration of symptom-free status among SP and SPAQ recipients who were parasite free on day 0 by qPCR. Our conclusions will reflect on the utility of the new WHO malaria chemoprevention efficacy study protocol follow-up to day 28 versus day 63.

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PARASITE CLEARANCE AND PROTECTION FROM *PLASMODIUM FALCIPARUM* INFECTION: CLINICAL RESULTS FROM A TWO-ARM, PARALLEL, DOUBLE-BLINDED, PLACEBO-CONTROLLED, RANDOMIZED TRIAL OF PRESUMPTIVE SULFADOXINE-PYRIMETHAMINE VERSUS ARTESUNATE MONOTHERAPY AMONG ASYMPTOMATIC CHILDREN 3-5 YEARS OF AGE IN ZAMBIA

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The World Health Organization's (WHO) 2022 malaria chemoprevention guidelines recommend the provision of sulfadoxine-pyrimethamine (SP) to asymptomatic children who reside in areas of high malaria transmission as perennial malaria chemoprevention (PMC). We will present results from a two-arm, parallel, double-blind, placebo-controlled, randomized trial in Zambia that is designed to evaluate the effect of parasite genotypes on the efficacy of single-dose SP among asymptomatic children between 3-5 years of age (NCT06166498). Our sample size has 77.4% power to detect a significant difference in duration of protection in the presence or absence of *Pfdhps* K540E, derived from 1000 simulations with the following assumptions: 10 infections per person per year, 37.8% prevalence by microscopy, 10% loss to follow up, 80% frequency of *Pfdhps* K540E, 30-day protection against *Pfdhps* 540K parasites, 18-day protection against *Pfdhps* 540E parasites and 85% genotyping success at *Pfdhps* codon 540. Children are randomly allocated to one of two groups for directly-observed treatment. Over seven consecutive days (days -7 to -1), children in the SP group (n=400) receive placebo artesunate (AS), then active SP (day 0). In contrast, children in the AS group (n=200) receive active artesunate for seven consecutive days, followed by placebo SP (day 0). Then, on days 0, 2, 5, 7, and weekly thereafter until day 28, children provide finger-prick blood for thick smear slides. Dried blood spots are collected on these same days for future qPCR analysis, and collected weekly thereafter until day 63. Children who become symptomatic are treated with artemether-lumefantrine if positive by malaria rapid diagnostic test. We will report unblinded results including: (i) time-to-parasite clearance among SP recipients who were positive on day 0 by qPCR and measured to day 63; (ii) mean duration of SP protection against infection, and (iii) mean duration of symptom-free status among SP recipients who were parasite free on day 0 by qPCR. Our conclusions will reflect on the utility of WHO's new malaria chemoprevention efficacy study protocol with its follow-up to day 28 versus day 63.

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PACRALIMA NITIDA FRUIT-RIND AND LEAF EXTRACTS EXHIBITED ANTIPLASMODIAL AND IMMUNO-MODULATORY EFFECTS AGAINST *PLASMODIUM BERGHEI*-INFECTION IN SWISSMICE

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Malaria has continued to remain a public health challenge, especially in some tropical and sub-tropical regions of the world. Although, a significant reduction in mortality and morbidity was recorded between 2005 and 2015, decreased susceptibility of *Plasmodium falciparum* to the current first-line antimalarial drug, artemisinin-based combination therapy (ACT), has been reported in Southeast Asia and other continents which further complicate the severity of the disease, especially in low-income countries like Nigeria. Numerous strategies have been employed to combat artemisinin resistance and one of them is the intensified efforts toward the discovery of novel drugs from plant sources that may be alien to the parasite. This study therefore evaluated the antiplasmodial and immuno-modulatory effects of chloroform-methanol extracts of *Pacralima nitida* fruit-rind and leaf in *P. berghei-infected* mice. The bioactive constituents of the plant were extracted using standard protocol. Extracts obtained were assessed for antiplasmodial activity by the standard four-day suppressive test on *P. berghei* (*ANKA*) infected mice (Swiss strain). The absorption spectra from the HPLC chemical finger-prints of the extracts revealed several peaks representing bioactive phytochemicals while the results from the animal study showed that the extracts were dose-dependently ($p < 0.05$) active against *P. berghei* parasite in comparison with the untreated infected mice (negative control). Dose-dependent decreases ($p < 0.05$) in some oxidative stress indices of the extracts-treated groups as against the infected control were observed. The pro-inflammatory cytokines levels were assessed and were found to be significantly low in the extracts-treated groups relative to the infected control. Results from the study suggest that methanol extracts of *P. nitida* fruit rind and leaf possess appreciable antiplasmodial properties with some immuno-modulatory effect against the *P. berghei* parasite.

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EFFECT OF SEASONAL MALARIA CHEMOPREVENTION IN STUNTING CHILDREN IN KOULIKORO, MALI

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Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine plus amodiaquine (SP+AQ) is an effective and promising strategy for controlling malaria morbidity and mortality in areas of intense seasonal transmission. Despite its effectiveness several controversies regarding the occurrence of clinical malaria among eligible children and challenges of the strategy in the context of high prevalence of malnutrition in area where it is implemented make questionable the benefit of SMC in malnourished children compared to those with normal nutritional status. This study investigated the risk of clinical malaria among stunting versus normal children eligible for SMC in Koulikoro, an area where the frequencies of the two diseases are high during the rainy season. A total of 2613 children eligible for SMC were enrolled just before the first round of SMC in July 2020. At baseline *Plasmodium falciparum (P.f)* infection and nutritional status was assessed for study participants and children were classified in

two comparison groups: normal and stunted. All participants were followed from the start to the end of SMC through passive case detection to determine the incidence of clinical malaria define as fever and malaria RDT or blood smear positive. The risk of malaria in both groups was estimated using the Wald test. The overall prevalence of asymptomatic malaria and stunting were 11.2% and 62% respectively. Ended, 847 children as normal and 89 as stunted. During the SMC season the overall incidence was 25.6%. Comparing the first occurrence of *P.f* parasitemia during the SMC season, the cumulative incidence of malaria was 20.6% in the normal group (n=336) vs. 33.7% in the stunted group (n=332). Stunted children had significantly more first malaria episodes RR= 1.97 (95% CI, 1.73-2.25). These results suggest a reduction of the effect of SMC treatment in preventing clinical malaria among stunted children compared to normal children. Thus, a combined intervention targeting the two diseases could increase the effectiveness of SMC in area where the two diseases are highly seasonal.

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EXPERIENCES FROM DIGITALIZING INSECTICIDE-TREATED NETS (ITNS) MASS DISTRIBUTION CAMPAIGNS IN ZAMBIA

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The Zambia National Malaria Elimination Programme conducts universal mass distribution of insecticide-treated nets (ITNs) every three years. In 2023/2024, Zambia used an Electronic Data Management Information System (EDMIS) to implement the ITN campaign for the first time. Prior to this, paper-based data collection was used, resulting in numerous challenges. Here we describe the development of EDMIS and lessons learned during its use to support deployment of ITNs targeting an estimated 20 million Zambians. A two-month consultation process was used that involved an assessment of the data infrastructure architecture. A data collection form was developed to collect information on household members, sleeping spaces, GPS coordinates, ITNs allocated and distributed, and data quality and validation checks. Over 10,000 phones and a HPE ProLiant DL380 Gen10 Plus server were procured to manage data entry, storage, and analyses. To address possible upload challenges and loss of data, paper-based registers were used as backup. A total of 20,664,899 persons in 3,883,195 households were registered, 17.45% less than the 4,560,912 projected households. As at March 27, 2024, 10,178,609 ITNs (one net per two people) were distributed and captured on EDMIS countrywide, translating to 89.4% of the enumerated population protected. During the process, bottlenecks were identified and support for about 10,000 data users was provided at full operating capacity. However, about 20% of data failed to upload to DHIS2 while in the field during registration and distribution, which was attributed to internet challenges in rural areas. This delayed the campaign by three months. The lessons learned and best practices established during the implementation of the EDMIS will contribute to the success of future campaigns, particularly by building staff capacity at district level in IT skills. However, with unpredictable outcomes in the digital space, the paper registers remain important in the execution of ITN campaigns.

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IMPROVING INTEGRATED COMMUNITY CASE MANAGEMENT (ICCM) BY COMMUNITY HEALTH WORKERS - AN EXAMPLE OF MALARIA MANAGEMENT IN NCHELENGE DISTRICT, ZAMBIA

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In Zambia, the 2021 national malaria prevalence was estimated to be 23%, according to data from the malaria indicator survey. Luapula Province, which includes Nchelenge District, had the highest prevalence at 63%. The Ministry of Health (MOH) plans to train 40,000 Community Health Workers (CHWs) nationwide by 2025 in integrated community case management (iCCM) including malaria. Between 2021 and 2023, trained CHWs increased from 382 to 405 in Nchelenge District. Although CHWs were being trained, many were not sufficiently equipped with malaria commodities, as it was reported in May 2021 that the availability of rapid diagnostic tests (RDTs) and the first-line antimalarials were at 0% and 5% respectively (56.7% reporting rate). During the regional supply chain review meeting with the MOH and partners in 2021, contributing factors to the commodity availability at CHW level, such as health facilities (HFs) not including CHWs' needs, low reporting rates, and low data quality, were identified. Following the findings, the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project partnered with the MOH to establish a consistent supply of commodities by working with provincial and district MOH staff to ensure that approved order quantities for HFs include CHWs' needs for iCCM and introduced a commodity ordering and tracking tool (COTT) for community level reporting for stock levels, consumption, losses, and adjustments. The tool provides an efficient way for CHWs to manage and track essential commodities with limited oversight and has now been integrated into the MOH-led iCCM trainings. These initiatives enhanced the availability of RDTs to 85%, and first-line antimalarials to 75% (80.6% reporting rate) in May 2023, at CHW level, and contributed to an increase in malaria case detection by CHWs from 79 cases in May 2021 to 5,366 cases for timely treatment in May 2023. These results indicate the importance of considering CHW expansion in commodity management. Strengthening CHW supply chain management skills may have helped the monitoring and maintenance of adequate commodities.

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QUANTIFYING FOR ROLE OF IMPORTATION ON SUSTAINED MALARIA TRANSMISSION IN SOUTHEAST UGANDA

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Importation of malaria parasites through human movement poses a threat to control. However, understanding the role of importation is challenging because it is difficult to differentiate between local and imported infections in areas with some level of transmission. We aim to quantify the role of importation on malaria in Kamwezi, Uganda, a region characterized by spatial variation in burden. We enrolled 400 households in a 2-year longitudinal study in summer 2023, collecting travel and movement histories, data on malaria episodes, and blood samples during bimonthly visits. Passive surveillance captured symptomatic infections at a local health facility alongside the cohort. Our outcomes included parasite positivity (asymptomatic infections) and symptomatic malaria cases. Regression models analyzed the association between travel and outcomes, stratifying by village-level transmission intensity. After four survey rounds involving

5,821 visits of 1,872 individuals, 3.8% (224) had recent malaria illness, and 16.6% (264) tested positive for asymptomatic infection at baseline. 8.3% (488) of individuals reported overnight travel and 6.9% (404) reported evening movement. We did not find evidence for an association between travel and asymptomatic infection, nor did we find an association between travel and symptomatic malaria in higher transmission villages. We found evidence supporting an association between travel and symptomatic malaria (incidence rate ratio = 2.45, 95% confidence interval 1.45-4.08) in lower transmission villages, such that travel accounted for 10% of malaria cases, with travel to higher transmission areas elevating risk. Furthermore, we found that movements during evening to higher transmission villages were associated with malaria illness. By the conference, 18 months of follow-up will be complete, allowing a probabilistic model estimating importation probability for all cases. We will also generate genotype data to differentiate between local and imported infections. Understanding these factors is crucial for developing interventions to reduce the impact of importation on sustained transmission.

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MALARIA ELIMINATION IN CABO VERDE: AN OVERVIEW ABOUT FOR HISTORY, CASE DATA FROM FOR LAST 35 YEARS (1985-2023) AND CHALLENGES AHEAD

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On January 12th, 2024, Cabo Verde was officially certified by the WHO as a malaria-free country after six consecutive years without local cases. This study analyses the malaria history of Cabo Verde, from 1953 to certification in 2024, brings some lessons learned and discusses challenges for the future as a malaria-free country. A literature review was conducted; descriptive analyses were done with the last 35 years' data (1988-2022), and cases were mapped using the Quantum GIS Software. Six reference stages and three periods of malaria interruption can be highlighted. The first interruption was for five years (1968-1972), the second for three years (1983-1985), followed by outbreaks, and finally, certification in 2024. From 1988 to 2022, 3,089 malaria cases were reported, being 2,381 (77.1%) local and 708 (22.9%) imported. To achieve elimination, after the last malaria outbreak in Cabo Verde in 2017, the NMCP reviewed the strategies and developed the new NSP for Malaria Elimination 2020-2024. It included implementing active and reactive foci investigations and effecting the vector control. The vector control strategies, included larval source management, indoor residual spraying (IRS) and environmental modification. Concerted efforts focusing on behavioural change and social mobilization were also crucial aspects in achieving elimination, associated with the robust epidemiological surveillance system in place, capable to detect timely, treat correctly and the follow-up of all cases. With the certification, Cabo Verde became an African country reference in the health sector organization, multisectoral and partnership in malaria control. Maintaining the certification imposes several challenges to the country's sustainability and perennially. The lessons learned and experiences about malaria control and elimination in Cabo Verde is an opportunity and hope to the others African countries that can benefit to save more lives and improve the quality of life of populations.

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ARE THERE GENDER DIFFERENCES IN FOR GAPS IN MALARIA TREATMENT CASCADE IN GHANA? IMPLICATIONS FOR MALARIA ELIMINATION

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Effective case management is critical to Ghana's malaria elimination agenda. Identifying gender differences in the malaria treatment cascade will help tailor interventions to address specific needs that will maximize benefits from scarce resources. We set out to explore gender differences in the malaria treatment cascade in Ghana. This was a nationally representative community-based survey among participants 18 years and older, in six randomly selected regions. The outcomes included gender differences in malaria treatment cascade of one-month and six-month prevalence of self-reported malaria. Overall, 3022 participants were engaged, including 1547 females, with a median age of 32(25-43) among males vs. 31(24-41) among females. The one-month self-reported malaria prevalence was 20.8% (19.4 - 22.3), 20.3% among males vs. 21.3% among females. A higher prevalence was observed among females in the Greater Accra region (17.5% vs. 10.5%) and the Central region (28.8% vs. 19.3%), $p<0.05$. Of the 628 malaria cases, 60% were tested, and 95.5% tested positive. Among the positive cases, 72,2% were prescribed orthodox medication, predominantly ACTs, 15.3% took complementary and alternative medicine (CAM), and 11.9% took both orthodox and CAM treatments. Stratified by sex, significant differences were not observed in the malaria treatment cascade except that, more females with negative tests took orthodox treatments, (38.5% vs. 0%, $p<0.05$), as well as CAM products (61.5% vs. 50.0%, $p <0.05$). Self-reported malaria in the past 6 months was 57.4% (55.6 - 59.1), and of 1733, 59.4% were tested, (males: 58.1% vs. females: 60.7%). Malaria RDT testing was significantly higher among females than males, 66.2% vs. 58.9%, ($p<0.05$). Fewer females tested positive (94.6% vs. 97.3%). Of the 695/1,733 cases, (40.1%) positive malaria cases treated with orthodox medicines, significantly more females (42.3%) were treated with orthodox medicines compared to males (37.8%), $p<0.05$. Exploring the factors that account for the relative gender differences in the treatment cascade gaps can potentially enhance malaria elimination efforts in Ghana.

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ONE HEALTH BY USING GREEN SYNTHESIS OF NANOPARTICLES TO IMPROVE COMMUNITY ENVIRONMENT

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Mosquitoes are main vectors of parasitic diseases such as dengue, malaria,filariasis,Japanese encephalitis, chikungunya and so on . These diseases cause death in humans and animals.The constant use of chemical insecticides against mosquitoes has led to a physiological resistance . Nanotechnology is a rapidly growing field due to its unique functionality and a wide range of applications. The aqueous extract of fresh leaves of *Ocimum basilicum* have been used to synthetize nanoparticles. The synthesized nanoparticles was characterized by using ultraviolet spectrophotometry, X-Ray diffraction, and Fourier transform infrared spectroscopy methods.The wavelengths between 400-600nm confirmed experimentally the formation of silver nanoparticles. They were crystalline in nature and constituted by the following chemical groups: Alcohols, amines,

alkyls, aldehydes and ketones. The larvicidal effect against *Anopheles gambiae* has been tested. The LC50 determinated after 24 h and 48 h. The results showed an increase in potency with time. The mortality of AgNPs *O. basilicum* having concentration of 2.0 to 2.5 ppm after 24 h. The LC_{50} for AgNPs *O. basilicum* were 1.54 ppm after 24 h, while after 48 h the LC_{50} reached 0. 95ppm.The green synthesis of silver nanoparticles using *O. basilicum* water extract were effective against *Anopheles gambiae* larvae. Their insecticide properties that do not require the presence of any harmful material. This method is eco-friendly, low-cost, and safe for human health and his environment Biocontrol agents derived from this methodology could be considered as a suitable alternative to control vector-borne diseases in developing countries.

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PREVALENCE OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN A MALARIA-ENDEMIC REGION OF COLOMBIA: IMPLICATIONS FOR RADICAL CURE OF *PLASMODIUM VIVAX*.

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Glucose-6-phosphate dehydrogenase deficiency (G6PDd) is a common genetic condition with important implications for radical cure of *Plasmodium vivax* (*Pv*), the most common malaria species in Colombia and Latin America (LA). G6PDd is associated with a higher risk of hemolytic events when using 8-aminoquinoline drugs. The prevalence of G6PDd and its relation to *Plasmodium sp*ecies infection is poorly known in this region. A cross-sectional study was conducted in Quibdó, Colombia. Participants were randomly selected among the general population (GP) (n=1267), indigenous communities (IC) (n=194), and outpatients with suspected malaria (OSM) (n=542). Participants were screened for G6PD levels using a quantitative finger-prick blood test and were classified as deficient, intermediate, or normal phenotype. *Plasmodium sp.* infections were determined by polymerase chain reaction (PCR). G6PDd and *Plasmodium* infection prevalence were calculated for each population and risk factors for G6PDd were explored. The study was conducted between July and November 2023. The prevalence of G6PDd was 10.4%, 0%, and 7.0% in the GP, IC and OSM, respectively. The prevalence of *Plasmodium sp.* infection was 17.8%, 40.7%, and 47.8% in GP, IC, and OSM, respectively. Among GP and IC, *Pv* was more frequent than *Pf* (GP Pv=11.2% & Pf=0.1%; IC Pv=26.2% & Pf=0.1%), and most *Pv* infections were asymptomatic. Being Afro Colombian (Prevalence ratio (PR) 6.81; 95% CI [3.21 - 18.08]) and male (PR 1.71; 95% CI [1.29 - 2.29]) were risk factors to be G6PDd, while being G6PDd resulted in lower *Plasmodium* infection (PR 0.41; 95% CI [0.25 - 0.63]). Afro-Colombian populations in Quibdó have a high G6PDd and thus, a higher potential risk of hemolysis, suggesting that a G6PD test must be implemented before the use of a high dosage of primaquine or tafenoquine. Effective malaria control is a big challenge in the study area due to the high burden of asymptomatic infections, caused by *Pv*. G6PDd was not found among the studied IC, which harbors the highest burden of *Pv* suggesting an opportunity for the adoption of new interventions for radical cure in this population.

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MASS DRUG ADMINISTRATION FOR MALARIA IN LOS CHILES, COSTA RICA: ITS IMPLICATIONS FOR ELIMINATION

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Despite the significant achievements, malaria is still a public health problem in Costa Rica (CR). Malaria cases are concentrated in a few regions from which, Los Chiles foci have been responsible for the 81% of the CR cases in 2022. To contribute to the elimination of malaria in the main active foci (Los Chiles) in Costa Rica, a MDA was proposed by the MOH and partners. Three localities were selected San Gerardo, Coquital, and Medio Queso; and two farms that overall reported 64% of the cases in Los Chiles canton (97% Plasmodium falciparum, Pf)). We reported the results of a non-interventional, observational study conducted between January and June 2023. Two MDAs cycles were implemented among people who provided verbal consent and without any contraindications. A preparatory phase (Jan-Mar 2023) included an updated census, protocol design, planning, and door-to-door sensitization of the selected communities. Chloroquine (CQ) full treatment was given supervised for 3 days to the selected population in 861 households, and 2 farms. Overall, the average CQ completeness (full CQ 3d course) in the MDA1 (Apr 1-7) and MDA2 (Jun 5-9) among the selected 3 localities was 82% and 59.2%, respectively. In contrast, the average CQ completeness among participants in the farms was 33.4% in MDA1 and 47.7% in MDA2. Among all groups, the CQ refusal rate was increased 5x times - from 3.1% in MDA1 to 15.8% in MDA2. Adherence to more than two CQ doses was 88% and 89% in MDA1 and MDA2, respectively. Malaria cases dropped to zero after the end of MDA1 for 12 months; surveillance activities (passive/active case detection) have been maintained. The addition of a MDA in Los Chiles was successful in eliminating malaria transmission in the target areas for 12 consecutive months. To our knowledge, this is the first MDA for malaria conducted in Latin America after the updated WHO recommendations for chemoprevention strategies in June 2022. MDA (and other chemoprevention strategies) should be considered, assessed its feasibility, and incorporated more frequently at NMCPs to accelerate elimination targets.

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TARGETED TREATMENT WITH PRIMAQUINE FOR THE ELIMINATION OF *PLASMODIUM VIVAX IN A BORDER AREA OF THE GREATER MAEKONG SUB REGION*

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Plasmodium vivax malaria's high incidence hampers the Greater Mekong Sub-region's (GMS) 2030 malaria elimination goals. Thailand's adoption of the 1-3-7 surveillance framework for rapid case detection and containment

is commendable, yet insufficient due to challenges like hypnozoite-induced relapses and poor adherence to the 14-day primaquine (PQ) regimen. Hence, additional control measures are imperative to meet elimination targets. This study integrated the 14-day PQ treatment with reactive case detection activities as part of the 1-3-7 surveillance approach, termed Targeted Primaquine Treatment (TPT). Three districts with the highest reported *P. vivax* incidence along the Thailand-Myanmar border were selected as study sites. Within each district, two villages with similar geographical and malaria prevalence profiles were assigned as treatment or control groups. While individuals in the control group received standard malaria prevention and control measures (SMPC), eligible individuals in the treatment group received TPT (PQ 0.25mg/kg/day for 14 days) under directly observed treatment, in addition to SMPC, with the target of 150 index cases per group. The impact of TPT will be assessed by comparing two indicators (incidence and prevalence) before and after TPT in both groups. From October 2023 to March 2024, 55 index cases were identified across the two groups, with over 300 individuals receiving the 14-day PQ regimen. The TPT will continue until July 2024 to cover the peak malaria transmission in these areas. Preliminary analysis with available results detected an impact of TPT on the infection rate in the treatment group but minimal change in the control group. Notably, no severe adverse effects related to PQ were reported. In conclusion, early results of TPT shows potential in reducing the burden of vivax malaria. Its integration into existing malaria elimination efforts, such as the 1-3-7 strategy, requires minimal additional resources. Thus, TPT offers a viable strategy to enhance *P. vivax* malaria elimination, not only in Thailand but also in the broader GMS and Southeast Asia regions where *P. vivax* remains prevalent.

7202

ADVANCING MALARIA DIAGNOSTIC AND TREATMENT ACCESSIBILITY: A COLLABORATIVE APPROACH TOWARDS ACHIEVING NATIONAL TARGETS IN BENIN

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In Benin, significant improvements have been made in combating malaria, evidenced by a notable decrease in incidence rates by over 20% in 2023. However, this positive development is counteracted by a 17% rise in malaria lethality, escalating from 1.2 to 1.4 per 1000 cases. Nonetheless, hospital lethality has remained steady at 1.6%. These statistics underscore a pressing issue in malaria-related fatalities and emphasizes the urgent necessity for enhanced commodity access, especially for severe malaria cases. To address the challenges related to commodity access, the National Malaria Control Program has undertaken various initiatives, including supply chain activities focused on supervision, healthcare facility training, central-level quantification activities and supply data reviews. While these efforts have led to a continuous decrease in stock outs across the country since 2021, the availability of testing and treatment remains moderate, fluctuating between 70% and 80%. This level falls below the national target of 95%. Availability of testing and treatment commodities were addressed with comprehensive data reviews aiming at strengthening malaria surveillance activities and leveraging data insights to strengthen commodities access. Since 2023, one annual coaching session has been conducted, empowering healthcare providers to deliver accurate and timely malaria diagnosis and treatment. Building upon the successes of the previous year's efforts, which were primarily centered around healthcare facility training, this coaching approach has evolved this year to include 40 hospitals. By broadening the scope of the coaching to include hospitals, the National Malaria Control Program aims to extend its reach and impact, especially regarding severe malaria, and ensuring that diagnostic and treatment accessibility is optimized across all levels of the healthcare system. To further strengthen this initiative, results from the collaborative efforts of the data reviews will be used to directly inform the content and focus of coaching sessions, ensuring alignment with evolving challenges and priorities.

7203

IMPROVING DATA QUALITY AND SUPPLY CHAIN SERVICE DELIVERY THROUGH TARGETED CAPACITY BUILDING IN RESOURCE-CONSTRAINED SETTINGS: A CASE STUDY OF TWO SELECTED LOCAL GOVERNMENT AREAS IN KANO STATE, NORTHERN NIGERIA

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Variances between dispensed-to-user data from the pharmacy and the number of patients accessing malaria prevention and treatment services have remained a source of concern in Kano State Nigeria. This mismatch can result in inaccurate quantification leading to overstocking or understocking of health facilities resulting in wastage which affects commodity security. For improved supply chain data management and accountability, formal refresher training is needed to retain institutional capacity amidst high attrition of personnel because of transfers, retirements, and migration. The Targeted capacity building (TCB) model was introduced to bridge the attrition gap of trained personnel without adequate resources for robust refresher training in all facilities. Twenty-four health facilities and 30 staff were selected in two local government areas (LGAs) with data triangulation variance greater than 10% and less than -10% indicating weak performance. A TCB session was planned to focus on the root causes and how to reduce the variance between the data sources. To ensure knowledge is retained after the training, a performance monitoring plan was developed with health facility workers and LGA personnel for follow-up. Before TCB, the cumulative average variance between dispensed to user data and the number of clients accessing malaria services recorded on the facility register and other registers collating malaria services between January and June 2023 was -44% and 25% respectively. These values improved to -22% and 8% for the respective LGAs following TCB from July to December 2023. The findings support the approach of using targeted capacity building in resource-limited areas, focusing on facilities and LGAs with performance issues. Continued analysis should be done to ascertain if the TCB approach can be sustained and continuously used.

7204

UTILIZATION OF MALARIA CORE TEAM STRATEGY ENHANCES STATE GOVERNMENT STAFF CAPACITY AND IMPROVES EFFICIENCY. A CASE STUDY OF OGUN STATE, SOUTHWEST NIGERIA

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Management Sciences for Health (MSH), a sub-recipient of Catholic Relief Services, implemented the Global Fund Malaria Grant, New Funding Model (NFM3) in 11 states in Nigeria from 2021-2023. One perennial challenge which the MSH project team sought to address during this period was that the State Malaria Elimination Programs (SMEP) staff lacked the capacity

to coordinate project activities and provide technical assistance to health workers, leading to a lack of ownership of grant interventions and making sustainability nearly impossible. MSH project team introduced the Malaria Core Team (MCT) strategy to enhance the capacity of SMEP personnel to address identified gaps. The MCT consists of SMEP technical staff and MSH state-based technical staff. MSH staff coached and mentored the government personnel in providing on-the-job training to service providers, through joint site visits. SMEPs now take ownership of grant interventions and ensure accountability for malaria health products, promoting sustainability. MCT members monitor project activities without MSH staff support and provide training to health workers using MSH-designed and national tools. Four SMEP personnel participated in a 2021-2023 MCT visit to Ogun State, visiting 180 health facilities, mentoring 450 workers, and advocating for smooth implementation, ensuring 40% of project-supported facilities were visited. The strategy of MSH, which involves working closely with governments, has significantly improved service delivery and reporting at the facility level. The Malaria Core Team's monitoring and supervisory visits have improved service providers' compliance with National Malaria Treatment guidelines, particularly in secondary health facilities. These visits have helped providers become more familiar with the guidelines and current treatment practices, especially for severe malaria. The MCT has resolved issues such as non-reporting, poor documentation, and poor data quality, reducing the risk of serious problems.

7205

INTEGRATING ACTIVE SURVEILLANCE AND ENTOMOLOGY FELLOWSHIP FOR SUSTAINABLE MALARIA CONTROL AND ELIMINATION IN SOUTHERN ANGOLA

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Synergy initiatives aimed at enhancing malaria surveillance for elimination in border regions of Southern Angola started in 2017. The Ministry of Health is strengthening efforts for a sustainable path for a malaria elimination together with its regional partners. Under the Elimination 8 funded program, a strategy for active surveillance, including malaria case-based notification tracker system, was rolled out. Recently, a training program was conducted in Cunene and Cuando Cubango Provinces focusing on building capacity and sustainability of interventions for active surveillance. Fifty-three health workers of selected health facilities and focal points of 5 districts were trained on DHIS2 tracker, data driven decision making, vector control and entomology as path to scale up interventions. In addition, a fellowship program was set up to implement an entomological surveillance programme building local capacity. The intensification of capacity building interventions and integration with fellowship activities will allow to increase the scope of sentinel sites and enhance foci classification, investigation and response. This collaborative effort, led by the Ministry of Health, aimed to strengthen malaria information systems and case-based reporting to identify local transmission foci. This integrated approach not only enhances intervention effectiveness but also strengthens overall health system capacity, ensuring long-term sustainability and resilience against disease resurgence in the region. This abstract highlights the significance of interlinking active surveillance programs with entomology fellowships to achieve sustainable malaria control and elimination goals.

7206

THE IMPACT OF 1-3-7 FOCUS INVESTIGATION SURVEILLANCE IN A PRE-ELIMINATION SETTING IN SOUTHERN ZAMBIA: A ZONAL-RANDOMIZED TRIAL

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Since 2016, eleven countries have been certified as malaria free, but none of these are in continental Africa, where elimination challenges are unique. Recommended elimination strategies, like 1-3-7 focus investigation, feature heightened case-based surveillance and focal community response to index cases. A passively detected malaria "index" case, be reported within one day, classified within three days, and followed up in its community with focal response within seven days. To date, no study has measured the effect of 1-3-7. Choma District, located in Southern Province, Zambia is a very low transmission setting (under-5 RDT prevalence is 3.3%). The MUSEMO study was a 24-month zonal-randomized study in two health center catchments areas in Choma District to measure the impact of 1-3-7 on the prevalence and incidence of malaria. 1-3-7 was deployed in a randomly-selected half of the zones in the study area. Surveys measured malaria prevalence in index-case communities 7 and 35 days after index case diagnosis to compare 1-3-7, "intervention", and non-1-3-7, "control" zones through multi-level logistic regression. Health facility data reported weekly zonal incidence and Poisson regression estimated changes in incidence rate across intervention and control areas. Community qPCR prevalence increased between the 7 and 35-day visits from 1.9% to 2.8%, but there was no significant difference across arms. The weekly zonal incidence as reported through surveillance was 81% lower in the zones using 1-3-7 surveillance (ratio of IRR: 0.19, 95% CI: [0.08,0.43], p-value <0.01). The increase in community-level prevalence suggests there is ongoing local transmission in the weeks after an index case, and that current focal 1-3-7 response does not interrupt this. The decrease in catchment-wide incidence provides evidence that the surveillance component of 1-3-7 may drive improved awareness of localized malaria risk and planning and response to mitigate it. These findings support the use of the 1-3-7 surveillance approach to focus investigation and to add additional focal response strategies to day-7 activities.

7207

VILLAGE HEALTH TEAMS IMPROVING THE MANAGEMENT OF MALARIA IN CHILDREN UNDER 5 YEARS IN UGANDA'S WEST NILE REGION: A CASE OF MOYO DISTRICT

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Malaria remains a significant health challenge in low- and middle-income countries, particularly affecting children under 5 years and pregnant women. In Uganda's West Nile Region, malaria prevalence is 22%. Moyo District in West Nile has been grappling with high malaria test positivity rates, ranging from 62% (January 2023) to 91% (December 2023). To address the problem, in September 2023, all 466/466 village health team members (VHTs) in Moyo were trained on case identification and fever management through integrated community case management (iCCM) of malaria, pneumonia, and diarrhea in children under five years of age. A cascaded training approach was used through the levels of service delivery in the district, starting from the district to the VHT. Training focused on case management and reporting of data and was followed by quarterly VHT meetings and mentorships to ensure compliance and accountability for commodity refills. At the start of the intervention, the

National Medical Stores (NMS) supplied 11,691 malaria commodities to 30 health facilities in Moyo, of which 70% (8,133) went to the VHTs. The availability of commodities for iCCM in Moyo ensured that malaria test and treatment ratios remained above the 95% national target. Following the iCCM training, VHT knowledge scores increased to an average of 75% from 39% at baseline. The number of children under five years attended to by VHTs within the community increased to 2,872 from 1,694 before the intervention. Fever cases attended to by VHTs also increased to 2,595 from 1,552. The success of this approach underscores the potential of VHT-led iCCM to significantly improve access to malaria case management services, particularly in hard-to-reach communities.

7208

MODELING THE IMPACTS OF SEVERE STORMS ON MALARIA INCIDENCE IN MOZAMBIQUE FROM 2016-2023

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Increases in frequency and severity of extreme weather events (e.g. cyclones, tropical storms, and severe storms) are a hallmark of climate change, and impact established programs to control and eliminate malaria. Mozambique is already experiencing these, with increases in tropical storms, tropical cyclones, and floods over the past 10 years impacting the entire population and currently does not have the capacity to respond to all of the infectious disease challenges that result. The National Malaria Control Program (PNCM) is charged with implementing and maintaining the infrastructure to support P. falciparum prevention, control, and elimination programs throughout the country. In this resource poor setting, the progress of these programs is under constant threat when infrastructure is damaged due to severe weather events because emergency response is limited to the highest impacted areas. Areas outside of direct impact, have not received support in the aftermath, and not specifically for malaria. We integrated malaria surveillance data and climate data for both named and unnamed storms to determine geographic areas in Mozambique that are at an increased risk of malaria due to infrastructure damage following severe weather events. We used databases from the World Meteorologic Organization database of named tropical storms and cyclones to identify the locations and tracts of the eyes of the storms. We quantified the areas impacted by these storms using NASA satellite precipitation data matched to the time and locations of the eyes of the storms. We integrated temperature data from NASA satellites also. We used daily precipitation data, monthly temperature data, and daily wind data (from NASA weather stations) to detect storms that don't reach the classification to be a named storm. We used these data with the malaria incidence data aggregated to the District level to quantify the population at risk in these areas following severe storms using a Bayesian time-series model. This study will present preliminary findings of our models for at the national level in Mozambique.

7209

EFFECTS OF COMMUNITY MALARIA CASE MANAGEMENT TO THE OVERALL MALARIA INCIDENCE IN BUSIA COUNTY KENYA 2022

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The objective of the study was to determine whether Case Management of Malaria (CCMm) by Community Health Volunteers (CHVs) affect the trends of malaria incidence in Busia Kenya from 2018 to 2023. The study determined the annual proportion and trends for malaria cases tested and treated at health facilities and Community Units and correlated the trends with annual malaria incidence out-patient malaria cases, weather patterns, climate change, and commodity availability at the community level. This was a retrospective cross-sectional involving the analysis of routinely collected malaria data as reported on the Kenya Health Information Systems. The proportion of Suspected Malaria Cases being tested by Community Health Volunteers compared to those tested at Health facilities increased from 11% in 2019 to 45% in 2022. The rate of malaria infections per month remained almost constant, with peak infections occurring in May annually, except in May 2020. Over time the contribution of CCMm in overall malaria case management and incidence has increased, with more malaria cases being treated in the Community as of mid 2022. The incidence of Malaria has remained high over the years. The study concluded that CCMm improves access to Malaria treatment services but does not reduce the Annual Malaria Incidence in Busia County.

7210

MALARIA AND ANAEMIA PREVALENCE AND ASSOCIATED FACTORS AMONG PREGNANT WOMEN INITIATING ANTENATAL CARE IN GHANA

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Malaria infection in pregnancy is associated maternal anemia and low birth weight. Although there are improving levels of implementation of recommended malaria and anemia control interventions in Ghana, there is no commensurate reduction in maternal anemia prevalence and low birth weight. A health facility-based cohort study was conducted between 2018 and 2020 to identify current risk factors of low birth weight and maternal anemia in 2 regions of Ghana. The baseline malaria infection and anemia prevalence and associated factors is reported here. Five thousand, one hundred and ninety-six pregnant women of all parities, ages and gestational ages were enrolled at first antenatal care visit in Ashanti and Volta regions of Ghana. Descriptive and inferential statistics were conducted on data collected on socio-economic and demographic characteristics, obstetric history, ITN ownership and use, presenting complaints and laboratory results of full blood count, G6PD and sickling status, malaria parasite, HIV, syphilis, Hepatitis B, schistosoma and helminth infections using STATA version 16. The mean (SD) age and gestational age were 27.3 (6.5) years and 15.5 (8.37) weeks respectively. ITN use was 59.8% compared to 80.8% ownership. Overall malaria parasite prevalence was 5.7%; higher in Ashanti (10.24% [95% CI: 8.92 - 11.68]; mean parasite density = 982/µl) compared to Volta (2.63% [CI: 2.07 - 3.29]; mean parasite density = 18226/µl). Overall anemia prevalence was 55.2%; higher in Volta region (65.6% [95% CI: 63.78 - 67.31]) than in Ashanti (42.6% [95% CI: 40.53 - 44.60]). Women with malaria infection were more likely to be resident in Ashanti, primipara, of lower wealth status and reported at least a clinical symptom. Women were more likely to be anemic if resident in Volta region, had malaria infection, were younger than 25years, booked ANC later and of lower wealth index (P<0.001). Although malaria infection prevalence is relatively low it still poses a risk to maternal anemia. Maternal anemia is high and of serious public health importance appearing to be related more to geographic location and wealth index.

7211

THE RELATIONSHIP BETWEEN PLACENTAL MALARIA AND PREECLAMPSIA

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Pre-eclampsia (PreE) and malaria are leading causes of perinatal morbidity and mortality in sub-Saharan Africa. Placental malaria (PM) has overlapping pathophysiology with PreE, causing abnormal angiogenesis in the placenta. Placental damage from PM may predispose patients to PreE. Previous studies have demonstrated an association between hypertensive disorders of pregnancy and PM but are limited by a failure to characterize the PM (acute v. earlier in pregnancy) and type of hypertensive disorder (PreE, eclampsia, all hypertensive disorders of pregnancy). Utilizing placental specimens and clinical data collected during a randomized

controlled clinical trial of intermittent preventive therapy during pregnancy in Malawi, we aimed to examine the association between PM and PreE. All individuals from the parent study with singleton pregnancies and placental histopathology and PCR available were included in this analysis. All patients were HIV-uninfected and primi- or secundigravid. No patients had chronic hypertension or advanced maternal age. Chi-squared tests were performed. Among the 751 individuals meeting inclusion criteria, 125 (16.7%) had evidence of PM. Of those, 105 had hemozoin pigment present, indicative of an infection earlier in pregnancy. Out of the 751 participants, 31 (5.0%) had PreE, 6 had eclampsia (1.0%) and 82 (13.1%) had any type of hypertensive disorder of pregnancy. There was no statistically significant difference in rates of PreE, eclampsia or hypertensive disorders of pregnancy based on the presence of PM or hemozoin pigment. Although, individuals with hemozoin pigment had nearly twice the rate of preeclampsia as those without (6.7% v. 3.7%, p=0.16). We suspect that placental infection in the 1st or 2nd trimester, rather than acute infection at the time of delivery may increase the risk of PreE. This study is limited by its sample size, and is likely underpowered to detect a difference in PreE rates based on PM. Further studies characterizing the relationship between PM and hypertensive disorders of pregnancy are warranted, with particular focus on the role of antimalarial treatments in reducing the risk of PreE.

7212

MALARIA-GUT MICROBIOTA INTERACTIONS WITHIN THE CONTEXT OF GEOGRAPHIC REGIONS, NUTRITION, PARASITIC CO-INFECTION & AGE IN RWANDA

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Malaria, caused by *Plasmodium* species, is a major health problem affecting the global south disproportionately. The gut microbiota (GM) play a critical role in health and disease including infections such as malaria. Evidence shows a significant interplay between the host GM and both the transmission and severity of malaria. Malaria-GM interactions may be shaped by several factors including, but not limited to, geographic location, nutrition, co-infections such as soil-transmitted helminths (STH) and age. Therefore, we used a multidimensional approach to explore interactions between malaria and the GM in Rwanda. Between 11/2021 and 09/2022, we conducted a study in three malaria-endemic provinces of Rwanda: East, South and West. We recruited 169 participants (85 females and 84 males) aged between 2-78 years. In addition to questionnaire-derived data, malaria diagnosis by rapid diagnostic test (RDT) and blood smear was followed by STH screening in stool by formalin-ether technique to make comparison groups. Fecal microbiota was analyzed using 16S rRNA gene sequencing. We discovered a significantly differential beta-diversity ($p < .002$, PERMANOVA) which may be explained by a 20-30% lower fiber intake ($p<.001$, ANOVA) observed in the West compared to both the other provinces. Relative abundance of *Faecalibacterium* and *Succinivibrio* was significantly higher in the West than in the East/South ($p<.001/p<.02$, Kruskal-Wallis) and lower in the West than in the South ($p<.01$, Kruskal-Wallis) respectively. Unlike age, infection status was not linked to GM composition differences. Moving forward, we are collecting samples with a better representation of asymptomatic and severes cases to perform metagenomic and micronutrional analyses.

7213

A REVIEW OF 15 YEARS OF CRYPTIC MALARIA IN THE UNITED KINGDOM

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Autochthonous malaria transmission has not been observed in the United Kingdom since 1953. Nearly all malaria cases diagnosed in the UK are imported, in individuals who acquire their infection during travel to a malaria-endemic region. Cryptic malaria cases where there is no history of recent travel of that nature and for which initial epidemiologic investigations cannot identify a plausible mode of acquisition are rare in the UK, making up less than 1% of cases since 2000. All cryptic malaria cases in the UK are investigated according to published national guidance. We reviewed 15 years of cryptic malaria in the UK between 2009 and 2023, to identify trends, compare investigation outcomes and inform updates to national cryptic malaria guidance. Nine cases of cryptic malaria, 8 *Plasmodium falciparum* and one *P. malariae*, were reported in the UK between 2010 and 2023, with the highest annual total of 3 cases in 2023. All cases were reported in Southern England, with the majority reported in London. Additional investigations were undertaken by the UK Health Security Agency's national Travel Health team, Malaria Reference Laboratory, local health protection teams and the national Medical Entomology team, to identify the potential source of infection for each case. Other stakeholders were included where appropriate. Five cases were classified as possible 'baggage' or 'airport' malaria, one as recrudescence in a semi-immune person due to pregnancy, one as a probable case of transfusion-transmitted malaria due to *P. malariae* and no clear sources were identified for the remaining two cases. Autochthonous transmission was excluded in all cases. Although it is considered unlikely that malaria will become endemic again in the UK, climate change could facilitate a re-emergence of natural transmission of malaria. Thorough investigation of cryptic malaria cases is essential in identifying potential sources of infection, and to ensure accurate and timely surveillance, which is vital to detect and prevent autochthonous malaria in the UK.

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KNOWLEDGE, ATTITUDES, AND PRACTICES OF MALARIA TREATMENT IN RWANDA: A CROSS-SECTIONAL STUDY

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Malaria remains a significant public health threat. Prompt diagnosis with effective treatment is a key malaria intervention and its success depends on communities having knowledge of and adhering to malaria treatment guidelines. Rwanda, the first African country to confirm partial artemisinin resistance, must promptly address this threat by ensuring optimal malaria treatment practices in the community. This study measured the malaria knowledge, attitudes, and practices (KAP) among febrile patients seeking treatment at government clinics, aiming to identify factors influencing malaria treatment practices across Rwanda. A cross-sectional study was

conducted in six health centers in areas of high malaria transmission in Rwanda. Patients or caregivers of children seeking treatment for fever were enrolled and interviewed using semi-structured questionnaires. The frequency and proportions of the KAP indicators were determined using descriptive statistics. From December 2023 to February 2024, 406 participants were enrolled, and 56% were female, most lived rurally (80%), and 50.2% attended primary school. Malaria knowledge was high: symptoms (86.7%), transmission (82.7%), and control (73.7%). Only 71.2% owned insecticide-treated nets (ITNs), 50.5% received indoor residual spraying (IRS). 44.3% (180/406) sought malaria treatment in the last 6 months; of those, 46.1% completed medication in 3 days, 36.7% stopped in 2 days, 10.6% over 3 days, 2.8% unsure. Furthermore, 26.8% (109/406) took antimalarials for fever without diagnosis; 54.1% got them from drug outlets/pharmacies. Malaria knowledge and positive attitudes towards treatment and prevention strategies among participants were high across all health centers. However, these positive attributes did not translate into malaria prevention and treatment behaviors. Specifically, poor adherence to malaria treatment was observed, which is likely potentiating the emergence of resistance. In an era of developing drug resistance, there is an urgent need to identify and implement effective interventions to boost malaria treatment and adherence practices in Sub-Saharan Africa.

7215

QUANTIFYING THE RELATIONSHIP BETWEEN MALARIA IN PREGNANCY AND MATERNAL ANEMIA USING ROUTINE ANTENATAL CARE-BASED SURVEILLANCE DATA IN TANZANIA

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Whilst malaria is associated with an increased risk of severe anemia, especially in first-time mothers, the relationship is not well characterized. To address this gap, we used routine antenatal care (ANC) surveillance data from mainland Tanzania (January 2016-September 2023) from pregnant women attending their first ANC visit. We evaluated trends in maternal malaria and severe anemia (hemoglobin (Hb) <85g/L) prevalence using descriptive statistics and used binomial mixed-effects logistic regression to estimate adjusted severe anemia prevalence, accounting for variation in Hb testing coverage. National malaria prevalence was 6.8% and severe anemia prevalence was 1.7%. Of the 17.2 million women attending first ANC, 91.8% were tested for malaria, but only 63.4% were Hb tested. Health facilities Hb testing <75% of attendees (compared to ≥ 75%) had higher malaria prevalence (8.37% vs 5.87%) and a higher percentage of women visiting after the first trimester (34.0% vs 25.2%), suggesting those who were not tested for severe anemia were likely those most at risk of severe anemia. After adjusting for variation in Hb testing coverage, our estimate of severe anemia cases increased 46.5% (unadjusted n = 184994, adjusted n = 271089). We found a weak positive correlation between malaria and adjusted severe anemia prevalence in different regions over time (Spearman's $\rho = 0.371$, $p<0.05$). From age-disaggregated data, we found that as malaria prevalence increased, the relative risk of severe anemia increased in younger women. When malaria prevalence in under 20s was 0, the risk of severe anemia in pregnant women under 20 compared to women over 25 was 0.98 (95% Confidence Interval (CI): 0.92, 1.04), and as malaria prevalence reached 30%, the relative risk increased to 1.44 (95% CI: 1.31, 1.58). Our work shows the value of routine ANC data in providing temporal and spatial granularity on ANC coverage and prevalence of malaria and severe anemia in pregnancy. This analysis will be used to inform Tanzanian maternal health policy on resource allocation and intervention coverage to reduce maternal malaria- and severe anemia-related morbidity and mortality.

7216

MALARIA HIGH RISK POPULATION ASSESSMENT IN ZANZIBAR, MAY-AUGUST 2023

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In malaria elimination settings, cases tend to cluster geographically and occur among certain subpopulations. Clustering is often related to certain factors such as occupation or mobility, which increase an individual's risk for malaria infection. The U.S. President's Malaria Initiative supported a case-control study to identify malaria high-risk populations (HRPs) in Zanzibar. Patients presenting with symptoms of malaria at selected facilities were recruited from historically high burden shehias in two urban districts (Mjini and Magharibi B) and two rural districts (Kati and Micheweni). Between May and August 2023, the study recruited 197 cases and 557 controls matched by age group and sex. Logistic regression was used to explore associations between risk factors and the epidemiological outcome of local malaria infection, classified as no travel outside Zanzibar in the prior three weeks. In urban districts, night watchmen/police (odds ratio [OR] 5.3, 95% confidence interval [CI]: 2.7-10.6, $p<0.001$), construction workers (OR 3.0, 95% CI: 1.8-5.0 $p=0.007$), and farmers (OR 1.6, 95% CI: 1.1-2.2, $p=0.01$) were found to be at risk for malaria infection. Other high-risk behaviours in urban districts included night-time activities (OR 2.8, 95% CI: 1.8-4.3, $p<0.001$), meals taken outside (OR 2.0, 95% CI: 1.1-3.4, $p=0.01$), and recent travel within Zanzibar (OR 3.3, 95% CI 1.5-7.1, $p=0.002$). In rural districts, night-time activities (OR 3.8, 95% CI: 1.5-9.9, $p=0.006$) and taking meals outside (OR 2.7, 95% CI 1.1-6.6, $p=0.03$) were risk factors for malaria; however, there were no significant associations between occupational group and infection. There was no statistical association between malaria infection and net use in urban districts, but in rural districts, prior night net use was protective (OR 0.38; 95% CI: 0.2-0.8 $p=0.015$). In urban populations, some occupations were associated with increased risk of malaria infection, while only behaviors were associated with increased risk of malaria infection in rural populations. These findings suggest intervention targeting occupational groups could reduce malaria risk among HRPs in urban areas.

7217

ASYMPTOMATIC MALARIA RESERVOIRS IN HONDURAS: A CHALLENGE FOR ELIMINATION

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Malaria elimination efforts have resulted in substantial progress during the last 25 years. In central America, Honduras has decreased the incidence of malaria to less than 2,408 cases in 2023 and aspires to reach elimination by 2030. However, reaching the elimination goal requires an evaluation of existing strategies, understanding the prevalence of asymptomatic and submicroscopic infections, and the incorporation of novel intervention tools tailored toward decreasing transmission in the country.
We conducted an active surveillance study during November 2023 in the community of Kaukira (Gracias a Dios Department), which is a major focus

of malaria transmission in Honduras. Households were randomly selected, and all eligible individuals were invited to participate. Participants provided sociodemographic and epidemiological data, and a finger prick sample for a rapid diagnosis test (RDT), photoinduced electron transfer PCR (PET-PCR), and conventional PCR testing.
A total of 138 participants were enrolled from 81 households. Most subjects were female (n=91, 65.9%) with a mean age of 42 years and all tested negative by RDT. Molecular testing detected 17 malaria positive samples (12.3%) with 15 of these typed, resulting in eight cases of *P. falciparum*, six cases of *P. vivax* and one mixed infection. Parasitemia levels were low, ranging from 100 parasites/µL to less than 0.25 p/µL. None of the positive cases were symptomatic during enrollment. Statistical analysis revealed that individuals who had previously lived with someone diagnosed with malaria were three times more likely to test positive for malaria (Fisher exact test p<0.05, OR 3.3, 95%CI:0.9-11.4).
Our study highlights ongoing transmission of malaria in Kaukira due to the presence of human asymptomatic malaria reservoirs which can hamper malaria elimination efforts. Furthermore, the association between previous malaria exposure in the household and current infection underscores the need for targeted interventions. Finally, our results highlight the need for highly sensitive detection methods as part of the surveillance strategy to achieve the goal of malaria elimination.

7218

EVIDENCE OF DECLINING MALARIA TRANSMISSION IN ZIMBABWE, 2014-2023

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While global malaria progress has stalled in recent years, Zimbabwe has reported declines in annual incidence. We sought to examine the malaria epidemiological trend and assess if changes were a result of decreased outpatient attendance, testing, or reporting. We used R to extract and analyze malaria data reported in the national health management information system from 2014-2023. Between 2014-2023, a mean of 95% of health facilities submitted monthly data reports on time, but only 44% of reports had all malaria variables completed. Confirmed malaria cases reported by health facilities and community health workers (CHWs) decreased from 552,305 in 2014 to 244,247 in 2023 (56% decrease), resulting in a 59% decrease in reported annual malaria incidence, from 39 to 16 cases per 1,000 individuals. On average, 44% of cases were diagnosed by CHWs, increasing from 23% in 2015, when CHW coverage increased, to 57% in 2023. Over 70% of cases were reported between February and June, aligning with the rainy season. Three of the 10 provinces, Manicaland, Mashonaland Central, and Mashonaland East reported 75% of total annual malaria cases. The malaria case fatality rate decreased from 0.156% to 0.124% (21% decrease). The number of all-cause outpatient visits decreased 34%, from 12.6 million visits in 2014 to 8.3 million in 2023; however, the increased proportion of cases diagnosed by CHWs did not account for decreased outpatient attendance. Test positivity decreased 43%, from 37% in 2014 to 21% by 2023. When adjusted for potentially decreased testing (provider discretion and rapid diagnostic testing stockout) and reporting completeness, the overall trend of testing decreased by 23%. Even when corrected for missing data and testing rates, reported malaria cases have decreased in Zimbabwe.

7219

IMPACT OF THE INTERRUPTION OF SEASONAL MALARIA CHEMOPREVENTION IMPLEMENTATION ON MALARIA INCIDENCE IN BANDIAGARA, MALI

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Malaria remains a major public health threat, with 249 million cases and 608,000 deaths in 2022. Most deaths were in the African region in children under five (WHO, 2023).Seasonal malaria chemoprevention (SMC) is an effective control strategy that has led to a significant reduction in morbidity. A decline in malaria incidence in Bandiagara, Mali, a vaccine testing site, following the combined implementation of control strategies that included SMC was observed in 2017-2018 compared to the previous decade. Since 2016, SMC has been a nationwide measure in Mali. This study aimed to assess the impact of a 2021 interruption of SMC in Bandiagara on malaria incidence. SMC resumed in 2022.A cohort of 240 children in three age strata (3 months-5 years, 6-10 years and 11-18 years) was followed from July 2021-December 2022 in Bandiagara, an area with intense seasonal malaria transmission. We measured malaria incidence in number of episode person-years for 2021 and 2022. Overall, malaria incidence was higher in 2021 compared to 2022 with, respectively, 2.04 and 0.96 episodes, IRR=2.12 (95% CI: 1.75- 2.55; p<0.001). The incidence in the 3 months-5 years age strata was, respectively, 1.7 and 0.5 episodes in 2021 and 2022, IRR=3.5 (95% CI: 2.3-5.7; p<0.001). For the 6-10 years strata, the incidence was higher in 2021, with 1.8 episodes vs 1.1 episodes in 2022, IRR=1.56 (95% CI: 1.13- 2.15; p=0.0025). For children 11-18 years, the incidence was also higher in 2021, with 2.5 episodes vs 1.1 episodes in 2022, IRR=2.31 (95% CI: 1.73- 3.08; p<0.001). In 2021, the malaria incidence for children aged 6-10 years was similar to children 3 months-5 years, IRR=0.96 (95% CI: 0.68- 1.37; p=0.42). That year, children under 10 years old had a lower malaria incidence than children above 10 years, IRR=0.68 (95% CI: 0.49- 0.94; p=0.0084).The high malaria incidence in 2021 is likely a consequence of the SMC interruption and indicates the need for further support for SMC efforts. Interestingly, SMC interruption also impacted malaria incidence in children outside the targeted age group, suggesting the need for further investigation of malaria spread and vulnerability in pediatric populations.

7220

CONDUCTING AND OVERCOMING PEDIATRIC CLINICAL TRIALS CHALLENGES IN LOW AND MIDDLE INCOME COUNTRY SETTINGS: EXPERIENCE IN THE DEMOCRATIC REPUBLIC OF CONGO

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Africa carries the major burden of malaria worldwide with children being the most affected. Despite increased efforts in pediatric drug development, a notable lack of approved pediatric formulations for anti-malarial drugs in young infants remains. Products intended for older children are often administered to young infants increasing the risk of misdosing and adverse reactions. Clinical trial conduct in children in low and middle-income countries (LMIC) poses challenges due to restricted funding, specific clinical needs, ethical and regulatory protections and lack of infrastructure. In 2020, we initiated the CALINA study in a regional, regulatory clinical trial naïve, Congolese hospital. The study evaluated a new dosage of arthemether-lumefantrine (5mg/60mg) in the treatment of uncomplicated malaria in neonates and infants < 5 kilograms of body weight. To enable this, a decentralized trial approach was set-up. This included training

and weekly communication with the referral health centers, enabling a community network, obtaining participant feedback and getting buy-in from local authorities. Between 2020 to 2023, 14'350 infants presented with suspected malaria at the peripheral centers for consultation (10km radius from the study site); 284 infants were pre-screened out of which 50 were transferred to the main hospital and screened at site. This lead to 21 infants being included in the study, with no loss to follow-up, the highest recruiting study site. Through understanding of the patient pathway and efficient site set-up and management, the study demonstrated the complexity and success in recruiting a highly vulnerable population in LMIC settings. Although, the return on investment for such intensive set-up is disputable, a conventional trial configuration does not necessarily work when reaching vulnerable patients. A decentralized approach set-up to the endemic sites with a focus on patient pathway is key to successful recruitment. The need for expertise, capacity strengthening and constant site support to ensure operational efficiency is paramount for successful completion of such trials.

7221

SCOPING REVIEW OF NEUROLOGICAL SEQUELAE DUE TO *PLASMODIUM FALCIPARUM* AND *VIVAX* CEREBRAL MALARIA, 1980-2023

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Malaria is a deadly vector-borne disease transmitted by Anopheline mosquitos with the majority of disease burden being caused by the parasites Plasmodium falciparum and vivax (*P.f.* and *P.v.*). Cerebral malaria (CM) is considered the most severe complication due to its high mortality rate and potential to leave survivors with residual neurological sequelae. We aim to describe the current data landscape of *P.f.* and *P.v.* CM neurological sequelae prevalence and duration by conducting a scoping review. Three databases (Pubmed, SciELO, Web of Science) were searched from 1980-2023 as were reference lists. Representative populations in locations endemic for *P.f.* or *P.v.* at the time of the study were included. We pre-registered the review protocol (PROSPERO ID CRD42023431162). We found 2,589 sources, 2,008 of which were excluded during title/abstract screening. After full text screening, 76 of the remaining 169 papers were excluded due to study overlap. 11 studies identified from the references of other malaria systematic reviews were also included. A total of 104 articles were extracted and analyzed, covering 26 countries. Most studies (76; 71.0%) were conducted in Sub-Saharan Africa, 17 in South Asia (15.9%), 10 in Southeast Asia, East Asia, and Oceania (9.35%), and 4 in North Africa and Middle East (3.74%). Across time, 18 (16.8%) studies took place in the 1980s, 49 (45.8%) in the 1990s, 33 (30.8%) in the 2000s, and 7 (6.54%) in the 2010s. There were no studies conducted in Latin America, the Caribbean, or in 2020-23. Although 47.7% (51) of studies provided information on the sequelae acquired, only 29.0% (31) included sequelae duration. 5 (4.67%) studies included data on *P.v.* CM, of which only 2 focused solely on *P.v.* The lack of studies in *P.v.*-prominent areas combined with the absence of more recent data indicate significant gaps in the current research. This work will be updated through 2024 and serve as the basis for a further systematic review and quantitative synthesis. As some countries approach elimination, studies on prevalence and duration of CM neurological outcomes are needed to accurately quantify malaria burden and track elimination progress.

7222

PLASMODIUM OVALE CURTISI AND P.O WALLIKERI CO-CIRCULATION AMONG MALARIA INFECTED PATIENTS IN THREE HEALTH FACILITIES IN DSCHANG, WEST REGION OF CAMEROON.

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Malaria is a vector-borne parasitic disease that continues to be a global public health threat to humans. Four different species of Plasmodium have been identified to cause malaria in African settings: *P. falciparum*, *P. malariae, P. ovale sp., and P. vivax*. Previous cross-sectional surveys in 2013 and 2017 have indicated the circulation of *P. vivax* in Cameroon prompting further investigation into the circulation of falciparum and non-falciparum species among patients presenting with symptoms consistent with acute uncomplicated malaria. This study evaluated the presence of malaria infection among these individuals using molecular methods in the West region of Cameroon. A cross-sectional facility-based study was carried out among 431 clinically suspected cases of malaria in 2020 from three health facilities in Dschang. Socio-demographic and clinical data were collected from all consenting patients. In addition, blood spots on Whatman chromatographic paper (number 03) were collected from the patients. These blood samples were subjected to DNA extraction and a real time PCR-based assay which detects the Plasmodium 18s rRNA gene. Samples positive for *P. ovale* were further characterised as *P.o curtisi* or *P.o wallikeri* using realtime PCR assay and custom primers. Among 431 samples, 215(49.9%) were positive for *P. falciparum*, 12(2.8%) for *P. ovale* in mixed infections with *P falciparum*, and 5(1.2%) mono infections. 1 for *P. malariae*(0.2%) mono infection and 3 for *P. falciparum* and *P. malariae* mixed infection (0.7%). 195(45.2%) samples were negative for any Plasmodium species. Speciation real time PCR detected 9 *P.o curtisi* and 5 *P.o wallikeri* infections. 3 samples identified as mixed, indicating co-circulation of *P. ovale* species in Dschang. Risk factors for infection will be assessed by bivariate analysis. Non-falciparum infection was present, but relatively uncommon in acutely febrile patients in 2020. No *P. vivax* infections were detected different from previous reports in the same region from 2017. The variation in non-falciparum prevalence needs to be further evaluated to determine the impact these species will have on malaria control.

7223

NOSOCOMIAL MALARIA: RISK OF MALARIA AFTER HOSPITALIZATION AT JINJA REGIONAL REFERRAL HOSPITAL, UGANDA: A COHORT STUDY

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In endemic settings, public hospitals may provide ideal grounds for malaria transmission, infection and disease. We determined risk of malaria among patients hospitalized with non-malaria illness at Jinja Regional Referral Hospital (JRRH), Uganda. This is an ongoing prospective cohort study. Eligible patients (negative malaria test at admission, requiring prolonged hospitalization, and provision of consent) are consecutively screened and enrolled at the Accident and Emergency Unit of JRRH. Upon enrollment, study participants undergo clinical assessment and a blood sample is collected for malaria testing (blood smear, RDT, and PCR). This assessment is repeated on days 7, 14, 21, 28, 35, and 42 after hospitalization, on the discharge day, and on non-scheduled days if fever is reported. Risk of malaria infection is reported as incidence. Associated factors are to

be determined using regression models. From July 2023 to March 2024, 301 patients have been screened; 133 excluded and 168 enrolled. Of 168 participants who have completed follow-up, 18 (11%) tested positive for malaria infection. Of the 18 positive patients, 15 (83%) were male, 14 were RDT and microscopy positive and four were RDT positive only. The median age and time to infection was 33 years (IQR 20-40) and 19 days (IQR 14, 24), respectively. Two patients turned positive on day 7, two on day 13, and rest after day 14. The geometric mean parasite density was 1086 (95% CI 290, 4058) parasites/ul of blood. One patient was symptomatic and *P. falciparum* accounted for all infections. Only one patient had a medical condition (tetanus), the rest had different fracture types. The cumulative incidence of malaria infection among patients hospitalized with non-malaria illness is high. Protective measures need to be considered among hospitalized patients in endemic regions. The magnitude of the problem, including possibility of transmission of non-malarial mosquito-borne diseases among hospitalized patients, needs to be further studied. Complete results will be presented at the conference.

7224

AN EXPERIMENTAL HUMAN BLOOD-STAGE MALARIA MODEL FOR STUDYING *PLASMODIUM KNOWLESI* INFECTION

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The zoonotic parasite *Plasmodium knowlesi* has emerged as a major threat to malaria control in Southeast Asia. *P. knowlesi* is now the only cause of indigenous human malaria in Malaysia and is increasingly reported in neighbouring countries. Human experimental induced blood stage malaria (IBSM) models of *P. falciparum*, *P. vivax*, and *P. malariae* have provided insights into parasite biology and disease pathogenesis, and enabled evaluation of diagnostics and therapeutic interventions for these species. The aim of this study was to develop an IBSM model for *P. knowlesi*. First, the laboratory-adapted YH1 *P. knowlesi* strain, previously adapted to grow in human erythrocytes, was further adapted to grow in human serum and expanded *in vitro* to produce a new malaria cell bank (MCB) designated YH1-HS. We are now undertaking a volunteer infection study to evaluate the safety and infectivity of this new *P. knowlesi* MCB, and to characterise replication rates, host response to disease, and pharmacodynamic response to artemether-lumefantrine. We will enrol up to 4 malaria-naïve healthy adults in cohorts of 1 participant each. Participants will be intravenously inoculated with *P. knowlesi*-infected erythrocytes. The first participant will receive ~2,800 viable parasites, with participants in subsequent cohorts receiving a higher dose of parasites depending on results from preceding cohorts. Definitive antimalarial treatment with artemether-lumefantrine will be initiated when parasitemia, as measured by qPCR, reaches ≥10,000 parasites/mL, or on day 21 if qPCR remains negative. This study will provide insights into *P. knowlesi* biology and host response to disease, in addition to establishing a model to evaluate therapeutic interventions against this emerging parasite. Data will be presented.

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MOLECULAR EPIDEMIOLOGY OF RESIDUAL PLASMODIUM SPP. TRANSMISSION IN A PERUVIAN AMAZON BASIN COMMUNITY

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Plasmodium vivax remains a health threat in the Peruvian Amazon. Malaria caused by P. vivax often manifests as submicroscopic infections, serving as reservoirs that could hinder elimination efforts and contribute to persistent transmission. Active disease surveillance is essential for detecting asymptomatic cases, estimating risk for military populations, and informing public health interventions.We conducted a prospective malaria cohort study in Santa Rita, a rural community in the Peruvian Amazon basin, from March 2021 to January 2022. The study included a baseline screening and eleven follow-ups among individuals aged three months and older. We collected socio-demographic, clinical, and epidemiological information, along with whole blood for malaria microscopy and molecular testing, and serum samples for serology. We enrolled 351 subjects with a mean age of 27.2 ± 20.5 years and a female to male ratio of 1:1. The mean number of follow-ups per subject was 7.5 with 77.8% (273/351) completing their first follow-up to 51.6% (181/351) by the twelfth follow up.Five subjects tested positive by microscopy for P. vivax (1.4% prevalence) and one for P. falciparum (0.28% prevalence). A subset of 153 participants (1,597 samples) that were visit at least nine times and/or had a positive microscopy result underwent RT-qPCR. A prevalence of 30.06% (46/153) for P. vivax and 0.65% (1/153) for P. falciparum was found. Among the 153, 47 tested positive for malaria by TaqMan real-time PCR at least once during the follow-up period and 10 participants tested positive by the same detection method more than five times during their follow-up visits, with the highest recording positivity in 10 out of 12 follow-up visits. Our study showed a high submicroscopic/microscopic malaria ratio of 24.8 in Santa Rita and a group of persistently positive asymptomatic individuals. This may hinder malaria elimination efforts and contribute to malaria transmission in the community. Furthermore, our results emphasize the need of diagnostic methods with higher sensitivity to detect infections on a submicroscopic level to strive toward successful elimination strategies.

7226

A NATIONAL MOLECULAR SURVEILLANCE PROGRAM FOR THE DETECTION OF *PLASMODIUM SPP.* AND *P. FALCIPARUM* MARKERS OF ARTEMISININ RESISTANCE IN PAPUA NEW GUINEA - 2019-2023.

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Background: Papua New Guinea (PNG) has the highest burden of malaria in the Western Pacific Region and is committed to regional malaria elimination targets. Strengthening surveillance and laboratory capacity is therefore a high priority in PNG to enable the National Malaria Control Program (NMCP) and Provincial Health Authorities (PHA) to make evidence-based decisions within their local context. STRIVE is a partnership-based implementation research and surveillance strengthening project that has established a molecular-informed sentinel surveillance system integrating real-time data dashboards and mapping tools that can be readily accessed and

utilised by the NMCP and provincial partners in a user-friendly manner to support planning, stratification and containment. Method: Eight sentinel health facilities capture febrile illness case data and collect dried blood spot on filter paper from a subset of patients. Samples are sent to a central laboratory and screened using polymerase chain reaction (PCR) that amplifies a conserved region of the 18S rRNA gene. Species-specific quantitative PCRs (qPCR) are then performed on positive samples and a qPCR specific for the kelch-13 C580Y gene is performed on *P. falciparum* positive samples. Result: Between 2019-2023, molecular surveillance confirmed the presence of Plasmodium spp. infections in 53.4% of febrile illness cases observed at the 8 sentinel sites. *P. falciparum* and *P. vivax* predominated, detected in 31.6% and 15.5% of cases respectively, with *P. malariae* and *P. ovale* rarely observed in 0.3% and 0.1% of cases respectively. Kelch13 C580Y mutations were detected in *P. falciparum* cases in at all sites, with the highest proportion in Buimo catchment in Lae, Morobe Province. In late 2022, an outbreak of *P. falciparum* was detected in the highlands fringe site, informing and guiding local response measures. Discussion: Establishing a molecular surveillance program to guide national and local decision-making in PNG has been feasible and is providing the priority evidence the NMCP requires for targeted therapeutic efficacy monitoring and responding to outbreaks in non-endemic settings.

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EXPLAINING TRENDS IN PLASMODIUM FALCIPARUM TRANSMISSION IN AFRICA SINCE 2000

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Concern has grown in recent years about the slowing rate of progress against malaria in Africa, with population growth in many places outpacing reductions in per capita incidence. The reasons for this are much speculated upon, but ultimately poorly quantified. In this analysis, spatio-temporal trends in key drivers of African malaria since 2000 - donor-funded intervention coverage, but also urbanisation, health-system strengthening, and an increasingly changing climate - are reconstructed using mathematical and statistical models. A geostatistical model then links these drivers to the Malaria Atlas Project's database of infection prevalence observations (>55k geolocated points), to estimate their individual and cumulative impact on trends in malaria prevalence and incidence since 2000. We find that within established transmission boundaries malaria control is responsible for the majority of change in burden this century, but that the impact of vector control has waned in recent years as coverage has failed to reach targets. Our results suggest improvements in horizontal interventions - strong health-systems offering accessible and efficacious treatment to those in need - have played a critical role in reducing malaria prevalence in children under five, but more needs to be done to target remote populations with low access to healthcare. Counterfactual analysis removing the impact of direct malaria control (ITNs, ACTs, IRS, SMC) reveals a changing baseline - socioeconomic development in Africa has fundamental altered inherent environmental and personal receptivity. Changes in receptivity attributable to the climate, meanwhile, are highly stochastic, highlighting vulnerabilities both at transmission fringes (where intervention coverage is low), and within high-burden settings (where intervention coverage levels are most threatened by indirect effects of climate change).

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CASE STUDY: ROYAL THAI ARMY SOLDIERS DEPLOYED FOR UN PEACEKEEPING OPERATIONS IN SOUTH SUDAN IN 2023 EXPERIENCE HIGH RATES OF *P. FALCIPARUM* AND *P. OVALE* MALARIA UP TO NINE MONTHS POST-DEPLOYMENT

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Peacekeeping operations in sub-Saharan Africa continue to be impacted by malaria both in-country and among returning service members. The Royal Thai Army (RTA) deploys an Engineering Company to Juba and Rumbek, South Sudan to conduct peacekeeping operations as part of the UN Peacekeeping Mission in South Sudan. Each deployment is approximately 12 months long and units are rotated yearly. The unit is provided doxycycline one week before travel and mefloquine via direct observation therapy during deployment and for four weeks after returning. Malaria diagnosis is conducted using rapid diagnostic tests and treatment is provided according to WHO guidelines. In 2023, the 273-person RTA unit experienced a high rate of prophylaxis failure with 27 Soldiers (9.9%) diagnosed and treated for malaria while deployed and another 37 Soldiers (13.6%) testing positive for malaria following return from deployment, including 18 cases of *P. ovale* (Po), 14 cases of Pf, 4 cases of mixed Pf/Pv, and 1 case of Pv; this constituted the largest single apparent Po cluster observed in a military unit in recent history. Eight malaria cases (all Pf) were identified within one week of returning from deployment during a unit-wide microscopy screening. The remaining 29 cases (6 Pf, 4 Pf/Pv, 18 Po, and 1 Pv) were identified 1-9 months following return from deployment and when Soldiers became symptomatic and sought medical care. Given that both Pf and Po are relatively rare in Thailand it is likely such infections were originally acquired in South Sudan. This case study highlights two significant areas of concern. First, there was a high rate of sub-clinical (18 of 273) and sub-microscopic (10 of 273) Pf malaria in returning Soldiers who were given mefloquine prophylaxis. Second, there was a high rate of latent Po infection among deployed Soldiers (18 of 273) that was only detected weeks to months after returning from deployment. These findings highlight shortcomings to existing malaria prophylaxis and screening strategies for military units deploying to endemic areas and underscore the importance of active surveillance and/or presumptive treatment when these units return.

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SPATIO-TEMPORAL EPIDEMIOLOGY OF URBAN MALARIA OVER DIFFERENT TRANSMISSION SEASONS IN ACCRA, GHANA.

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Urban malaria has largely been ignored, but evidence is emerging that urban areas in Africa are receptive to malaria transmission. In Ghana, despite urban communities of greater Accra being considered low malaria risk and some areas earmarked for a push for elimination, pockets of moderate malaria transmission remain. This study aims to use three surveys spanning different transmission cycles to better understand the spatiotemporal malaria epidemiology in the Greater Accra Region of Ghana to support appropriate interventions towards malaria elimination. For each cross-sectional survey, 13 health facilities, stratified by malaria risk, and 100 households per catchment area were randomly selected. This was repeated at 3 time points throughout the transmission season.

All consenting household members were tested for malaria and anaemia and completed a questionnaire. QGIS™ and R/Rstudio software were used to map malaria cases and the number of malaria episodes. Spatio-temporal analysis with Anselin local Moran's I and Getis-Ord Gi* statistics were conducted. Preliminary results from the dry season survey include 2930 individuals sampled from 1313 households (average household size of 3.6). Of these, the average age was 29.8 (SD 18.7), with 42.9% males and 52.1% females. The overall malaria prevalence was 2.2% (95% CI: 1.7 - 2.8) but ranged from 0.8 to 5.9 per facility catchment area. The prevalence of anaemia was 7.1%% (95% CI 6.2-8.1) but ranged from 1.8 to 18.2% per facility catchment area. Low utilisation of insecticide-treated bednets (10%) the night before the survey was reported. The predominant forms of vector control employed in households were fumigation (15.9%) and mosquito repellents (5.1%). Our preliminary data confirms a low but heterogeneous prevalence of malaria infections during the dry season in Accra and a low-reported use of vector control methods typically employed in rural settings. Combined with the seasonal patterns observed, these results will fill an important gap in understanding urban malaria risk in Accra and other similar settings and help inform intervention strategies appropriate for this context.

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DESCRIPTION OF INPATIENT MALARIA CASE MANAGEMENT AT HEALTH FACILITIES IN SOUTHEASTERN TANZANIA, 2023

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In Tanzania, malaria service quality is assessed through Malaria Services and Data Quality Improvement (MSDQI) supportive supervision (SS). In 2023, PMI supported the National Malaria Control Program in Tanzania to investigate factors associated with malaria hospitalization and mortality rates using facility registers and SS data in Lindi, Mtwara, Pwani, and Ruvuma regions. A descriptive analysis of inpatient MSDQI data from 36 (28%) health facilities was conducted. Selection prioritized facilities with high malaria case counts and/or poor performance during previous MSDQI rounds. Stock availability of emergency medicines used to treat severe malaria complications, diagnostic accuracy, and health worker competence managing severe malaria cases were assessed. Scores from record review and MSDQI assessments were categorized as poor (below 50%), moderate (50- to 75%), and good (75% and above). From January to December 2023, the facilities reported 109,132 admissions, of which 10,834 (9.9%) were for severe malaria (31% of all [34,948] malaria cases) and 134 malaria deaths (1.2% case fatality rate [CFR] among severe admissions). Among the 10/36 (29%) facilities reporting severe malaria cases and malaria deaths, "good" scores were obtained by 97% for injectable artesunate preparation and administration; 70% for severe malaria treatment dose per patient weight; 54% for adequate emergency medicine stock, such as anticonvulsants and oxygen; 64% for management of associated emergency conditions; and 64% for adherence to national guidelines for treating complications associated with severe malaria. Despite an overall low CFR, serious remaining gaps in the inpatient management of severe malaria highlight the need for a comprehensive assessment of emergency commodity availability and ongoing support to improve service delivery. Improving healthcare providers' skills in managing severe malaria at the primary level could lower mortality rates and enable prompt treatment of complications.

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MAPPING MALARIA SEASONALITY IN SUB-SAHARAN AFRICA: METHODOLOGY AND INSIGHTS

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Seasonality is an important aspect of the epidemiology of malaria, and seasonal signals are evident in many metrics that measure transmission intensity and burden of disease. Understanding intra-annual variation, especially when attributable to epidemiologically-sensible environmental signals, can provide insight vital for accurate burden estimation, near-term predictions of outbreaks, evaluating the efficacy of seasonally-timed interventions, and the strategic planning of intervention campaigns and of clinical trials. Furthermore, understanding and combating malaria in highly seasonal areas will be critical for reducing global burden of this disease, as some of the highest burden areas are highly seasonal.

We have developed a geostatistical modelling framework to describe the intra-annual variation in the monthly proportion of P.*falciparum* incidence for sub-Saharan Africa between 2000 and 2020. Our model is trained using a comprehensive new data base of publicly available malaria time-series observations and incorporates a range of temporally dynamic environmental covariates. We derive key seasonal characteristics from the predictions of this model including season timing (onset, peak, and duration), seasonal intensity, and the number of seasons. We use inter-year variation of these characteristics to gauge temporal variation.

We present a range of products including maps of the derived characteristics: season timing, seasonal intensity, and inter-year variance. We discuss the apparent spatial structure in the arrangement of these characteristics, and the demarcation of seasonal and non-seasonal locations. Additionally, we provide insight into the influence of environmental factors; including maps illustrating the spatially heterogeneous relationship between the observed signals and the underlying climatic drivers. These findings provide useful insight into malaria seasonality and have the potential to improve the cost-efficacy of seasonally timed campaigns, which is critical those individuals currently living in areas with seasonal malaria.

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LONG-ACTING FORMULATION OF IVERMECTIN FOR EFFECTIVE MALARIA CONTROL: INSIGHTS FROM AN AGE-STRUCTURED MODELLING STUDY.

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Despite a great decrease of malaria cases and deaths starting from the twenties, a stagnation, and even an increase in the last years, highlight the limits of available tools for controlling the disease. A novel approach, complementary to existing ones, is to render Anopheles blood meals toxic by treating hosts using systemic insecticides like ivermectin. Efficacy of this strategy is hampered by the short remanence of approved oral dose, and thus, the requirement of repeated dosing to achieve full coverage. Hence, long-Acting Ivermectin Formulations (LAIFs) would increase efficacy with costs and logistical reliefs. In the frame of the IMPACT project, a LAIF candidate from the BEPO® technology has been selected using cattle model. Pharmacokinetics and pharmacodynamics (PK/PD) data showed sustained entomocidal efficacy for at least 3 months after a single injection. Here, we developed a mathematical model to predict associated

transmission blocking effects. Unlike other mathematical models in this context, we incorporated continuous structural variables, including humans age, and time post-LAIF injection (for both humans and vectors). Hence, we captured the longitudinal dynamics of (i) ivermectin systemic concentrations in the human bloodstream, and (ii) ivermectin associated effects on mosquitoes' life span after a blood meal on treated human.
Using our experimental PK/PD data, the model was run in a context of perennial transmission with a baseline of 30% clinical case prevalence and 80% Plasmodium prevalence in the population. Different scenariii were tested where efficacy duration, formulation dose and proportion of the population treated were adjusted. A 70% coverage of the 6-60 years old with LAIF at a dose of 1mg/kg (three months efficacy) would decrease malaria case prevalence from 30 to 19% (36% decrease) for 89 days. Translated to entomological parameters, this corresponds to a 65% decrease of infectious Anopheles' population. Using our model, we therefore demonstrated that MDA using our candidate LAIF would meet the WHO requirements of more than 20% decrease of clinical case prevalence for novel malaria vector control tools.

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BACTERIAL VAGINOSIS IS ASSOCIATED WITH INCREASED RISK OF PLACENTAL MALARIA

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Bacterial vaginosis (BV) is a common cause of vaginal discharge characterized by a shift in the microbiota from a *Lactobacillus*-dominant community towards a diverse set of anaerobic and facultative species. BV is associated with increased risk of adverse birth outcomes (low birth weight, preterm birth, chorioamnionitis) and reproductive tract infections (STI acquisition, HIV transmission). Although malaria and BV are considered independent risk factors for adverse birth outcomes, there are no published studies examining the vaginal microbiota within the context of malaria in pregnancy. Here, we demonstrate a novel association between BV and/or decreased vaginal lactobacilli during pregnancy and increased risk of placental malaria (PM). We analyzed data from an ongoing double-blinded randomized trial of intermittent preventive treatment during pregnancy (IPTp) in Uganda. In multigravida with evidence of malaria parasitemia during pregnancy, we found that BV at delivery was associated with increased odds of moderate-to-severe past-chronic PM, defined as histopathology with ≥ 10% HPF with hemozoin pigment deposited in fibrin (aOR=2.3 [95% CI: 1.4-3.8]). In a subset of participants, we used 16S rRNA amplicon sequencing to characterize the vaginal microbiota during pregnancy (at 12-20 and 32 weeks gestation). Among multigravida, we found a positive correlation between microbial diversity (suggestive of BV) and PM severity. BV-associated taxa—*Atopobium* and *Gardnerella*--were significantly more abundant with increasing PM severity. To test whether the vaginal microbiota was correlated with PM in an independent cohort, we analyzed data from an IPTp trial in Malawi and Tanzania (IMPROVE). In participants assessed for BV at 16-28 and 32-35 weeks gestation, vaginal fluid Gram stain with decreased *Lactobacillus* morphotypes was associated with increased risk of PM (OR=1.6, 95% CI: [1.0-2.4]). Overall, our data support a previously undescribed link between vaginal microbiota and PM. Further studies are needed to determine whether interventions targeting the vaginal microbiota impact severity of PM and related birth outcomes.

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ASSESSMENT OF THE INFECTIVITY OF MALARIA PARASITES FROM ASYMPTOMATIC SCHOOL CHILDREN TO *ANOPHELES* MOSQUITOES IN A HIGH TRANSMISSION AREA IN GHANA

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Asymptomatic malaria is prevalent in Ghana. Majority of these infections are sub-microscopic, and carriers would normally not seek treatment. They would therefore serve as infectious reservoirs for malaria transmission. This study assessed the infectivity of parasites from asymptomatic children to *Anopheles* mosquitoes in a high transmission area in Ghana. Ninety-eight healthy children were screened for malaria by microscopy and nested polymerase chain reaction using sequence specific primers targeting the 18rna of the *Plasmodium* gene. Presence of sub-microscopic gametocyte was determined by amplification of the *Pf*g377 gene by reverse transcriptase polymerase chain reaction. Whole blood samples from the asymptomatic children were used in a direct membrane assay using laboratory raised colonies of *Anopheles gambiae.* Infectivity was determined by the presence of oocysts in mercurochrome-stained dissected midguts viewed under the light microscope. Mosquito infection rate as well as oocyst density were recorded. Out of the 98 children who were screened, 73 (74.49%) were asymptomatic for malaria. Out of these, 13.70% (10/73) carried microscopic densities of parasites. Parasite density (geometric mean (95% CI)) amongst these participants was 2,560(1,383.29-6,903.39(parasites/µl). Molecular analysis indicated that 82.46% (57/73) had malaria parasites. Amongst these, 64.38% (47/57) were classified as having sub-microscopic infections. None of the participants carried gametocytes by microscopy, however *Pf*g377 gene amplification was observed in 33.33% (19/57) participants. Blood samples from 4 out of these 19 individuals (21.05%) were infectious to mosquitoes. These infections were observed in 9 midguts out of a total of 862(1.04%) midguts dissected for all feeding experiments. The total oocyst density observed was 28. Prevalence of asymptomatic malaria infections was high, and were associated with carriage of sub-microscopic densities of gametocytes which were infectious to mosquitoes. The asymptomatic children would therefore serve as a reservoir for onward transmission of malaria within the community.

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G6PD DEFICIENCY VARIANTS AND MALARIA: INSIGHTS FROM A HOSPITAL BASED STUDY IN AWKA, SOUTHEAST NIGERIA

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Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is prevalent in malaria-endemic regions, has been linked to a reduced risk of severe malaria due to impaired parasite growth in deficient erythrocytes. Conversely, it poses a high risk of hemolytic anemia in patients treated with the antimalarial drug primaquine. This study aims to investigate the prevalence of G6PD deficiency variants, their impact on hemoglobin levels, malaria parasite density, and their implications for malaria treatment policy in Awka, Anambra State, Nigeria. **Methods**: A subset of 100 malaria patients at Chukwuemeka Odimegwu Ojukwu Teaching Hospital in Awka, Nigeria, underwent screening for common G6PD mutations (A376G and G202A), which are particularly prevalent among individuals of West African descent. Malaria infection was confirmed using Rapid Diagnostic Test kits. The G6PD gene region was amplified using PCR, and Sanger sequencing techniques were employed to study the polymorphisms associated with G6PD variants.
Results: Molecular analysis revealed that the B variant (normal) was predominant, with 83% of the participants possessing this variant, while

17% had the mutant A+ (A376G) variant associated with mild G6PD deficiency. None of the participants tested positive for the A- (A376G/G202A) variant associated with severe G6PD deficiency. Both the B variant and the A+ variant (moderate) showed no significant impact on the hemoglobin and parasitemia levels of the study participants.
Conclusion: This study found only a low prevalence of the G6PD A+ (moderate variant) mutation among the participants, with no significant impact on their hemoglobin and parasitemia levels. This suggests that the observed G6PD deficiency variants may not have substantial implications for the management of malaria in this population.

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DECLINE IN THE INCIDENCE OF MALARIA IN BENIN IN 2023: INVESTIGATION OF ASSOCIATED FACTORS AND HOW TO MAINTAIN THE TREND

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Consecutively over past 4 years, Benin has observed a steady upward trend in incidence of malaria, despite the various interventions implemented to control the disease. For the first time in 2023, a drop in incidence was observed. The poor quality of routine epidemiological surveillance data and the low care seeking behavior were the main hypotheses put forward for this decline.Routine malaria data collected monthly and hosted on DHIS2, the repository for all health system data in Benin were analyzed. We analyzed indicators related to confirmed malaria cases with assessment of the temporal and spatial trend from 2020 to 2023 in relation the specificities in some interventions scaled-up nationwide for the first time in 2023.The number of confirmed malaria cases rose by 10.3% from 2020 to 2021(that is from 2.19 million cases to 2.42 million cases), then an upward trend was maintained between 2021 and 2022, with the number of cases rising from 2.42 million to 2.67 million (this is an increase of 10.2%). Between 2022 and 2023, an opposite trend was observed, with a 22.1% drop in the number of confirmed cases, from 2.67 million to 2.08 million. Compared to 2022, the number of tested cases increased by 1.5% and the positivity rate fell by 16%. This drop maybe attributable to the combined effect of several interventions: i) a new monthly data quality assessment method with the used rapid diagnostic test (RDT) cassettes verification as proof, which improves indicators relating to data quality; both campaigns of ii)the seasonal malaria chemoprevention (SMC) implemented in eligible areas in the northern side of the country; and the mass mosquito net distribution campaign, achieved good coverage of targets nationwide; and iii) the intensification of community-based interventions with the commitment of civil society organizations through the Zero Malaria Alliance. Malaria incidence in Benin declined in 2023, probably due to the synergistic effect of three majors' interventions put in place to control the disease. These interventions need to be reinforced in 2024 to maintain the improvement trend in malaria epidemiological surveillance indicators in Benin

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MODELING THE TEMPORAL INCIDENCE OF FEVER AND CLINICAL MALARIA IN DANGASSA, DISTRICT OF KATI, MALI FROM 2014 TO 2016

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Malaria remains one of the leading causes of morbidity and mortality in much of sub-Saharan Africa. Our objective was to study the temporal variations of the incidence of malaria and fever in Dangassa from October 2014 to December 2016 and to make an analytical comparison of these incidences.
Our study was conducted in Dangassa on the right bank of the Niger River with year-round access to the river water. This was a longitudinal study consisted of following healthy participants between cross passages: - 526 participants from October 2014 to June 2015 - 825 participants from June 2015 to November 2015 - 1234 participants from November 2015 to June 2016 - 987 participants from June 2016 to December 2016.
The Poisson regression model with the number of person months offset was used to estimate the person-month incidence of fever and malaria as a function of age class, season and sex parameters.
Results: The incidence rate of fever in the 5 to 9 year age group was 1.81 times that of children under 5 with a significant p ($p = 0.001$). Malaria during the high transmission season was 2.3 higher than the low transmission season with a significant p ($p < 0.001$).
Conclusion: This study has a significant variation in the variation of the incidence of fever and malaria in particular according to the age group of the season with a strong tendency during the period from June to November corresponding to the period of strong transmission in Mali.

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UNDERSTANDING RELATIONSHIPS BETWEEN ENVIRONMENTAL TEMPERATURE, RAINFALL, AND MALARIA IN CHILDREN UNDER 5 YEARS OF AGE IN SENEGAL

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Malaria transmission is greatly affected by weather conditions; thus, climate change is one of the main factors that could affect future trend of malaria cases in endemic countries. This research aimed to investigate the effect of temperature and precipitation on malaria in children under 5 years of age (U5) in five regions of Senegal (Diourbel, Kédougou, Kolda, Sédhiou, and Tambacounda). Monthly, district-level data on population and reported U5 children with malaria were gathered from the Senegal's national health management information system (HMIS) between 2018 and 2022. Monthly temperature and precipitation were estimated using remote sensing data from MODIS and from the Global Precipitation Climatology Centre. Time series analyses were performed to describe the trend of malaria incidence and weather indicators. The relationship between malaria incidence and weather indicators was investigated using generalized additive random effect models. From January 2018 to December 2022, 121,030 malaria cases in CU5 were reported in the HMIS for the study area. Malaria incidence declined from 68.2 cases per 1,000 CU5 to 18.6 cases per 1,000 CU5 (-72.1%) from 2018 to 2022, with a substantial decrease in 2020 and 2021. From 2018 to 2021 average temperatures decreased (MD: -4.2%; IQR: -2.7%; -5.7%) linked with increased precipitation (MD: 10.8%, IQR: 1.1%; 16.7%). In 2022, precipitation diminished (MD: -24.8%, IQR: -16.9%; -30.3%) and temperature increased (MD: 5.2%, IQR: 3.4%; 7.6%). Malaria incidence was significantly associated with weather conditions occurring in the previous 5 months. The association between malaria incidence and rainfall was larger than with temperature. Understanding climate-malaria links could help health systems to adapt their surveillance and intervention systems to address malaria vulnerability and adapt to a changing climate.

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TOWARDS ELUCIDATING THE IMPACT OF TRANSMISSION HETEROGENEITY ON THE RELATIONSHIP BETWEEN MALARIA PARASITE GENETICS AND CLINICAL INCIDENCE

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Molecular surveillance is emerging as a critical tool for malaria genomic epidemiology, and the integration of genetic metrics could synergize with and improve malaria transmission studies. In Senegal, we showed that clinical incidence and genetic metrics such as the frequency of multiple strain infections or complexity of infection (COI, the number of strains per infection) have a complex relationship. Specifically, relations between genetic metrics and clinical incidence differ sharply in regions with an annualized incidence greater than 10 cases per thousand year (‰) versus regions with less than 10‰. We hypothesize that changes in parasite genetics in higher transmission areas (>10‰) largely reflect differences in bulk transmission intensity, while those in lower transmission areas (<10‰) are more sensitive to differences in transmission heterogeneity (variation in transmission structure among populations, individuals, and vectors). To explore this hypothesis, we use GenEpi, a model which layers parasite genetics over a detailed, agent-based malaria transmission model (EMOD) to identify the parameter regimes where parasite genetics is more sensitive to changes in bulk transmission intensity or transmission heterogeneity. Here, we describe the model design and calibration strategy that will be used to address these questions. This involves: 1) fitting the model to the observed incidence and genetic metrics of three moderate-to-high transmission (>100‰) sites in Senegal, 2) comparing model predictions to genetic data collected from three low transmission settings (≲ 10‰), and 3) modeling different forms of transmission heterogeneity to determine whether they could be responsible for any deviations between modeled and observed values. Distinguishing genetic signals associated with transmission heterogeneity from those with bulk transmission intensity could inform tailored intervention campaigns designed to disrupt the transmission structure of a target population and, hence, be of great value to national malaria control programs.

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PLASMODIUM FALCIPARUM GENE SIGNATURES OF MALARIA DISEASE SEVERITY IN KENYAN CHILDREN

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We present signatures of disease severity from our analysis of *Plasmodium falciparum* (*Pf*) transcriptomes (n=60) obtained from pediatric patients with malarial anemia in a holoendemic transmission region: Siaya, Kenya. The statistical signal was enriched with several strategies including the exclusion of patients coinfected with HIV and/or bacteremia, to reduce alternative sources of variance. LASSO model selection identified 13 genes associated with low hemoglobin (Hb) levels and five associated with high Hb levels with a univariate *P*-value (by Welch two-sample t-test) less than 0.1. The majority of the 13 genes associated with poor outcomes (*i.e.*, low Hb) are central to known virulence mechanisms in blood-stage malaria and several have been investigated as potential malaria drug targets, *i.e.*, histone H3, mitochondrial ATP synthase, type I signal peptidase, plasmepsin X, STPP-2B (calcineurin), *Pf*EMP1 and RIFIN. LASSO model selection applied to particular subsets of the genes, such as kinases, metabolic genes, secretion systems, and those interacting with erythrocytes identified additional genes that may be linked with disease severity. Sequedex, a metagenomic analysis technique based on signature peptides, identified redox-related functional groups in the human host transcriptome that were elevated in severe disease (Hb<6.0 g/dL) but had no functional categories for *Plasmodium*. To better understand how genetic variation and gene expression patterns of highly divergent genes such as *Pf*EMP1 in the dataset were associated with low Hb levels, *Pf* transcriptomes were mapped onto the 14 *Plasmodium* chromosomes of the Kenya reference isolate (pfKE01) derived from plasmoDB. Our methodology included using peptide 10-mer analysis to address low complexity regions and genome duplications, read mapping with Bowtie2, and gene assignment using HTSeq. Using this approach, we aim to gain an enhanced understanding of the relationship between gene expression patterns and malaria severity.

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PLASMODIUM FALCIPARUM GENETIC DIVERSITY IN THE BLOOD STAGE VACCINE CANDIDATE ANTIGEN PFCYRPA IN SENEGAL

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Malaria represents a public health burden. Current estimates revealed a plateaued curve of the disease-associated morbidity and mortality, while approved vaccines are yet to show strain-transcendent protection. Our present study evaluates the breadth of genetic diversity of one of the malaria vaccine candidates in early phase I clinical trials, *P. falciparum* Cysteine-Rich Protective Antigen (PfCyRPA) and also predicts the functional impact. Samples used in this study were collected from informed consents patients diagnosed with symptomatic malaria infections in Kédougou, Senegal. *P. falciparum* gDNA was extracted prior to *PfCyRPA* amplification. *PfCyRPA* genomic sequencing were obtained through targeted deep amplicon sequencing using the NovaSeq 6000 platform and sequence reads analyzed using the Geneious Prime Software. Non-synonymous single nucleotide polymorphisms were called relative to the 3D7 reference sequence using a minimum variant frequency of 0.02 and minimum coverage of 1000 reads. To predict the functional impact, PfRh5-CyRPA complex was constructed using Pymol (PDB ID: 4U0Q and 6MPV) and structural predictions with mAb binding was performed. A total of 93 *Pf* clinical isolates were included in this experiment. Overall, we identified 15 distinct SNPs, of which only four (F41L, V165I, N270T and V292F) have previously been reported. The majority of the novel SNPs were rare and only identified in a single isolate, except for R236N (N=4), R50C (N=2), I196F (N=2) and K211Q (N=2). Furthermore, our structural threading analysis revealed 3 novel SNPs occurring near epitopes bound by inhibitory monoclonal antibodies, potentially impacting immune evasion, while other SNPs were predicted to impact *PfCyRPA* structure or interactions with its binding partner PfRH5. Our data demonstrate that *PfCyRPA* exhibits a relatively greater genetic diversity than previously described. The structural

studies reveal that novel SNPs could have functional implications on *PfCyRPA* recognition by inhibitory antibodies, complex formation, or structural modelling, all hypotheses that we are exploring functionally.

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EFFECTS OF RECOMBINATION ON LINKAGE DISEQUILIBRIUM IN THE EPIDEMIOLOGY OF PLASMODIUM FALCIPARUM MALARIA

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When multiple beneficial alleles are present in a population, there is no general evolutionary result guaranteeing that recombination will speed up or slow down the emergence and evolution of genotypes carrying multiple beneficial alleles. Translated to infectious disease control, this evolutionary ambiguity means that when multiple types of drug resistance are present, we cannot be sure whether recombination will act more strongly (1) to bring together single-resistant genotypes into multi-drug resistant (MDR) genotypes, or (2) to break apart MDR genotypes into single-resistant genotypes. We introduce a new version of an established and validated individual-based malaria transmission model where we have added individual mosquito bites, interrupted feeding by mosquitoes, and individual recombination events of different Plasmodium falciparum genotypes inside the mosquito's salivary glands. Recombination among P. falciparum genotypes occurs from two sources of variation: multi-clonal infections and interrupted feeding by mosquitoes, and the results from our modeling analysis show that 80% to 95% of recombinant falciparum genotypes are created from single uninterrupted bites on hosts with multi-clonal infections. However, higher rates of interrupted feeding accelerate the emergence of double-resistant genotypes from single-resistant genotypes through recombination. A comparison of drug-resistance management strategies with this new model shows that, over a 15-year timeframe, triple ACT strategies show the largest reductions in treatment failures, multiple first-line therapy approaches show the second-largest reductions, and ACT cycling approaches show the smallest reductions in future treatment failures.

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ASSESSING CHANGES IN *PLASMODIUM FALCIPARUM* GENETIC DIVERSITY IN NIGERIA POST-ACTS IMPLEMENTATION

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Understanding parasite genetic diversity over time and across regions can help gauge the impact of ACTs on parasite populations. We utilized a high-resolution method that employs targeted sequencing of microhaplotypes to evaluate changes in Plasmodium falciparum transmission intensity in Nigeria, 15 years post-ACTs introduction. We utilized 593 DBS samples from children aged 12-60 months collected from therapeutic efficacy studies performed across six States at four time points between 2010 and 2020. We extracted genomic DNA and performed amplicon sequencing of 100 highly diverse microhaplotypes. The median expected heterozygosity (He) of the microhaplotypes was 0.56 (interquartile range: 0.43-0.73) across all States and not significantly different across time. A majority (61%) of the microhaplotypes had He>0.5 indicating sustained genetic diversity over time and across States, comparable to findings in Mozambique. Notably, 85% of infections were polyclonal, with mean complexity of infection (COI) of 3.4, suggesting high within-host diversity. The mean intra-host relatedness among parasite clones was 0.63, suggesting significant inbreeding and a major role of cotransmission in maintaining polyclonal infections within all populations; this however, resulted in an effective COI of 1.95. Spatio-temporal pairwise comparison using identity by descent showed low proportion (<3%) of significantly related parasites across all States, consistent with the high genetic diversity observed across all States regardless of the Year. This is in line with previous studies from Nigeria. Our study indicates no genetic evidence of reduction in malaria transmission intensity over the study period, aligning with national survey reports from 2010 and 2018. The persistent high genetic diversity and lack of decline in transmission underscore the need for ongoing surveillance of the malaria parasite's genetic landscape. This analysis suggests that merely increasing the coverage of existing interventions may not suffice. Instead, exploring new strategies or enhancing existing ones to effectively combat malaria in Nigeria is imperative.

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MALKINID (MALARIA KINSHIP IDENTIFIER): A LIKELIHOOD MODEL FOR IDENTIFYING PARASITE GENEALOGY RELATIONSHIPS BASED ON GENETIC RELATEDNESS

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Pathogen genomics is a potent tool for tracking infectious disease transmission. In malaria, sexual reproduction and recombination in mosquitoes can generate genetically related progeny whose genomes contain identical-by-descent (IBD) segments. In theory, IBD can be used to distinguish genealogical relationships (parent-child [PC], full-sibling [FS], etc) to reconstruct transmission history or identify parasites for genotype-to-phenotype quantitative-trait-locus (QTL) experiments. We developed a new likelihood model, *MalKinID* (Malaria Kinship Identifier), based on genomic data from three laboratory-based genetic crosses (yielding 440 PC and 9060 FS comparisons). *MalKinID* uses the genome-wide IBD proportion and the per-chromosome max IBD segment block and IBD segment count distributions to identify parasite genealogical relationships. *MalKinID's* performance was assessed using empirical lab-cross data and simulated, point importations. *MalKinID* accurately identified lab-generated F_1 progeny with >80% sensitivity and showed that 0.39 (95% CI: 0.28, 0.49) of the second-generation progeny of an NF54 and NHP4026 cross were F_1s and 0.56 (0.45, 0.67) were backcrosses of an F_1 with the parental NF54 strain. For simulated, outcrossed point importations, *MalKinID* accurately reconstructs genealogy history with high precision and sensitivity. The F1-scores for PC, FS, second-degree, and third-degree relatives were 0.95 (0.84, 1.0), 0.94 (0.72, 1.0), 0.84 (0.60, 1.0) and 0.84 (0.64, 0.94), respectively. However, when importation involves inbreeding, such as during serial cotransmission, the precision and sensitivity of *MalKinID* declined, with F1-scores of 0.76 (0.56, 0.92) and 0.23 (0.0, 0.4) for PC and FS and <0.05 for second-degree and third-degree relatives. *MalKinID* lays the foundations for identifying different parasite genealogical relationships, which can be used to reconstruct transmission lineages in outcrossed parasite populations or used to separate progeny for QTL experiments.

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PLASMODIUM FALCIPARUM ADAPTS TO FRONTLINE DRUG CHANGES THROUGH NEW HAPLOTYPES AT OLD TARGETS

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Populations of *Plasmodium falciparum* regularly confront orchestrated changes in frontline drug treatment that drastically alter the parasite's selection landscape. When this has occurred, the parasite has successfully adapted to the new drugs through novel resistance mutations. These novel

mutations, however, may emerge in a genetic background already shaped by prior drug selection. In some instances, selection imposed by distinct drugs has targeted the same loci in either synergistic or antagonistic ways, resulting in genomic signatures that can be hard to attribute to a specific agent. Here, we use two approaches for detecting sequential bouts of drug adaptation: haplotype-based selection testing and temporal changes in allele frequencies. Using a set of longitudinally acquired samples from French Guiana, we determine that since the introduction of the new drug artemether-lumefantrine (AL) there have been rapid hard selective sweeps at both known and novel loci. We additionally identify genomic regions where selection acted in opposing directions before and after widespread AL introduction. At four high-profile genes with demonstrated involvement in drug resistance (*crt*, *mdr1*, *aat1*, and *gch1*), we saw strong selection before and after drug regime change, however, selection favored different haplotypes in the two time periods. Similarly, the allele frequency analysis identified numerous coding variants whose frequency trajectory changed sign under the new drug pressure. These selected alleles were enriched for genes implicated in artemisinin and/or partner drug resistance in other global populations. Overall, this suggests that subtle changes throughout the genome impact drug resistance, and this may explain the observation that some *P. falciparum* populations experience novel evolutionary trajectories—rather than a return to "wildtype"—after drug removal.

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HMMIBD-RS, AN ENHANCED IMPLEMENTATION OF *HMMIBD* FOR PARALLELIZABLE IDENTITY-BY-DESCENT DETECTION FROM HAPLOID GENOMES

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Identity-by-descent (IBD) is a key tool in malaria parasite population genomics to infer genetic relatedness, selection signals, and population demography. The hidden Markov Model-based probabilistic method *hmmIBD* has been widely used to infer IBD in species with high recombination rates and low marker density, such as *Plasmodium falciparum* (*Pf*). In previous work, we found that *hmmIBD* had higher accuracy in detection of IBD segments compared to identity-by-state-based methods. However, the power of the *hmmIBD* algorithm is currently limited by its non-parallelizable implementation, and the assumption of uniform recombination rate across the genome, limiting its application to large data sets or to genomes with variable recombination. Here, we present a new tool, *hmmibd-rs,* that reimplements the original *hmmIBD* algorithm in a memory-safe language, Rust. The tool allows the direct input of a common genotype data format (BCF), the specification of a non-uniform recombination rate map, and the utilization of multi-core CPU for parallelization, with performance increasing almost linearly with the number of threads. Using simulation, we showed that *hmmibd-rs,* can detect IBD segments from 30,000 simulated *Pf*-like 100-centimorgan (cM) chromosomes in 9 hours using 64 threads, compared to 3-4 weeks when using single-threaded *hmmIBD*, demonstrating scalability for large data sets such as MalariaGEN Pf7 (n > 20,000 isolates). We also found that the incorporation of a recombination rate map into *hmmibd-rs* largely reduced detection of false positive IBD segments (≥ 2 cM) in low recombining regions and moderately decreased false negative rates in high-recombining regions in genomes simulated with non-uniform recombination rates, compared to *hmmIBD*, which uses an average rate. Ongoing work will apply this new tool to the MalariaGEN Pf7 data set to measure the computation time used for IBD detection and determine the extent to which the incorporation of variable recombination rates (estimated from population samples or existing genetic cross data) impacts downstream inferences of parasite demography in different malaria transmission settings.

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GENETIC SURVEILLANCE REVEALS THE CLONAL REPLACEMENT DYNAMICS AND SPATIAL STRUCTURE OF *PLASMODIUM FALCIPARUM* IN SÃO TOMÉ AND PRÍNCIPE

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Despite ongoing efforts to eliminate malaria in São Tomé and Príncipe (STP), there has been an increase in case numbers in recent years. Understanding the composition of the remaining transmission is crucial for tailoring effective elimination strategies. In this study, we collected amplicon sequencing data from 980 samples and integrated it with longitudinal surveillance data from 2010 to 2016 to examine the genetic composition of the parasite population. The mean multiplicity of infection (MOI) was 1.3, and the proportion of polyclonal infections was 11%, indicating that transmission intensity was low. Notably, the temporal trends of these genetic metrics did not align with incidence rates. In low transmission settings, where parasite population size is small, genetic metrics are expected to be highly influenced by stochastic fluctuations in the composition of circulating infections. Our results suggest that temporal changes in genetic metrics may not necessarily reflect changes in transmission intensity. Furthermore, while the majority of samples (87%) were genetically linked to other samples, suggesting limited genetic diversity, we observed continuous turnover in genetic clusters accompanied by changes in drug-resistance haplotypes during the study period. Principal component analysis suggests that the STP samples were genetically similar to those from Central and West Africa, pointing to the possibility of importation. The parasite diversity was lowest at the end of the study period, which is indicative of successful malaria control efforts. In summary, our study reveals dynamic changes in the parasite population in STP, highlighting the need to not only prioritize targeted interventions against hotspots of transmission but also to implement reactive case detection and collect travel histories to prevent the introduction of new parasites into this island nation as it approaches elimination. This study also serves as a case study for implementing genetic surveillance in a low transmission setting.

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APPLICATION OF HIGHLY MULTIPLEXED AMPLISEQ TARGETED NGS ASSAYS FOR GENOMIC SURVEILLANCE USE CASES FOR *P. FALCIPARUM* AND *P. VIVAX* IN ASIA, AFRICA AND LATIN AMERICA

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Malaria remains a major global health problem. Research has advanced our knowledge of malaria epidemiology and ecology, but emerging drug and diagnostic resistance highlight the urgency of continuous surveillance. Genomic surveillance, a field of study using genetics to track diseases, aids in decision-making and policy for malaria control and elimination. While genomic surveillance of viral and bacterial pathogens is becoming mainstream, genomic tools are not routinely used in malaria surveillance, partly due to the size and complexity of the parasite genome. Here we

present a set highly-multiplexed sequencing assay (AmpliSeq) which have been developed for cost-effective targeted deep sequencing of *P. falciparum* or *P. vivax* of specific genomic regions of interest. These assays combine phenotypic and population genetic markers to study parasite dynamics, which has been successfully piloted in several countries, including Burkina Faso, Democratic Republic of Congo, Peru, Vietnam, and in travelers and migrants in Belgium.We demonstrate genetic surveillance use cases, such as drug-resistance of *P. falciparum* in Vietnam, Burkina Faso and DRC, the increasing rate of *hrp2/3* deletions in Peru, and the origin of imported *P. vivax cases* in Belgium. High-resolution identity-by-descent relatedness analysis in Vietnam indicated a high level of *P. vivax* parasite connectivity in coastal provinces, and a distinct highly-related population in a remote highland province. An imported clonal *P. vivax* outbreak in a Peruvian Amazon border community was detected. In addition, we are investigating *Pfcsp* diversity in a vaccine trial site in Burkina Faso. This approach can effectively differentiate and characterize parasite isolates over time and space, and is easily adaptable to diverse epidemiological contexts. It can guide, surveillance and implementation of core control interventions such as vector control, chemotherapy and prophylaxis, and vaccine deployment strategies, among others. The priority is to make this tool available to key actors in endemic countries to increase ownership and ensure data usage for decision-making and policy.

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TEMPORAL GENOMIC ANALYSIS REVEALED MAINTAINED GENETIC DIVERSITY AND COMPLEXITY OF INFECTION AMONG PLASMODIUM FALCIPARUM INFECTIONS IN MAINLAND TANZANIA:2021-2022

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Plasmodium falciparum infections in endemic countries exhibit high genetic diversity, posing challenges to malaria control efforts. Recent studies have reported the heterogeneous genetic diversity of P. falciparum in mainland Tanzania, highlighting the need for integrated approaches in malaria surveillance. Understanding the temporal dynamics of genetic diversity and the complexity of infection (COI) is crucial for effective malaria control and elimination strategies. Here we present the preliminary analysis for countrywide temporal dynamics of P. falciparum genetic diversity and COI of malaria parasites in 13 regions of Mainland Tanzania from 2021 to 2022. About 34,550 individuals were screened by malaria rapid diagnostic tests (RDTs) through cross-sectional surveys conducted between February and July 2021-2022, of which 14,871 were malaria positive. DNA extraction was done using the Chelex 100+Tween20 method and sequenced by molecular inversion probes (MIPs). The data was analyzed using MIPtools and R software. The mean COI was 1.53 (ranging from 1.55 in 2021 to 1.51 in 2022) and did vary across years (p-value =0.02), indicating the persistence of heterogeneous genetic diversity within the country. The proportion of polyclonal infections was 40.4% in 2021 and 46.1% in 2022. The mean COI was heterogeneous across the studied regions, with the lowest mean COI of 1.27 in Dodoma and the highest being 2.01 in Kagera. The COI correlated with regional transmission intensities (correlation ratio = 1). The expected heterozygosity was 0.28 in 2021 and 0.36 in 2022, indicating little genetic diversity. The principal component analysis did not detect parasite population structure over time. The results reveal a striking persistence of moderate genetic diversity and complexity of infection over time, indicative of ongoing supper infection/co-transmission within individual hosts. Further analysis will be performed to fully assess temporal parasite genetic diversity to support effective malaria management and elimination in the country.

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DIVERSITY AND MULTIPLICITY OF *PLASMODIUM FALCIPARUM* INFECTIONS AMONG ASYMPTOMATIC SCHOOL CHILDREN IN ANKAZOABO, SOUTHEN MADAGASCAR

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< Malaria remains a major public health problem in Madagascar. Understanding *Plasmodium falciparum* population diversity and transmission dynamics provides information on the intensity of malaria transmission, which is needed for assessing malaria control interventions. This study aimed to determine P. *falciparum* allelic diversity and multiplicity of infection (MOI) among asymptomatic school-age children between five to fifteen year-old in Ankazoabo district, South of Madagascar in December 2023.From 360 asymptomatic study participants, a total of 99 samples positive for *P. falciparum* were included for molecular analysis. Samples were characterized by nested PCR and genotyping the polymorphic regions of *msp-1* and *msp-2*. For *msp-1*, 86.87 %(86/99), and *95.95*% (95/99) for *msp-2* were detected. In *msp-1* ,K1 was the predominant allelic family detected in 80.23% (69/86) of the isolates followed by MAD20 and RO33. For *msp-2,* the frequency of IC/3D7 and FC27 were 82.11%(78/95) and 70.53%(67/95) respectively. Fifty three percent of isolates had multiple genotypes and the overall mean of multiplicity of infection (MOI) was 2.3. Correspondingly, the excepted Heterozigosity(He) value for *msp-1*(He=0.54) and *msp-2*(He=0.51).The findings of this study revealed higher genetic diversity of the *msp-1* and *msp-2* allele families in *P.falciparum* isolates in this malaria endemic area. However continued monitoring of status of the local genetic diversity profile in *P.falciparum* population is required to support malaria control and elimination strategies. >

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REVEALING NOVEL GENETIC VARIANTS IN THE MALARIA TRANSMISSION BLOCKING VACCINE CANDIDATE PFS25

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Malaria remains a significant global health challenge, causing nearly a quarter of a billion cases worldwide in 2022. The approval of 2 new liver-

stage vaccines is a major advance, but there remains an urgent need for more effective vaccines that target other stages of the parasite's life cycle. Transmission-blocking vaccines (TBVs) offer promise for malaria elimination by reducing transmission within communities through targeting the sexual stages. However, the genetic diversity of the parasite antigens presents a significant obstacle to vaccine development. We employed next-generation amplicon deep sequencing to identify Pfs25-associated non-synonymous SNPs in 209 *Plasmodium falciparum* samples from four African countries: Senegal, Tanzania, Ghana, and Burkina Faso. Using a very sensitive threshold of 1% variant frequency, we identified 24 SNPs including 25 novel variants, and assessed their population prevalence and variant frequency in complex infections. Five variants were detected in multiple samples (L63V, V143I, S39G, L63P, and E59G), while the remaining 21 were rare variants found in individual samples. Analysis of country-specific prevalence revealed varying proportions of mutant alleles, with Ghana exhibiting the highest prevalence (55.3%), followed by Senegal (27.6%), Tanzania (6.9%), and Burkina Faso (6.9%). We further categorized SNPs based on their frequency, identifying dominant variants with frequencies exceeding 25% and rare variants with frequencies below 2%. Threading analysis of the Pfs25 protein structure revealed SNPs in two categories: 1) SNPs that have the potential to influence the binding between Pfs25 and antibodies and can lead to immune evasion, and 2) SNPs that can potentially modify the structure of Pfs25 protein. Our results show that while Pfs25 remains a relatively highly conserved gene, we identified additional SNPs beyond the 9 previously reported. Most of these newly discovered SNPs display low variant frequency and population prevalence. Further research exploring the functional implications of these variations will be important to elucidate their role in malaria transmission.

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AMPLICON AND SNP GENOTYPING OF *P. FALCIPARUM* AND *P. VIVAX* CASES IDENTIFIES HIGHLY RELATED SAMPLE CLUSTERS AS BHUTAN APPROACHES ELIMINATION

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Bhutan is slated for malaria elimination by 2025, and cases have declined sharply over the last 20 years. Approaching elimination, malaria cases are often imported and occur in border regions. Understanding genetic relatedness between parasites can help distinguish imported from local cases. DNA was extracted from dried blood spots for 114 *Plasmodium vivax* and 30 *Plasmodium falciparum* isolates collected from individuals with clinical infection in Bhutan from 2016 to 2021. *P. falciparum* genotyping was conducted using the 129-amplicon AMPLseq panel, and *P. vivax* genotyping using a SNP barcode comprised of 130 variable sites. The resulting amplicon and SNP genotypes were compared to the same sites extracted from publicly available whole genome sequence data (MalariaGEN Pf7 and Pv4 for *P. falciparum* and *P. vivax*, respectively) from isolates collected in India, Bangladesh, and Myanmar. Isolates with poor genotyping coverage and polyclonal isolates without a clear predominant clone were excluded, resulting in 64 genotyped *P. vivax* isolates and 12 *P. falciparum* isolates for analysis. Dcifer was used to estimate genetic relatedness, and InfoMap community network detection was performed to identify clusters of highly related parasites. We identified two clusters of identical *P. falciparum* isolates, each with 100% identity at the 104 genotyped amplicons, and 7 clusters of identical *P. vivax* isolates, with 100% identity at the 130 variable sites. One *P. vivax* and one *P. falciparum* cluster contained isolates from non-consecutive collection years, suggesting persistence of parasite clones over time in this very low transmission area. Neither *P. vivax* nor *P. falciparum* isolates from Bhutan clustered with isolates from neighboring countries, likely due to limited representation of sequences from border regions in the MalariaGEN database. This lack of data from immediately adjacent districts limits our ability to infer whether cases were imported or locally-acquired based on genotyping data alone; such inferences will require integration with additional epidemiologic data on the timing of diagnosis, travel history, and patient proximity.

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PULSED MICROWAVE IRRADIATION INDUCES APOPTOSIS LIKE CELL DEATH IN *PLASMODIUM FALCIPARUM* VIA FAS/FASL DEATH RECEPTOR PATHWAY

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Pulsed Microwave Irradiation Induces Apoptosis-Like Cell Death in *Plasmodium falciparum* via FAS/FASL Death Receptor PathwayMost of the signaling pathway events involved in the apoptotic process of protozoa remain unknown, and *P. falciparum* is no exception. A previous study by our research group demonstrated that the parasite *P. falciparum* exhibits regulated cell death markers when exposed to microwaves (MW). In this study, we investigated the presence of proteins in *P. falciparum in vitro* following exposure to pulsed MW irradiation at 2.45 GHz frequency. After MW exposure, we used a commercial human dot-blot array to identify 43 target proteins associated with programmed cell death (PCD). We compared protein expression levels between control and treated samples using ImageJ, a digital image analysis software. Notably, MW-treated samples showed significantly higher signal intensity for the death receptor Fas and its ligand FasL, which are known to activate the caspase cascade in multicellular organisms and in some eukaryotic single-celled microorganisms. We also observed increased expression of HSP70, HSP60, BID, and BAX, proteins that participate in the Fas/FasL mediated apoptosis pathway leading to mitochondrial outer membrane permeabilization (MOMP) and cell death. Interestingly, *P. falciparum* possesses metacaspases encoded by the PfMCA1, 2, and 3 genes. Our results suggest that the activation of death receptor FAS/FASL like in *P. falciparum* triggers the activation *of P. falciparum* metacaspases. We propose that FAS/FASL like proteins are present *in P. falciparum* and play a significant role in the parasite's apoptosis-like cell death.

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SETTING A MRDT-BASED STRATEGY FOR MONITORING THE OCCURRENCE OF *PLASMODIUM FALCIPARUM HRP2* AND *HRP3* DELETIONS IN MADAGASCAR

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In the island of Madagascar – where *Plasmodium falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* coexist, the malaria rapid diagnostic test (mRDT) has become an essential tool for improving malaria case management since 2006. The most used mRDT in the Malagasy health system detects both the pan-specific LDH and the *P. falciparum* HRP2. However, the deletion of the *pfhrp2* gene threatens the accuracy of the HRP2-based test. There therefore is a need to set a robust method for monitoring the occurrence of *pfhrp2* and *pfhrp3* gene deletions. During malaria detection in August 2023 in 373 children aged from 5 to 14 years in Ankililoaka in the dry southwestern part of the island, blood samples were collected by finger-prick for mRDT and molecular analysis using dried blood spots. Of the 194 (52%) mRDT positive samples, 105 were mRDT pan LDH and HRP2 positive, 76 mRDT HRP2 positive but pan LDH negative, and 13 mRDT pan LDH positive but HRP2 negative. These 13 HRP2 negative samples

were PCR analyzed. Five samples contained *P. falciparum* and one case of *pfhrp2* and *pfhrp3* double deletions (0.5%), and two cases of *pfhrp3* single deletions (1.1%) were confirmed. Our results demonstrated the occurrence of *pfhrp2/3* deletions among *P. falciparum* isolates from the southern part of Madagascar at a low level. Above all, the standard operating procedures for detecting *P. falciparum hrp2/3* deletions were successfully established for developing a national survey to guide the national malaria control program on the mRDT choice.

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GUT MICROBIOTA-INDUCED IMMUNE TOLERANCE IMPAIRS SYSTEMIC IMMUNITY AGAINST SEVERE MALARIA

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Severe malaria caused by *Plasmodium* spp. infection leads to hundreds of thousands of deaths annually. Our lab uses *P. yoelii* and C57BL/6 mice from diverse vendors to study the influence of gut microbiota on malaria severity. Recently, we showed microbiota-dependent germinal center contraction and reduced antibody quality post-infection, leading to hyperparasitemia. This phenotype is replicated by introducing cecal material from hyper-parasitemic mice into regular and germ-free mice. While the causality is established, the intricate mechanisms remain unclear. Here, we found that susceptible mice had increased T regulatory cells in their Peyer's Patches and spleens after infection, correlated with reduced IFN-γ production. When exposed to sub-colitis doses of DSS, malaria-resistant mice developed colitis, while susceptible mice were resistant to weight loss, confirming the tolerogenic nature of their microbiota. Both groups showed similar levels of intestinal damage and bacterial translocation post-infection, suggesting malaria-dependent microbiota-independent gut injury. Moreover, modulation of splenic adenosine immunosuppressive pathways involving A2AR and CD39 is enhanced by tolerogenic microbiota in different leukocytes during malaria infection. Treatments to repair the gut barrier or to antagonize A2AR after intestinal damage post-infection significantly mitigate parasitemia, weight loss, and mortality while enhancing immunity. These findings highlight the vital role of the gut microbiota in shaping systemic immunity during infections, underscoring the potential of therapeutic interventions targeting the gut barrier to mitigate malaria severity and enhance outcomes.

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AGEING OF *PLASMODIUM FALCIPARUM* MALARIA SPOROZOITES ALTERS THEIR MOTILITY, INFECTIVITY AND REDUCES IMMUNE ACTIVATION *IN VITRO*

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Sporozoites (SPZ), the infective form of *Plasmodium falciparum* (Pf), can be inoculated into the human host skin by Anopheline mosquitoes. These SPZ migrate at ± 1µm/s to find a blood vessel and travel to the liver where they infect hepatocytes. At the skin they are still low in number and vulnerable to immune attack by antibodies and macrophages. This is why whole SPZ and SPZ proteins are used as the basis for most malaria vaccines. Mosquitoes inoculate SPZ into a human host between 14 and 25 days after infectious blood meal. However, it is unknown whether residing time within the mosquito affects the SPZ. We aimed to unravel how the age of *Pf* SPZ in salivary glands (14, 17, or 20 days post blood meal) affects their infectivity and the ensuing immune responses. We investigated SPZ numbers, viability, motility using dedicated sporozoite motility orienting and organizing tool software (SMOOT) and infectivity of HC-04.j7 liver cells. *In vitro* co-culture assays with SPZ stimulated monocyte-derived macrophages (MoMϕ) and $CD8^+$ T-cells, analyzed by flow cytometry, were used to investigate immune responses. We found that SPZ age did not result in different SPZ numbers or viability. However, we observed a markedly different motility pattern, whereby motility decreases from 89% at day 14 to 80% at day 17 and 71% at day 20 (p=<0.0001). Similarly, infectivity of day 20 SPZ dropped to 50% as compared with day 14 SPZ (p=0.004). MoMϕ were better able to take up day 14 SPZ (7.6%) than day 20 SPZ (4.1% p=0.03) and displayed an increased expression of pro-inflammatory CD80, IL-6 (p=0.005) and regulatory markers PDL1 (p=0.02), IL-10 (p=0.009) upon phagocytosis of younger SPZ. Interestingly, co-culture of these cells with $CD8^+$ T-cells revealed a decreased expression of activation markers CD137 and IFNγ as compared to their day 20 counterparts. These findings suggest that older (day 17-20) *Pf* SPZ are less infectious and have decreased immune regulatory potential. Our data shows a first step in enhancing our understanding of how mosquito residing time affects *Pf* SPZ and could impact our understanding of the *Pf* infectious reservoir and the potency of whole SPZ vaccines.

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LEVERAGING BIRTH COHORTS TO TRACE COMPLICATED MALARIA RISK AND ITS IMMUNOLOGICAL CORRELATES AT EACH INFECTION IN INFANCY

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Infections with *P. falciparum* range from asymptomatic to life-threatening. Protection from severe disease is usually acquired in the first few years of life, though it is unknown how this protection is encoded immunologically. Uncovering this mystery holds promise for developing and evaluating interventions that prevent severe disease and death. We leveraged three birth cohorts from high-transmission settings in Uganda for a detailed view of malaria risk and associated immunological changes in infancy. Monthly, active case finding allowed the faithful capture of each infection in more than 900 children aged 8 weeks to 2 years. Across thousands of *P.falciparum* infections, we find that the risk of complicated malaria is highly dynamic in early life. First infections tended to have lower parasitemias and were mostly uncomplicated. Median parasitemia increased in subsequent infections but reached a plateau after about three infections. The probability of symptoms, given a parasitemic episode remained constant in early life. In contrast, complicated disease risk peaked around malaria episode 5 and then quickly, exponentially declined thereafter,while median parasitemia remained unchanged. In multivariate analyses, the order of infection, more than age or parasitemia, significantly predicted complicated malaria risk in our cohort. Single-cell analysis of *P.falciparum*-specific T cells revealed changes in activation and differentiation associated with high and low-risk infections. Our data suggest that protection from severe disease is acquired after just a few malaria episodes. This occurs even when median parasitemias remain unchanged, and thus represents a mechanism of disease tolerance. This tolerance mechanism is likely distinct from clinical immunity, as the probability of developing symptoms remained constant in this cohort.

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REACTIVITY OF ANTIBODIES AGAINST MALARIA AND OTHER PARASITIC DISEASES TO THE ANTIGENS N, S AND S1 SUBUNIT RDB951 USED IN COVID-19 SEROLOGY

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In response to the SARS-CoV2 (COVID) pandemic, several antibody (Ab) sero-surveillance assays were developed. However, studies suggesting that samples from malaria endemic areas have Ab that cross react with

COVID serology assays may limit their utility in these settings. We used a multiplex bead assay (MBA) to assess if Ab from parasite positive samples from United States (US) patients reacted against three COVID antigens: nucleocapsid (N), the spike protein (S) or its subunit RDB951 (R). The study tested 816 pre-COVID samples: 704 from the US with Ab positive results (Ab+) for malaria or 13 other parasitic diseases, 91 from Africa with Ab+ for filariasis, and 21 from US individuals with no reactivity for parasitic diseases. Controls were 33 samples collected during the COVID pandemic. Resulting data were assembled in contingency tables and analyzed by Chi-square/ Fisher's exact tests. Among pre-COVID samples, Ab+ against the COVID antigens were found in 14 (1.7%) samples for N, 26 (3.2%) for S, and none for R. No sample was Ab+ for N and S. Among the 33 samples from the COVID period, 10 (30.3%) had Ab+ for N, 20 (60.6%) for S and 19 (57.6%) for R, and 18 (54.5%) had simultaneous Ab+ for S and R. Among pre-COVID US samples positive for a parasitic disease, significant associations were found between filariasis positive samples (6/72, 8.3%) and Ab+ to S ($p=0.015$). Among 35 malaria Ab+ samples, one sample had Ab+ for N, and another had Ab+ for S. Among the 91 African pre-COVID samples, only 6 had Ab+ for N and 2 for S. Meanwhile, the COVID pandemic control group had Ab+ against the N, S and R antigens that were significantly associated with the COVID period ($p<0.001$). The MBA data showed that US malaria positive sera were not associated with Ab+ for COVID antigens N, S or R, and that Ab developed against other etiologies, as determined by MBA in pre-COVID samples, could contribute to some cross reactivity against either the N or S antigens but not likely against the R antigen.

7259

A NOVEL MURINE MODEL FOR INVESTIGATING THE PATHOGENIC ROLE OF COAGULATION IN MALARIA-ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME

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Malaria-associated acute respiratory distress syndrome (MA-ARDS) is a complication of severe malaria, characterized by pulmonary complications such as edema, inflammation, hemorrhages, and alveolar damage. The role of coagulation in the pathogenesis of MA-ARDS is poorly understood. Aiming to understand the pathogenic pathways that lead to lung malaria, including dysregulated coagulation, we developed an experimental murine model that lacks endothelial tissue factor (TF), the primary initiator of the extrinsic coagulation cascade. We hypothesized that altered TF expression would suppress the inflammatory response, oxidative stress, and endothelial disruption, resulting in reduced vascular leakage in the lung. We further hypothesized that sexual dimorphism would influence disease severity, with males being more susceptible. We assessed disease progression in P. berghei NK65 infected (IV, 105) endothelial tissue factor-deficient ($F3^{flox/flox}$ Tie-2^{Cre}) mice. Parasitemia, anemia, and body condition were measured longitudinally over 16 days. At 16 days post-infection, lung tissues were weighed and processed for histology and molecular analysis. Body condition score as measured by activity and behavior was significantly reduced in males relative to females regardless of TF expression. Females lacking endothelial TF had significantly lower parasite burden in comparison to males, while tissue factor intact female and male mice had similar parasitemia. Lung index, anemia, and body weight in all experimental groups were similar. Ongoing studies are examining lung histology and the expression of inflammatory, anti-oxidant, pro- and anti-coagulant associated genes to further assess the extent to which TF expression and sex influence lung pathology in this model.

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COMPARING MIXTURE MODELING APPROACHES FOR CLASSIFYING LONG-TERM MALARIA SEROLOGICAL MARKERS IN NORTHERN LAOS

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In Lao People's democratic (Lao PDR), malaria is hypo-endemic and *Plasmodium vivax* is a common cause of malaria infection; current diagnostic tools are insufficient for detection of malaria infection. Serological assays can be a valuable tool for elucidating infection timelines and estimating the likelihood of *P. vivax* hypnozoite presence. Challenges in serology include defining antigenic targets, and classification of individuals based on semi-quantitative assays. This study presents a comparison of two statistical models to classify parasite exposure based on Luminex assays. We also apply regression models to quantify factors associated with historical exposure. A cross-sectional study in Lao PDR was conducted in four providences. Participants provided biological samples and demographic information. The prevalence of four putative long-term markers was classified using two mixture models: (1) deterministic finite mixture model (dFMM), and (2) novel probabilistic finite mixture model (pFMM) using a Weibull distribution in a Bayesian framework. Thirty-eight individuals (0.8%) were PCR-positive for current parasitemia. The seronegative proportion of the population by model is as follows for each marker: PvAMA1 (59.3% by dFMM, 11.9% [80% CrI: 3.5, 31.8] by pFMM); PvMSP119 (18.0% by dFMM, 17.4% [80% CrI: 1.0, 42.9] by pFMM); PfAMA1 (57.5% by dFMM, 23.6% [80% CrI: 21.6, 25.5] by pFMM); PfMSP119 (58.2% by dFMM, 26.9% [80% CrI: 24.7, 29.2] by pFMM). Seroprevalences based on the pFMM model are consistent with expectations in this region which is approaching elimination. Factors including age, geography, sex, and occupation were associated with individual-level seropositivity (cumulative exposures). This was consistent with expectations of long-term markers. While serology is a useful tool, the lack of validated classification methods leads to arbitrary cut-points under strong assumptions. This pFMM provides a complimentary and nuanced framework to interpreting serological data. A probabilistic approach can better capture the uncertainty found in this inherently complex data.

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TARGETS OF CSP-BASED MALARIA VACCINES: WHAT WE MISSED IN 1987 AND WHAT IS MISSING NOW

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The current circumsporozoite protein (CSP) based licensed malaria vaccines can be improved by the inclusion of novel CSP targets. In the wake of increasing relevance of non-*falciparum* species, a cross-species vaccine is desirable. In this study, we profiled the CSPs of *Plasmodium falciparum, Plasmodium malariae,* and *Plasmodium ovale* in terms of protein sequence and structure, and naturally-acquired CSP-specific IgG in malaria-exposed individuals. We sought to uncover cross-species conserved domains to prioritize in the design of a cross-species vaccine. Also, we probed potentially protective CSP motifs by comparing immune responses between malaria "protected" and "at-risk" cohorts. Sequence alignments were done using Clustal Omega. Protein structures were predicted using

ColabFold and compared using TM-align. Total IgG, IgG avidity, and IgG subclass measurements against full-length proteins (PfCSP, PmCSP, PoCSP) and peptides (20mer with 10aa overlap) were done by indirect ELISA. Western/dot blotting was done to confirm ELISA results and identify immunodominant CSP peptides. Sequence and structural similarities were low across full-length proteins; highest in the C-terminus. We observed the conservation of essential sequences cross-species; the PEXEL motif, the protease cleavage site, and region II+. There was similar anti-PfCSP and PoCSP and a lower anti-PmCSP total IgG levels. We uncovered 16/27(PfCSP), 16/26(PmCSP), and 13/26(PoCSP) seropositive peptides by dot-blot. IgG profiles of the PEXEL (N-terminus), minor repeat (junctional), major repeat (central repeat), and region II+ (C-terminus) peptides reveal high and diverse peptide recognition in the malaria "protected" cohort; IgG was polarized to peptides of the central repeat and the C-terminus in the at-risk cohort. Our study reaffirms CSP-specific antibody feedback inhibition in naturally malaria-exposed individuals. We propose cross-species targets; the PEXEL, protease cleavage site, and region II+. Our data suggests that a potent anti-CSP response is high and diversified across CSP domains. This study contributes to the design of effective vaccines.

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INVESTIGATING THE ASSOCIATION BETWEEN MALARIA INFECTION AND AUTOANTIBODY PRODUCTION IN MURINE AND HUMAN STUDIES.

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The relationship between malaria and autoimmunity remains controversial, with previous studies showing that infection promotes or inhibits inflammatory conditions. We, therefore, set out to investigate the link between *Plasmodium* infection and autoimmunity using murine models and studies in patient cohorts. The development of rheumatoid arthritis associated anti-citrullinated protein autoantibodies (ACPA) responses were assessed in *Plasmodium chabaudi* infected mice. Subsequently, we evaluated the impact of these heightened ACPA responses on the development of a model of experimental arthritis in mice following infection with *P. chabaudi* infection. We demonstrate that infection with *P. chabaud*i leads to increased ACPA peaking at two weeks post infection; and remaining high even after parasite clearance compared to naïve mice. Under the conditions used in our study these autoantibodies did not appear to influence the outcome of experimental autoimmune arthritis. Extending our findings to humans, we measured the levels of ACPA in individuals residing in areas of either low or moderate malaria transmission. Using microarray, we assessed the range of autoimmune markers exhibited by ACPA high individuals and flow cytometry was also used to assess T cell phenotypes associated with an autoimmune profile. As in the murine studies, individuals living in higher malaria transmission areas had elevated levels of ACPA. Individuals with higher ACPA exhibited diverse autoantibody profiles, suggesting a general increase in autoreactivity. We also noted lower FOXP3 regulatory T cell levels in individuals with higher ACPA levels compared to those with lower responses. These data suggest that malaria infection induces a range of autoantibody responses in both mice and humans. In our murine model, the pre-existing ACPA response following a single infection did not influence the development of experimental autoimmune arthritis. However, the impact of multiple malaria infections on the risk of developing autoimmune disease warrants further investigation.

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PROTEIN SEQUENCE AND STRUCTURE, AND ANTIBODY PROFILE OF THE AMA1 FROM THREE *PLASMODIUM* SPECIES.

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The need for an effective malaria vaccine is imperative. The prevalence of non-*falciparum* species in the clinical setting calls for the design of broad-spectrum intervention tools. To achieve this in vaccine design, it is necessary to establish species-specific immune mechanisms. The Apical membrane antigen (AMA1) is an advanced vaccine candidate with its potential evidenced by neutralizing antibodies. In this study, we investigated sequence and structural conservation between AMA1 proteins of *P. falciparum, P. malariae,* and *P. ovale* using *in silico* techniques and characterized IgG responses in six different populations in Ghana. Protein sequence comparison was done using Clustal Omega (significant at similarity >30%). Protein structures were predicted by homology modeling using Swiss-Model. Monoclonal antibody cross-reactivity was determined by Western blot. Our study cohorts include community, hospital (follow-up days 0,7,21), and a malaria "protected" and "at-risk" cohort sampled in the same geographic area. Total IgG, IgG subclasses, and IgG avidity were measured by indirect ELISA , and data was analyzed in R. There was high sequence similarity(>50%) and structural concordance(TM>0.9) between all antigens. All antigens were recognized by malaria-hyperimmune IgG in Western blot with intensities of PfAMA1>PmAMA1>PoAMA1. Using PfAMA1-generated monoclonals, we observed cross-reactivity between PfAMA1 and PmAMA1 for MAb N3-1D7. Comparing immune response against the three antigens, PfAMA1 recorded the highest IgG levels and seropositivity in all sample groups corresponding with species transmission intensity. Across the three antigens, anti-PfAMA1 IgG avidity was highest only in our clinical follow-up cohort on day zero. Dominating IgG subclasses were IgG1 and IgG2. This study affirms species transmission intensity in Ghana and the conservation of AMA1 in terms of sequence and structure. This is the first study that profiles and compares cross-species immune responses against AMA1 in naturally immune individuals. This study contributes to anti-AMA1 immunology towards vaccine design.

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MALARIA EXPOSURE RISK AND NATURALLY ACQUIRED IMMUNITY AMONG STUDENTS FROM SOUTHERN AND NORTHERN GHANA

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In Ghana, malaria remains a significant public health issue, with different regions experiencing varying levels of transmission intensity. This study examined the differences in malaria exposure and the development of naturally acquired immunity between students from Ghana's northern and southern regions. A cross-sectional study was conducted on a group of 189 healthy students from the Nyankpala Campus of the University for Development Studies (UDS) using a structured questionnaire to assess their malaria exposure history, risk, and prevention-seeking behavior. In addition, the study measured their IgG levels against *P. falciparum* 3D7 crude antigens, HB3VAR06, and IT4VAR60 using an indirect ELISA. This study uncovered that though individuals from the northern regions showed

a nearly significant difference in malaria susceptibility (p=0.054), there were no notable differences in malaria prevention-seeking behaviors compared to those from the southern region. Furthermore, no significant differences were observed in the levels of IgG antibodies against crude antigens, however, variations were found in the levels of IgG antibodies against HB3VAR06 antigens. The HB3VAR06-specific IgG levels were relatively higher among individuals from the north (p=0.027), whereas those from the south had higher levels of IT4VAR60-specific IgG but not significant (p=0.155), suggesting that individuals from the two regions may have been exposed to different VAR clones of the parasite. In general, the levels of naturally acquired IgG antibodies showed no correlation with the risk of malaria exposure. The result of this study provides valuable insights into the prevalence and risk factors associated with malaria in the study population and a potential geographical selection of parasites between southern and northern Ghana.

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UNVEILING IMMUNODOMINANT REGIONS OF PFCERLI1: INSIGHTS FOR MALARIA VACCINE DEVELOPMENT

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Malaria is a disease of major global health concern. *Plasmodium falciparum* is the deadliest human *Plasmodium* parasite. An effective malaria vaccine would be an important additional tool in the fight against malaria. Merozoite proteins of Plasmodium falciparum have been studied for malaria vaccine development. One of such antigens is the Plasmodium falciparum Cytosolically Exposed Rhoptry Leaflet Interacting protein 1 (*Pf*CERLI1). *Pf*CERLI1 is essential for red blood cell invasion by merozoites; antibodies against *Pf*CERLI1 are inhibitory to red blood cell invasion. In this study, we determined the immunodominant regions of PfCERLI1 to prioritize as targets for vaccine development. Five overlapping peptides were designed and synthesized to cover three-quarters of the full-length protein. Full-length protein structure was predicted using ColabFold. The predicted structure was visualized and edited in PyMol. Initial peptide seroreactivity using hyperimmune IgG purified from Ghanaian adults was determined by dot blot. Total IgG was measured using indirect ELISA. Sera samples were obtained from Madina (community samples and malaria-diagnosed hospital samples) and Lekma (clinical follow-up with days 0,7,21). All *Pf*CERLI1 peptides are reactive to naturally-acquired IgG. Our findings reveal varying levels of recognition among *Pf*CERLI1 peptides. Notably, peptides 5 and 7 exhibited immunodominance in the Madina cohort in both community and clinical samples. All anti-peptide IgG increased with age moderately in the clinical cohort. Adjusted for age, we observed higher total IgG levels in the community cohort compared to the hospital cohort except for peptide 3. In the clinical cohort, peptides 3, 4, and 5 were immunodominant at all time points. We observed significant IgG decay at day 7 for all peptides except 3 and 7. Our results show a correlation of peptide IgG with the development of anti-malaria immunity in naturally-exposed individuals. We are inclined to conclude that *Pf*CERLI1 is an essential target for vaccine design. Understanding the immunodominant regions of *Pf*CERLI1 brings us closer to a targeted and effective malaria vaccine.

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EARLY MALARIA IMMUNE SIGNATURES IN NAÏVE ADULTS EXPERIMENTALLY INFECTED WITH *PLASMODIUM FALCIPARUM* REVEAL HIGH AND LOW RESPONDERS

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The immune response to *Plasmodium falciparum* (Pf) is complex, involving innate responses that induce regulatory mechanisms, which determine infection outcomes and acquired immunity. In malaria-naive adults inoculated with Pf sporozoites via needle injection in Barcelona, we conducted analyses including genome-wide gene expression, cytokine and antibody profiling, and dendritic cell (DC) phenotyping. There were minimal responses on days 1 and 7. However, low density infections at day of parasite detection by thick blood smear (TBS) elicited robust innate responses, with 1251 differentially expressed genes compared to baseline (|log2FC|>0.6 & FDR<0.01), increased plasma cytokines and frequencies of activated DC ($CD86^+$, $PDL1^+$ & $CD40L^+$). Top upregulated genes included CXCL10, CXCL9, and CCL2, correlating with their elevated plasma concentrations. Upregulated blood transcriptional modules (BTMs) were related to interferon, DC activation, and cell cycle regulation, while downregulated BTMs were linked to NK, T and B cells, which correlated with lymphocyte cell counts (rho>0.7, p<0.01). Interestingly, transcriptional analysis revealed 'high' and'low' responders, with larger gene expression changes in high responders. BTMs associated with innate responses (DC, monocytes, platelets, interferons, inflammation, and chemokines) were upregulated in high responders. This coincided with higher cytokine concentrations and increased frequencies of activated DC. Consistently, cell deconvolution showed more activated DC and M1 macrophages. Instead, BTMs linked to adaptive responses (B & T cells, plasma cells) and NK cells were more downregulated. No significant differences were observed in pre-patent period (12.17 *vs* 12.27 days) and TBS parasite density at patency between the two groups. However, time to positive qPCR was longer in low responders (9.33 *vs* 7.73 days, p=0.02). Furthermore, high responders exhibited significantly more neutropenia and fever at patency. Innate responses to a first Pf infection in adults are highly variable and may impact parasite kinetics, clinical outcome, and whole parasite vaccine responses.

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ANTI-CIRCUMSPOROZOITE PROTEIN ANTIBODIES AS MARKERS FOR MALARIA TRANSMISSION MONITORING

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Malaria, remains a global burden, despite progress towards elimination in some endemic areas. Researchers are renewing efforts to track transmission to assess anti-malarial interventions. This correlation underscores the need for robust methods for monitoring malaria exposure and transmission. Antibodies to the *Plasmodium* antigen, circumsporozoite protein (CSP), is a promising alternative to the existing methods used for transmission intensity estimation. However, this may vary within populations and could be compromised by CSP antigen polymorphism. This study aimed to assess the use of anti-CSP antibodies as markers of recent exposure to malaria, taking antigen polymorphism into consideration. Sixty children and 120 adults from 2 regions of Ghana were sampled monthly for a year. Malaria infection status and parasite density were assessed by PCR. Enzyme-linked immunosorbent assays were used to determine anti-CSP antibody seroprevalence against the recombinant PfCSP (3D7 strain) and two conserved 24-mer peptides (NANPNANP repeats and NVDPNANP repeats) from the central repeat region of PfCSP. The *csp* genes were

amplified using Sanger sequencing and analyzed using MEGA 11 software. Parasite prevalence was 65% and 1% among children and adults respectively. Seropositivity varied significantly by month among children for anti-CSP (p-value<0.001), Anti-24 mer peptide 1 (p-value=0.001) and anti-24 mer peptide 2 (p-value=0.004). Seropositivity however did not significantly vary amongst adults. Parasite prevalence was significantly higher in children than in adults over the period, but antibody seropositivity was high in both children and adults. This study supported previous works on anti-CSP antibody method for monitoring malaria transmission. Further, these results showed that anti-CSP antibody measurement could be more useful in adults in low malaria transmission areas with undetectable levels of *Plasmodium* parasites even by PCR. Although *csp* gene is polymorphic, this did not significantly affect the levels of antibodies as measured with a standard strain for estimating malaria exposure among our study participants.

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PLASMABLAST IG REPERTOIRE DYNAMICS THROUGH REPEAT *PLASMODIUM FALCIPARUM* CHALLENGES REVEAL SIGNATURES OF NEGATIVE SELECTION

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To understand the development of immunity against malaria, a controlled human malaria challenge (CHMI) model was used to expose malaria-naïve individuals to the same *P. falciparum* (*Pf*) strain (NF54) four times over two years. Consistent with the gradual immunity observed naturally, the time to parasite detection increased significantly (delayed patency (DP)) by the 3rd CHMI. Plasmablast Ig repertoire maturation was tracked 7 days after peak parasitemia at each CHMI. Clone copy numbers and CDR3 counts for the major clones (CDR3 >200 or clone copy >20 000) increased significantly after exposure to Pf in all participants with DP and peaked at CHMI-2 in most DP. In contrast, the participants without DP had no significant increase in clone copy number or CDR3 count until CHMI-4. In these major clones, the ratio of replacement to silent mutations (R/S) declined from baseline through the 4 CHMIs and there was a significant decrease in R/S for the 12 Ig heavy chain variable genes associated with anti-Pf immunity in DP only. Phylogenetic analysis indicated that clones with longer tree lengths (more divergence) correlated with increasing negative selection (omega). These patterns suggest that a certain level of B cell activation is needed to reduce parasite replication and DP. However, there is a limit to the maturation of specific clones, possibly because most additional replacement mutations do not improve affinity and are selected against. Disclaimer: The opinions and assertions expressed herein are those of the authors and do not reflect the official policy or position of all the affiliated Institutions. The authors do not have a financial interest in any commercial product, service, or organization providing financial support for this research.

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VENOUS BLOOD GAS ANALYSIS IN UGANDAN CHILDREN WITH SEVERE MALARIA

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Acidosis, defined as base deficit (BD) >8mmol/L, is a criterion of severe malaria (WHO guidelines 2023). If the BD is not available, a plasma bicarbonate concentration [HCO_3^-] of <15mmol/L or venous plasma lactate ≥5mmol/L can be used to define acidosis. Kussmaul respirations may also suggest acidosis. We examined the agreement between markers of acidosis and their predictive value for mortality among children with severe malaria. Venous blood gas measurements (i-STAT biochemistry analyzer, Abbott Point of Care) from children <5 with severe falciparum malaria enrolled in a past clinical trial (July 2011 to June 2013) were examined retrospectively. Inclusion criteria were: (1) <5yr of age; (2) *P. falciparum* detected by both microscopy and rapid diagnostic test; (3) met criteria for severe malaria; and (4) venous blood gas measurement recorded at admission. 124 children (median age 2yr, 44% female) were included. Acidosis (BD > 8 mmol/L) was present in 59/124 (48%), hypobicarbonatemia in 51/124 (41%), hyperlactatemia in 42/121 (35%), and Kussmaul respirations in 58/124 (47%). Base deficit was inversely correlated with [HCO_3^-] (ρ= -0.93, p<0.0001), directly correlated with lactate level (ρ=0.38, p<0.0001), and was significantly higher in patients with Kussmaul respirations (9.7 mmol/L (IQR 4.5-14) versus 5.7 mmol/L (IQR 2.9-11), p=0.0064). Using BD>8mmol/L as a reference standard, hypobicarbonatemia, hyperlactatemia, and Kussmaul respirations were 85%, 53%, and 59% sensitive, and 98%, 83%, and 65% specific for detection of acidosis, respectively. There were 11 deaths (8.9%). All 11 deaths occurred in children with acidosis (OR >3.1, p=0.00018). Hypobicarbonatemia, hyperlactatemia, and Kussmaul respirations increased the odds of death by 17-fold (95%CI 2.3 - 760, p=0.00063), 3.1-fold (95%CI 0.68 - 16, p=0.094), and 13-fold (95%CI 1.8 - 590, p=0.0029), respectively. Our findings support the current WHO definition of acidosis: BD>8mmol/L is a strong predictor of mortality in children with malaria. Other markers of metabolic acidosis (hypobicarbonatemia and Kussmaul respirations) also have prognostic value.

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DYSREGULATION OF NETOSIS IN PEDIATRIC PATIENTS WITH SEVERE MALARIAL ANEMIA

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Human malaria remains among the leading global causes of childhood morbidity and mortality, accounting for 249 million cases and 608,000 deaths annually. The World Health Organization African Region accounts for the majority (95%) of fatalities of which 80% occur in children <5 years. In western Kenya, a holoendemic *Plasmodium falciparum* area, severe malarial anemia (SMA, Hb<6.0 g/dL) is the primary manifestation of severe childhood malaria. Although antimalarials are pivotal for malaria control, rising drug resistance underscores the importance of defining novel molecular targets to support drug discovery efforts. As such, we explored the entire expressed transcriptome (Illumina® NovaSeq 6000) in the peripheral blood of Kenyan children with either SMA (n=18) or non-SMA (Hb≥6.0 g/dL, n=39), excluding cases of sickle cell disease. There were 1,682 differentially expressed genes (DEGs, *padj*<0.05) in SMA relative to non-SMA: 1,403 up-regulated and 279 down-regulated. Pathway analysis using MetaCore™ (threshold: $\log_2$foldchange=0.585, *padj*<0.05) revealed that NETosis in Systemic Lupus Erythematosus (SLE) was the top disrupted pathway (*padj*=8.134E-5) in children with SMA. NETosis is a cellular process initiated by pathogen products, antibodies, immune complexes, and cytokines for the formation and release of neutrophil extracellular traps

(NETs), composed of decondensed chromatin DNA and neutrophil granule peptides/proteins (e.g., PERM, alpha-defensin, leukocyte elastase, and histones). Consistent with chromatin decondensation and formation of NETs,
children with SMA had up-regulation of PERM (+1.77), alpha-defensin (+2.20), leukocyte elastase (+1.68), histone H1 (H1-0:+1.1 and H1-2:+0.71) and H2 (H2AC6:+1.04). In addition, NETs activate the classical complement pathway by interacting with C1q which was also upregulated in children with SMA (C1QA:+1.34, C1QB:+1.33, and C1QC:+1.52). Collectively, these results identify molecular mechanisms associated with enhanced chromatin decondensation and formation of NETs as potential therapeutic targets to reduce tissue hypoxia and organ dysfunction.

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ASYMPTOMATIC *P. FALCIPARUM* INFECTION IS NOT ASSOCIATED WITH EXPOSURE TO SOIL TRANSMITTED HELMINTHS IN CHILDREN FROM A MULTI SCHOOL-BASED STUDY IN ESSE, CAMEROON

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Asymptomatic *Plasmodium* carriage is a major public health threat affecting both children and adults and hindering malaria eradication, yet the mechanisms that allow for asymptomatic malaria are unclear. Many LMICs are endemic for both malaria and soil-transmitted helminths (STH). Studies have confirmed that helminths secrete various proteins during infection to regulate host immune responses as a survival strategy meanwhile reducing host immune responses to other inflammatory processes. We conducted a two-part study to evaluate if STH infection drives the phenotype of asymptomatic *Plasmodium* infection. First, a one-month longitudinal study of 134 primary school children across 3 school-based study sites in Esse, Cameroon (where both malaria and STH are endemic) was performed to identify the prevalence of asymptomatic *P. falciparum* infection, factors associated with subsequent development of symptomatic malaria, and the prevalence of STH co-infection. Blood samples determined malaria status and anemia, daily temperature checks were used to monitor for symptomatic disease development, and stool samples screened for STH infection using the Kato Katz method. Due to presumed falsely low Kato Katz results, a secondary retrospective study was conducted to establish STH IgG positivity. Overall, 85.8% of children had asymptomatic *P. falciparum* infection by microscopy, 88.8% had serologic positivity for at least one STH antigen, and 76.1% had asymptomatic *P. falciparum* plus STH exposure. We found no significant difference in the proportion of children with STH exposure and asymptomatic vs. symptomatic *P. falciparum* carriage (88.7% vs 83.3%, p >0.05), or in the proportion of asymptomatic *P. falciparum* carriers who were STH-exposed vs. STH-unexposed (85.7% vs. 86.7%, p > 0.05). The quantity of reactive antibody to STH was no different in asymptomatic vs. symptomatic *P. falciparum* carriers (p>0.05), and, for asymptomatic children, there was no correlation between anti-STH antibody level and *P. falciparum* load (p > 0.05). While limitations exist, we observed no association between STH exposure and asymptomatic *P. falciparum* infection.

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UPREGULATION OF GENE TRANSCRIPTS FOR SEVEN CRITICAL *PLASMODIUM FALCIPARUM* GLYCOLYTIC ENZYMES IN PEDIATRIC SEVERE MALARIAL ANEMIA

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The potential of novel therapeutic targets for severe malaria infections caused by *Plasmodium falciparum* is essential. This can be achieved by harnessing components of the parasite's metabolic pathways vital for its viability and infectivity in human hosts. One such target is the glycolytic pathway responsible for energy generation for the parasite's activities. This pathway is catalyzed by enzymes that control the flow of glycolytic metabolites. Enzymes in the pathway also influence non-glycolytic processes essential for the infectivity of the parasite such as: (i) the motility of sporozoites towards the liver cells and the subsequent attachment and entry into the hepatocytes, (ii) the egress of merozoites, (iii) infection of red blood cells, and (iv) the adherence of the parasites to the endothelial vessels. To explore if genes encoding key enzymes in the glycolytic pathway of *P. falciparum* contribute to the pathogenesis of severe malaria anemia [SMA, hemoglobin (Hb)<6.0 g/dL], a major manifestation of severe malaria, we performed *P. falciparum* transcriptome profiling on the peripheral blood of pediatric malaria patients in Siaya County Referral Hospital, Kenya, stratified into two clinical groups: SMA (n=20) and non-SMA (Hb≥6.0 g/dL, n=40). Our results revealed significant upregulation (FDR-adjusted $P<0.05$) of genes encoding seven key parasitic enzymes in the glycolytic pathway in children with SMA: pyruvate kinase 2 (*PykII*, $\log_2$FoldChange=1.262), phosphoglycerate mutase (*PGM*, $\log_2$FoldChange=0.710),phosphoglycerate kinase (*PGK*, $\log_2$FoldChange=0.645), enolase (*ENO*, $\log_2$FoldChange=0.609), triosephosphate isomerase (*TIM*, $\log_2$FoldChange=0.608), phosphoglycerate mutase (no gene symbol, $\log_2$FoldChange=0.533), and 6-phosphofructokinase (*PFK9*, $\log_2$FoldChange=0.519). Harnessing key enzymes in the glycolytic pathway of *P. falciparum* presents a promising avenue for targeting severe malaria infections, as evidenced by significant upregulation of these enzymes in pediatric patients with SMA, suggesting their potential role in disease pathogenesis.

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HEME AND HEMOGLOBIN SCAVENGING DEFICIENCIES IN PEDIATRIC SEVERE MALARIAL ANEMIA-- INSIGHTS FROM PLASMA PROTEOMICS

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Severe malarial anemia (SMA: Hb<6.0 g/dL, with any density parasitemia) is the primary clinical manifestation of severe malaria and among the

leading causes of morbidity and mortality in children under five years in holoendemic *Plasmodium falciparum* transmission regions, such as Siaya County, western Kenya. *P. falciparum* infection causes hemolysis of infected and uninfected human erythrocytes, resulting in the release of heme and free hemoglobin (Hb) into peripheral circulation. These molecules act as blood toxins to exposed cells and can promote organ failure when not promptly scavenged. To define molecular signatures associated with severe disease, we utilized an aptamer-based technology (SomaScan) to quantify 6,612 circulating human proteins in plasma samples collected from children (3-36 months) with non-SMA (Hb≥6.0 g/dL, n=20) and SMA (n=20) upon enrollment (pre-treatment: day 0). The proteomics revealed that levels of 670 plasma proteins were significantly higher in SMA relative to non-SMA (P<0.05, FDR<0.25), whilst the circulating levels of 665 proteins were significantly lower in SMA vs. non-SMA (P<0.05, FDR<0.25). Of the 1,335 differentially expressed proteins (DEPs), two critical heme scavengers, hemopexin and alpha-1-microglobulin, as well as the sole Hb scavengers, haptoglobin isoforms, were all down-regulated in the SMA group: hemopexin (log_2FoldChange= -0.842, P=3.753E-4); alpha-1-microglobulin (log_2FoldChange=-0.385, P=3.660E-3); haptoglobin, mixed type (log_2FoldChange=-3.961, P=8.089E-3); and haptoglobin isoform 2 (log_2FoldChange=-3.944, P=4.372E-3). Collectively, these proteomic results demonstrate that SMA is characterized by a deficiency of scavenging capability for heme and free hemoglobin during severe malaria infections.

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TRANSCRIPTOMIC INSIGHTS INTO COMPLEMENT-ASSOCIATED GENE DYSREGULATION IN CHILDHOOD SEVERE MALARIAL ANEMIA

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Severe malarial anemia (SMA: Hb<6.0 g/dL) is among the leading causes of global childhood morbidity and mortality. In holoendemic *Plasmodium falciparum* transmission regions, such as western Kenya, severe malaria primarily manifests as SMA. We have previously demonstrated that genetic variations in complement components alter the longitudinal risk of SMA and mortality. To extend these findings, we examined the entire expressed transcriptome in peripheral blood samples collected from children (1-59 mos.) with non-SMA (Hb≥6.0 g/dL, n=41) and SMA (n=25). Of the 585 human complement-associated genes identified in NCBI, 566 of the genes were contained within the RNA-Seq data with 189 genes differentially expressed in children with SMA relative to non-SMA at FDR≤0.050. Of the 189 genes, 79 were up-regulated and 110 were down-regulated. Gene ontology (GO) enrichment analysis using clusterProfiler in R revealed complement activation (FDR=$8.49x10^{-22}$), humoral immune response (FDR=$1.09x10^{-21}$), and complement activation (classical pathway, FDR=$6.60x10^{-15}$) as the top-enriched biological processes. Collagen-containing extracellular matrix (FDR=$5.25x10^{-15}$), blood microparticle (FDR=$1.61x10^{-13}$), and secretory granule lumen (FDR=$1.46x10^{-12}$) were the most enriched cellular processes. Glycosaminoglycan binding (FDR=$8.02x10^{-09}$), cytokine binding (FDR=$1.62x10^{-06}$), and extracellular matrix structural constituent (FDR=$2.97x10^{-06}$) as the top associated molecular functions. Functional pathway enrichment analyses using MetaCore™ (threshold: log_2foldchange=0.585 and FDR<0.05) showed that SMA was characterized by dysregulation in Plasmin Signaling (FDR=$2.93x10^{-8}$), Classical Complement Pathway (FDR=$4.32x10^{-8}$), and C3a Signaling (FDR=$6.32x10^{-6}$) related to the immune response. Collectively, these findings illustrate that acute malaria, and particularly SMA is associated with dysregulation in several complement signaling cascades.

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PLASMODIUM KNOWLESI INFECTION IS ASSOCIATED WITH ELEVATED CIRCULATING BIOMARKERS OF BRAIN INJURY AND ENDOTHELIAL ACTIVATION

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Introduction: Malaria remains a major public health concern with substantial morbidity and mortality worldwide. In Malaysia, the emergence of *Plasmodium knowlesi* has led to a surge in zoonotic malaria cases and deaths in recent years. Signs of cerebral involvement have been observed in a non-comatose, fatal case of severe *knowlesi* infection, but the potential impact of this malaria species on the brain remains underexplored.
To address this gap, we investigated circulating levels of brain injury, inflammation, and vascular biomarkers in a cohort of *knowlesi*-infected patients and controls.
Methods: Archived plasma samples from 19 patients with confirmed symptomatic *knowlesi* infection and 19 healthy, age-matched controls from Peninsular Malaysia were analysed. A total of 52 plasma biomarkers of brain injury, inflammation, and vascular activation were measured using Luminex and SIMOA assays. Wilcoxon tests were used to examine group differences, and biomarker profiles were explored through hierarchical clustering heatmap analysis.
Results: Bonferroni-corrected analyses revealed significantly elevated brain injury biomarker levels in *knowlesi*-infected patients, including S100B (p<0.0001), Tau (p=0.0007), UCH-L1 (p<0.0001), αSyn (p<0.0001), Park7 (p=0.0006), NRGN (p=0.0022), and TDP-43 (p=0.005). Compared to controls, levels were lower in the infected group for BDNF (p<0.0001), CaBD (p<0.0001), CNTN1 (p<0.0001), NCAM-1 (p<0.0001), GFAP (p=0.0013), and KLK6 (p=0.0126). Hierarchical clustering revealed distinct group profiles for circulating levels of brain injury and vascular activation biomarkers.
Conclusions: Our findings highlight for the first time the impact of *Plasmodium knowlesi* infection on the brain, with distinct alterations in cerebral injury and endothelial activation biomarker profiles compared to healthy controls. Further studies are warranted to investigate the pathophysiology and clinical significance of these altered surrogate markers, through both neuroimaging and long-term neurocognitive assessments.

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TRANSCRIPTOME PROFILE OF BLOODSTAGE *PLASMODIUM FALCIPARUM* IN CHILDREN WITH SEVERE MALARIAL ANEMIA

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About 80% of malaria-related deaths in the World Health Organization African region occur in children <5 years, who develop severe malarial anemia [SMA, hemoglobin (Hb)<6.0 g/dL] as the primary clinical manifestation of severe malaria. However, differential expression of *Plasmodium falciparum* genes in SMA vs. non-SMA remains largely unexplored. As such, we characterized the entire *P. falciparum* transcriptome in peripheral blood obtained from children (3-36 months) with non-SMA (Hb≥6.0 g/dL, n=40) and SMA (n=20) at enrollment. Next-generation sequencing was performed at a depth of >20 million high-quality mappable reads. Reads were mapped to a Kenyan isolate (*pf*KE01) reference genome using the HTSeq platform, revealing 3,155 *P. falciparum* mRNA transcripts. Expression levels of 566 genes were significantly ($p \leq 0.05$) altered in SMA (499 up- and 67 down-regulated). Principle component analysis revealed that the first two principal components explained 72.9% of the variance. Gene expression deconvolution analysis showed a higher proportion of trophozoites ($p=0.028$) and a lower proportion of ring stages ($p=0.008$) in SMA, but comparable proportions of schizont and gametocyte stages between SMA and non-SMA. Notably, the male gametocyte proportion was higher than the female gametocyte proportion across all malaria patients ($p=1.000E-6$). Weighted gene co-expression network analysis of the 566 differentially expressed genes identified five modules enriched in the following functional terms: molecular function-threonine-type endopeptidase activity ($p=3.780E-5$); biological process- proteasomal ubiquitin-independent protein catabolic process ($p=4.780E-6$); cellular component- proteosome complex ($p=1.710E-12$), and KEGG-proteasome ($p=6.060E-8$). This study provides the first transcriptional profile of blood-stage *P. falciparum* in children with SMA, highlighting the parasite's reliance on proteasome-mediated protein degradation pathways for survival within the host and suggesting potential targets for therapeutics.

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PROBING THE RELATIONSHIPS BETWEEN COAGULATION, INFLAMMATION, AND OXIDATIVE STRESS IN PLACENTAL MALARIA PATHOGENESIS

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Plasmodium falciparum infection in pregnancy contributes to poor birth outcomes via adherence of infected erythrocytes in the placenta, precipitating maternal responses that induce placental damage and dysfunction. This syndrome, termed placental malaria (PM), is characterized by placental oxidative stress and dysregulated inflammatory and coagulation responses, though the extent to which these responses are molecularly linked is unclear. Preliminary data in human PM identifies correlations between key markers of these processes, but do not prove causation. To pursue this question, a mouse model was utilized. *P. chabaudi* infection in *Tnf*$^{-/-}$ and endothelial tissue factor-deficient (*F3*$^{flox/flox}$ Tie-2^{Cre}) mice and ablation of tumor necrosis factor (Tnf) and anticoagulant treatment in mice infected with the rodent-infective parasite improved pregnancy outcomes. Relative to infected C57BL/6J (B6) controls, infected *Tnf*$^{-/-}$ mouse embryos showed two to four-fold reduced expression of protease activated receptor 2 (*F2rl1*), which links activated coagulation with inflammatory responses. Tissue factor (*F3*) expression was 50% reduced, while endothelial protein C receptor (*Procr*) transcripts increased three to five-fold, supporting the notion that coagulation and inflammation are co-regulated in PM, with reduced inflammation promoting natural anticoagulant function. With anti-coagulant drug treatment of the dam, transcripts for cytokines and chemokines (*Ifng, Tnf, Il10, Il1b,* and *Ccl2*), antioxidants (*Sod1*, *Sod2*, and *Nfe2l2*) and *F3* were significantly downregulated relative to sham-treated, infected B6 mice, whereas *Procr* transcripts were elevated. These results support the assertion that inflammation, coagulation and oxidative stress are functionally linked in PM pathogenesis, and suggest that targeting of one or more of these responses therapeutically may be broadly protective by disrupting all three pathogenic processes.

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REGULATED CELL DEATH IN PLACENTAL MALARIA: NECROPTOSIS ASSOCIATES WITH INFECTION AND INFANT BIRTH WEIGHT

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Placental damage and dysfunction are key features of malaria infection during pregnancy and associate with poor birth outcomes. Necrotic shedding of villous trophoblast is a key feature of placental malaria (PM), but the molecular basis for this outcome has not been explored. Toward this end, primary human trophoblast (PHT), villus explants and placenta from malaria-infected women and mice were used to assess markers of necroptosis by RT-qPCR, western blot, bead-based protein complex detection, and immunostaining. Receptor interacting protein kinase 3 (RIP3) and phosphorylated mixed lineage kinase domain-like protein (pMLKL), as well as RIP1/RIP3 necrosomal complexes, all indicators of activation and execution of necroptosis, were significantly higher in human placenta with PM. RIP3 levels in infected placenta inversely correlated with infant birth weight and positively correlated with placental hemozoin load. In contrast, while *in vitro* exposure of syncytialized PHT to hemozoin induced elevated transcripts for *RIPK1* and *RIPK3*, no RIP3 or pMLKL was detected in isolated cells. Furthermore, *in vitro* treatment of PHT with activators of necroptosis (tumor necrosis factor, cycloheximide and carbobenzoxy-valyl-alanyl-aspartyl-[O-methyl]-fluoromethylketone (Z-VAD)) failed to induce this cell death pathway, instead driving trophoblast apoptosis. Only treatment conditions that included the caspase inhibitor Z-VAD, which suppresses apoptosis, were able to restore PHT viability to control levels. Thus, under the *in vitro* conditions used in this study, PHT was resistant to necroptosis, yet, *in vivo*, this cell death pathway appears to play an important role in PM pathogenesis and associated poor birth outcome. Regulation of cell death pathways in the syncytiotrophoblast requires further investigation to establish critical triggers that can precipitate placental loss of function and pregnancy compromise in PM. Current work is assessing this cell death pathway in placental tissue explants which more accurately model the native physiological and architectural context of the syncytiotrophoblast.

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THE RELATIONSHIP BETWEEN PLACENTAL MALARIA INFECTION, HIV, INTESTINAL PERMEABILITY, AND INFLAMMATION IN POST-PARTUM KENYAN WOMEN

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Placental malaria, which compromises maternal health and causes poor infant health outcomes in association with *Plasmodium falciparum* infection, has long been associated with intense and damaging inflammatory responses in the maternal peripheral and placental blood. HIV infection further exacerbates these outcomes. Maternal responses to these infections lead to significant placental dysfunction, but how they impact other organ systems in pregnant women has been less well studied. The aim of this study was to determine the relationships between placental malaria (PM), HIV serostatus, markers for intestinal permeability (lipopolysaccharide (LPS), LPS-binding protein (LBP), and zonulin), and markers of inflammation (interleukin-6 (IL-6), IL-8, IL-10, Tumor Necrosis Factor (TNF), TNF receptor II (TNFRII), and interferon γ-induced protein 10 (IP-10)) in post-partum women exposed to malaria and HIV in Kenya. Clinical and diagnostic parameters (i.e., infection status, self-reported maternal health pre-partum, and infant outcomes), as well as levels of these biomarkers in the peripheral venous blood (measured by ELISA), were analyzed. LPS and zonulin levels weakly to moderately positively correlated with placental parasite load, and

zonulin was significantly elevated with PM and PM/HIV co-infection as well as self-reported recent malaria infection. LPS was elevated in women with low birth weight infants relative to normal birth weight infants, and positively correlated with markers of inflammation (TNF, IL-6, IL-8, IL-10, and IP-10). These data suggest that infection-associated inflammatory cytokine and chemokine responses coincide with induction of gut permeability in pregnant women, and may synergize to exacerbate poor maternal and infant outcomes. Future investigations to establish the causal relationships between these responses in malaria and HIV infected women could reveal potential new targets for diagnostics and therapeutic intervention.

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BIOCHEMICAL AND BIOINFORMATIC CHARACTERISATION OF UNDERSTUDIED ERYTHROCYTE SURFACE EXPRESSED HYPERVARIABLE PROTEIN FAMILIES IN PLASMODIUM FALCIPARUM

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Title: BIOCHEMICAL AND BIOINFORMATIC CHARACTERISATION OF UNDERSTUDIED ERYTHROCYTE SURFACE EXPRESSED HYPERVARIABLE PROTEIN FAMILIES IN *PLASMODIUM FALCIPARUM.* **Abstract:**Malaria, is a vector borne disease, caused by infection with Plasmodium species, responsible for approximately 608 thousand deaths and 249 million cases worldwide in 2022, with 94% cases in sub-Saharan Africa, the majority caused by infection with Plasmodium falciparum (Pf). Parasite virulence is partly caused by evasion of the human host immune system during the blood stage of infection. Sequestration and cytoadherence are characteristic Pf virulence factors, enabled by parasite-derived proteins expressed on the surface of infected erythrocytes (IEs). These proteins are associated with acquired immunity to Pf and with antigenic variability also called Variant Surface Antigens (VSAs). VSAs are translocated from blood stage Pf to be expressed on the surface of the IE membrane. STEVOR is a VSA protein family encoded 40 stevor gene copies per parasite, expressing single variant per parasite. Members of the family differ mostly in their hypervariable region, which is exposed to the circulation and possesses antigenic epitopes. The variable domain is associated with P. falciparum exposure and potentially clinical outcome. Seroreactivity and recognition to the variants are age and exposure dependent, with higher reactivity in adults and higher domain recognition in individuals with clinical disease. This study demonstrates successful expression of isolated domains of STEVOR proteins as recombinant proteins, characterizes their antigenicity and expands understanding of the Pf proteome. By developing specific in-silico model, this study characterizes STEVOR variants into clusters for the selection and subsequent development of a library of variants to explore the breath of antibody responses to the library in various Sub-Saharan African populations, characterized with different malaria endemicity levels.

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PRECARIOUS SECURITY CONTEXT AND ADAPTATIVE METHODS TO IMPLEMENT SEASONAL MALARIA CHEMOPREVENTION (SMC) IN BURKINA FASO

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Burkina Faso's Permanent Secretariat for Malaria Elimination, SP/Palu, has been organizing Seasonal Malaria Chemoprevention (SMC) campaigns since 2014 to prevent malaria illness and deaths in children under five years during the rainy season. SMC treatments are administered by community distributors (CDs) through door-to-door visits and at fixed distribution points at health facilities. The USAID-funded Integrated Health Services (IHS) project supports SMC distribution in 19 districts in 3 regions. Since 2015, the country has been contending with insecurity, leading to a surge of internally displaced persons (IDPs), many of them children. This has implemented SMC a challenge in many areas, including 16 out of 19 IHS-supported districts. In addition, during the 2023 SMC campaign, 37 of 598 health facilities in these districts were closed, and affected health and community workers relocated. To ensure that all eligible children receive treatments, the IHS project adapted its SMC interventions to facilitate the reach of eligible targets. This included introducing a "tick card" for children at IDP sites, training additional CDs, increasing the number of CD trainers, selecting an IDP to raise awareness with the public crier jointly, and verifying insecticide-treated net availability in affected districts. 16 IDP sites were encountered in IHS-supported districts during the 2023 SMC campaign. 5,957 internally displaced children were treated during cycle 0 (7 districts) and 26,944 during cycle 4 (19 districts). IDPs reached with SMC in IHS-supported districts represented 9% of IDP children who benefitted from SMC nationwide; children benefiting from SMC in HIS area represent 21% of all children treated in the country. In IDP sites, challenges encountered included difficult access to some IDP sites, inadequate communication between CDs and households, and a lack of data to estimate the number of children at IDP sites for planning and drug quantification. Coverage isn't ensured, but substantial efforts are being made to reach vulnerable and displaced populations.

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PERFORMANCE OF A NEW COMMUNITY HEALTH POLICY IN BENIN FOR DISTRIBUTING INSECTICIDE-TREATED NETS: EXPERIENCE OF 2023 MASS CAMPAIGN

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The national insecticide-treated bed net (ITN) policy in Benin is universal coverage of 1 ITN for 2 people per household. Benin recently adopted a community health policy in which paid community health workers (*Relais Communautaire*, [RC]) deliver a package of non-clinical interventions to their communities. For the 2023 campaign, RCs conducted door-to-door ITN distribution (Community-based approach [CBA]) to about 200 households (HH) as part of their routine work. We compared CBA distribution with traditional distribution (Employee-based approach [EBA]), in which employees are hired to distribute ITNs at fixed points in villages. Both approaches included training for HH enumeration, and ITN distribution using the RedRose digital platform (RCs had work smartphones, hired staff were lent smartphones). The data collected included HH location and the number of residents by age while the RedRose application generated HH ITN targets. The ITN coverage (ITNs delivered/HH ITN targets) from the six CBA and eight EBA districts was compared using a Chi-square test in R Studio. ITN coverage was significantly higher in CBA compared with EBA districts (98% [373,706/381,247] vs. 92% [436,548/473,884]; $p<0.05$) though the CBA required more distribution days than EBA (8-15 vs. 4 days, respectively). CBA HHs benefited from individual messages regarding ITN use and maintenance rather than group messaging at EBA delivery sites. CBA did not require additional labor costs for distribution as these were incorporated into RC salaries. ITN distribution coverage was higher using door-to-door CBA delivery vs traditional fixed-point EBA delivery. Additional evaluations of the two systems will help to determine future delivery modes.

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EVALUATION OF SEASONAL MALARIA CHEMOPREVENTION IMPLEMENTATION IN THE UPPER EAST REGION OF NORTHERN GHANA

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AbstractGhana adopted the WHO-recommended Seasonal Malaria Chemoprevention (SMC) in 2016 following a pilot study as a vital strategy for malaria control. This study monitored the implementation of SMC to ensure the intervention is achieving its target.We conducted a prospective longitudinal study in four administrative districts of the Upper East Region of Ghana. Children aged between 3 and 59 months were sampled and followed up one week after each cycle of SMC dosing to complete a questionnaire. SMC status was determined through the caregiver's report and child welfare cards, if available. Caregivers were asked if the participant had been treated for malaria since the last cycle. Simple and multiple logistic regressions were employed to determine associations between SMC adherence and the independent variables, with all results interpreted at a 95 % confidence level (CI).A total of 2099 participants were enrolled in this study. This study reported an average SMC coverage of 87% (CI: 86.7-89.5) per cycle with a 2% dropout after the first cycle. SMC adherence rate remained above 82% (CI: 1.4-2.5), with malaria incidence decreasing in those who received all four doses of SMC compared to partial recipients. The main reasons reported for non-adherence were the participant not available/in school (74%), caregiver refusal (14%), and forgetfulness (5%). Significant predictors of adherence were household size (aOR=1.04, 95% CI: 1.01-1.08), sleeping under bednets (aOR=1.88, 95% CI: 1.44-2.48), and indoor residual spraying (IRS) presence (aOR= 0.83, 95% CI: 0.69-1.99). Despite achieving an average coverage of 87% per cycle, it falls short of the national target of 90%. Notable reasons for drop-outs and non-adherence were, the caregiver being unavailable
during the distribution, highlighting the need for diversified approaches in SMC campaigns to enhance coverage and adherence, and maximize intervention benefits.

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LOCALIZATION IN ACTION: TRANSITIONING INDOOR RESIDUAL SPRAYING MANAGEMENT TO HOST COUNTRY GOVERNMENT IN ANKAZOABO DISTRICT, ATSIMO ANDREFANA REGION, MADAGASCAR, 2023

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Localization in action: Transitioning indoor residual spraying management to host country government in Ankazoabo District, Atsimo Andrefana Region, Madagascar, 2023

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ABSTRACT

As part of PMI's approach to promoting shifting power to local actors, PMI Evolve is committed to strengthening capacity of the national malaria program (NMP) to manage indoor residual spraying (IRS) operations while promoting gender equality, social inclusion and climate change mitigation. For the 2023 spray campaign, after a memorandum of understanding was signed between NMP and PMI Evolve to delineate the roles and responsibilities of both parties and ensure standardized procedures across different phases of IRS operations, the NMP led all stages of IRS implementation in Ankazoabo Sud district. NMP and district health services coordinated and monitored IRS implementation, trained actors, handled logistics and environmental compliance and provided trainings. PMI Evolve provided technical guidance to NMP, procured spray materials, funded expenses and supported NMP in national results dissemination. The intervention covered 20,613 structures (93.8% of structures found), and 85,385 people. With support from local, district and regional health systems, NMP successfully coordinated and planned activities, managed staffing, and social mobilizations through community meetings. Along with the district health team, NMP and PMI Evolve will prioritize IRS implementation sustainability plan and preparation for 2024.

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SEASONAL MALARIA CHEMOPREVENTION IN NORTHERN MOZAMBIQUE: A COST-EFFECTIVENESS ANALYSIS

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Malaria is endemic in Mozambique and one of the leading causes of death in children under five years old. In 2020 the country adopted the WHO-recommended Seasonal Malaria Chemoprevention (SMC) strategy, and started delivering the intervention in 2, 4 and then all 23 districts of Nampula province by 2023. The aim of this study was to estimate the cost-effectiveness of SMC in Nampula, Mozambique. Costs were analyzed from a health care provider perspective and reported in 2023 US$. Data on resource use were collected from intervention records by the Malaria Consortium, data on the beneficiaries were collected from surveys after Cycle 4, and malaria cases and deaths averted by SMC were estimated based on prevalence data obtained from available data sources, e.g., Global Burden of Disease 2019 and the Malaria Incidence Survey 2018. Incremental cost-effectiveness ratios (ICERs) were estimated by round, for the three rounds conducted between 2020 and 2023, and sensitivity analyses were conducted to test the robustness of the ICERs. We found that the total financial cost of SMC in Mozambique was US$ 8,994,226.90 (2023) for three rounds implemented between 2020 and 2023. We estimated a cost per targeted child of $5.99; a cost per household with eligible children visited by a community distributor at $7.00; a cost per child who received day 1 SPAQ at $7.37; a cost per child who received day 1 SPAQ by community distributor adhering to DOT at $7.73; and a cost per child who received 3 full-day course SPAQ at $7.49. In addition, we estimated a cost per malaria case averted at $27.20, and a cost per malaria death averted at $3,107.97. Cost-effectiveness was higher in round three, suggesting substantial economies of scale. The ICERs were robust to a variety of alternative assumptions on benefit estimates as well as discounting rate. Finally, we found that $1,670,827.55 could have been saved if the program did not include ineligible children (60-119 months old). In line with existing evidence from other African countries, SMC is cost-effective in Mozambique: SMC is a beneficial prevention strategy to improve under-five health in the country, at a relatively low-cost.

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ACCEPTABILITY OF A SCREENING AND TREATMENT STRATEGY TO THE POPULATION AS PART OF STRENGTHENING THE IMPACT OF SEASONAL MALARIA CHEMOPREVENTION IN BURKINA FASO

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Population screening and treatment strategies are now making considerable headway in the fight against malaria. In order to improve the effectiveness of seasonal malaria chemoprevention **(**SMC), which has been recommended since 2014 for the prevention of malaria in children, the SMC-RST project has been implemented in Burkina Faso. This project consists of screening and simultaneous treatment of roommates of children under SMC coverage. This study aims at determine the social, cultural and behavioural factors that facilitate or hinder adoption and adherence to the newly added antimalarial treatment. We conducted a qualitative study of 41 roommates, 5 health care workers, 5 field workers between October 2022 to January 2023 using purposive sampling in 5 rural villages in the Health District of Nanoro. Data collection combined in-depth interviews and observations of interactions between housemates and data collectors. Interviews were conduct in local language audio recorded and transcribed. Data were coded and a thematic analysis was carried out using QSR N'vivo 12 software. Our findings reveal good acceptability of this new screening and simultaneous treatment intervention for roommates of children with SMC coverage. Indeed, participants perceive an improvement in the health of children under 5 years of age under SMC coverage through the intervention. They appreciate the fact that they can be screened and treated at home, free of charge, and that they can prevent illness or treat themselves before it gets worse. Health care workers mentioned that they received fewer consultations from children under 5 since the start of the intervention, despite the fact that this is a time of high malaria rates. Overall, the study had a positive impact on the health of children under 5 and their housemates. It demonstrated a positive perception of simultaneous screening and treatment of roommates of children under SMC coverage.

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LEVERAGING PERENNIAL MALARIA CHEMOPREVENTION (PMC) PILOT IMPLEMENTATION TO PAVE THE WAY FOR PMC AND MALARIA VACCINE CO-IMPLEMENTATION IN THE DEMOCRATIC REPUBLIC OF CONGO

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The World Health Organization recommends both PMC and malaria vaccine for the prevention of Plasmodium falciparum malaria in children in areas of moderate to high malaria transmission. Although the funding sources are currently different (i.e. through the malaria program and immunization program), these two interventions are recommended to be delivered through the same EPI platform and target the same age group. Furthermore, the rollout phase involves similar steps, including the establishment of coordination mechanisms between the malaria program and EPI, the development of an optimal delivery schedule, the modification of national Health Information Management System (HIMS) tools, and the development of a community engagement plan to ensure uptake. The DRC recently introduced PMC with rollout starting in December 2023. The country has opted for a six-contact model administering Sulfadoxine-Pyrimethamine (SP) at 10 and 14 weeks of age, 6, 9, 12 and 15 months. The country has also been approved by Gavi to receive support for initial subnational malaria vaccine introduction, with a four-dose schedule at 6,7,9 and 24 months. As the service provision is integrated at the point of delivery (i.e. health facility), meaning the same healthcare provider will deliver both PMC and malaria vaccine, an approach leveraging PMC introduction to prepare for malaria vaccine rollout was taken. Hence, the coordination mechanism created to co-develop the PMC schedule was leveraged for vaccine introduction. The coordination platform includes the Malaria Program, EPI, Nutrition Program (NNP), Health Promotion and Communication Program, HMIS department, National Program to fight Cholera and Diarrheal Diseases, the National Supply Chain for Essential Drugs, and implementing partners. During PMC introduction, through an inclusive and consensual decision-making process, all normative documents and HMIS data collection and reporting tools updated to capture PMC data incorporated aspects related to malaria vaccine. These include the vaccination register, the tally sheet, the child vaccination card as well as the national DHIS2 platform.

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ACCEPTABILITY OF INTEGRATING NOVEL MALARIA PREVENTION TOOLS INTO ROUTINE IMMUNIZATION VISITS IN CAMEROON

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Cameroon is among the 11 countries with the highest malaria burden worldwide. In the past year, Cameroon began implementing the RTS,S/AS01 malaria vaccine and perennial malaria chemoprevention (PMC) for children <24 months of age. We conducted a 2-phase health facility cross-sectional study (Nov-Dec 2023 dry season and April-June 2024 rainy season) to examine vaccine acceptability and PMC uptake through routine immunization services at Cameroon Baptist Convention Health Services (CBCHS). We selected 7 CBCHS clinics in 5 regions in Cameroon with varying malaria prevalence. Caregivers of children presenting for immunizations were randomly selected for a brief survey. In the dry season phase, we surveyed 353 caregivers: median age 29 years (IQR 25-32), 96.6% female, 64% with at least secondary education; 84% reported the child slept under a mosquito net the night before, and 11% reported that the child had fever/malaria in the prior 2 weeks. Only 47% of caregivers knew of the malaria vaccine, and 91% said they would accept it for their child at CBCHS. However, 33% expressed concerns about the vaccine: fear of side effects (23%), uncertain about safety (9%), possible interaction with other vaccines (7%), uncertain of efficacy (7%), other (13%). 23% said ≥1 neighbor would not accept the vaccine. A higher proportion (76%) had heard of PMC ("Fansidar for infants"), and 50% reported that their child had received ≥1 dose. Few caregivers expressed concerns about PMC. In multivariable logistic regression, caregivers in the highest vs lowest wealth quartile were less likely to be willing to accept malaria vaccine (OR 0.08 [95% CI: 0.01-0.78]). Having fever/malaria in the prior 2 weeks was associated with not expressing concerns about the vaccine (OR 2.89 [1.10-7.57]). The rainy season survey and dried blood spot analyses are ongoing. Integration of malaria vaccine and PMC into routine immunization visits is acceptable to caregivers of young children attending CBCHS, although

continued efforts are needed to increase confidence in these interventions. Alternative strategies are needed to reach those who do not regularly attend routine immunization visits.

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IMPACT ON PREGNANCY OUTCOMES OF INTERMITTENT PREVENTIVE TREATMENT WITH SULPHADOXINE-PYRIMETHAMINE IN URBAN AND PERI-URBAN PAPUA NEW GUINEA - A RETROSPECTIVE COHORT STUDY.

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Background Intermittent preventive treatment in pregnancy with sulphadoxine-pyrimethamine (IPTp-SP) prevents low birth weight (<2,500 g) and other adverse pregnancy outcomes through malaria and non-malarial mechanisms. Malaria transmission in Papua New Guinea (PNG) is highly heterogeneous. The impact of IPTp-SP in settings with little or no malaria transmission, such as the capital Port Moresby, is unknown.
Methods A retrospective cohort study was conducted amongst HIV-negative women with a singleton pregnancy who delivered at Port Moresby General Hospital between 18 July and 21 August 2022. The impact of IPTp-SP doses on adverse birth outcomes and anaemia was assessed using logistic and linear regression models, as appropriate.
Results Of 1,140 eligible women amongst 1,228 consecutive births, 1,110 had a live birth with a documented birth weight. A total of 156 women (13.7%) did not receive any IPTp-SP, 347 women (30.4%) received one, 333 (29.2%) received two, and 304 (26.7%) received the recommended ≥3 doses of IPTp-SP. A total of 65 of 1,110 liveborn babies (5.9%) had low birth weight and there were 34 perinatal deaths (3.0%). Anaemia (haemoglobin <100 g/L) was observed in 30.6% (243/793) of women, and 14 (1.2%) had clinical malaria in pregnancy. Compared to women receiving 0-1 dose of IPTp-SP, women receiving ≥2 doses had lower odds of LBW (adjusted odds ratio [aOR] 0.50; 95% confidence interval [CI] 0.26, 0.96), preterm birth (aOR 0.58; 95%CI 0.32, 1.04), perinatal death (aOR 0.49; 95%CI 0.18, 1.38), LBW/perinatal death (aOR 0.55; 95%CI 0.27, 1.12), and anaemia (OR 0.50; 95%CI 0.36, 0.69). Women who received 2 doses versus 0-1 had 45% lower odds of LBW (aOR 0.55, 95%CI 0.27, 1.10), and a 16% further (total 61%) reduction with ≥3 doses (aOR 0.39, 95%CI 0.14, 1.05). Birth weights for women who received 2 or ≥3 doses versus 0-1 were 81 g (95%CI -3, 166) higher, and 151 g (58, 246) higher, respectively.
Conclusions Provision of IPTp-SP in a low malaria-transmission setting in PNG appears to translate into substantial health benefits, in a dose-response manner, supporting the strengthening IPTp-SP uptake across all transmission settings in PNG.

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A RANDOMIZED CONTROLLED TRIAL OF DIHYDROARTEMISININE PIPERAQUINE FOR SEASONAL MALARIA CHEMOPREVENTION IN CHILDREN UNDER 10 YEARS OLD IN KOULIKORO, MALI

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Seasonal malaria chemoprevention (SMC) with sulfadoxine-pyrimethamine-amodiaquine (SP-AQ) was recommended by the Word Health Organization (WHO) in 2012 for children under five year-old living in highly seasonal malaria transmission areas. Efficient SMC implementation has been met with challenges with treatment compliance and adverse drug effects. Also, increasing resistance markers among *Plasmodium falciparum (P.f)* to both SP and AQ in these countries require more attention when scaling up SMC for malaria elimination initiatives. This study aimed to assess the effectiveness of Dihydroartemisinine-piperaquine (DHA-PQ) as an alternative to the standard regimen for SMC while extending the age limit to up to 9 years. In 2019 and 2020, six villages within the health district of Koulikoro, Mali were cluster-randomized to receive either SP-AQ or DHA-PQ. The primary outcome was malaria incidence, defined as the presence of fever plus a positive malaria rapid diagnostic test. Cross-sectional surveys were used to determine the effect of each treatment regimen on asymptomatic malaria and anemia at the start and the end of the SMC campaign in each cohort. Adverse side effects, and compliance to treatment were assessed through monthly household survey. Over 95% of children received the first dose of SMC treatment under direct observation in both study arms, and about 71.5% (SP-AQ arm) and 82.0% (DHA-PQ arm) received 3 to 4 rounds of SMC yearly. Nausea (OR: 0.37, 95% CI: 0.29–0.47]) was the most frequent SAE reported and more frequent in the SP-AQ arm. Asymptomatic *P.f* prevalence decreased by 18% (95% CI: 0.66–1.97) in the SP-AQ arm versus 26% (95% CI: 0.57–0.94) in the DHA-PQ arm. DHA-PQ was associated with reduced the risk of malaria disease over SP-AQ by 49% (incidence risk ratio [IRR]: 0.51, 95% CI: 0.46–0.55). Our findings show that both treatment regimens are highly effective among children between under 10 years-old with more advantages for DHA-PQ such as fewer side effects, and significant reduction in both asymptomatic infection carriage and incidence. The findings are relevant to countries were SMC with SP-AQ has shown high impact on malaria burden.

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EVALUATION OF CLOTHIANIDIN INDOOR RESIDUAL SPRAYING (IRS) AND PIPERONYL BUTOXIDE (PBO) INSECTICIDE-TREATED NET (ITN) CO-DEPLOYMENT COMPARED TO PBO ITNS ONLY USING HEALTH MANAGEMENT INFORMATION SYSTEM DATA IN SIERRA LEONE, 2017-2023

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Indoor residual spraying (IRS) and pyrethroid/piperonyl-butoxide (PBO) insecticide-treated nets (ITNs) are proven malaria vector control tools; however, the impact of their combined use is not well studied. To combat increasing insecticide resistance and high malaria burden, the Sierra Leone National Malaria Control Program conducted a mass distribution of PBO ITNs between May-June 2020. Clothianidin-based (CTD) IRS was co-deployed in Bo and Bombali districts between May-June 2021 and 2022. Using an observational study design, six years of routinely reported Health Information System data (May 2017-April 2023) and 20 months of vector density data (July-April from 2020-2022) were evaluated to estimate the epidemiological and entomological impact of IRS and PBO ITN co-deployment in Bo and Bombali compared to PBO ITNs alone in two control districts, Karene and Port Loko. Negative binomial mixed effects modeling frameworks were used to independently estimate confirmed malaria case

incidence, human biting rate (HBR), and indoor resting density (IRD) over time. In both intervention groups, there were significant post-intervention declines in confirmed case incidence compared to baseline (IRS + PBO ITNs: -43.4% [95% credible interval (CI): -44.5%, -42.4%]; PBO ITNs only: -41.9% [95% CI: -43.0%, -40.8%]). However, there was no significant difference in confirmed case incidence overall between areas that received co-deployment or PBO ITNs alone (-1.5% [95% CI: -3.6%, 0.5%]). Only during the third year post-PBO ITN distribution did the co-deployment areas observe greater reductions in confirmed case incidence (2.7% [95% CI: 0.2%, 5.2%]). Co-deployment was also associated with a 10% greater reduction in HBR (IRR: 0.90, 95% CI: 0.82-0.99, p-value: 0.04) but no significant difference in IRD (IRR: 0.95, 95% CI: 0.75-1.21, p-value: 0.68). These results leveraging routine data sources could suggest that PBO ITNs may not be providing sufficient protection for their intended duration, but IRS may provide some protection.

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SUB-NATIONAL AND SUB-ANNUAL COVERAGE OF SEASONAL MALARIA CHEMOPREVENTION IN AFRICA 2012-2023

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The use of seasonal malaria chemoprevention (SMC) to prevent malaria in children has expanded rapidly since it was recommended for use by the WHO in 2012. SMC has been shown to be highly effective at reducing malaria incidence in control trials, suggesting that the rapid scale up of SMC will have important implications for the burden of malaria. To quantify this impact and adequately incorporate SMC when mapping and predicting burden, detailed information on the spatiotemporal intervention coverage of SMC will be required. SMC coverage is measured either during campaigns, where data is collected on the number of children receiving SMC drugs per distribution cycle, or in surveys where the proportion of children receiving SMC drugs is recorded. Campaign data is available for most country-years, however, coverage estimates often exceed 100%, which may indicate inaccurate estimates of target populations or that drugs were going towards non-target populations (e.g., older children). While surveys are perhaps a more robust measure of coverage, they were only conducted in a subset of administrative units and years and thus cannot provide complete Africa-wide coverage estimates. Here, we use the geographically complete campaign estimates to provide a binary (yes/no) coverage layer of where and when SMC was deployed and then estimate proportional SMC coverage from the survey results and an infilling methodology. Our results provide sub-annual and sub-national estimates and maps of SMC coverage for sub-Saharan Africa for years 2012-2023. By producing monthly results, we standardise for shifts in the timings of SMC campaigns and changes in the number of cycles distributed. Key findings of this research include (a) affirming the well documented geographical expansion of SMC and quantifying this expansion in terms of population coverage; and (b) enumerating the considerable heterogeneity in coverage levels achieved in early SMC campaigns, which became more consistent and higher by 2021.

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DEVELOPMENT OF AN ELQ-331 LOADED IMPLANT FOR LONG-TERM PROTECTION AGAINST MALARIA

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Protection of US military personnel in regions around the world endemic with malaria currently rely on the prophylactic use of oral medications that must be taken on a daily basis. This situation is not ideal and introduces the challenge of compliance under the stress of warfare and active combat. Development in other fields (HIV, contraception, and psychiatry) suggest that long-acting injectables and implantables could be developed as a long-acting preventative, providing 3 months or longer of broad protection from malaria infection and transmission. With support from the PRMRP program of the US Department of Defense, we have designed and developed a subdermal implant, loaded with the prodrug ELQ-331, using the patented Proneura® implant technology. After iterative rounds of testing, our most advanced implant design provided steady release of the active antimalarial agent, ELQ-300, in low bloodstream concentrations that were sufficient to protect mice from multiple sporozoite challenges (10,000 sporozoites/challenge) for at least 16 weeks, which was the duration for this efficacy evaluation. Full details of our successful findings, together with long-term strategies to advance this technology for the prevention of malaria infection and transmission in humans, in soldiers and civilians alike, will be presented. Note: Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s), and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense. Research was conducted under an IACUC-approved animal use protocol in an AAALAC International-accredited facility with a Public Health Services Animal Welfare Assurance and in compliance with the Animal Welfare Act and other federal statutes and regulations relating to laboratory animals.

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THREE YEARS OF MONITORING AND EVALUATING SEASONAL MALARIA CHEMOPREVENTION DELIVERY IN NEW LOCATIONS IN EAST AND SOUTHERN AFRICA: RESULTS AND LESSONS FROM THREE COUNTRIES

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The scale-up of seasonal malaria chemoprevention (SMC) in West and Central Africa has been widely considered a success story. Updated World Health Organization guidelines for malaria no longer restrict SMC to specific geographies. This provides greater flexibility which enables malaria-endemic countries to adapt chemoprevention strategies to suit local epidemiology. Since 2021, SMC has been introduced and delivered in new geographies in East and southern Africa (ESA). We present results and lessons from three years of implementing, monitoring and evaluating SMC programs using sulfadoxine-pyrimethamine plus amodiaquine(SPAQ) targeting children under five in Mozambique, South Sudan and Uganda. End-of-cycle household surveys using lot quality assurance sampling (LQAS) methods

and end-of-round surveys were conducted in the 2021-2023 rounds. Surveys were used to monitor program performance against coverage, quality, safety and community awareness, knowledge and acceptability standards. Data were analyzed to compute estimates for each performance indicator by monthly cycle and location, expressed as percentages with 95% confidence intervals (CI). SMC programs targeted a population of around 200,000 eligible children in Mozambique and Uganda in 2021, increasing to 1.6 million children in the three countries in 2023. Coverage in terms of receipt of Day 1 SPAQ by eligible children exceeded 90% in most cycles and locations, ranging from 77.2% (95% CI: 70.8-82.5) to 100.0%. Similar levels of administration of Day 1 SPAQ as directly observed therapy and receipt of the full three-day course of SPAQ were maintained. Results also indicate that SMC was generally delivered to high safety, community awareness, knowledge and acceptability standards. There were however notable within-country variations in coverage and other indicators between locations and over time. Overall, results demonstrate the feasibility and sustainability of SMC when delivered at scale in new geographies in ESA. Observed sub-national disparities in program performance have implications for instituting program improvement efforts in future SMC campaigns.

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FACTORS ASSOCIATED WITH MALARIA INCIDENCE AMONG CHILDREN RECEIVING SEASONAL MALARIA CHEMOPREVENTION IN NINE STATES IN NIGERIA.

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Seasonal malaria chemoprevention (SMC) is an intervention used to prevent malaria among vulnerable populations, particularly children under five years of age. Understanding the factors associated with malaria incidence among SMC-eligible children is essential to optimize the impact of this intervention. This study aimed to understand the relationship between caregiver's characteristics, such as gender, education, occupation, adherence to dosing schedule, reporting of adverse reactions to SMC drugs and belief in SMC effectiveness and delivery factors; community drug distributors (CD) visit to household, are associated with malaria incidence. We extracted data from 11,880 caregivers of SMC-eligible children randomly sampled during SMC end-of-round surveys conducted in November and December 2023 across nine SMC implementing states in Nigeria. A Pearson chi-square test was used to determine the association between each independent variable and children reported with malaria. Mixed-effects logistic regression was used to identify adjusted association between the independent and outcome variables. A total of 2,365 (19.91%) caregivers reported their child had a fever in the past month, of which 1,539 (53.6%) received a diagnostic test and 1,266 (21.6%) tested positive for malaria. The odds of testing positive for malaria were lower in caregivers who adhered to dosing schedule (aOR = 0.667, 95% CI = 0.53 - 0.85 p<0.001), believed SMC is effective (aOR = 0.484, 95% CI = 0.36-0.64 p<0.001) and were employed in skilled manual work (aOR = 0.602, 95% CI =0.45-0.79 p<0.001) and sales (aOR = 0.535, 95% CI = 0.44-0.64 p<0.001). Individuals who experienced adverse reactions related to SMC drugs were almost three times more likely to be malaria positive than those who did not (aOR = 2.606, 95% CI =2.066-3.286 p<0.001). The study concludes that adherence to dosing schedule of SMC drug and caregiver's belief in SMC effectiveness are associated with reduced malaria incidence in SMC eligible children. Further research is required to better understand the causal pathway of increased malaria incidence among children reporting adverse reaction to SMC drugs.

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CLUSTER RANDOMIZED CONTROLLED TRIAL TO ASSESS THE SAFETY AND TOLERABILITY OF FIVE MONTHS' REPEATED DOSES OF DIHYDROARTEMISININ PIPERAQUINE AND SULFADOXINE PYRIMETHAMINE PLUS AMODIAQUINE WHEN USED FOR SEASONAL MALARIA CHEMOPREVENTION IN CHILDREN UNDER FIVE IN UGANDA.

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Seasonal malaria chemoprevention (SMC) with sulfadoxine pyrimethamine plus amodiaquine (SPAQ) is recommended for children at risk of severe malaria living in areas of seasonal transmission. Previous studies have demonstrated the safety of monthly SPAQ courses for up to four SMC cycles annually. However, the safety of additional cycles remains unexplored. A potential alternative SMC drug regimen is dihydroartemisinin piperaquine (DP) but there is a paucity of data on its safety when administered monthly for SMC. This study evaluated the safety and tolerability of five monthly cycles of SMC with SPAQ versus DP in children under five in Karamoja, Uganda. A three-arm open-label superiority and non-inferiority cluster-randomized controlled trial (cRCT) was conducted in 2022 as part of a hybrid effectiveness-implementation study. A total of 3,749 children were randomized to receive SMC with either SPAQ (1,698) or DP (1,667), while 384 acted as control and relied on standard malaria care over the five-month high-transmission period. Adverse events following SPAQ or DP administration were collected from caregivers during end-of-cycle surveys. A total of 115 (7.0%) children in the SPAQ arm and 168 (10.3%) in the DP arm experienced at least one adverse event following administration of the medicines over the five monthly cycles (p=0.001). Across both arms, the most reported adverse events were fever (33.1% of reported events in the SPAQ arm and 31.5% in the DP arm), vomiting (26.9% in the SPAQ arm and 23.8% in the DP arm) and headache (15.7% in the SPAQ arm and 17.9% in the DP arm). However, reports of nausea (p<0.001), vomiting (p<0.001) and skin rashes (p=0.02) were significantly higher in the DP arm than in the SPAQ arm. Adverse events occurred more frequently in the earlier cycles across both arms. Less commonly reported adverse events across both arms included abdominal pain, cough and dizziness. No serious or fatal adverse events were reported in either arm. The administration of DP and SPAQ for SMC over five cycles were found to be safe and well-tolerated among children in Karamoja, Uganda.

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DIRECT EVIDENCE OF FACTORS ASSOCIATED WITH SEASONAL VARIATIONS IN THE USE OF INSECTICIDE-TREATED NETS IN NIGERIA

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Despite the substantial contribution of insecticide-treated nets (ITNs) to malaria reduction in Africa, encouraging their consistent use remains challenging. Understanding underlying factors is important for developing strategies to improve ITN use. Several studies have shown perceptions related to heat and mosquito abundance are important determinants of ITN use in populations with access, but there has been limited direct evidence linking seasonal climatic variations with ITN use. We conducted repeated household surveys, in different seasons in Ondo State of Nigeria, to investigate seasonal changes in ITN use rates and the potential determinant factors.Five household surveys were conducted, using similar study design and sample sizes, before an ITN distribution campaign in December 2021 and post-campaign in April 2022, and June, August and October 2023.

A multi-stage stratified cluster sampling design was used to select 832 households in 52 wards during each survey. Household interviews were conducted using a digital questionnaire. Satellite-driven data on rainfall estimates and temperature were analysed in relation to ITN use rates overall and among populations with access. Data on household characteristics, types of available nets, and age and gender of household members were also collected and used in the analysis. The study showed significant seasonal variations in ITN use among populations with access. Reasons for non-use of available nets included feeling hot, perception of mosquito abundance, climate, urban-rural residence, age and condition of nets, and availability of extra nets in the households. The study confirmed the crucial effects of seasonality and climatic factors, especially rainfall and temperature patterns in determining ITN use rates, with increases in the rainy season and reductions in the hot, dry season. ITN use among populations with access is determined by interactions of multiple factors that should be considered when designing behavioral change communication strategies, as well as timing of distribution campaigns, promotional messages, and surveys to evaluate outcomes of the intervention.

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PROMOTING THE USE OF THE INTERCEPTOR DUAL AI G2 INSECTICIDE TREATED NETS TO REDUCE MALARIA INFECTIONS THROUGH FOCUSED SOCIAL BEHAVIOR CHANGE CAMPAIGNS IN NAMAYINGO DISTRICT, UGANDA.

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PACE, with support from BASF, is running the hang-up, keep-up campaign to promote Interceptor G2 dual Active Ingredient Insecticide Treated Nets (ITNs) against malaria in Namayingo district, Uganda. This follows the Ministry of Health's distribution of IG2 ITNs to 9.4 million households across 18 districts, via a universal net coverage campaign. A post-distribution Social and Behavioral Change (SBC) campaign in Namayingo Town Council and Buswale sub-counties aims to enhance net use to reduce malaria infections in district. A baseline assessment was conducted in to provide benchmarks against which changes in knowledge, attitude and practices (KABs) regarding net use would be measured. A cross-sectional study design employed quantitative methods of data collection. 8,238 household were targeted to participate in the baseline whether they received nets or not. We administered questionnaires to 8,195 household in 63 villages to identify KABs that impact the utilization of nets. Analysis conducted using STATA version 14. Findings revealed that 94% of households, confirmed that they had received IG2 Dual AI ITNs; while 6,158 (80%) did not hang or use the newly distributed nets one month post ITN distribution. Among those who did not use/hang up the nets, cited reasons that included concerns about the smell or irritation caused by the net 497 (32%), the perception that it was too hot 399 (26%), and the intention to hang it later (24%) among others. 85.3% were aware of the correct net hanging and usage practices and believed that ITNs were effective in protecting them against mosquito bites. SBC and monitoring of net use should be implemented during, and post universal ITN distribution campaign foster to positive knowledge, attitude and practices regarding net use for malaria prevention.

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CLOSING THE ACCESS-USE GAP: INVESTIGATING INFLUENCERS OF BEHAVIOR AROUND INSECTICIDE-TREATED NET USE IN NIGERIA AND UGANDA

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Over the last two decades insecticide-treated nets (ITNs) have been distributed as a method to prevent malaria and were responsible for 68% of the cases averted between 2000 and 2015. However, the consistent use of ITNs among communities is low, even in areas where access is high, which limits the impact of this intervention and poses a barrier to the control of the disease. To date information on barriers to net use have been collected as part of routine surveys which provide limited insights into the motivations that influence human behaviour. This formative phase - conducted between April and August 2024 - uses a mixed-method approach to explore factors that influence ITN use in areas of Nigeria and Uganda where access to ITNs is high and use rates are low. The findings from this formative research will be used to inform co-created interventions with communities that encourage ITN use. A pilot study will also be conducted to test the feasibility and acceptability of these interventions. This research will guide the design and deployment of appropriate behavioural change intervention strategies to improve ITN use in similar contexts across Africa. We are conducting a desk review of published literature and analysis of existing survey data to inform tools for primary data collection. Qualitive research, using purposive sampling, will then be carried out to investigate the factors identified in more depth. We will conduct focus group discussions with target communities, and local and national stakeholders are invited to participate in in-depth interviews. Direct observations will also be carried out in communities to observe the user experience with ITNs. Results will be analysed using a behavioural science lens to identify which factors can be targeted with behaviour change interventions. We present key findings on the barriers and enablers to ITN use in communities where access rates are already high. Our results provide a comparison across two countries, and offer evidence-based recommendations to enhance ITN uptake.

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PREDICTORS OF COHORT RETENTION AMONG ELIGIBLE CHILDREN RECEIVING SEASONAL MALARIA CHEMOPREVENTION IN NINE STATES IN NIGERIA

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Seasonal malaria chemoprevention (SMC) with sulfadoxine/pyrimethamine plus amodiaquine (SPAQ) has shown high protective efficacy against malaria in children under five during the high transmission season. Adherence to a full three-day course of SPAQ over four or five cycles (cohort retention) is required to confer adequate protection. This study measured cohort retention and identified child, caregiver and health systems-related predictors of retention among eligible children. Data were extracted from SMC end-of-round (EoR) survey conducted between November and December 2023 in nine states in Nigeria. The EoR survey randomly sampled 11,880 primary caregivers of eligible children aged 3-59 months. Mixed effects multivariable logistic regression models were fitted to explore the child, caregiver and health systems factors associated with cohort retention. The results indicate that 82.9% (95% CI: 82.2-83.6) of children received full three-day course of SPAQ in all cycles. We observed lower odds of retention among children with history of fever (aOR: 0.82, 95% CI:0.70-0.95) or adverse drug reactions (aOR: 0.76, 95% CI: 0.64-0.92), children whose primary caregivers were not responsible for

child medical decisions (aOR:0.78, 95% CI:0.64-0.94), children whose caregiver had post-secondary education (aOR: 0.71, 95% CI:0.57-0.88). Conversely, higher odds were observed as child age increased (p<0.01), where caregivers were knowledgeable about SMC eligibility (aOR: 1.59, 95% CI:1.21-1.89), in households that were visited by lead mothers (aOR: 2.39, 95% CI:2.09-2.73), when SPAQ was administered under direction supervision by drug distributors (aOR: 1.47, 95% CI:1.21-1.80), and when drug distributors were known to caregivers (aOR: 1.59, 95% CI:1.41-1.80). Understanding the factors that influence SMC cohort retention can help programmes design appropriate interventions to improve cohort retention throughout the SMC round. Further research may be required to understand the negative association between retention and caregivers' education status.

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A REVISED TOOLKIT TO SUPPORT PLANNING, IMPLEMENTATION AND MONITORING OF CONTINUOUS DISTRIBUTION OF INSECTICIDE TREATED NETS

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Despite the deployment of more than 1.3 billion insecticide-treated nets (ITNs) in the past five years, ITN access and use remains below the levels observed in 2017. Approximately half of countries that distribute ITNs expect no more than an average of two years of useful life from their nets and some national malaria programmes (NMPs) have considered shifting their ITN mass campaign cycle from every three to every two years. However, recent modelling for ITN distribution strategies has shown that full scale deployment of continuous distribution (CD) can provide better ITN access for 20% fewer ITNs compared to 3-year mass campaigns, assuming ITNs have a median useful life of at least 2.5 years. Implementation experience from Ghana, Madagascar, Senegal and Tanzania at different subnational scales shows that ITN CD maintains access and is operationally feasible and cost-effective. However, widespread uptake of CD strategies (like community- and school-based distribution) has not occurred, and best practice guidance has not been systematically updated since 2017. The CD working group of the Alliance for Malaria Prevention has revised the CD Toolkit (available at www.continousdistribution.org) in 2024 to provide new step-by-step guidance, tools and editable resources necessary to support planning, implementation and monitoring of CD. New guidance on ITN quantification for CD channels is presented alongside country success stories and lessons learned. The online toolkit has been developed with NMPs and technical partners implementing and supporting CD and is designed to remove barriers to initiating CD as part of a national vector control strategy. Website and material use will be monitored during 2025, with elements adapted based on user feedback. Expanding CD offers opportunities to improve and maintain ITN access. NMPs are encouraged to align with WHO Malaria Guidelines and donor recommendations, review operational and financial data, and consider increasing CD to complement or replace ITN mass campaign distribution, using resources available through the CD Toolkit to support planning and implementation.

7302

IMPACT OF SEASONAL MALARIA CHEMOPREVENTION ON THE INCIDENCE OF MALARIA AMONG CHILDREN UNDER THE AGE OF FIVE YEARS IN LAU LOCAL GOVERNMENT AREA OF TARABA STATE, NIGERIA

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Malaria continues to pose a significant threat to public health, particularly among children under the age of five, in many parts of sub-Saharan Africa, including Nigeria. Lau Local Government Area (LGA), situated at the bank of river Benue in Taraba State, Nigeria, faces significant challenges in combating malaria due to factors such as high transmission rates, limited access to healthcare services, and socio-economic disparities. With financial support from The Global Fund to fight AIDS, TB and Malaria, Management Sciences for Health implemented Seasonal Malaria Chemoprevention (SMC) across nine LGAs within Taraba State, including Lau. This paper explores the impact of the SMC campaign on the incidence of malaria among children under the age of five in Lau LGA of Taraba State. To examine the impact of the SMC campaign on malaria incidence among children under five years old, we analyzed the malaria test positivity rates (TPR) among this age group before the initiation of SMC (January 2020 to June 2021) and during the period of SMC implementation (July 2021 to November 2023) across all supported public health facilities in the LGA. The data used for this assessment was obtained from DHIS2, and data analysis was conducted using Statistical Package for Social Sciences (SPSS). The TPR ranges from 64.82% to 83.84% prior to SMC and from 34.98% to 62.78% two months after the start of SMC. The average TPR before SMC initiation stood at 74.74%, whereas it decreased to 51.25% two months after the commencement of SMC. Analysis of variance revealed a significant difference ($p < 0.05$) in the mean TPRs before the initiation of SMC and two months thereafter. These results suggest that the SMC campaign has significantly reduced malaria incidence among children under five in Lau LGA from an average of 74.74% to 51.25%. The decrease in malaria TPR observed among children at health facilities indicates the effectiveness of SMC in preventing and controlling malaria within the target population.

7303

THE IMPACT OF THREE ADDITIONAL DOSES OF PMC ADMINISTERED THROUGH EPI SCHEDULES ON VITAMIN A SUPPLEMENT UPTAKE IN CAMEROON

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Vitamin A is crucial for child development and deficiency is associated with increased morbidity and mortality, particularly from infectious diseases. In Cameroon, four vitamin A doses (6-11 months: 100000 IU, 12-59 months: 200000 IU) are recommended as part of the expanded program on immunization (EPI) but attendance is typically poor, especially for the three doses in the second year of life. As part of one visit, Cameroon's national malaria programme (NMP) recommends administering sulfadoxine-pyrimethamine (SP) for perennial malaria chemoprevention (PMC) which may provide additional attendance incentive. This study evaluates the

impact on vitamin A coverage of three additional doses of SP to the PMC schedule, during EPI visits that coincide with vitamin A. Data come from a prospective cohort of children under 2 years of age in Cameroon beginning July 2023. The study took place at two sites, Soa, the intervention area with up to eight PMC doses co-implemented with four vitamin A contacts, and Mbankomo, the control with up to five PMC doses co-implemented with one vitamin A contact. Beginning May 2023, all children residing in the study areas with parental consent were enumerated, and any EPI visits recorded using their EPI book. All subsequent PMC and/or EPI visits for participants were recorded by field workers based in health facilities using an assigned ID in the EPI book or through a name look-up form. Generalized estimating equations (GEE) were used to estimate a marginal model for the effect of intervention area and time on the proportion of children who received at least one dose of vitamin A supplementation. Preliminary results from the recruitment cross-sectional survey found 10.1% (397/3921) of children under 2 years received initial vitamin A supplements as indicated by their EPI books. In terms of the first vitamin A visit only, the contact point consistent between the two sites, coverage was 10.3% and 9.6% (p>0.05) in Soa and Mbankomo, respectively. Findings from this study will provide valuable insights for policymakers and NMPs into the impact of integrating additional doses of SP into the EPI schedule on improved vitamin A uptake.

7304

DOES MOSQUITO NET USE CONTRIBUTE TO MALARIA PREVENTION: AN ANALYSIS OF LOT QUALITY ASSURANCE SURVEY AND ROUTINE HEALTH FACILITY DATA FOR CONFIRMED MALARIA CASES

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Mosquito net use is generally recognized as an effective protection against malaria infection globally (WHO 2017). This abstract compares net coverage, condition, use, and malaria test positivity rates (TPR) in five high-burden regions of Uganda: Acholi, Busoga, Karamoja, Lango, and West Nile. We analyzed Lot Quality Assurance Survey (LQAS) August 2022 - September 2023 household-level data of 7,224 respondents with 5,311 observed household nets and malaria TPR from 3,420,496 fever cases and 2,066,367 confirmed malaria cases for October 2022 - September 2023 health facility level DHIS2 data extract to understand the relationship between net use and malaria. Data was analyzed for key mosquito net coverage and use indicators: Proportion of households with at least one ITN for every two people; proportion of the population that slept last night under an ITN, correlated to conditions of ITN observed and annual regional malaria TPR from routine DHIS2 data. On average, nearly 81% (5,846) of households had a net, and at least 49% (3,541) of the households had a net for every two people; 74% (5,346) of the respondents had slept under a net the night before the survey and 5,311 mosquito nets were observed with 57% (3,049) in good condition and appropriately hung over beds. Analyzed DHIS2 data showed that higher malaria TPR was found in regions with lower observed nets in good condition and appropriately hung (62% TPR compared to 40% in Acholi and 52% TPR compared to 45% in West Nile, respectively) while lower TPR was found in regions with nets in good condition and appropriately hung (47% TPR compared to 69% in Busoga, 44% TPR compared to 51% in Karamoja, 62% TPR compared to 77% in Lango, respectively). Regardless of the proportion of availability of at least one ITN for every two people, high TPR was observed in the age groups 29 days-4 years and 10-19 years and lower TPR among 0-28 days and 20+ years of both sexes. Low malaria TPR may be associated with proper net maintenance, hanging and use as observed during the survey. Ensuring people at risk of malaria infection repair damaged nets, correctly and consistently use the nets can be an effective strategy for malaria prevention.

7305

LEVERAGING BEHAVIORAL SCIENCE FOR ENHANCED MALARIA PREVENTION IN UGANDA: HOUSEHOLD ACTION AGAINST MALARIA

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Malaria is the leading cause of illness and death in Uganda, despite being preventable and treatable. The PMI Uganda Malaria Reduction Activity (PMI MRA) builds community and household capacities to prevent malaria through the household action against malaria (HAAM) approach, adapted from the Ministry of Health's Mass Action Against Malaria. HAAM empowers communities to own malaria prevention at household level to achieve malaria smart home status: malaria-free for six consecutive months. Adhering to behavioural science principles—empowerment, inclusivity, community involvement, feedback loops, and collaboration—underpin HAAM success. HAAM is implemented in 12 high malaria-burden districts through health facility staff who line-list malaria cases from HMIS registers, map villages with >5 cases (high burden villages) and cluster households for all-village inclusion. Households are assessed for malaria transmission drivers using the HAAM assessment tool and action plans are co-created with household members to address them. Monthly follow up visits are conducted to monitor progress. During implementation, household malaria champions reinforce accountability and follow up malaria response plans. District/village health teams and other stakeholders are engaged to ensure community involvement. From October 2022-February 2024, 57,677 households were assessed, clustered and sensitized using the HAAM checklist. Results from HAAM assessment data show a reduction in household malaria episodes from an average of 61% to 32% from visit 1 to visits 3 or 4 in this time period. Households clearing breeding spots increased from 55% to 96%, while consistent net use among pregnant women increased from 85% to 100%. Households planting locally available mosquito repellents rose from 23% to 81%. By co-creating prevention actions with households based on locally available resources and strategies and, and clustering households for follow-up, HAAM fosters and local empowerment and community ownership for malaria prevention.

7306

CONTRIBUTION OF SOCIAL BEHAVIOR CHANGE THROUGH COMMUNITY HEALTH WORKERS AND LOCAL LEADERS IN REDUCING MALARIA INCIDENCE IN KAYONZA DISTRICT, EASTERN PROVINCE OF RWANDA

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Malaria remains a major public health problem in Rwanda and is considered among the leading cause of morbidity and mortality. The National Malaria Strategic plan objective five states that by 2024, 85% of the population at risk will have correct and consistent practices and behaviors towards malaria control interventions. In 2019, Kayonza district ranked in the top 10 with the highest malaria incidences nationwide requiring an integrated approach of malaria control. SFH in partnership with the Ministry of Health started implementation of social behavior change communication project complementing other existing interventions. Inclusive SBC intervention through different channels like community education, peer education and community outreach implemented by community health workers and local leaders at community level which yielded a significant reduction in malaria

incidence. These interventions are spearheaded by the theme "Zero Malaria Starts with Me" promoting community ownership in malaria prevention. We conducted a desk review to assess the contribution of SBC using Ministry of health data and reports from Health Management information System (HMIS) and score cards from 2019 to 2023. Data analysis showed that social behavior change complementing existing interventions has contributed to the significant reduction of malaria incidences in Kayonza district. Results show that malaria incidences reduced from 452 per 1000 population (total malaria cases =190,464) in 2019 to 12 (total malaria cases =5,277) in 2023. Social Behavior Change in Kayonza was proven to be a successful intervention towards adapting proper behaviors like use of Bed nets (LLINs), accepting Indoor Residual Spraying (IRS), early treatment seeking behavior and integrated vector control management (IVM) that yielded a substantial reduction in malaria incidences and thus contributing towards the goal of malaria elimination in Rwanda.

7307

TRENDS AND LEVELS OF MALARIA INCIDENCE DURING INDOOR RESIDUAL SPRAYING IN HOMABAY COUNTY, 2019-2023

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Malaria in Kenya accounts for 16% of all outpatient visits. Vector control interventions are implemented according to malaria risk stratification. Homa Bay County (HBC) is in a malaria endemic zone that has implemented indoor residual spraying (IRS) from 2018-2023 to supplement long-lasting insecticide nets (LLINs), resulting in high coverage rates over the 85% recommended by WHO for community effectiveness. We describe the trends of malaria incidence using reported program data during IRS intervention. This was a cross-sectional retrospective review of data from HBC extracted from the Kenya Health Information Systems (KHIS) and National Malaria Control Program activity reports from 2019-2023. Number of all suspected malaria cases and those tested were used to calculate test positivity rate (TPR) and malaria incidence was calculated as cases per 1000 population at risk. Geospatial maps were developed in QGIS to visualize incidence patterns over time. On average the IRS coverage was 93.8% and 95.8% of population targeted were protected. While there was an initial decline in incidence from 197.3 in 2018 to 106.7 in 2020, there was a gradual increase during the IRS period, up to 359.6 in 2023. TPR increased from 21.0% in 2019 to 42.2% in 2023. Number of malaria cases detected in the community increased from 16,690 in 2021 to 80,595 in 2023. The malaria incidence risk maps showed a gradual increase of malaria transmission intensity from 2019 that covered the whole county by 2023. The initial decline in malaria incidence may be attributable to IRS intervention. Due to implementation of community case management, the number of malaria cases detected in the community increased, contributing to increased incidence despite IRS. Comparing malaria incidence over time has limitations given its dependence on data completeness and quality. Reporting in KHIS have improved over time, resulting in what appears to be increased incidence. The malaria program data demonstrate that HBC is still receptive to malaria transmission and close monitoring of malaria data and insecticide resistance are critical in the period after IRS withdrawal.

7308

ENHANCING MALARIA DIAGNOSIS, TREATMENT, AND DATA MANAGEMENT THROUGH TRAINING AND SUPERVISION OF HEALTHCARE PERSONNEL IN SIX NORTHERN PROVINCES OF ANGOLA, 2018-2023

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Malaria remains a health challenge in Angola, with high incidence rates (267/1000 cases in 2023) and associated mortality. Effective diagnosis, treatment, and accurate data recording are key in malaria control efforts. Since 2018, a comprehensive training and supervision program was implemented targeting health workers (HWs) in 6 hyper-endemic provinces in Angola, with support from PMI. The program emphasized parasitological confirmation over clinical diagnosis, adhering to standardized treatment protocols, and improved data recording practices. In total 11,704 HWs were trained in-person or via the KASSAI online platform on rapid malaria diagnostics, 9,032 HWs were supervised on malaria diagnostics and 1,021 data verification visits to health units (HUs) were conducted. To assess the impact of this program, we used routine surveillance data from 2018 to 2023 and compared malaria diagnostic practices against 4 non-PMI provinces with high malaria burden. Results shows the percentage of clinically diagnosed cases declined from 16% to 2% in 6-PMI focus provinces from 2018 to 2023, as compared to no change (28%) in 4 non-PMI-focus provinces. Malaria incidence rates increased across all PMI-focus provinces: 207/1000 in 2018 and 467/1000 in 2023, likely due to improved case detection rather than a surge in actual cases, indicative of enhanced diagnostic practices, increased reporting rates (70.0% in 2018 and 92.0% in 2023) and improved data quality (quality scores rose from 84.3% in 2021 to 91.5% in 2023). The case fatality rate decreased from 0.28% in 2018 to 0.08% in 2023, suggesting improved treatment outcomes. The use of diagnostic tests over clinical diagnosis signifies a shift towards evidence-based practices, while improved data recording enhances the reliability of surveillance data for decision-making. The use of online platforms like KASSAI enhanced the scalability and accessibility of training initiatives. These findings underscore the importance of continuous training via multiple platforms and of target supervisions, in strengthening healthcare systems and combating malaria in resource-limited settings like Angola.

7309

BUILDING A LOCAL INSTITUTION WITH GLOBAL REACH: INVESTING IN AFRICA UNIVERSITY FOR ENTOMOLOGICAL SURVEILLANCE TO FIGHT MALARIA IN ZIMBABWE

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Localization is a commitment to shift program ownership and leadership to local institutions with the capability and credibility to drive positive change in their own countries and communities. We describe our multi-year journey to strengthen capacity to achieve rigorous entomological surveillance through Africa University in Zimbabwe. In 2017, the U.S. President's Malaria Initiative (PMI) began a stepwise, iterative process with Africa University, the National Malaria Program (NMP), and key partners to design activities, set performance milestones, and collaborate during implementation and monitoring. The key prerequisite was demonstrable success in conducting entomological surveillance as a sub-awardee under a global contract. In 2021, PMI awarded Africa University a three-year performance-based, fixed-amount cooperative agreement (total $1,650,000 USD). Concurrent

capacity strengthening included construction of an insectary and provision of equipment to the existing molecular laboratory. Existing and new cadres of field and laboratory staff received training. Entomological samples analyzed annually averaged 1,827 (range: 858-3,407) and increased to 8,872 post-localization (range: 6,453-11,291). Live reference colony mosquitoes supplied annually to the Health Ministry increased from a mean of 20,665 to 47,525. Direct upload of entomological data into the national database was established for program decision-making. Africa University also became a member of the Malaria Vector Control Subcommittee which provides technical support to NMP. Cost savings and capacity have permitted the geographical expansion of entomological and insecticide resistance monitoring. Building off this investment, Africa University has established a new malaria institute and entomological center of excellence with a new applied science curriculum for faculty and graduate student research, and student internships. Localization with Africa University is a model for improved local ownership and performance, cost savings, public-private partnership, impact, and sustainability of PMI investment.

7310

USING MALARIA ROUTINE DATA QUALITY AUDITS TO IMPROVE MALARIA DATA QUALITY IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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In the Democratic Republic of the Congo, malaria data are collected in DHIS2, the national platform for the collection and analysis of health information data. Despite continuous efforts by the National Malaria Control Program (NMCP) and its partners, data quality issues persist. To better understand root causes of this poor data quality, we conducted malaria routine data quality audits (mRDQA) in 61 health facilities in Haut Katanga, Kasai Central, Kasai Oriental, South Kivu, and Tanganyika provinces in 2023. Sites were selected based on accessibility and historically low performance on data quality metrics. The mRDQA is an open-source digital tool accompanied by a District Health Information System 2 (DHIS2) package used to collect information on data quality for routine malaria reporting from health facilities as part of routine supervision. mRDQA results revealed that 84 percent of sites had complete data in their reports, 66 percent did not use the standard national registers, and 67 percent did not have congruent data between the primary source documents and aggregate monthly reports for the period audited. We found that only 11 percent of health facility providers had received training on data collection and analysis in the past two years, and 77 percent of providers had poor understanding of malaria data elements and indicators used in DHIS2. Based on the mRDQA results, NMCP and partners identified and corrected 6,031 instances where cases were misclassified as malaria deaths and supported more than 278 providers in data analysis. The mRDQA revealed that inaccurate compilation from source documents, use of non-standard data collection tools, and lack of training contributed to observed data quality issues. Future efforts should focus on providing standard data collection tools to all 179 supported health zones, organizing targeted training in malaria surveillance, monitoring, and evaluation to improve data quality for informed decision making.

7311

INSECTICIDE RESISTANCE DATA TO INFORM INTERVENTION SELECTION AND TARGETING IN UGANDA

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Uganda represents 5.1% of the global malaria burden as per the World Malaria Report (2023). Long Lasting Insecticide Nets (LLINs) and indoor residual spraying (IRS) are core interventions utilized to disrupt malaria transmission and reduce illness in at-risk populations. Although existing strategies led to a decline in incidence by 48% between 2000 and 2015, incidence has plateaued to between 200 to 300 cases per 1,000 population alongside growing resistance to insecticides used in vector control interventions. Routine entomological surveillance is implemented in Uganda and includes insecticide testing for the presence, intensity, and mechanism of resistance to the common insecticide classes used for LLINs and IRS. Despite growing resistance to insecticides data collected at sentinel sites is underutilized. Understanding where resistance has developed helps the National Malaria Control Division (NMCD) to optimize procurement and distribute more effective nets where they will have most impact. To improve data-driven decision making, CHAI (Clinton Health Access Initiative) supports NMCD to collate, analyze, and interpret insecticide resistance data to tailor vector control interventions. The 2017 analysis identified increasing resistance to pyrethroids and was used to advocate for procurement of 25% Piperonyl-butoxide (PBO) nets for the 2017/2018 mass LLIN campaign. Analysis of 2021 data showed in 7/11 sites that submitted data, PBO did not restore susceptibility to pyrethroids. In 2022 data, 14/17 sentinel sites across the country had confirmed resistance to pyrethroids. These analyses informed a shift in procurement toward more dual active ingredient (AI) nets in the 2023 mass campaign from 0-19%, though due to cost implications most nets were PBO (71%) and the remaining 10% pyrethroid-only. Annual analysis and advocacy informed the latest global fund application where the country requested to increase the proportion of dual AI nets procured to 50% due to growing resistance. Routine use of entomological surveillance data is vital to ensure that resources are used to procure and deploy the most effective vector control tools.

7312

DECADAL TRENDS IN UNDER-5 MALARIA MORTALITY; INSIGHTS FROM AN ENDEMIC HDSS SITE IN RURAL WESTERN KENYA

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WRAIR AFRICA, KISUMU, Kenya

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causes, 878 were attributed to malaria (10.6%). Malaria mortality rates showed a decline from 180 deaths per 100,000 population in 2013 to 42 deaths per 100,000 population by the conclusion of 2023. Peaks in malaria mortality were observed in 2014 (337 per 100,000) and 2017 (203 per 100,000 population).

Conclusion: The real-world effectiveness of the various malaria interventions, as well as its impact on under-5 mortality in endemic settings, remains to be fully understood. As these interventions are rolled out in regions where malaria burden is high, it is essential to monitor its performance in reducing malaria-related deaths among children under five years old.

7313

NAVIGATING VILLAGE BOUNDARIES: A COMPARATIVE EXPLORATION OF THREE MAPPING TECHNIQUES

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Clear, well-defined village boundaries are vital for community-based intervention trials, vector control studies and malaria surveillance. They facilitate spatial analysis, capturing population denominators for more precise monitoring of infection transmission dynamics. Existing boundary mapping tools may not capture variations in land use or building characteristics (commercial vs residential). We examine three distinct techniques for mapping village-level spatial boundaries: i) village walk-around - traversing the entire village perimeter with a GPS receiver; ii) structure mapping- identifying and recording GPS coordinates for all physical structures in a village; and iii) centroid mapping - using a local expert to map perceived “centers” of the village and utilizing geospatial techniques to calculate centroids and Voronoi polygons to generate village boundaries. We evaluated practicality (ease of use, flexibility, precision, and scalability) and cost-effectiveness (operational cost analysis, time efficiency in data collection and processing) in various operational contexts, providing a detailed comparison for diverse field settings. Each technique presents unique advantages, challenges, and uncertainties, with practicality varying based on mapping objectives and study area characteristics. Structure mapping generates a fine-grained resolution dataset but is labor-intensive and at $112 per village is 5.3 times costlier than walk-around and centroid techniques. Boundary walk-around can be done relatively quickly (2 villages per day), but precision relies heavily on local area knowledge. Centroid mapping is an easy to deploy technique but may be limited by geographical orientation and estimation skills of local experts. Terrain complexity, population density, budget, and data processing timelines are key considerations in technique selection. Our findings offer valuable insights into technical aspects of village-level boundary mapping and provide a framework for selecting the most appropriate mapping method, optimizing spatial data collection and use.

7314

ASSESSING THE TRENDS AND CONCORDANCE OF MALARIA PREVALENCE BETWEEN PREGNANT WOMEN ATTENDING ANTENATAL CLINICS AND ASYMPTOMATIC INDIVIDUALS IN THREE REGIONS OF MAINLAND TANZANIA

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Tracking the burden and transmission of malaria using reliable data is crucial for designing and implementing effective control strategies and accurately monitoring the impacts of interventions and progress towards the elimination targets. Surveillance of malaria in Tanzania is based on different types of data including those obtained from screening of pregnant women at their first antenatal care clinic (ANC) visits since 2014. ANC malaria prevalence is highly correlated to prevalence in under-fives but the correlation with other age groups has not been established. This study assessed the trends and concordance of malaria prevalence between asymptomatic individuals of all age groups from community cross-sectional surveys (CSS) and pregnant women attending ANC clinics in three regions of Kigoma, Ruvuma and Tanga in Mainland Tanzania from 2021 to 2023. In both CSS and ANC clinics (from 2021 to 2023), testing for malaria was done using malaria rapid diagnostic tests (RDTs) and covered 8,096 asymptomatic individuals in CSS and 819,103 women. Malaria prevalence in CSS was 32.7% (95% confidence interval (CI), 31.7-33.7) in 2021, 36.8% (95% CI, 35.8-37.9) in 2022 and 30.5% (95% CI, 29.5-31.5-32.7) in 2023. The prevalence in pregnant women was 8.63% in 2021, 7.30% in 2022, and 7.93% in 2023 with higher prevalence among women aged <20 years (12.26%) compared to older women (7.14%). In both CSS and ANC, there was a significant positive correlation between malaria prevalence in CSS and ANC (r=0.719, P=0.03). The strongest positive correlation was among children <5 years and pregnant women aged <20 years (r=0.84,p=0.005); and school children aged 5-15 years and pregnant women aged >20 years (r=0.85, p=0.018). Malaria prevalence in pregnant women provided a close match to both under-fives and school aged children. The findings support previous studies and suggest that ANC data can be used as a sentinel surveillance group to monitor the trends of malaria prevalence in these groups rather than surveys that focus on presence or absence of asymptomatic infections in time points.

7315

TRANSFERRING CAMPAIGN DIGITIZATION EXPERTISE TO NATIONAL ENTITIES AND STRENGTHENING MALARIA CONTROL ACTIVITIES IN BENIN

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In 2022 malaria incidence was 21,7% among general population and 43,1% among under five children, in Benin. As the country is dedicated to achieving malaria elimination by 2030, it’s important to leverage on digital transformation to reach the target. Since 2019, the Ministry of Health has initiated campaign digitization initiatives with the technical support of Clinton Health Access Initiative. To ensure that the investments made in digitizing campaigns in Benin are sustainable, the Clinton Health Access Initiative, World Health Organization worked with the Ministry and other partners to expand and integrate the key components of campaign activities into disease control programs, while building capacities to lead digitization in the long term. The process of transferring the expertise on digitizing campaigns in Benin starts with strengthening and consolidating governance initiatives of the digitization campaign, led by the Information Systems Direction, followed by ensuring that the tool selection and deployment process leads to the adoption of suitable platforms and software addressing country specific needs, then, progressively improving digitization and integration of public health campaigns, and finally determine the sustainable ways to capacitate the government for the improvement of campaign operations. In result, leadership and coordination mechanisms were established, with steering committee that meets routinely to agree on the implementation plan for Integrated Campaigns Digitization across all Ministry of Health programs, departments and partners. The Information Systems Direction supported the malaria program to run nets distribution campaign and

Seasonal Malaria Chemoprevention campaign, engaged with technical and implementing partners to build a comprehensive platform to visualize, use and share the campaign data across programs, engaged steering committee and technical committee on design and requirements for review of existing tools and elaboration of new tools. Strengthening and transferring expertise to national entities ensure campaigns autonomous implementation by national stakeholders.

7316

UNDERSTANDING DHIS2 DATA LIMITATIONS FOR MALARIA BURDEN ESTIMATION: A COMPARISON WITH GOLD STANDARD MEASUREMENTS FROM A COHORT STUDY IN ZAMBIA

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To achieve public health goals and effectively respond to epidemics, robust health management information systems are indispensable. Platforms such as DHIS2, an open-source system, offer broad geographic coverage and timely disease incidence data, which can be helpful for malaria programming and intervention targeting. However, DHIS2 data inherently have limitations and may not provide a true estimate of community malaria incidence. Factors that contribute to these limitations include treatment-seeking behaviors, case management practices, and data quality concerns. This study aims to assess the differences in malaria incidence rates between passively-detected DHIS2 data and a gold standard measurement method, involving a prospective cohort with active case detection from a trial conducted in Western Province, Zambia for evaluating attractive targeted sugar baits (ATSB) from 2021 to 2023. Specifically focusing on children aged 12-59 months from the ATSB cohort that were cleared of parasites at the start of the malaria season and followed up monthly for 6 months to capture malaria incidence cases. These cases will be compared to the malaria incidence trends from matching health facility catchment areas using line plots. Concordance between the two estimates will be assessed via z-score scatter plots and Bland-Altman diagrams. Associations between health facility characteristics, patient preferences, and differences in estimates will be assessed through linear regression. Finally, Poisson regressions will be used to model the relationship between the outcome of monthly malaria incidence with both estimates, incorporating health facility characteristics and patient preferences. Examining the disparities between DHIS2 data and a gold standard measurement, and assessing the effects of contributing factors, may provide valuable insights into the limitations of DHIS2 estimates, aiding in their interpretation and informing their use in malaria programming efforts.

7317

CREATING COMMUNITY RESOURCES TO MAKE MALARIA GENOMIC DATA ANALYSIS MORE ACCESSIBLE BY EVALUATING, IMPROVING, AND HARMONIZING SOFTWARE TOOLS

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Major advances in *Plasmodium* sequencing approaches, pipelines, and data analysis tools have provided valuable insights from parasite genomic data on malaria epidemiology. However, translating genetic data into actionable information for NMCPs is still challenging. Important barriers still limit integration of these advances into a seamless data analysis ecosystem that produces standardized, interpretable results for use by NMCPs. The PlasmoGenEpi network convened 18 subject matter experts to landscape available tools, evaluate software standards, improve documentation, and evaluate next steps in the context of key use cases at the: **R**eproducibility, **A**ccessibility, **D**ocumentation, and **I**nteroperability **S**tandards **H**ackathon (RADISH23). We defined eight use cases for Plasmodium genetic data informing malaria surveillance, based on data analysis and functionality requirements. For each use case, we mapped out workflows with respect to information flow through each analysis functionality. In combination with the landscaping of tools and their functionalities, each step of the workflow can be mapped flexibly to available tools and can be used to identify gaps where new software is needed. These resources are available on **PGEforge** (mrc-ide.github.io/PGEforge), a community resource built during RADISH23. We identified 40 Plasmodium genomic analysis tools, of which 17 were prioritized for resource development. PGEforge contains the tool landscaping, software standard guidelines, and fully reproducible tutorials showing example usage of each tool using canonical target and whole genome sequencing datasets (empirical and simulated). Installation of R-based tools is simplified by our implementation of a centralized "R-universe" package repository. PGEforge now serves as a central, open repository for current and future resources for malaria genetic data and analysis workflows, greatly improving accessibility. Ongoing and future work will focus on rigorous benchmarking of tools and modular workflows to tackle the more ambitious goal of developing best practices in malaria genomic surveillance.

7318

USING ROUTINE SURVEILLANCE DATA TO ASSESS ADHERENCE TO MALARIA TREATMENT GUIDELINES IN THE COUNTY REFERRAL HOSPITALS IN KENYA

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The WHO recommends early diagnosis and prompt, effective treatment of malaria by observing appropriate weight-based dosing and rational use of antimalarial agents to reduce the spread of drug resistance. Kenyan malaria treatment guidelines recommend the appropriate dosage of Artemether Lumefantrine (AL) as the initial line of treatment for test-positive uncomplicated malaria. Cases are entered into registers; monthly summaries are uploaded to the Kenya Health Information System (KHIS). We assessed the adherence to the guidelines in Kenya's 47 County Referral Hospitals (CRHs) during the biannual commodity review meetings in November 2023. Suspected malaria cases are tested and recorded in a laboratory register (MOH 706); this information is replicated in the commodity summary report (MOH 743), which contains a summary of malaria tests, AL dispensed, and patients by weight category. A standard template was shared with the 47 counties to collect aggregated data from KHIS for Sept 2023, the most recent reporting month. Analysis of the total no. of patients who tested positive in both reporting tools, the total no. of patients treated with AL compared to the total no. of patients who tested positive in MOH 706 and MOH 743 for all CRHs. The conversion of doses dispensed to the number of tablets that should have been dispensed for the reported total no. of patients by weight category to cater for substitutions of AL packs. A total of 7,176 patients were treated with AL, yet only 3,080 (43%) tested positive for malaria, translating to overtreatment of

4,096 (57%) patients. A comparison of MOH 743 with MOH 706 (source document for laboratory test data), revealed over-reporting by 24% on the number of patients who tested positive. Only 580 (8%) of the total patients treated with AL were tested and treated correctly, with 11 CRHs (23%) giving correct dosing to positive patients. Data quality audits should be carried out to address data discrepancies, and data review meetings to be sustained for peer learning. Capacity building of health workers is also critical for rational drug use and inventory management.

7319

ADAPTING MALARIA INDICATOR SURVEYS TO INVESTIGATE TREATMENT ADHERENCE: A PILOT STUDY ON BIOKO ISLAND, EQUATORIAL GUINEA

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Adherence to antimalarial treatment regimens is an important aspect of understanding and improving the impact of malaria case management. However, both adherence to artemisinin combination therapies (ACT) and the factors driving it vary widely. While many other evaluation activities have been conducted on Bioko Island, until now adherence to antimalarial treatments, and in particular ACTs has not been evaluated. The implementation of a malaria indicator survey (MIS) conducted on Bioko in 2023 was leveraged to evaluate adherence to ACTs provided to individuals testing positive following the survey. A follow-up team visited the targeted households, physically observed treatment blisters where possible, and provided messaging to household members on the importance of adhering to the treatment guidelines to household members. The team used survey data from the targeted households to make messaging as relevant to the household's particular context as possible. Overall ACT adherence on Bioko Island was low, around 50%, and this varied demographically and geographically. Some of the highest transmission areas had exceptionally low adherence, but no systematic relationship between proper adherence and *P. falciparum* prevalence was detected. Estimates of adherence from follow-up visits were much lower than survey-based estimates in the same households (52.5% versus 87.1%), suggesting that lack of proper adherence may be a much larger issue on Bioko Island than previously thought. Anecdotally, the data-driven communication approach taken in this study was more effective in achieving desired behaviors than previous approaches focused on delivering a core set of messages to as many people as possible. The large discrepancy between adherence as measured in this study and survey-based estimates on Bioko Island suggests a health facility-based study to quantify adherence among the population receiving treatment for symptomatic malaria may be necessary.

7320

MALARIA OUTBREAK INVESTIGATION IN THE ARID NORTHERN WAJIR COUNTY, KENYA, DEC 2023-FEB 2024

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From Jan–Feb 2024, Wajir County reported 373 malaria cases, compared to an expected <10 cases, in what is considered a low transmission zone. Rainfall in Oct–Nov 2023 (2992mm) was significantly more than the same period in 2022 (110mm). We investigated the outbreak to ascertain the case characteristics and implement intervention measures. We reviewed data from Dec 2023–Feb 2024 in registers from health facilities that reported confirmed malaria cases higher than the sum of the median and 3rd quartile of cases reported in the past 5 years. We conducted a data quality audit (DQA) by comparing data in the registers against data in the Kenya Health Information System (KHIS). Key informant interviews were conducted with questionnaires to assess epidemic preparedness in coordination structures, surveillance, emergency commodities, and field response. Environmental risk factors were assessed in villages with the most cases and we evaluated community knowledge, attitudes, and practices on malaria. Frequencies and proportions were calculated for quantitative variables and qualitative data were analyzed thematically. Of the 710 positive cases investigated, 471 (66.3%) were male and 587 (82.7%) were ≥ 5 years of age. Most cases 499 (70.3%) were from Jan 2024, 2 months after the peak rainfall. There were 20 (2.8%) *P. vivax* cases, 57 (8.0%) severe malaria cases, and 4 deaths (CFR 0.6%). The county lacked epidemic preparedness and response coordination structures, and adequate stocks of key diagnostic and treatment commodities. Mosquito breeding sites were identified, and the community was aware of malaria treatment, prevention, and risk factors. DQA found only one-third of the suspected malaria cases were reported in KHIS. After the increased rainfall from Oct–Nov 2023, Wajir saw a >30-fold increase in malaria. Challenges included commodity stockouts, presence of *P. vivax* (new for the area), and lack of a coordinated county response. Strengthening diagnostic and treatment capacity, and improving data quality for surveillance to guide intervention strategies are key to minimizing morbidity and mortality in future malaria outbreaks.

7321

QUALITY OF MALARIA SERVICE DELIVERY BY HEALTH CARE WORKERS FOR PATIENTS PRESENTING WITH FEBRILE ILLNESS IN HEALTH FACILITIES IN SOUTHEASTERN TANZANIA, 2023

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High quality clinical management improves patient outcomes. Clinical management of febrile patients depends on the skills of health care workers (HCWs). To assess and improve malaria service delivery quality by HCWs in Tanzania, we supported the National Malaria Control Program to assess services via the Malaria Services and Data Quality Improvement (MSDQI) platform and conduct supportive supervision (SS). Using standard MSDQI checklists that generate composite competency scores in the areas of clinical history taking, physical examination, malaria testing, malaria diagnosis, malaria treatment, and provider counseling, we analyzed clinical observation data from 1,822 febrile patient visits collected from 590 health facilities in the high-burden southeastern PMI coverage regions of Lindi, Mtwara, Ruvuma, and Pwani from January to June 2023. If reporting data were complete for a given competency area, then the competency score for that area was analyzed descriptively, with the national competency standard defined as a score of >=75% ("good"). During 1,822 reported febrile patient visits, HCWs met area-specific national competency standards for 370/923 (40%) clinical histories, 717/1622 (44%) physical examinations, 1534/1615 (95%) malaria testing, 1596/1607 (99%) malaria diagnosis, 1522/1570 (97%) malaria treatment, and 1080/1790 (60%) counseling. HCWs met overall competency standards for all six categories in 948/1822 (52%) of visits. Despite high proportions of HCWs meeting competency standards for malaria testing, diagnosis, and treatment, we found that provider history taking, physical examination, and counseling contributed to degradation

of the overall quality of service delivery. Facility-based service delivery in southeastern Tanzania could be improved by identifying and intervening on factors contributing to weakness in these areas.

7322

OPERATIONAL FACTORS INFLUENCING TIMELY MALARIA CASE REPORTING BY PRIVATE HEALTH FACILITIES IN URBAN DISTRICT, UNGUJA ZONE, ZANZIBAR

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In Zanzibar, an area targeted for elimination, delayed reporting of malaria cases remains a challenge. Healthcare providers in public and private facilities are required to report malaria cases through the Malaria Case Notification system within 24 hours of diagnosis using a mobile reporting application. In 2021, reporting timeliness was 72.7%, and District Malaria Surveillance Officers observed private health facilities had lower malaria reporting timeliness. A cross-sectional explorative study using a phenomenological qualitative approach was conducted to examine operational factors impacting timeliness of case reporting among private health facilities in Urban Districts of Unguja. Sixteen study participants were selected using purposive sampling due to their reporting responsibilities. In-depth Key Informant Interviews were conducted using semi-structured guides, and thematic data analysis was performed using NVIVO software version 12. Of healthcare workers who participated in the study, 94% (15/16) demonstrated awareness of the reporting process and all (100%) received training on timely reporting. All participants also (100%) reported communicating with other staff at their facilities about reporting responsibilities, despite some challenges including effective communication, workloads, and lack of collaboration within facilities. Furthermore, 56% of healthcare workers reported receiving incentives including meeting allowance and best-performing rewards for timely reporting, which they found motivating. All respondents acknowledged operational resources like smartphone and internet bundles also played a role in reporting timeliness. The findings suggest that incentives, effective communication, and availability of resources can influence reporting timeliness for malaria cases from private healthcare facilities. Strategies to address communication challenges and ensure adequate provision of operational resources might be further assessed to enhance timely reporting of malaria cases, ultimately contributing to improved malaria surveillance and control efforts in Zanzibar

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RETROSPECTIVE ANALYSIS OF MALARIA INCIDENCE IN GUINEA 2018 TO 2022

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The objective of this study was to analyze the trend in malaria incidence in Guinea at the level of health districts and identify factors associated with high or low incidence. We used malaria surveillance data from 2018 to 2022, along with demographic data and results from national surveys (DHS 2018 and MIS 2021). The analytical methods included estimation of adjusted malaria incidences, time series decomposition, and the Mann-Kendall test ($p < 5\%$). We also employed Sen's slope to determine the direction and quantify the intensity of the trend, as well as multivariable analysis to identify factors associated with increased incidence. The results showed that nationally, between 2018 and 2022, the annual crude incidence increased by 36.7%, and adjusted incidence (completeness + testing) increased by 34.4%, with a variation rate ranging from 0 to 27% depending on the health district (HD) and year. In total, 27 out of 33 districts exhibited a significant upward trend (coef: 20 to 60%), 1 district (Siguiri) showed a significant downward trend (coef: -20 to -40%), and in 5 districts, the incidence trend was not significant. Multivariable analysis identified factors related to intervention and the healthcare system associated with high or low incidence in the districts. In summary, this study highlights a significant increase in malaria incidence in Guinea between 2018 and 2022, with notable variations among districts. The results suggest particular concern for the 27 districts showing an upward trend, and the identified factors associated with this increase provide factual insights to guide malaria control efforts in Guinea.

7324

COST-UNIT ANALYSIS OF VECTORCAM: A NOVEL COMMUNITY-BASED AI TOOL FOR VECTOR SURVEILLANCE TO IDENTIFY MOSQUITOES' SPECIES IN RURAL UGANDA

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Introduction: Advancements in digital tools have revolutionized mosquito surveillance for malaria control. VectorCam, is a novel tool that utilizes computer vision algorithms enabling low-cost, user-friendly mosquito identification at the village level. This study conducted collaboratively by the Johns Hopkins University, Makerere University, and the Ugandan Ministry of Health, aims to evaluate the cost per unit using VectorCam compared to traditional surveillance methods. **Methods:** In the randomized control trial in Uganda the village health team members (VHTs) in each arm collected mosquitoes using standard methods CDC light traps and pyrethrum spray catch from community households. Vector Control Officers in the control group, use microscopes and paper-based systems to morphological identify mosquitoes whereas in the study group, the VHTs employ the VectorCam app. Data in the control arm is manually transferred to the Ministry of Health's DHIS2 platform, whereas the study group's data is directly transferred via the app. **Preliminary Results:** Preliminary findings demonstrate VectorCam's ability to analyze a substantial volume of mosquitoes. Since September 2023, over 52,000 mosquitoes were imaged and analyzed, with 20.5k identified as *Anopheles* mosquitoes, of which 88% were female *Anopheles*. VectorCam's cost per mosquito analyzed was $0.50 per female *Anophelines* compared to the control arm of $0.64 per female *Anophelines*. **Conclusion:** Although both arms demonstrate an economy of scale the study arm maintains a consistently lower cost per unit. These findings highlight that in a country where scalability of their surveillance system is a priority, VectorCam could offer a financially advantageous alternative in high-volume settings than paper-based surveillance systems. VectorCam emerges as a robust tool for vector surveillance enhancing data collection and analysis, providing valuable insights for targeted interventions at the community level. This study highlights the importance of innovative digital solutions in advancing global health initiatives, particularly in resource-limited settings.

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ASSESSING THE FEASIBILITY OF IDENTIFYING AND VALIDATING SEROLOGICAL MARKERS OF RECENT LOW DENSITY *PLASMODIUM FALCIPARUM* INFECTIONS IN A PRE-ELIMINATION SETTING

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Serological markers of recent malaria infection are promising tools to measure malaria epidemiology. Previous work has identified serological markers of recent infection in moderate transmission settings; however, the generalizability of these findings to pre-elimination settings, where low parasite density infections elicit low antibody responses, remains unclear. Using a multiplex bead assay (MBA), we measured IgG responses to 19 *Plasmodium falciparum* antigens within a longitudinal cohort in Southern Province, Zambia. Monthly samples collected between October 2018 and September 2020 were tested for *P. falciparum* using ultrasensitive qPCR and quarterly samples with the MBA. The MBA was run on 1940 samples from 277 individuals, 59 of whom had at least one qPCR positive event with parasite density below 100 parasites per microliter. We found no differences in antibody responses to any antigens comparing participants with a qPCR positive event to those without, nor between pre- and post-qPCR positive events, demonstrating the limited feasibility of identifying markers of recent low-density infections. Using multilevel linear regression models, between person variability explained 63% to 86% of overall variability in antibody responses. Furthermore, while antibody responses of participants with no qPCR positive events overlapped with responses of serum from U.S. samples, the variability among serially negative participants was at least twice that of U.S. serum across all antigens suggesting that U.S. control serum fails to adequately capture the full range of antibody responses of negative serum from malaria endemic regions. Antibody responses of 56 participants showed variability in responses greater than 10 times the median within-host variability, this was not associated with age, sex, or infection. A timeseries analysis of antibody responses showed autocorrelation between -0.2 and 0.2 for all timepoints, suggesting random variation. These findings highlight the potential importance of incorporating longitudinal controls from malaria endemic areas, particularly in settings where biomarkers produce low signal.

7326

IMPACT OF ROUTINE DATA QUALITY AUDITS (RDQA) IN IMPROVING DATA QUALITY AND MALARIA MANAGEMENT STANDARDS IN HEALTH FACILITIES IN THE DEMOCRATIC REPUBLIC OF CONGO (DRC)

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The fight against malaria requires the production of quality data to monitor disease trends and enable evidence-based decision-making. An assessment of the DRC malaria surveillance system conducted in 2021-22 revealed significant inaccurate reporting of malaria data, with only about 20% accuracy. The NMCP, with support from PATH, has developed and piloted a decentralized approach to implementing Routine Data Quality Audits (RDQAs) in 36 health facilities in 4 health zones in Haut-Katanga Province. The approach favors ownership and accountability by the peripheral level of the health system around data quality. Health teams were trained on the RDQA approach, malaria data quality assurance procedures, and management of malaria interventions and indicators. During the pilot phase (June 2023-March 2024), purposive sampling was used for the selection of RDQA sites (n=36) for logistical reasons. The following indicators were included in the RDQA: outpatient consultation, suspected malaria, RDT performed, positive RDT, confirmed uncomplicated malaria, uncomplicated malaria treated according to national policy, confirmed severe malaria, and severe malaria treatment. Two RDQA rounds were carried out in each health facility in June 2023 and November 2023. During each visit, malaria data checks were carried out to compare data between registers, monthly HMIS reports, and data reported in DHIS2. During field visits, health workers were interviewed about malaria case management and a qualitative assessment of the data management system was conducted. Several data quality attributes were analyzed, including the average accuracy of all data elements for each round. The overall improvement in mean data accuracy from round 1 (30%) to round 2 (56%) was statistically significant ($p<0.0001$) by paired T-test. Given the promising results seen during the pilot phase, the NMCP is planning a national harmonization of RDQA approaches and developing RDQA malaria implementation manuals and training materials. Current efforts are focused on harmonizing and digitizing the RDQA tool in the country to facilitate further expansion beyond the pilot area.

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DESCRIPTION OF FACTORS ASSOCIATED WITH MALARIA PREVALENCE IN TWO TRANSMISSION SETTINGS IN SIAYA COUNTY, WESTERN KENYA (2022-2024)

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Malaria remains a public health challenge in western Kenya, with persistent transmission despite ongoing prevention and control efforts. Understanding the prevalence and associated factors among malaria cases is crucial for effective control. A continuous malaria indicator survey was conducted from April 2022 to March 2024 in Rarieda and Alego Usonga sub-counties, Siaya County, western Kenya. A total of 1,960 compounds were randomly selected from sub-county censuses to be surveyed. Demographic information, temperature, history of fever, and insecticide-treated net (ITN) use, were collected from consenting persons of all ages, and a malaria rapid diagnostic test (RDT) was administered. Correlates of malaria infection, including age, current fever, fever in the past 2 weeks, and ITN use were assessed using Poisson generalized linear regression models stratified by sub-county. In total, 7,490 (3,738 in Alego Usonga and 3,752 in Rarieda) individuals were included (1,008 (13.5%): <5yrs, 2,223 (29.7%): 5-14yrs and 4,259 (56.9%): 15+ yrs old). Malaria prevalence was 39.2% [95% CI: 38.1-40.3] with a higher prevalence in Alego Usonga (54.4% [95% CI: 52.7-56.0]) vs. Rarieda (24.1% [95% CI: 22.7-25.5]). Most cases were afebrile at the time of testing (99.6% [95% CI: 97.3% - 100%); 3.4% [95% CI: 3.0-3.8] reported fever in the past 2 weeks. Most (81.6%, 95% CI: 80.7-82.5) reported ITN use the night prior. Compared to those <5yrs, those 5-14yrs had higher risk (aPR: 1.31 [95% CI: 1.15 - 1.50] in Alego Usonga and 1.67 [95% CI: 1.37 - 2.06] in Rarieda) while those >15 had lower risk (aPR= 0.68 [95% CI: 0.60 - 0.78] in Alego Usonga and 0.71 [95% CI: 0.58 - 0.88] in Rarieda). Self-reported fever in the past 2 weeks was associated with an increased malaria risk (aPR: 1.51 [95% CI: 1.20 - 1.87] in Alego Usonga and 2.64 [95% CI: 2.09 - 3.28] in Rarieda). The findings highlight that children ages 5-14yrs remain a key risk group for malaria, emphasizing the need for additional tools and strategies to control transmission particularly targeting this key risk group. Given the high ITN use, factors including ITN quality, use duration, and time of entry and exit will be explored.

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IMPORTANCE OF A STRONG LOGISTIC MANAGEMENT INFORMATION SYSTEM TO REDUCE MALARIA COMMODITY LOSSES IN MADAGASCAR

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Between 2009 and 2020, Madagascar used a locally-designed, centrally-managed software called CHANNEL to facilitate the management of health sector commodities. Its specific purpose was to track stock levels and the movement of commodities between district pharmacies and health facilities with the aim of optimizing stock levels of essential commodities at both levels. In 2021, the Ministry of Health abandoned CHANNEL because it was inaccessible online and computer viruses destroyed the database behind the software. Since 2022, while awaiting the acquisition of new software for its logistics management system, which has been delayed, Madagascar has been using an ad hoc offline tracking platform centrally and peripheral health facilities continued reporting limited monthly stock data to DHIS2. Since 2009, the US President's Malaria Initiative has supported the Ministry of Health through an implementing partner to improve commodity management in all 115 districts. We assessed overall loss of malaria commodities through expiration, loss, or damage using data from DHIS2, comparing losses in 2022 and 2023 to those in 2021. Expiration, loss, or damage of 34,431 courses of Madagascar's first-line artemisinin-based combination therapy (ACT) and 49,715 malaria rapid diagnostic tests (mRDTs) was reported nationally in 2021. In 2022 and 2023, the number of ACTs that expired or were lost or damaged increased, respectively, to 142,925 courses (+315%) and 189,607 (+450%) courses. The number of expired, lost, or damaged mRDTs also increased in 2022 (198,471 mRDTs [+299%]) and 2023 (226,068 mRDTs [+354%]). The total procurement cost of these losses is equivalent to $24,730 in 2021, $90,532 in 2022, and $130,225 in 2023. In the absence of a supply chain management platform that integrates supply and demand data at all levels, Madagascar has experienced increased commodity loss. A supply chain system that tracks commodity movement, is accessible at all levels, and integrates supply- and demand-side data, and resources to redeploy excess stock, are crucial to improve the use of commodities in the context of limited resources and heterogenous transmission.

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MOLECULAR SURVEILLANCE OF MALARIA IN ENDEMIC REGIONS IN UGANDA REVEALS HIGH GENETIC DIVERSITY OF *PLASMODIUM FALCIPARUM* AND CORRELATION WITH TRANSMISSION INTENSITY

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Despite significant progress in genetic research enhancing our understanding of malaria, integrating these findings into practical strategies, especially concerning malaria transmission, remains underexplored. Although malaria epidemiology and parasite population genetics have developed distinct viewpoints, this study merges these perspectives. We explore the genetic diversity of P. falciparum and its link to transmission intensity using initial data from Uganda's first extensive molecular surveillance campaign in malaria-endemic areas. Our objective is to analyze the variability in transmission intensity across high endemic regions of Uganda, utilizing P. falciparum specific genomic data and epidemiological measures. We examined 2400 dried blood spot samples from symptomatic cases across 24 health facilities, averaging 100 samples per site. We calculated malaria incidence as cases per 1000 person-years over the three months before sample collection. The facilities represent varying transmission levels: high (over 500 cases per 1000 person-years in 9 centers), moderate (250-500 cases, 6 centers), and low (1-250 cases, 9 centers). We employed the MAD4HatTeR technique targeting 165 microhaplotypes and used MOIRE to assess infection complexity and within-host parasite relatedness. Early results showed a high average complexity of infection at 3.19, with significant within-host relatedness averaging 0.65. Interestingly, complexity decreased with patient age and increased with higher transmission levels, suggesting a link between transmission intensity and genetic diversity. These findings indicate potential superinfection and cotransmission rates, with ongoing analysis focused on identifying genetic indicators most predictive of local transmission intensities.

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THE INTEGRAL ROLE OF GIS IN THE SEASONAL MALARIA CHEMOPREVENTION CAMPAIGN TO IMPROVE MONITORING_A CASE STUDY OF TARABA STATE, NORTHEAST, NIGERIA

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Malaria in Nigeria is a persistent issue that requires strategic interventions. Mass Drug Administration (MDA) is crucial, especially in Taraba State, with a population of over 3.2 million. Seasonal Malaria Chemoprevention campaigns are key to malaria control. The Management Sciences for Health Global Fund Malaria has integrated geographical information systems (GIS) into MDA campaigns for better planning, implementation, and assessment. The study investigates the use of the Geographic Information System (GIS) in Taraba State's 2023 Seasonal Malaria Chemoprevention Campaign, to address inadequate supervision by monitors during mass drug distribution, focusing on intervention efficacy tracking, coverage examination, and monitoring at various levels. The SMC campaign used GIS technology to map and analyze key activities, including medicine delivery locations, demographic analysis, and malaria-prone regions. Geocoordinates were collected using platforms like Redrose and Kobocollect and placed on GIS platforms with basemaps from Google Maps and Google Satellite. SMC supervisors used handheld devices to take geo-coordinates at CDD drug administration sites. The GIS-based SMC campaign monitoring identified high-risk zones, streamlined logistics, evaluated campaign coverage, determined mass mop-up locations, and improved communication tactics. Monitoring of SMC supervisors' coverage. Real-time monitoring enabled aggressive responses to new challenges from 2021 to 2023, the supervisory coverage across supported wards increased from 60 to 90, resulting in a 65% to 89% increase. The 2023 Seasonal Malaria Chemoprevention campaign in Taraba State utilized GIS for targeted actions, logistics, and understanding of campaign dynamics. This demonstrates the potential of GIS in improving supervisors' coverage and visibility at sites, mass drug administration exercises, and providing crucial information for Nigeria's future malaria elimination plans. Consistent integration of GIS into MDA microplanning is recommended for long-term success.

7331

EXTENDED INTERVAL REGIMEN OF PREQUALIFIED MALARIA VACCINE R21 ADJUVANTED WITH 3M052 ELICITS HIGH AVIDITY ANTI-CIRCUMSPOROZOITE PROTEIN ANTIBODIES IN NON-HUMAN PRIMATES

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R21 is a WHO prequalified malaria vaccine targeting the pre-erythrocytic stage of *Plasmodium falciparum* (*Pf*) life cycle, exhibiting 74-77% efficacy in clinical trials in malaria endemic regions. By quantifying the binding kinetics of sera from multi-dose R21 immunized rhesus macaques to antigens (Ags) that include a recombinant *Pf* circumsporozoite protein (CSP), NANP6 (represent *CSP* central repeat region) and PF16 (represent *CSP* C-terminal region) measured using biolayer interferometry, we investigated whether varying adjuvants (3M052, GLA-LSQ or Matrix-M), immunization routes (subcutaneous (SC) or intramuscular (IM)) and/or vaccine schedules (standard regimen (weeks 0, 4, 8, and 62; SR) or extended interval regimen (weeks 0, 8, 23, and 72; ER)) influence R21-induced CSP targeting antibody (Ab) response and avidity. Among all combinations, IM groups with 3M052 or Matrix-M showed the highest Ab responses for CSP and NANP6 at post 3rd vaccination (PD3). Compared to Matrix-M IM-SR, the 3M052 IM-SR group showed comparable CSP and NANP6 responses but lower trending PF16 response, with the trend continuing at post 4th vaccination (PD4). Compared to 3M052 IM-SR, the 3M052 IM-ER group elicited >3 fold higher PF16 response but lower NANP6 response at PD3 and PD4 as well as showed 2.8-12.3 fold more retention of high Ab responses between PD3 and PD4 for CSP and PF16. Our avidity quantification further dissected the dissociation time course of Ag-sera interaction into components of different dissociation rates using Polyclonal Antibody Avidity Resolution Tool (PAART). Compared to 3M052-IM-SR, the 3M052-IM-ER group showed improved Ag occupancy by high avidity Abs at PD4 with 3 fold higher avidity over PD3 for NANP-targeting antibodies (binding to NANP6), despite low response at PD4. Additionally, for high responders in all 3M052 groups, high avidity Abs maintained >90% Ag occupancy between PD3 and PD4 despite decreasing Ab response. These results suggest that adjuvanting with 3M052 with an extended interval dosing schedule could increase the abundance and quality of R21-induced anti-CSP Abs and potentially improve Ab-mediated protection.

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IMPACT OF RTS,S MALARIA VACCINE ON *PLASMODIUM FALCIPARUM* INFECTION IN SCHOOL-AGED CHILDREN: INTERIM RESULTS FROM INDIVIDUALLY RANDOMIZED CLINICAL TRIAL IN MALAWI

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The burden of *Plasmodium falciparum (Pf)* malaria, including malaria-related anemia, is shifting towards school-aged children (SAC), who often have limited access to malaria interventions such as long-lasting insecticidal nets and prompt diagnosis and treatment. The RTS,S/AS01 malaria vaccine, the first vaccine recommended for under-five children in 2021, could potentially reduce the burden of clinical malaria in SAC. However, the effect of RTS,S/AS01 on SAC has never been assessed. As part of the first, individually randomized clinical trial assessing efficacy of RTS,S/AS01 in SAC, we evaluated the impact of the vaccine on *Pf* infection in children aged 6-15 years attending 5 primary schools in rural southern Malawi. This report is based on 3,884 children with median age 10 years (interquartile range [IQR] = 8-12 years), who were randomized to one of 4 intervention arms: 1) RTS,S/AS01 alone (963 children), 2) RTS,S/AS01 + parasite clearance with artemether-lumefantrine (AL) at enrollment (970 children), 3) parasite clearance with AL at enrollment alone (978 children), and 4) control receiving only Vitamin A (Vit A) (973 children). Participants were followed for detection of clinical malaria through a surveillance system at school clinics to which they reported whenever they felt symptoms. Malaria diagnosis was confirmed through microscopy (primary) and malaria rapid diagnostic test (mRDT). At this point, all participants in the 4 arms have received the 1st dose of the assigned intervention; 88% of participants in the two RTS,S/AS01 arms have received 2 doses and 82% all three doses of the vaccine. In 10 months of follow-up to date, median time to first mRDT positive malaria episode was 4 months (IQR: 2-6 months), with disease-free survival rates of 46% (95% CI: 42%-50%) overall, and 46% (95% CI: 37%-55%) RTS,S/AS01, 52% (95% CI: 42%-61%) RTS,S/AS01+AL; 48% (95% CI: 41%-55%) AL and 42% (95% CI: 36%-49%) Vit A. Thus far, neither of the RTS,S/AS01 arms show reduced time to *Pf* infection by mRDT. Results of an additional 7 months of exposure, and test results using both mRDT and microscopy, will be available from October 2024.

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ACCELERATED STABILITY STUDY OF CGMP DRUG PRODUCT INTERMEDIATE PVS230D1-EPA CONJUGATE

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Pvs230 is a promising *Plasmodium vivax* malaria transmission-blocking vaccine (TBV) candidate antigen. Pvs230 is expressed by gametocytes in the human host and displayed on the surface of gametes in the mosquito host. Antibodies generated against Pvs230 disrupt parasite development in the mosquito. To increase the immunogenicity of a *Pichia pastoris*-expressed domain 1 of Pvs230, recombinant Pvs230D1M was conjugated to the recombinant, non-toxic *Pseudomonas aeruginosa* ExoProtein A (rEPA), a carrier protein, in conformance with current good manufacturing practices (cGMP). To assess the stability of this conjugated vaccine candidate during storage, transportation and administration, an accelerated stability study was performed. The non-formulated cGMP Drug Product Intermediate, a 200 µg/mL Pvs230D1-EPA conjugate, was stored at -80ºC, -20ºC, 4ºC, 25ºC and 40ºC, and sampling was conducted at Days 0, 1, 3 and 7 for testing. The stability of the vaccine candidate was evaluated by appearance; pH; protein content by UV (A_{280}); SDS-PAGE with silver staining; Western blot with a transmission-blocking anti-Pvs230D1 monoclonal antibody 1H3, and an anti-exotoxin A polyclonal antibody; RP-UPLC; and size exclusion chromatography with multi-angle light scattering (SEC-MALS). Our results showed that the Pvs230D1-EPA conjugate is stable for at least 7 days after storage at 4°C and 25ºC. Storage at 40ºC showed a significant time-dependent decrease (Δ~15%, $p<0.05$) in molar mass of the conjugate when evaluated by SEC-MALS, although it is unknown whether this change impacts potency. Some changes by Western blot were observed including lower molecular weight bands when probed by both mAb 1H3 and the anti-exotoxin A polyclonal antibody after storage for 3 days at 40ºC. Storage at -20ºC showed a trend toward an increase in molar mass, suggesting minor aggregation after 1 day. These results indicate the Pvs230D1-EPA DPI maintains good stability characteristics when stored at various temperatures. More stability studies are warranted to better understand the implications of the observed changes and impact on vaccine efficacy in future formulations.

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DEVELOPMENT OF VACCINE CANDIDATES AGAINST PLACENTAL MALARIA USING PEPTIDE-DECORATED ANTIGENIC LIPOSOMES

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The WHO reported over 13 million pregnancies exposed to malaria infection in 2021, endangering both the mother and fetus. *Plasmodium falciparum* causes placental malaria by infecting red blood cells that accumulate in the intervillous space and bind to the syncytiotrophoblast of the placenta. Infected cells express the parasite virulence factor VAR2CSA that binds to chondroitin sulfate A (CSA) chains on proteoglycans in the placenta. The sequestration of infected red blood cells (iRBC) is associated with low birth weight, pre-term birth and fetal growth restriction. A vaccine against VAR2CSA is highly desirable to prevent these birth outcomes. In pre-clinical studies, we identified two peptides that mapped to conserved epitopes on VAR2CSA, P6 (in DBL3X) and P10 (in DBL4ε), and induced antibodies that prevented binding of iRBCs to CSA *in vitro.* We hypothesize P6 and P10 can be combined into a liposome-based multivalent peptide vaccine to induce synergistic inhibitory antibodies against VAR2CSA. Strain promoted azide-alkyne cycloaddition chemistry was employed to conjugate the peptides to a lipid linker prior to preparation of the liposomes via thin film hydration. We prepared single and multi-epitope liposomes with encapsulated ovalbumin to enhance the immunogenicity of the liposomes. The lipophilic adjuvant monophosphoryl lipid A was incorporated into the formulation as it is a TLR4 agonist and implicated in T cell activation. The resulting peptide-decorated liposomes were 189.8 nm (± 46.8) in size with a polydispersity index ranging from 0.2-0.4. Conjugation of both peptides to the liposomes was confirmed by ELISA. C57BL/6 mice were immunized subcutaneously with the antigenic liposomes and the sera will be tested for recognition of iRBCs infected with parasite strains expressing different alleles of VAR2CSA in an inhibition-based assay. Overall, our goal is to develop immunogenic liposomes against placental malaria to contribute to the urgent need for effective malaria vaccines.

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SAFETY AND REACTOGENICITY OF THE MALARIA VACCINE CANDIDATE ANAPN1 IN HEALTHY ADULTS IN GABON: PRELIMINARY DATA OF A RANDOMIZED, CONTROLLED, PHASE1 DOSE-ESCALATION CLINICAL TRIAL

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Malaria remains a major global public health issue in endemic regions. In preclinical studies, the recombinant AnAPN1 vaccine candidate has shown promising activity. Here, we assessed the safety, tolerability, and reactogenicity of three doses of the AnAPN1 vaccine, formulated with and without the GLA-LSQ (glucopyranosyl lipid containing QS21/saponin) adjuvant, administered to healthy adults. A randomized, double-blind, controlled, dose-escalation phase1 clinical trial was conducted in Lambaréné, Gabon among 33 healthy male and female volunteers aged 18-45 years. Participants were randomly assigned to one of 3 ascending dose groups. In each cohort, 9 participants received AnAPN1 with GLA-LSQ and 2 received the vaccine without adjuvant. The 20µg, 50µg, and 100µg vaccine doses were administered intramuscularly at days 0, 28, and 56-day in the first, second, and third cohorts, respectively. The vaccine's safety and reactogenicity were evaluated by means of close participant monitoring for any adverse effects occurring during and after vaccinations. The trial is registered with ClinicalTrial.gov, NCT05905432 and is still ongoing. Between October and December 2023, 55 participants were screened, of whom 33 eligible participants were recruited and allocated to either the 20µg, 50 µg, or 100µg dose in 3 sequential cohorts of 11 individuals each. The median age of enrolled participants is 27 years (range: 18-43 years). At the time of this analysis, participants in cohort 1 (n=10), cohort 2 (n=10) and cohort 3 (n=11) received the complete 3-dose vaccination schedule. The most frequently solicited local adverse events were mild to moderate injection site pain, representing 92% (44/48) of local events, and mild headache 36% (29/81) and nausea 19% (15/81) at a systemic level. There were no vaccine related serious adverse events reported. Overall, these preliminary results suggest that the administration of the AnAPN1 malaria candidate vaccine is safe and well tolerated in healthy Gabonese adults. Subsequent immunogenicity studies will determine whether it induces adequate IgG responses to justify a future phase2 clinical trial.

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CAREGIVER PERCEPTION AND ACCEPTABILITY OF THE MALARIA VACCINE RTS,S PRIOR TO INTRODUCTION IN THE FAR NORTH REGION OF CAMEROON

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Malaria is a recurrent public health challenge that requires a combination of strategies to address it in view of elimination. Currently, the malaria vaccine RTS,S vaccine is being introduced in several African malaria endemic countries while in Cameroon, the vaccine was introduced in January 2024. In view of interventions to evaluate the effectiveness of the RTS,S vaccine in Cameroon, pre-introduction caregiver perceptions and acceptability of the malaria vaccine was investigated in the Far North region, which poses the greatest risk of malaria related morbidity and mortality among under 5 children in Cameroon. A household survey was conducted in December 2024 involving 1240 parents/guardians in 4 randomly selected semi-urban and rural health areas of the Maroua 3 health district in the Far North region of Cameroon. The acceptability was explored. Quantitative data was analysed using regression analysis and qualitative data in Atla.ti using both inductive and deductive approaches. Among the 1203 participants, 79.3% were aged between 20 and 40 years and 71.1% had at most primary education. About 1 in 4 respondents were aware of the malaria vaccine Overall, 95.4% of caregivers interviewed were willing to accept the malaria vaccine if available. Confidence of vaccine efficacy,[5,78(aOR:1,27 ; 26,39), p=0.023], or were not concerned[aOR:3,75(1,09 ; 12,88)]. Believe in vaccine presenting low risk of serious reactions, independently affected acceptability. Community health workers were generally favorable to a combination of routine delivery through EPI and campaign style to implementation of the malaria vaccine given the high seasonality of malaria and experience with SMC. Overall, caregivers and community health workers expressed positive perception of the efficacy, health benefits and reduced out of pocket costs due to malaria infection of the RTS,S vaccine. Concerns on serious adverse reactions were expressed by <5% of respondents. Caregivers preferred vaccines delivered at home and community health care workers advocated for a hybrid approach to malaria vaccine delivery given their experience with other vaccines and SMC.

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EFFECTIVENESS AND IMPACT OF THE RTS,S/AS01$_E$ MALARIA VACCINE ONE YEAR AFTER THE PRIMARY VACCINATION IN REAL-LIFE SETTINGS IN THREE SUB-SAHARAN AFRICAN COUNTRIES: INTERIM RESULTS

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In the framework of the WHO-coordinated Malaria Vaccine Implementation Programme (MVIP), the RTS,S/AS01$_E$ malaria vaccine was introduced in selected areas in Ghana, Kenya and Malawi through routine national immunization programs. Within selected MVIP areas, a prospective cohort

disease surveillance study (EPI-MAL-003, NCT03855995) is conducted to assess safety, effectiveness and impact of the RTS,S/AS01$_E$ vaccine in children under 5 years old. Children were followed up through home visits and continuous monitoring of outpatient visits and hospitalizations in selected sites where the vaccine was introduced (exposed clusters) and comparator sites where the vaccine was not initially introduced (unexposed clusters). Vaccine effectiveness and impact were assessed on the incidence of malaria, hospitalizations, anemia and mortality. Results (crude estimates) up to one year after the 3-dose primary vaccination are presented here. This interim analysis (study period: 2019-2023) included 44,912 children uniformly distributed between exposed and unexposed clusters. In the exposed clusters, the primary RTS,S/AS01$_E$ vaccination coverage was 85%. Incidence rate (IR, 95% confidence interval [CI]) per 100,000 person-years (PY) of severe malaria was 252.9 (182.3-341.9) in vaccinated vs 591.3 (489.9-707.6) in unvaccinated children (vaccine impact: 57%). IR (95% CI) per 100,000 PY of all-cause hospitalization was 8,713.0 (8,269.8-9,173.8) in vaccinated vs 10,644.3 (10,198.3-11,104.8) in unvaccinated children (vaccine impact: 18%). IR (95% CI) per 100,000 PY of malaria-attributed hospitalization was 2,342.3 (2,115.3-2,587.1) in vaccinated vs 3,513.3 (3,259.1-3,782.1) in unvaccinated children (vaccine impact: 33%). No vaccine impact was observed on anemia cases at hospital entry. Vaccine impact on all-cause mortality was 17% but did not reach statistical significance (IR ratio: 0.83 [95% CI: 0.64-1.08], p=0.162). The RTS,S/AS01$_E$ vaccine showed positive impact in reducing severe malaria, malaria-attributed hospitalization and all-cause hospitalization over one year after the primary vaccination in real-life settings.

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CHARACTERIZING HUMAN MONOCLONAL ANTIBODIES INDUCED BY VACCINES AGAINST PLASMODIUM VIVAX DUFFY-BINDING PROTEIN

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There are no licensed vaccines against *Plasmodium vivax*, the second most common cause of malaria in humans. Vaccine candidates targeting *P. vivax* Duffy-binding protein region II (PvDBPII), an antigen expressed during the blood-stage of the parasite life cycle, have recently been tested for efficacy in controlled human malaria infection trials in adults. These showed that delayed boosting with a protein-in-adjuvant vaccine partially inhibited parasite growth and that the level of *in vivo* growth inhibition correlated with antibody responses. However, the mechanism(s) of antibody-mediated parasite growth inhibition are not well defined. To determine the breadth of antibody responses that humans generate in response to PvDBPII-based vaccines and the mechanisms of protective antibody responses, we have isolated a large panel of over 150 IgG monoclonal antibodies (mAb) from humans vaccinated against PvDBPII. Anti-PvDBPII specific single cell sorted B cells were isolated from blood and recombinant mAbs were expressed in mammalian cells. The antibody variable gene sequences were analysed using IMGT V-quest. ELISA and high throughput surface plasmon resonance are being used to determine binding characteristics of each mAb and to identify mAb communities of with competitive epitope binding interactions. The functional activity of mAbs was assessed with an *in vitro* parasite growth inhibition activity (GIA) assay using transgenic *P. knowlesi* expressing PvDBP, which showed that the majority of mAbs are GIA positive over a range of potency. Data from this large panel of anti-PvDBPII mAb will be used to define characteristics that determine the functional potency of mAb across different epitopes within PvDBPII. This will help guide the rational redesign of new PvDBPII-based vaccines to improve on efficacy as well as development of prophylactic mAb against blood-stage *P. vivax*.

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COMPARATIVE STUDY OF ANTIBODY EFFECTOR FUNCTIONS IN UK INDIVIDUALS AFTER VACCINATION EITHER WITH RTS,S AS01$_B$ OR R21 MATRIX-M ENROLLED INTO CONTROLLED HUMAN MALARIA INFECTION STUDIES

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In 2022, malaria remained a leading cause of death in Sub-Saharan Africa, with more than 249 million cases and 608,000 deaths, *Plasmodium falciparum* (*Pf*) being the most widespread and deadly form of the parasite. Highly efficacious vaccines are valuable additions to core interventions to reduce malaria incidence and mortality. Recently, two pre-erythrocytic malaria vaccines based on a *Pf* antigen circumsporozoite protein (CSP), RTS,S/AS01$_B$, and R21/Matrix-M, have been licensed for the prevention of malaria in children. Vaccine-induced IgG antibodies against the central NANP repeat region of the CSP are known as the main driver of protection. The identification of the mechanism by which vaccine-induced antibodies provide protection at the individual level after CSP-based vaccines is still needed to facilitate rapid clinical development of new vaccine candidates. In this study, we performed a comprehensive antibody profiling using serum of UK adults enrolled in Controlled Human Malaria Infection studies and vaccinated either with RTS,S (N=24) or R21 (N=33), to provide information regarding the quantitative and qualitative functions of vaccine-induced antibodies associated with protection. Associations with protection were assessed for the two vaccines at the time of challenge (one month after three doses of vaccines). For RTS,S vaccinees, we observed higher FcγRIIIa binding (*P*=0.03) in protected compared with unprotected participants. For R21 vaccinees, we observed increased ability of antibodies to inhibit sporozoite invasion (*P*=0.04) in protected compared with unprotected participants. For both vaccines, complement deposition was higher in protected participants (RTS,S *p*=0.02; R21 *p*=0.04). In conclusion, antibody characterisation after vaccination at the time of challenge highlighted different functional humoral immune profiles between protected and non-protected participants across RTS,S and R21 vaccines. These findings may help to assess vaccine immunogenicity of new CSP-based vaccine candidates.

7340

SAFETY AND IMMUNOGENICITY OF THE MALARIA VACCINE R21/MATRIX-M™IN UGANDAN CHILDREN LIVING WITH HIV

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Malaria remains one of the main causes of mortality in children in Sub-Saharan Africa. Despite the initial success of preventive programmes, progress in reducing malaria incidence has stalled in recent years. A safe and highly effective vaccine is paramount to reduce malaria incidence in this population and to progress towards eradication. R21/Matrix-M™ malaria vaccine has been shown to be safe and highly effective in a phase 3 trial (73% vaccine efficacy [95% CI 70 to 76] to first malaria episode within 12 months) which resulted in the WHO recommendation in October 2023 and pre-qualification in December 2023. In sub-Saharan Africa, the areas most affected by malaria overlap substantially with the areas most affected by HIV. For successful deployment of R21/Matrix-M™, it is necessary to assess the safety and immunogenicity of R21/Matrix-M

in this vulnerable population. Although children living with HIV may have been enrolled in the R21/Matrix-M™ phase 3 trial as HIV-infection itself was not an exclusion criterion, this is the first trial to specifically assess the safety and immunogenicity of the R21/Matrix-M™ in this population. 100 HIV positive and 20 HIV negative children, aged 5-36 months, were recruited and received 3 doses of R21/Matrix-M™. We collected safety data for solicited adverse events for 7 days after each vaccination and unsolicited adverse events for 30 days after each vaccination. Serious adverse events are collected for the duration of the trial. Blood samples to assess immunogenicity were taken before enrolment, before administration of the third dose, and one, 6 and 12 months after the third dose and results will be presented in the meeting. R21/Matrix-M™ was well tolerated, and the adverse events observed were similar to the adverse events observed in previous R21/Matrix-M™ trial in children. Most of the solicited and unsolicited adverse events were mild or moderate, and short- lived. There were no observed trends in unsolicited adverse events. There were no serious adverse events assessed as related to the vaccine. These data support the safety of R21/Matrix-M™ in children living with HIV.

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A NOVEL *EX VIVO* ASSAY TO EVALUATE FUNCTIONAL EFFECTIVENESS OF *PLASMODIUM VIVAX* TRANSMISSION BLOCKING VACCINE USING PVS25 TRANSGENIC *P. BERGHEI*

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Plasmodium falciparum and *P. vivax* account for >90% global malaria burden. Transmission intervention strategies encompassing transmission-blocking vaccines (TBV) and drugs represent ideal public health tools to eliminate malaria at the population level. The availability of mature *P. falciparum* gametocytes through *in vitro* culture has facilitated development of a standard membrane feeding assay (SMFA) to assess efficacy of transmission interventions against *P. falciparum*. The lack of *in vitro* culture for *P. vivax* has significantly hampered similar progress on *P. vivax* and limited studies have been possible using blood from infected patients in endemic areas. The ethical and logistical limitations of on-time access to blood from patients have impeded the development of *P. vivax* TBVs. Transgenic murine malaria parasites (*P. berghei*) engineered to express TBV candidates of *P. vivax* offer a promising alternative for evaluation of *P. vivax* TBVs through *in vivo* studies in mice and *ex vivo* membrane feeding assay (MFA). In this study, we describe the development of transmission-competent transgenic *P. berghei* parasites expressing Pvs25 (TgPbvs25), and the optimization of parameters to establish a robust *ex vivo* MFA using TgPbvs25. We validated the reliability and applicability of this MFA for evaluating transmission-reducing activity (TRA) using two transmission-blocking mAbs targeting Pvs25. Furthermore, TRA of IgG from sera of mice immunized a Pvs25 DNA vaccine was demonstrated in *ex vivo* MFA using TgPbvs25, and the results were comparable to those tested in direct membrane feeding assay (DMFA) using *P. vivax*-infected patient blood in the field. This novel assay is expected to expedite Pvs25-based TBV development without dependence on blood from *P. vivax*-infected patients in endemic areas for evaluation. Additionally, the *ex vivo* MFA approach developed can be widely employed for various transgenic *P. berghei* parasites expressing different TBV antigens from both *P. vivax* and *P. falciparum*.

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MALARIA VACCINE INTRODUCTION REDUCED CLINICAL MALARIA IN KENYA: TIME-SERIES ANALYSIS OF ROUTINE HEALTH FACILITY SURVEILLANCE DATA (2020-2022)

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Following the introduction of RTS,S/AS01 (RTS,S) through the Malaria Vaccine Implementation Programme (MVIP) in Kenya, we examined monthly routine malaria surveillance data from the Kenya Health Management Information System (KHIS) to assess the impact of RTS,S on outpatient malaria cases in children <5 years of age. Due to KHIS data aggregation at <5 and ≥5 years, the proportion of vaccine age-eligible children (RTS,S doses at 6, 7, 9, and 24 months) among <5y was initially small but increased over time. The monthly number of confirmed malaria cases reported to KHIS from outpatient facilities and community health workers was included from 23 vaccinating and 23 comparator sub-counties. Analysis was restricted to facilities reporting at least 11 months each year from January 2015 through December 2022 (139 vaccinating; 141 comparator). We estimated the case reduction as the difference between monthly reported cases <5y and forecasted cases <5y (January 2020-December 2022). Forecasts were based on time-series models of pre-vaccination data (January 2015-December 2019). To account for factors unrelated to MVIP, such as decreased clinic attendance during the COVID-19 pandemic, IRS, and bednet distributions, the analyses included a covariate for malaria cases ≥5y, as well as adjustment for trends in comparator areas. The annual percent reduction in <5y cases in vaccinating facilities was 15% in year 1, 17% in year 2, 24% in year 3, and 18.4% across 3 years. Attributing the reduction of clinical malaria to RTS,S was supported by evidence that the impact was greatest (32.9% overall) when excluding 31 (22%) comparator facilities whose population may have received vaccine due to their proximity to a vaccinating facility (<5km). Routine health facility data may be an effective source for estimating vaccine impact following broad scale-up, but has several important limitations such as age aggregation to initially include vaccine ineligible children, assumptions about vaccination status based on population-level coverage, availability of data from comparable non-vaccinating facilities, incomplete reporting, and impact of non-vaccine factors.

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IMMATURE DENDRITIC CELL TARGETING MRNA VACCINE ENHANCES PROTECTION FROM *PLASMODIUM* LIVER STAGE INFECTION BY ENHANCING T CELL RESPONSES AND ANTIBODY TITERS AGAINST CSP REPEAT REGIONS

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In 2021, there were 247 million clinical cases and 619,000 deaths from malaria. RTS, S, the first and only WHO approved vaccine for malaria, targets the pre-erythrocytic stage antigen circumsporozoite protein (CSP) and provides only limited efficacy, reducing clinical malaria by a modest 30%. For RTS, S and other pre-erythrocytic stage targeting vaccines, the ability to produce a robust immune response, eliciting high antibody titers and engaging a strong T cell are the primary obstacles to achieving vaccine-induced protection. Here, we describe the creation of a novel CSP mRNA, chemokine fusion vaccine, designed to overcome these challenges. Vaccination with mRNA expressing full-length CSP fused to macrophage inflammatory protein 3 alpha (MIP3α), provided significantly greater protection against sporozoite challenge than vaccination with mRNA expressing full-length CSP alone. The CSP-MIP3α fusion vaccine enhanced antibody titers against highly neutralizing NANP repeat epitopes and stimulated both CD4+ and CD8+ T cell responses. Protection from sporozoite challenge correlated significantly with titers against NANP repeats and T cell stimulation, particularly CD4+ T cytokine responses.

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THE PVRBP2B-TFR1 INTERACTION IS NOT ESSENTIAL FOR RETICULOCYTES INVASION BY *PLASMODIUM VIVAX* ISOLATES FROM CAMBODIA

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Reticulocyte invasion by *Plasmodium vivax* (Pv) involves different receptor-ligand interactions. For decades, only the Duffy Binding Protein (DBP) was known to be critical for this process. Recently, the Reticulocyte Binding Protein 2b (RBP2b) has been described as an essential ligand for Pv invasion by binding the transferrin receptor 1 (TfR1) on the surface of reticulocytes. Anti-RBP2b mouse monoclonal and rabbit polyclonal antibodies (Abs) were shown to inhibit RBP2b-TfR1 binding as well as the invasion of a few clinical Pv isolates from Thailand and Brazil. Human monoclonal anti-RBP2b Abs have been isolated, epitopes determined, and shown to block the binding of rRBP2b to reticulates *in vitro*. However, their capacity to neutralize Pv invasion has not been evaluated. Here, we aim to determine if these same mouse, rabbit and human anti-RBP2b Abs can inhibit invasion of Pv isolates collected in Cambodia. Using a robust in vitro flow cytometry-based assay allowing unambiguous reticulocyte invasion scoring and a total of 49 different Pv clinical isolates, we show that none of the mouse monoclonal, rabbit polyclonal and human monoclonal Abs inhibit invasion even at high concentration (500 µg/ml), despite anti-DBP inhibited by nearly 60% invasion of Pv. The anti-TfR1 OKT9 Abs that inhibits the RBP2b-TfR1 binding does not inhibit Pv invasion either. Combinations at high concentrations of human monoclonal Abs targeting different RBP2b epitopes do not inhibit invasion. Combinations of anti-RBP2b with anti-DBP do not enhance invasion inhibition caused by anti-DBP Abs alone. We also show that invasion of Cambodian Pv is trypsin-resistant while TfR1 is trypsin-sensitive and we demonstrate that TfR1 is not recycled following trypsin treatment. We determined the RBP2b sequence of all isolates used in the invasion assays and analyzed polymorphism within epitopes recognized by anti-RBP2b Abs. We show that polymorphism does not explain the absence of neutralization. In addition, rabbit anti-RBP2b polyclonal Abs recognized all four isolates tested in IFA. Thus, RBP2b is not be essential for Pv isolates from Cambodia to invade reticulocytes.

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THE EFFECTS OF VACCINE ADJUVANTS & MAJOR HISTOCOMPATIBILITY COMPLEX (MHC) ON THE IMMUNOGENICITY OF A SUBDOMINANT EPITOPE IN *PLASMODIUM VIVAX* DUFFY BINDING PROTEIN

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We are developing a vaccine that targets a specific epitope within the *Plasmodium vivax* protein PvDBP. The challenge is that this epitope (in subdomain-1, or SD1) is subdominant & not immunogenic within the recombinant protein. We hypothesized that mutations in other regions of PvDBP (subdomains 2 and 3) may alter the immunodominance hierarchy to expose this epitope. To test this, we expressed various PvDBP mutants, measured their affinity toward a mouse monoclonal antibody (3D10 mAb) specific to SD1, & measured their immunogenicity in mice. Recombinant wild-type PvDBP (Sal1 allele) & four mutants (DEKnull, DEKnull-2, DEKnull-3, DEKnull-4) were expressed in *E. coli*, purified & refolded. The affinity of the 3D10 mAb against each recombinant protein was measured by mass photometry. BALB/c and C57BL/6 mice were immunized with Sal1 & the mutant proteins alone or with Titermax, GLA-SE, or Alum as adjuvants. Immunogenicity was determined by enzyme-linked immunosorbent assay (ELISA) against a synthetic SD1 peptide. Among the five proteins, the 3D10 mAb had the highest affinity for DEKnull-4. When comparing the IgG titers specific to SD1, vast differences were observed depending on the immunogen, strain of mouse and the choice of adjuvant. SD1 remained subdominant in BALB/c mice immunized with Sal1 without adjuvant or with Titermax, but was strongly immunogenic when adjuvanted with GLA-SE and Alum. The immunogenicity of SD1 was increased further when DEKnull-4 was adjuvanted with GLA-SE or Alum. Conversely, anti-SD1 IgG responses were significantly masked in C57BL/6 mice under similar immunization conditions, indicating an important contribution of the Major Histocompatibility complex (MHCII) to SD1 immunogenicity. Supporting this, immunization of B10.D2 congenic mice (BALB/c MHCII on a C57BL/6 genetic background) with either Sal1 or DEKnull-4 adjuvanted with Alum fully restored the immunogenicity of SD1. These results demonstrate that the antigen structure, the choice of adjuvant, & most significantly, MHC restriction, drive epitope-specific immunogenicity following vaccination with subunit vaccines.

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VACCINE DESIGNS TO ELICIT PROTECTIVE ANTIBODIES AGAINST *PLASMODIUM FALCIPARUM* CSP

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Vaccines and monoclonal antibodies (mAbs) that target the *P. falciparum* 3D7 circumsporozoite protein (CSP) have proven effective in blocking infection in humans but extending the length of protection likely requires improving immunogenicity and durability of CSP-based immunogens. CSP contains a central repeat region composed of 38 NANP tetramers and a minor repeat region composed of three alternating NVDP and NANP tetramers. The junctional region is located immediately upstream and is also a target of humoral immunity. Based on knowledge gained from structures of mAbs bound to these regions and with the goal of understanding and improving protection against infection, eight immunogens (IMV1-8) targeting the major and minor repeats and junctional peptide region have been designed and produced. Structural data have demonstrated that IMV1-8 display the proper structure and the anticipated antibody valency on the repeat regions. To promote immunogenicity, the purified recombinant immunogens were bound to the capsid virus-like particle (cVLP) AP205 using a split-protein conjugation system to generate stable isopeptide bound antigen-cVLP complexes. Groups (n=6) of female C57BL/6N mice were immunized three times at 3-week intervals with equimolar amounts (180 pmol) of cVLP-IMV1-8, using AddaVax as an extrinsic adjuvant. The calculated geometric mean titers, using 2A10 mAb as a reference, indicated immunogenicity was proportional to the length of the immunogen. To test infection blocking efficacy in vivo, immune sera against the different constructs were injected intravenously (IV) into mice, which were challenged IV with 2,000 tg*Pb-Pf*CSP sporozoites. Significant inhibitions were observed

for cVLP-IMV2 and cVLP-IMV8 at levels comparable to those induced by anti-RTS,S antisera. Thus, constructs presenting either the major (cVLP-IMV2) or the minor (cVLP-IMV8) repeats performed similarly to RTS,S/AS01 in producing infection blocking antibody responses in this mouse model. Whether such antibody responses might act in synergy is being investigated.

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AMA1-SPECIFIC HUMAN MONOCLONAL ANTIBODIES INHIBIT *PLASMODIUM VIVAX* PRE-ERYTHROCYTIC AND BLOOD STAGE INFECTION

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One-third of the human population is at risk of contracting *Plasmodium vivax* (Pv). Developing novel Pv-specific therapeutic options such as monoclonal antibodies is vital to decreasing the worldwide burden of Pv. Apical Membrane Antigen 1 (AMA1) is an essential invasion protein that when expressed binds to Rhoptry Neck Protein 2 (RON2), an interaction utilized by sporozoites and merozoites during host cell invasion. PBMCs from a Pv-exposed individual were screened for AMA1-RON2 blocking antibodies using a competition ELISA. 12 PvAMA1-specific human monoclonal antibodies (humAbs) were produced and their functional characteristics were analyzed. One humAb, 826827, blocks invasion of human reticulocytes using Pv clinical isolates *in vitro* (IC_{50}= 48 µg/mL). 826827 also inhibited sporozoite invasion of a human hepatocyte cell line and primary human hepatocytes (IC_{50} = 0.3 - 3.7 µg/mL). The crystal structure of recombinant PvAMA1 with the antigen-binding fragment of 826827 shows that 826827 partially occupies the highly conserved hydrophobic groove in PvAMA1 that binds its known receptor, PvRON2. Competition ELISAs confirm that 826827 competes with a PvRON2 peptide for PvAMA1 binding with a higher affinity, accounting for its potency. *In vivo* testing using a liver-humanized mouse model that supports Pv liver stage infection showed a log-fold reduction in parasite burden in the liver with 826827 compared to mice treated with an isotype control antibody (Mann-Whitney, P = 0.0143). 826827 binds to highly conserved residues on PvAMA1, explaining the observed strain-transcending properties. To our knowledge, 826827 is the first humAb reported specific to PvAMA1 and is one of the first antibodies to show potent inhibition against blood stages and pre-erythrocytic stages.

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DESIGN AND EVALUATION OF CHIMERIC *PLASMODIUM FALCIPARUM* CIRCUMSPOROZOITE PROTEIN-BASED MALARIA VACCINES

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Efficacy data on two malaria vaccines, RTS,S and R21, targeting *Plasmodium falciparum* circumsporozoite protein (*Pf*CSP), are encouraging. Efficacy may be improved by induction of additional antibodies to neutralizing epitopes outside of the central immunodominant repeat domain of *Pf*CSP. We designed four r*Pf*CSP-based vaccines in an effort to improve the diversity of the antibody response. We also evaluated *P. falciparum* merozoite surface protein 8 (*Pf*MSP8) as a malaria-specific carrier protein as an alternative to hepatitis B surface antigen. We measured the magnitude, specificity, subclass, avidity, durability, and efficacy of vaccine-induced antibodies in outbred CD1 mice. In comparison to N-terminal or C-terminal focused constructs, immunization with near full-length vaccines, r*Pf*CSP (#1) or the chimeric r*Pf*CSP/8 (#2), markedly increased the breadth of B cell epitopes recognized covering the N-terminal domain, junctional region, and central repeat. Both r*Pf*CSP (#1) and r*Pf*CSP/8 (#2) also elicited a high proportion of antibodies to conformation-dependent epitopes in the C-terminus of *Pf*CSP. Fusion of *Pf*CSP to *Pf*MSP8 shifted the specificity of the T cell response away from *Pf*CSP toward *Pf*MSP8 epitopes. Challenge studies with transgenic *Plasmodium yoelii* sporozoites expressing *Pf*CSP demonstrated high and consistent sterile protection following r*Pf*CSP/8 (#2) immunization. Noteworthy, antibodies to conformational C-terminal epitopes were not required for protection. These results indicate that inclusion of the N-terminal domain of *Pf*CSP can drive responses to protective, repeat, and non-repeat B cell epitopes and that *Pf*MSP8 is an effective carrier for induction of high titer, durable anti-*Pf*CSP antibodies.

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ASEPTIC, PURIFIED, VIALED *PLASMODIUM VIVAX* SPOROZOITES FOR CONTROLLED HUMAN MALARIA INFECTION

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Malaria caused by *Plasmodium vivax* (Pv) is 2nd to *P. falciparum* (Pf) in incidence and impact. Unlike Pf, chemoprophylactic measures against Pv do not prevent relapses due to re-activation of persistent liver-stage sleeping forms of the parasites called hypnozoites. Primaquine and tafenoquine are the only licensed drugs that target Pv hypnozoites, but cause life threatening acute hemolytic anemia in patients with G6PD deficiency. Drug and vaccine development are hampered by inability to propagate blood stages of Pv parasites *in vitro* and mosquitoes for controlled human malaria infection (CHMI) can only be generated with Pv-infected blood from patients. We produced Pv sporozoites (SPZ) of the Chesson strain by feeding infected blood from specific pathogen free (SPF) *Saimiri boliviensis* (Sb) monkeys to aseptic *Anopheles stephensi* mosquitoes and these PvSPZ were highly infectious to FRG mice with humanized livers and produced hynozoites. We then manufactured in compliance with GMPs 1) a master cell bank of Pv (Chesson) asexual RBC stage parasites in the blood of SPF Sb, 2) small lots of aseptic PvSPZ with all in-process samples of aseptic eggs, pupae, blood meals and adult mosquitoes, and the final product testing negative for microbial growth using U.S. Pharmacopeia USP<71> tests for sterility, and 3) One lot of aseptic, purified, vialed cryopreserved PvSPZ, Sanaria® PvSPZ Challenge (Chesson) that is aseptic, pure, and potent. Our pre-IND package to the FDA including our chemistry, manufacturing, and controls, quality control (QC) assays, and a proposal for a clinical trial, received positive feedback and recommendations. PfSPZ Challenge has revolutionized CHMI studies for Pf malaria. We expect PvSPZ Challenge will similarly provide the larger malaria community with a radically enhanced tool to assess anti-Pv interventions, as a safe quality-controlled reagent with minimal variability in potency, that is logistically simpler to administer, not subject to geographical limitations for application, compared to mosquito bite CHMI. The characteristics of the SPF Sb, aseptic mosquito infections, and GMP-produced PvSPZ will be presented.

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ANTIMICROBIAL RESISTANCE OF *SHIGELLA* AMONG CHILDREN UNDER FIVE YEARS WITH DIARRHEA OVER A DECADE IN THE GAMBIA

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Antimicrobial resistance (AMR) is a major public health concern globally, especially in low- and middle-income countries (LMICs). Resistance among the leading cause of bacterial diarrhea and dysentery, *Shigella* spp., limits antibiotic options for children vulnerable to mortality and linear growth faltering. A high burden of *Shigella* spp.-attributable diarrhea was found among African sites in the Global Enterics Multicenter Study (GEMS). We describe AMR among *Shigella* spp. from children with diarrhea enrolled in the GEMS (2007 - 2011), Vaccine Impact on Diarrhea in Africa (VIDA, 2015 - 2018) and Enterics For Global Health (EFGH) *Shigella* surveillance study (August 2022 - March 2024) in Basse, The Gambia. We enrolled children with diarrhea aged 6-35 months in the EFGH study and children with moderate to severe diarrhea (MSD) aged 0-59 months in the GEMS and VIDA studies. *Shigella* spp. isolated from stool and rectal swab samples by microbiological culture are reported. Antimicrobial resistance was assessed for 114, 214, and 99 *Shigella* spp. isolates from GEMS, VIDA and EFGH diarrhea cases, respectively. *S. flexneri* was the leading serogroup in all three studies constituting 69.0%, 67.6% and 57.3% of isolates in GEMS, VIDA and EFGH, respectively, followed by *S. sonnei* (20.7%; 18.2%; 36.9%), *S. boydii* (6.0%; 11.8%; 2.9%) and *S. dysenteriae* (4.3%; 2.3%; 1.0%). AMR in the GEMS, VIDA and EFGH studies was 93.9%, 93.0% and 97.9% to trimethoprim-sulfamethoxazole, 57.9%, 41.6% and 26.6% to ampicillin, 0.0%, 0.9% and 15.1% to nalidixic acid, 0.0%, 0.0% and 7.0% to azithromycin, 0.0%, 0.5% and 0.0% to ceftriaxone and 0.0%, 0.0% and 2.0% to ciprofloxacin, respectively. Resistance to pivmecillinam, only assessed in the EFGH study, was 10.0%. These findings suggest AMR patterns parallel drug usage, with AMR increasing in the recommended treatment for dysentery (trimethoprim-sulfamethoxazole, ciprofloxacin, azithromycin) and decreasing in ampicillin, which is no longer recommended. This emphasizes the importance and urgent need for *Shigella* vaccine introduction and implementation of strategies to prevent the further increase in AMR burden.

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COMPARING WHOLE CELL PSORALEN INACTIVATED SHIGELLA VACCINE VERSUS FORMALIN INACTIVATED SHIGELLA VACCINE IN MICE

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Shigella is responsible for approximately 600,000 annual deaths worldwide, predominantly among children, yet no licensed vaccines are currently available. This study evaluates the immunogenicity of a psoralen plus ultraviolet A-inactivated (PSIV) Shigella vaccine, which may enhance immunity by better preserving protein epitopes compared to traditional methods. We utilized a mouse model to compare the immunogenicity of PSIV versus formalin-inactivated (FIV) Shigella sonnei vaccines. Four groups of five mice each received one of the following treatments: PSIV with and without a double mutant heat-labile toxin (dmLT) adjuvant, and FIV with and without the adjuvant. Vaccinations were administered on days 0 and 28. Pooled sera from days 0, 28, and 49 were tested for the presence of anti-Shigella antibodies using whole-cell enzyme-linked immunosorbent assays. We found that PSIV with adjuvant resulted in the highest total antibody titer among the pooled samples, which was 30% higher than that of FIV. The mean fold change in antibody titer between days 28 and 49 across all arms was 13.5, indicating a strong booster effect. The PSIV Shigella vaccine is qualitatively superior and statistically non-inferior to an FIV Shigella vaccine in eliciting a broad antibody response. Further research is required to evaluate specific epitope responses. Our results suggest that PSIV may be an effective approach for developing a Shigella sonnei vaccine.

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ESTABLISHING CHOLERA SURVEILLANCE IN RURAL NEPAL DURING COVID-19 PANDEMIC: LESSONS LEARNED

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The ongoing upsurge of Cholera cases with multiple outbreaks, alarming numbers and mortality rates is a global public health concern. The situation underscores the importance of strengthened Cholera surveillance for accurate outbreak detection and response. Cholera outbreaks have been frequently reported in Nepal since early 1800's, but the country still lacks an effective surveillance system for its detection. Assessing the need, International Vaccine Institute (IVI) with the support of Global Disease Eradication Fund (GDEF) from Korea collaborated with Sudurpaschim Provincial Government of Nepal, to establish Cholera surveillance in Kailali district of Nepal in 2019. A network of 10 sentinel sites for enrollment and rapid laboratory testing of suspected Cholera cases and refurbishment of local laboratory to serve as regional reference laboratory for Cholera culture confirmation was planned. Throughout 2019, multiple engagements between stakeholders were held and project implementation was planned from 2020 through 2023 but had to be put on hold due to declaration of Covid-19 pandemic in March 2020. Finally, a collaboration agreement was signed on March 2022 after numerous virtual/on-site meetings even during Covid pandemic. Laboratory upgradation was completed in April 2023 and sentinel sites were trained on use of common protocol for diarrheal disease surveillance. The Cholera surveillance in Kailali formally kicked-off in June 2023 with the first culture confirmed Cholera case being reported in August 2023. Here we present our experience with lessons learned from planning and implementation of the project to reporting first case of Cholera from Kailali district of Nepal during Covid-19 pandemic.

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A COMPARISON OF SEROLOGIC, MOLECULAR, AND GENOMIC APPROACHES FOR SEROTYPING *SHIGELLA FLEXNERI* STRAINS ISOLATED FROM THE PERUVIAN AMAZON

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Shigellosis is one of the leading causes of bacterial gastroenteritis and dysentery in children under the age of 5 living in Iquitos, Peru. *Shigella* spp., a gram-negative bacillus, is the causative agent of this disease. Consequences of Shigellosis include persistent diarrhea, intestinal protein loss and intestinal inflammation, as well as linear growth faltering. Agglutination with antisera against lipopolysaccharide O-antigen is utilized as the gold standard for serotyping *Shigella flexneri*. However, molecular serotyping methods, including a qPCR-based approach, and a genomic based approach have been developed. In this study we compare the results obtained for serotyping *Shigella flexneri* isolates using serum agglutination, genomic sequencing, and qPCR of the matched rectal swabs. *Shigella* spp. isolates were obtained from the Enterics for Global Health Shigella Surveillance Study (EFGH) conducted in Iquitos, Peru. Between August 2022 and December 2023, 86 Shigella strains were isolated from unique rectal swabs from children with medically attended diarrhea. Of these, 78 had a matched qPCR result. Of these, 54 were identified as *S. flexneri*, 22 as *S. sonnei* and 1 as *S. dysenteriae*. Of the 54 *S. flexneri*, 37 (68.5%) ha a matched serotype assigned by agglutination and qPCR (1a (n=2), 2a (n=23), 2b (n=11), 3a (n=1), and 17 (31.5%) had discordant results by agglutination and qPCR. All strains were sequenced using Illumina based methods, and both reads and contigs were analyzed using ShigaTyper and ShigaPass bioinformatic programs. So far, of the 17 discordant pairs, sequencing results are available for three strains. Two of these were classified as 4a by agglutination, were not typed by qPCR and were classified as Yv by genomic serotyping. The third was classified as 1a by agglutination and 1b by qPCR and genomic serotyping. Sequencing will be completed in August 2024, and results of the pending matched and discordant serotyping will be presented at the meeting.

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INTERIM SAFETY DATA FROM A PHASE 1/2A, RANDOMIZED, CONTROLLED, OBSERVER-BLIND TRIAL TO EVALUATE THE SAFETY, REACTOGENICITY AND IMMUNOGENICITY OF A TRIVALENT VACCINE AGAINST INVASIVE NONTYPHOIDAL SALMONELLOSIS (INTS) AND TYPHOID FEVER IN HEALTHY EUROPEAN AND AFRICAN ADULTS.

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Invasive nontyphoidal Salmonellosis (iNTS) and typhoid fever are major public health concerns causing a significant burden, particularly in resource-limited settings of sub-Saharan Africa. There is no licensed vaccine for iNTS, and the licensed Typhoid Conjugate Vaccines (TCVs) are not widely used in Africa. A novel trivalent iNTS-TCV vaccine, aimed at preventing both diseases, is under development by GSK Global Health Vaccines R&D (GVGH). This abstract presents interim blinded safety results from an ongoing phase 1/2a study in healthy adults. In stage 1, 50 European adults were randomized in a 2:2:1 ratio to receive either iNTS-TCV vaccine and concomitant saline in different arms, or separate iNTS-GMMA and TCV vaccines in different arms, or placebo and saline in different arms intramuscularly, on Days 1, 57 and 169. Of these, 10 subjects received low doses of the study vaccines and 40 received full doses. In stage 2, 105 African adults were randomized in a 3:3:1 ratio to receive full doses of the same vaccines or comparators. Menveo, Boostrix and Typhim Vi are administered as controls for the 1st, 2nd and 3rd doses respectively. After all administrations in European adults and at least one administration in 92/105 (87.6%) African adults, majority of the adverse events (AEs) observed are of mild to moderate intensity. Injection site pain is the most reported local solicited AE, while myalgia, fatigue and headache are the most frequent systemic solicited AEs. Severe unsolicited AEs related to vaccination were reported in 4 subjects overall. No serious AE considered related to vaccination has been reported. In conclusion, based on available data, the anticipated benefit/risk profile of the iNTS-TCV vaccine continues to be positive, with no safety concerns precluding further clinical development. First immunogenicity results are expected later in 2024 and would be presented at the congress.

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POLYCHROMATIC FLOW CYTOMETRY PANELS TO CHARACTERIZE ANTIGEN-SPECIFIC MEMORY B-CELLS INDUCED BY ENTEROTOXIGENIC ESCHERICHIA COLI VACCINES

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Enterotoxigenic *Escherichia coli* (ETEC) is one of the significant pathogens causing moderate-to-severe diarrhea in travelers. ETEC is also a leading cause of morbidity in children under 5 years of age especially in resource-poor regions. Current approaches to ETEC vaccine development predominately target the colonization factors, which are involved in ETEC adhesion, and the diarrheagenic heat labile toxin (LT). Combination of colonization factor antigens and mucosal mutant LT adjuvants (mLT or dmLT) aim to induce systemic and mucosal immune responses capable of blocking infection and neutralizing LT. Here, we report on the development of antigenic probes to enable monitoring the induction and response rates of antigen-specific memory B cells induced by vaccination with intradermally administered subunit vaccine targeting the colonization factor antigen I (CFA/I) using the mLT adjuvant. This study was technically challenging due to the nature of the ETEC antigens (CfaE, LT), which bind to intestinal epithelial cells thus potentially resulting in non-specific binding to cells rather than to the antigen-specific B cell receptors. We summarize the various strategies applied to develop a highly specific and sensitive flow cytometric panel. The presentation will provide guidance on how to approach the design of antigenic probes for B cell analysis. The completed flow cytometric panel allowed simultaneous monitoring of LT- and CfaE-specific memory B cells, their functional status, and the expression of homing receptors associated with migration to intestines.

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RETAINING AZITHROMYCIN SUSCEPTIBILITY IN THE FACE OF INCREASING USE IN SUB-SAHARAN AFRICA-THE ROLE OF EFFLUX PUMP INHIBITORS

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Mass drug administration (MDA) of azithromycin is being considered to prevent child mortality in some high mortality settings. Although azithromycin resistance is uncommon in enteric bacteria in sub-Saharan Africa (SSA), resistance may rise with MDA. Azithromycin resistance in *Escherichia coli* (*E. coli*) can result from ribosomal mutations, macrolide-

modifying enzymes, or by efflux pumps expelling intracellular antibiotics. We sought to establish the minimum inhibitory concentration (MIC) of azithromycin and relative importance of efflux pumps in explaining azithromycin resistance in *E. coli* isolates cultured from children recently discharged from hospitals Western Kenya. *E. coli* was isolated from children aged 6-59 months enrolled in a randomized control trial testing post-discharge azithromycin efficacy against mortality and re-hospitalization. Azithromycin MICs were established by E-test in the presence or absence of 50µg/mL Phe-Arg-β-Naphthylamide (PAβN), an efflux pump inhibitor. *E. coli* was isolated from 1220 of 1400 enrolled children and 757 (62%) isolates were resistant to azithromycin (≥32 mg/L), with 565 (75%) having the highest MIC (≥256 mg/L). In the presence of PaβN, the prevalence of azithromycin resistance was reduced by more than half (357 [29%] isolates). MIC_{50} and MIC_{90} in the absence of PaβN were 128 mg/L and 256 mg/L respectively while in the presence of PaβN were 4 mg/L and 256 mg/L respectively. Almost 75% (908/1220) of the isolates had > 2-fold change in MIC values with PaβN, of these 300 (33%) had a 16-fold change in MIC. Azithromycin resistance in *E. coli* was common among children discharged after a non-traumatic hospital admission and highlights the importance of the potentiating effect of efflux pump inhibitors in azithromycin antibacterial activity in *E. coli*. Efflux pump inhibitors, or associated mechanisms such as increased membrane permeability, may hold promise for retaining azithromycin susceptibility in enteric bacterial infections in SSA.

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ESTIMATING THE COST-OF-ILLNESS RELATED TO CHOLERA IN MOZAMBIQUE AND NEPAL

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Cholera is endemic and epidemic in some developing countries. This disease not only tests a country's health systems resilience, but also has direct financial implication to patients and the country alike. Knowing the economic burden of cholera in different settings provides policymakers with appropriate evidence for development, budgeting, and implementation of the national cholera plan (NCP). We carried out a cost-of-illness (COI) study on cholera in Mozambique and Nepal. Using convenience sampling, confirmed cholera cases selected during active outbreak and endemic settings in these countries were surveyed in 2023. A structured questionnaire was used for collection of personal cost (direct medical, direct non-medical and indirect cost) associated with the disease. Healthcare provider costs were also collected. Total 204 and 119 patients were enrolled for COI survey in Mozambique and Nepal respectively. All patients in Mozambique were enrolled from inpatient ward, while 60.5% (72/119) of enrolled patients in Nepal were from emergency ward. Though patients in both countries received governmental subsidies for treatment, more people received subsidy in Mozambique (203/204; 99.5%) than Nepal (32/119; 26.9%). Compared to Mozambique (4/204; 0.019%) more participants from Nepal (19/119; 15.97%) visited pharmacy prior to seeking treatment at health facility. Average cost from patient perspective in Mozambique and Nepal was direct medical (USD0.33, and 52.42 respectively), direct non-medical (7.83, 9.30) and indirect cost (6.42, 35.92). In Mozambique, average total cost from patient perspective ranged from USD17.25 in Niassa to USD26.02 in Zambezia whereas in Nepal, for inpatient was USD153.93 and for outpatient USD47.28. There was substantial difference in cholera related COI in different settings within and between Mozambique and Nepal. If we compare these costs with the income of minimum wage workers, which is approximately USD62.5 for Mozambique and USD130 for Nepal, it becomes evident that cholera poses a considerable financial burden and also challenges in accessing affordable healthcare.

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SINGLE DOSE AZITHROMYCIN AMONG CHILD CONTACTS OF CHOLERA PATIENTS CAN REDUCE CHOLERA AT HOUSEHOLD LEVEL: A DOUBLE-BLINDED RANDOMIZED CONTROL TRIAL

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Vibrio cholerae causes 3 million cholera cases and 100,000 deaths annually with over half of deaths in children. Children who are household (HH) contacts of cholera patients are at high risk for cholera infection and are not well protected by cholera vaccines compared to adults. Azithromycin is an effective treatment for cholera and is widely used as prophylaxis against other childhood infections. Our objective of this trial is to determine whether a single dose of azithromycin given to children aged 1-15 years who are HH contacts of cholera patients will reduce the risk of *V. cholerae* infection. We are conducting a double-blinded cluster-randomized controlled trial of single-dose azithromycin (20mg/kg) compared with the non-antibiotic placebo group. After index cases are identified at icddr,b Dhaka hospital, we enroll HH children aged 1-15 years living in or around Dhaka city within 12 hours. HH contacts are assigned to receive azithromycin or a placebo. We then collect their rectal swab samples as well as clinical data with follow-up for up to 6 months post-intervention (days 1-7, day 30, and day 180). We initiated the study on 31st October 2021 and it is ongoing. A total of 1044 diarrheal patients were screened for *V. cholerae* through 29th February 2024 and 235 were cholera-positive by RDT. 84.26% of RDT-positive cases were positive by culture. Many index patients reported prior receipt of antibiotics, and 41.48% reported taking metronidazole. We enrolled 375 HH contacts from the 235 index cases. Among the HH contacts, 135 were <5 years of age, and 240 were 5-15 years of age. 36 HH contacts (9.6%) were culture-positive for *V. cholerae* O1 and only one was symptomatic. Baseline levels of antibiotic resistance, including macrolide resistance genes, were high among all participants. We report the early-stage results of a randomized clinical trial of single-dose azithromycin to prevent cholera in children. The results of the study when unblinded will inform the clinical management of close contacts of patients with cholera and provide new data about the impact of single-dose azithromycin on short- and long-term carriage of antibiotic-resistant bacteria.

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TYPHOID CONJUGATE VACCINE INTRODUCTION: DECISION-MAKING IN THE CONTEXT OF LIMITED DATA USING A BURDEN AND RISK ASSESSMENT FRAMEWORK

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Since WHO recommended typhoid conjugate vaccine (TCV) introduction in 2018 for all typhoid endemic countries, only six countries have introduced TCV. National decision-making for TCV introduction is limited by lack of typhoid burden data. To address this challenge, WHO and CDC, supported by a group of experts, developed a burden and risk assessment framework to provide a standardized approach to collating, scoring, and interpreting available typhoid data in six areas: incidence, prevalence, antimicrobial resistance (AMR), outbreaks, intestinal perforations, and risk factors. The framework underwent an iterative revision process through pilots in 4 purposively selected countries. Blood culture data and *Salmonella* serotype confirmation were available from tertiary hospitals, but quality and quantity varied by country. Typhoid diagnosis was frequently based on clinical symptoms and antigenic test results. AMR data were limited by the number

of available isolates and data quality varied by country. Intestinal perforation data lacked causality and outcome information. High quality WASH data were derived from national household surveys but were generally not available sub-nationally. Data on outbreaks were consistently lacking. Data collection comprised a desk review (incidence, outbreaks, risk factors) and health facility visits (prevalence, AMR, intestinal perforations), facilitated by an electronic tool, and focused on health facilities with blood culture capacity. Data collectors needed to have laboratory and moderate data management experience. Technical support and funding were required for implementation. Data interpretation required expertise in typhoid epidemiology and laboratory diagnostic methods and was nuanced to each country. The framework can help to provide an overall inference of typhoid burden in a country, even in settings where blood culture confirmation is not routine. Results may inform national typhoid control decision-making, including TCV introduction. However, technical support for implementation and data interpretation are necessary for success.

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MEASURING THE EFFECTIVENESS AND IMPACT OF TYPHOID CONJUGATE VACCINE FOLLOWING NATIONAL INTRODUCTION IN MALAWI (MITIMA)

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Typhoid conjugate vaccine (TCV) has demonstrated robust efficacy in randomized controlled trials in low- and middle-income countries, including Malawi. Liberia and Zimbabwe were the first sub-Saharan African countries to introduce TCV in April and May 2021, respectively. In May 2023, Malawi became the third African country to introduce TCV. We aim to measure TCV effectiveness and impact post-introduction in a typhoid-endemic sub-Saharan African setting and inform policy decisions across Africa. We are conducting passive blood culture surveillance for typhoid fever in Blantyre. Individuals aged 9 months to 45 years presenting with febrile illness (subjective fever for ≥72 hours, axillary temperature ≥38°C, or hospitalisation with a history of fever) have a blood culture. Vaccine effectiveness will be measured post-introduction among children age-eligible for vaccination (9 months to 15 years) using a test-negative study design. Cases are blood culture positive for *Salmonella.* Typhi (*S*. Typhi); controls are blood culture negative for *S.* Typhi. TCV impact will be assessed using an interrupted time series analysis of blood culture surveillance data collected from one-year pre-introduction and two years post-introduction. We will calculate changes in *S*. Typhi-positive blood culture incidence in vaccine-eligible and 16-45-year-old participants, using the latter as a comparator for temporal trends. TCV was introduced in Malawi from 15 May to 24 May 2023. Between 18 April 2022 and 12 Apr 2024, 240,062 participants were screened; 8537 met the febrile illness definition, 6762 were enrolled, and 6704 had blood cultures collected. The blood cultures yielded 190 *S.* Typhi and 23 *Salmonella* Typhimurium cases. Among the *S*. Typhi isolates, 94.8% were multidrug-resistant, 2.1% fluoroquinolone-resistant, and 3.1% susceptible to all or some first-line antibiotics. Blood culture surveillance before and after the TCV campaign has been consistent. The data are unadjusted for vaccine coverage or other temporal trends. Surveillance continues and will provide important data on TCV effectiveness and impact in an endemic African setting.

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EVALUATING THE IMPACT OF VACCINATION WITH ORAL CHOLERA VACCINE ON CHOLERA BURDEN IN HIGH TRANSMISSION AREAS OF DHAKA, BANGLADESH AN INTERRUPTED TIME SERIES ANALYSIS

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Bangladesh, a cholera endemic country, experiences two seasonal peaks: one from April to May, another from August to September. In 2022, Dhaka experienced the largest surge in cholera-related hospitalizations in last 60 years. More than half of the came from Jatrabari, Dakshinkhan, Sabujbagh, Mohammadpur-Adabor, and Mirpur regions. In response, the government of Bangladesh requested oral cholera vaccine (OCV) from the global stockpile. A targeted, two-dose vaccination campaign was implemented in the aforementioned areas in June and August 2022. This study aims to evaluate the impact of the OCV campaign on cholera burden in vaccinated areas. A pre- and post-evaluation was conducted using routinely collected surveillance data from the icddr,b hospitals. Since 1996, every 50th patient presenting for care with acute watery diarrhea is included and a stool sample is tested for cholera by culture. The proportion of cholera cases averted in the 5 vaccinated regions was calculated. An interrupted time series analysis compared the proportion of culture cholera confirmed cases in vaccinated and non-vaccinated areas of Dhaka. In the first year of the post-OCV campaign period (September 2022-September 2023), the culture confirmed cholera positivity among hospitalized diarrheal patients from vaccinated areas decreased by 46% compared to the pre-OCV campaign period (June 2017-May 2022; except 2020). In the five high burden vaccinated areas, the hospitalization rates per year during pre- and post-OCV campaign periods were 9.1 and 6.4 per 1000 population respectively. There was no significant difference in the positivity among patients from the unvaccinated areas during the same two periods. Also the cholera positivity in the post-OCV campaign period was 51.1% lower than predicted by the model. Both the cholera positivity and hospitalization rate among vaccinated areas in Dhaka decreased following the OCV campaign. While data on other factors that may have contributed to this reduction were not collected, this evaluation provides evidence to support the impact of cholera vaccination on burden reduction in the first year following vaccination.

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GENETIC DETERMINANTS OF EXTENDED-SPECTRUM BETA-LACTAMASE RESISTANCE IN *SHIGELLA* SPECIES IN KENYA

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Shigella spp have increasingly become resistant to mostly used antimicrobials, which account for over 165 million cases and 1.1 million deaths annually worldwide, significantly, due to its low infective dose and high transmission rate in areas with poor hygiene and in low income areas. The emergence of multidrug-resistant *Shigella* spp complicates the treatment and management of shigellosis which has put more strain to the already paltry resources in the developing countries. This study sought to detect the presence of Extended spectrum β-lactamases (ESBLs) resistance genes markers in *Shigella* spp. isolates from diarrheal patients in Kenya. A retrospective analysis of 515 *Shigella* spp stool specimens

initially tested for phenotypic antimicrobial susceptibility was performed using molecular PCR to detect resistance markers. Specifically, we targeted ESBL resistance gene markers, that included: TEM, SHV, OXA, OXA-48, CTX Groups 1, 2, 9, 8, and 25, CTX-M, ACC, FOX, MOX, DHA, CIT, EBC, GES, PER, VEB, IMP, VIM, and KPC. After results analysis, we found two major ESBL resistance gene markers in *Shigella* isolates; blaTEM and blaOXA in the same proportion 14% (71/515). Additionally, blaVIM was found in 1.4% (7/515) and blaIMP in 0.2% (1/515). The other gene markers were not detected from the isolates; SHV, OXA-48, CTX Groups 1, 2, 9, 8, and 25, CTX-M, ACC, FOX, MOX, DHA, CIT, EBC, GES, PER, VEB, IMP, and KPC. This study concludes that, blaTEM and blaOXA are the most commonly seen genes among the *Shigella* isolates from Kenyan patients. Further analysis using whole genome sequencing could be done to detect mutations or virulent genes that could be associated with the resistance conferred by *Shigella* isolates.

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MOLECULAR CHARACTERIZATION AND PHENOTYPIC ANTIMICROBIAL RESISTANCE PROFILE OF DIARRHEAGENIC *ESCHERICHIA COLI* ISOLATED FROM PATIENTS WITH ACUTE DIARRHEA VISITING KERICHO COUNTY REFERRAL HOSPITAL, KERICHO, KENYA.

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Diarrheal disease caused by diarrheagenic Escherichia coli (DEC) is the second leading (after pneumonia) cause of morbidity and mortalities in children under five years in low-income countries. The emergence of multi-drug resistant (MDR) variant of DEC poses a formidable challenge infection control efforts. This study aimed to determine the phenotypic antibiotic resistance profiles of DEC isolated from patients with acute diarrhea visiting Kericho County Referral Hospital between January 2022 to December 2023. A total of 149 stool samples were collected from patients presenting with symptoms of acute diarrhea over a two-year period, shipped to the Microbiology Hub Laboratory-Kericho, cultured and isolated. DEC pathotypes were identified by multiplex Polymerase Chain Reaction assays targeting nine virulence genes; *Enteroaggregative E.coli (*EAEC*_aatA,aaiC),* Enteropathogenic *E.coli (*EPEC*_eae,bfpA),* Enterotoxigenic *E.coli (*ETEC*_LT, ST),* Enterohemorrhagic *E.coli (*EHEC*_StxI,StxII)* and Enteroinvasive *E.coli (*ETEC*_ipaH).* DEC positive isolates were subjected to antimicrobial susceptibility testing using BD Phoenix Gram Negative NMIC/ID-431 panel run on the M50 identification system.15 out of 149 (10.10%) stool samples tested positive for DEC pathotypes. The most commonly isolated pathotype was EAEC 7/15 (46.67%), followed by EPEC in 5/15 (33.33%), and EIEC in 3/15 (20%). No ETEC and EHEC were detected during this period. Majority of the strains were resistant to trimethoprim/sulfamethoxazole 13/15 (86.66%), ampicillin 12/15 (80%), amoxicillin/klauvanate 6/15 (40%), cefazolin 6/15 (40%), cefuroxime 3/15 (20%), ceftriazone 3/15 (20%), imipenem 3/15 (20%), and tigercycline 3/15 (20%). 5/15 (33.33%) of the isolates were resistant to three classes of antibiotics. However, none of the isolates were resistant to amikacin, ceftolozane-tazobactam, gentamicin, piperallicin/tazobactam. Results showed that EAEC is the most frequently detected pathotype. While many of these isolates show resistance to commonly used antibiotics, there is still potential treatment options for diarrhea caused by EAEC.

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CAMPYLOBACTER SPP AND ANTIMICROBIAL RESISTANCE IN A DIARRHEAL CASE-CONTROL STUDY IN KENYA

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Campylobacter is one of the most commonly isolated enteric pathogens among patients with diarrhoea worldwide and has been listed among the WHO high priority pathogens due to emergence of fluoroquinolone resistant strains. Complications associated with campylobacteriosis are rare but infection may be concurrent with recurrent colitis, Guillain-Barré Syndrome (GBS), irritable bowel disease, pancreatitis, cystitis and reactive arthritis. We describe the results of surveillance of *Campylobacter spp* in a diarrheal case control study in Kenya between January 2013 and December 2020. A total of 4,062 stool samples from cases and controls were collected and cultured to determine bacterial diarrheal pathogens, including *Campylobacter spp*. *Campylobacter spp* were identified using biochemical tests and confirmed using the MALDI-TOF Mass Spectrometry System (Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility tests were performed using E-test and interpreted according to CLSI guidelines. *Campylobacter spp* was isolated from 91 (2.2 %) stool samples. Out of the 91 *Campylobacter spp* isolated, 55 (60%; p = 0.04) were from diarrheal cases while 36 (40%) were from controls. Majority of the *Campylobacter spp* were *C. jejuni* (78/91; 86%) which were mainly isolated from cases (46/78; 59%) as compared with controls. Additionally, the *Campylobacter spp* were mainly isolated from children ≤5 years (60/1705; 66%; p <0.0001). Antimicrobial susceptibility test was done for ciprofloxacin, chloramphenicol, ampicillin, azithromycin and tetracycline and they all showed 100% susceptibility. However, 24% of the isolates were resistant to trimethoprim sulphamethoxazole. Our results show that *Campylobacter sp*p disproportionately infects children ≤5 years and emphasizes the importance of continued surveillance and monitoring of antimicrobial resistance patterns to combat antimicrobial resistance.

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TIMING OF CHOLERA CASES ADMISSIONS AND IMPLICATIONS FOR CASE MANAGEMENT IN THE DEMOCRATIC REPUBLIC OF THE CONGO

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Clinical care for cholera is free in cholera treatment centers (CTCs) in many settings. In the DR Congo (DRC), where out-of-pocket payments significantly contribute to health facility revenues, CTCs attract few resources and attention from health care providers and managers. During night and weekend shifts, CTCs are often staffed by newly recruited or insufficiently trained nurses with limited access to pharmacy stocks including critical supplies for cholera treatment like rehydration solutions and antibiotics. We examined the drivers of night and weekend admissions in CTCs in Uvira, a cholera endemic city in eastern DRC. Between August 2021 and April 2024, 2,605 patients were admitted for cholera treatment, for whom time of admission data was available for 2,413. 40.5% of admissions were registered at night and 35.5% during weekends. There was no difference in age or sex between patients admitted during the day and night, but children < 5 years old were more likely to be admitted during weekends (OR 1.42; 95% CI: 1.11–1.83) than older individuals. Patients living closer to the CTCs were more likely to be admitted at night (OR 0.96; 95% CI: 0.92–1, distance measured in km). Those admitted at

night were more likely to be severely dehydrated (OR 1.16; CI 0.99–1.36) and were admitted for longer (≥ 2 days vs <1 day, 1.71; 1.23–2.38). The odds of seeking care within the first 24 hours of symptoms onset were 1.6 higher (95% CI 1.21–2.12) for patients admitted at night than those admitted during the day. During weekends, patients were twice as likely to be admitted at night than during the day (OR 2.06; CI 1.74–2.45). As both severe cases, for whom prompt and aggressive dehydration is crucial, and young children, for whom dehydration is more challenging, are more likely to be admitted to CTCs during night and weekend shifts, the provision of healthcare services in CTCs should be organized to ensure sufficient resources are available at all hours to improve clinical outcomes. Building CTCs in remote neighborhoods might improve access to cholera care in settings like Uvira, where public transport at night is sparse to non-existent and private pharmacies are closed.

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ANTIMICROBIAL RESISTANCE PATTERNS AT AN URBAN REFERRAL HOSPITAL IN BLANTYRE, MALAWI

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Antimicrobial resistance is one of the biggest new threats to global health security in Africa. Recent studies in Malawi document the emergence of carbapenemase-producing Enterobacter as well as other resistant pathogens. We obtained an antibiogram for positive blood and urine cultures from September 2021 through March 2022 at Blantyre Adventist Hospital, a 40-bed pediatric and adult hospital in southern Malawi which sees an average of 75,000 patients per year. A total of n=685 cultures were obtained, with 17.6% positive specimens. Findings were notable for 39.1% ceftriaxone resistance and 40.6% ciprofloxacin resistance in tested E. coli specimens. These findings were similar or worse in tested Klebsiella specimens (57.1% ceftriaxone and/or ciprofloxacin) and tested Proteus specimens (38.5% cefuroxime and/or 23.1% ciprofloxacin). A chi-square test of independence showed a correlation between ceftriaxone and ciprofloxacin resistance, both for all gram negatives (p=4.74E-06) as well as E. coli alone (p=1.77E-05). Of note, resistance to meropenem and/or imipenem was also seen in 14.3% of tested Klebsiella specimens and 15.4% of tested Proteus specimens. Additionally, a significant number of tested urine culture specimens displayed resistance to commonly prescribed outpatient medications, including trimethoprim (E. coli 30.9%, Klebsiella 57.1%, Proteus 38.5%) and less so nitrofurantoin (E. coli 11.6%, Klebsiella 14.3%, Proteus 53.8%). In addition, tested Staphylococcus species demonstrated significant resistance to some commonly used outpatient antibiotics (36.3% trimethoprim, 27.2% third-generation cephalosporins), less so other antibiotics (4.5% clindamycin, 9% second-generation cephalosporins). Further studies should attempt to develop a full program of antibiotic stewardship at Blantyre Adventist and other regional hospitals, assessing resistance genes, uniform identification and susceptibility testing across locations, and provider education.

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SPATIAL PATTERNS OF HANSEN'S DISEASE AND WASH RISK FACTORS IN MINAS GERAIS, BRAZIL

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The mode of transmission of *M. leprae*, the causative agent of Hansen's Disease (HD), remains uncertain due to the long incubation period of HD and the inability to culture *M. leprae* in the lab. Our research investigates the role of environmental and household-level water, sanitation, and hygiene (WaSH) factors on HD transmission. We conducted a cross-sectional study of 1,315 participants living in four municipalities of a HD-endemic area of Minas Gerais, Brazil. Data were collected on participants' *M. leprae* infection status and household WaSH factors. *M. leprae* infection was determined via antibody testing against LID-1, a recombinant *M. leprae* protein. Among the study population, the highest anti-LID-1 positivity rates were found in the municipality of Mantena (12.26%). Clustering of anti-LID-1 positivity was identified using the Kuldorff spatial scan statistic and relative risk surfaces. Due to the large areas between municipalities where data were collected, clustering was examined on both a regional scale encompassing all of the study data as well as at the municipality level. Examining the whole region, clustering of anti-LID-1 positivity was identified in the municipality of Mantena. Selected household-level WaSH factors were not significant using logistic regression controlling for residence in rural areas, suggesting other factors associated with rural residence may be driving HD transmission. To investigate this, we plan to incorporate neighbors' household WaSH characteristics and environmental characteristics including elevation and proximity to natural water source.

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THE IMPACTS OF THE CROSSTALK BETWEEN BACTERIAL VAGINOSIS ASSOCIATED BACTERIA AND *TRICHOMONAS VAGINALIS* ON THE PATHOGENESIS AND HOST IMMUNE RESPONSES

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Bacterial vaginosis (BV) is an enigmatic polymicrobial condition characterized by a depletion of health-associated *Lactobacillus* and an overgrowth of anaerobes. Trichomoniasis, caused by *Trichomonas vaginalis*, is a common infection of the urogenital system. Notably, BV-associated bacteria (BVB) and *T. vaginalis* are linked to adverse gynecologic outcomes, including an increased risk of sexually transmitted infections and cervical cancer. In this study, we aim to investigate whether BVB act as pathobionts of *T. vaginalis* infection by altering pathogenic capabilities of the parasite, focusing on adhesion to vaginal substrates and regulation of host immune responses. We established a co-culture system to investigate the interaction of *T. vaginalis* and vaginal bacteria (*Lactobacillus crispatus, Escherichia coli, Prevotella bivia*, and *Lactobacillus iners*), forming a polymicrobial infection on ectocervical cell (Ect). The gene expression of *T. vaginalis* adhesin AP65 was significantly increased after the interaction with *P. bivia*. Upon interaction with *P. bivia*, promoting *T. vaginalis*growth,and affected the survival of Ects, causing higher cytotoxicity and upregulation of IL-6, IL-8, CXCL1, and IP-10. However, *L. crispatus* suppressed the *T. vaginalis*-induced chemokines. Additionally, the crosstalk between *T. vaginalis* and *P. bivia*activated of PI3K, ERK1/2, and MAPKpathways, enhanced the EMT event (the loss of E-cadherin and increased expression of Snail) in Ect, and promoted the pathogenic effects of the parasite. Together, this study demonstrate the impacts of the crosstalk between BVB and *T. vaginalis* on the pathogenesis and host immune responses, and BVB accompanying by *T. vaginalis* infection function as pathobionts to enhance the pathogenic capabilities of this parasite.

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PHYLOGENETIC AND PHENOTYPIC CHARACTERIZATION OF *BURKHOLDERIA PSEUDOMALLEI* ISOLATES FROM GHANA REVEALS A NOVEL SEQUENCE TYPE AND COMMON PHENOTYPES

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We previously confirmed the presence of *Burkholderia pseudomallei* in the environment of Ghana, unmasking a new area of endemicity for this tropical pathogen. Here, we describe the genetic characteristics of isolates obtained from that environmental survey. Twenty-one isolates were subjected to whole genome sequencing and found to represent three discrete sequence types (ST), one of which was novel, and designated ST 2058. Phylogenetic analysis places this novel isolate within a *B. pseudomallei* clade that includes genomes derived from the Americas, although it is closely related to a sub-clade that includes isolates from Burkina Faso. Importantly, phenotypic characterization demonstrates common features including API20NE profiles and *B. pseudomallei* CPS to support existing diagnostics, and susceptibility to standard of care antibiotics often used in the clinical management of melioidosis. These findings add to our knowledge about the presence and distribution of *B. pseudomalle*i in Africa and represent the first published genomes out of Ghana.

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REAL TIME PCR-HIGH RESOLUTION MELTING ANALYSIS FOR PATHOGENIC *LEPTOSPIRA* SPP. IDENTIFICATION

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Leptospirosis is an important zoonotic disease widespread worldwide. The etiological agent, *Leptospira* spp., is a highly heterogeneous bacterial genus divided into pathogenic and saprophytic species. The high resolution melting (HRM) analysis was already described as an important tool for *Leptospira* spp. typing at the species and subspecies levels. The present study aims to evaluate the performance of real time PCR-high resolution melting (qPCR-HRM) analysis, targeting the housekeeping gene *mre*A, in the identification of pathogenic species of *Leptospira* spp. isolated from human cases of leptospirosis. Eighteen reference strains belonging to five *Leptospira* pathogenic species (*L. interrogans*, *L. kirshneri*, *L. noguchii*, *L. borgpetersenii* and *L. santarosai*) and six strains isolated from Brazilian human blood cultures were initially selected for this study. Human isolates were previously identified at species level by 16S DNA sequencing. All the strains were obtained from the *Leptospira* Collection/IOC/Fiocruz. Primer pairs *mre*A-1 and *mre*A-2 were designed based on the *in silico* analysis of the core genomes of these species deposited at the GeneBank. Amplification reactions were performed with 2X Type-it HRM PCR Kit (Qiagen) using the Rotor Gene-Q (Qiagen) instrument. HRM analysis was obtained using the software Rotor Gene Q Series version 2.3.2.(Qiagen). The qPCR-HRM assay using the primer pair *mre*A-2 was able to successfully distinguish *L. interrogans, L. kirshneri* and *L. noguchii*, although with low accuracy, and improvements in our qPCR-HRM assay are still necessary. On the other hand, primer pair *mre*A-1 produced distinct melting curve profiles for *L. borgpetersenii* and *L. santarosai* (Tm 84.4 and 85.6°C, respectively). This is an important finding since *L. santarosai* was already described as one of the predominant species in many countries from Central and South America. The qPCR-HRM assay we designed could be a simple tool for species identification, especially considering the prevalence of *L. santarosai* in Brazil.

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MULTI-DRUG THERAPY IS REQUIRED TO EFFECTIVELY TREAT *BARTONELLA* INFECTION IN DIFFERENT ENVIRONMENTS

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Bartonella is a gram negative, facultative intracellular bacterium that manifests as different clinical syndromes collectively known as bartonellosis. The well-known diseases caused by these bacteria are cat scratch disease (*Bartonella henselae*), trench fever (*Bartonella quintana*) and Carrion's disease (*Bartonella bacilliformis*). Excluding *B. bacilliformis*, which is evolutionarily more distinct than the 30+ other species, *Bartonella* infections often result in subclinical or undiagnosed disease that is left untreated. Individuals with compromised immune systems may experience life-threatening clinical manifestations. Bartonellosis can affect cardiac, circulatory, digestive and neurological function and needs to be treated with effective antibiotics. To date, there is no standard treatment course for these infections and many doctors prescribe antibiotics based on limited case studies. It has been shown that *Bartonella* can grow extracellularly, intracellularly, and in biofilms. To determine an effective antibiotic strategy, it is important to understand *Bartonella* susceptibility in each of these growth conditions. **We hypothesize that combination antibiotic treatments are required to effectively eliminate *Bartonella quintana* and *Bartonella henselae* growth, particularly in biofilm and intracellular environments**. Our previous work has shown that *B. henselae* treatment with single antibiotics in different media, as well as in DH82 canine macrophages, was ineffective in eliminating bacteria. We plan to expand this work with different antibiotics supported by case reports, as well as double and triple combination therapy in erythrocytes and biofilms. The following antibiotics were tested: doxycycline, gentamicin, azithromycin, azlocillin, rifampin, tobramycin and clarithromycin. We found that while monotherapy may inhibit growth extracellularly, it is ineffective when used against intracellular bacteria or pre-existing biofilms. The effectiveness of combination therapy supports the notion that *Bartonella* species utilize target cells and biofilms as an antibiotic tolerance strategy.

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EPIDEMIOLOGY OF INVASIVE *STAPHYLOCOCCUS AUREUS* IN PATIENTS SEEN AT AN OUTPATIENT CLINIC IN THE GAMBIA

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Staphylococcus aureus is a major cause of infection globally, particularly in low-and middle- income countries. In The Gambia, *S. aureus* is a common cause of infection in children. However, comprehensive data on the epidemiology of and antibiotic susceptibility of *S. aureus* is limited. We describe the epidemiology and antibiotic susceptibility of invasive *S. aureus* causing invasive disease in The Gambia. 134 *S. aureus i*solates obtained from clinical specimens of patients seen between 2018 and 2020 at the MRCG at LSHTM outpatient clinic in Fajara, The Gambia were analyzed. *S. aureus* strains were characterized using Multilocus Sequence Typing (MLST) and antimicrobial susceptibility was determined using the Kirby-Bauer disc diffusion method. 60.3% of strains were recovered from males while children < 2 years contributed the highest number of isolates (65.0%). 82.6% of the isolates were obtained from blood cultures. Antibiotic susceptibility to trimethoprim-sulphamethoxazole, chloramphenicol, cloxacillin and methicillin was 12.7%, 97.0%, 97.0% and 96.3% respectively. MLST identified 10 Sequence Types. Our study has provided essential information on invasive *S. aureus* strains in The Gambia. Antibiotic susceptibility patterns show that invasive *S. aureus* infections can be successfully treated with widely available antibiotics in The Gambia. Methicillin Susceptible *Staphylococcus aureus* (MSSA) strains continue to be the major cause of invasive staphylococcal infection in The Gambia. Discovery of Methicillin Resistant *Staphylococcus aureus* (MRSA) strains although in small numbers emphasizes the need for continuous surveillance and better antibiotic stewardship to avoid increase in antibiotic resistance.

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CLINICAL CHARACTERIZATION OF HUMAN LEPTOSPIROSIS IN A REGION OF THE COLOMBIAN CARIBBEAN

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Leptospirosis is the emerging and re-emerging zoonosis with the highest distribution and prevalence worldwide with important repercussions on human and animal health. A prospective longitudinal descriptive study was carried out, with non-probabilistic sampling, which included 339 patients suspected of leptospirosis during July 2017 to February 2021. The cases were confirmed by the Microagglutination Test (MAT) and Polymerase Chain Reaction (PCR). The 16S rRNA gene amplification products obtained from blood or urine samples of confirmed patients were sequenced. 67 cases of the 339 suspects were confirmed. The most frequent serogroups associated with acute cases were Sejroe, Australis and Pomona. The 16S rRNA gene sequences showed L. *interrogans* and L. *borgpetersenii* as species associated with acute cases of leptospirosis. At the time of admission, the symptoms reported by the positive patients showed that 86.6% (n=58) presented the triad of symptoms: fever, headache and myalgia. In 40.3% (n=27) of cases, the triad was accompanied by jaundice and in 17.9% (n=12) by hepatomegaly. For the operational case definition, there is a greater possibility of having leptospirosis when patients presented hepatomegaly, jaundice, conjunctival injection, triad plus jaundice and triad plus hepatomegaly with statistically significant differences. In the early stages of the disease, patients with the presence of the triad (fever, headache and myalgia) associated with conjunctival injection were more likely to suffer from the disease. This symptomatology must be taken into account for the operational case definition in the study area. Leptospirosis clinical protocols in Colombia should include not only diagnostic but also clinical algorithms that guide the timely and adequate management of the disease, whose transmission is not only occurring in rural areas as has traditionally been described, but also in the urban environment.

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SEROLOGICAL ASSESSMENT OF *HELICOBACTER PYLORI* INFECTION AND ITS ASSOCIATED RISK FACTORS IN ASYMPTOMATIC GHANAIAN PATIENTS, ATTENDING AGONA GOVERNMENT HOSPITAL

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Helicobacter pylori infection poses a considerable global health challenge, exhibiting high prevalence rates in developing countries. This disease lacks a definitive treatment in Ghana and is often treated with a combination of antibiotics— posing risk of antibiotic resistance. Evidence suggests that gastric cancer risk might increase due to helminths colonizing the gastric epithelium following H. pylori-induced gastric atrophy. We carried out a cross-sectional clinical survey in Ghanaian asymptomatic patients to determine the exposure rate of *H. pylori* infection, the presence of intestinal helminthic flora, and identify related risk factors for gastro-duodenal diseases. A 2ml venous blood and 3 g stool samples were collected from 275 asymptomatic patients (mean age: 29.4 ± 9.2 years) for serological tests that detected *H. pylori* serum antibodies (human IgG) and stool antigens. A portion (1 g) of the stool samples was analyzed for intestinal helminthic flora using the formo-ether concentration technique. Structured questionnaires were utilized to collect demographic information and assess risk factors. Serum antibody testing revealed *H. pylori* exposure in 63.3% of participants, while 71.3% tested positive for *H. pylori* stool antigens. Females exhibited higher positivity rates for both tests (72.3% for stool, 65.1% for serum). More individuals (60.7%) tested positive for both *H. pylori* serum antibodies and stool antigens. Microscopic examination showed that 90.6% of the participants had no intestinal helminths. Employment status did not significantly affect *H. pylori* positivity rates (X^2=01.92; p=0.908). Logistic regression identified a long-term high-fat diet as a significant predictor of *H. pylori* occurrence (p=0.003). The high exposure and occurrence of asymptomatic *H. pylori* infection in the study area highlights the need for routine screening and early intervention to prevent the development of serious gastro-duodenal diseases. Targeted public health efforts should address modifiable risk factors like dietary habits to reduce the burden of *H. pylori*-related morbidity.

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ASSESSING PROGRESS TOWARDS THE ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF SYPHILIS IN PERU

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To eliminate and control the mother-to-child transmission (MTCT) of Syphilis, the World Health Organization (WHO) recommends meeting the following targets: (1) 95% coverage of syphilis screening during pregnancy, (2) reducing the incidence of congenital syphilis in less than or equal to 0.5 cases per 1000 newborns, and (3) 90% reduction in the incidence of maternal syphilis between 2018 and 2030. We evaluated the progress in the Peruvian context at the national and department level. A retrospective epidemiological analysis was performed using national data collected by the Peruvian Ministry of Health of reported cases of congenital and maternal syphilis from 2015 to 2022. The incidence rates were calculated by dividing the number of cases over the number of live births each year by department. Syphilis screening and sociodemographic data were obtained from The Demographic and Health Survey (DHS). In addition, we described departments with higher rates of congenital and maternal syphilis and higher percentages of extreme poverty and low maternal education (primary or no education). In 2022, nationwide syphilis screening during pregnancy was 82.6% (95% CI: 80.7% - 84.5%), the congenital syphilis rate was 0.82 cases per 1000 newborns, and the maternal syphilis rate increased by 53.7% from 2018. At the department level, only one department achieved all targets; 14, either target (2), (3) or both; while 10, didn't meet any targets. Among those living in extreme poverty, the jungle region exhibited the highest rate of congenital syphilis. Additionally, for maternal syphilis, this trend extended to include the highlands. When stratified by low maternal education, the jungle showed the highest rate of congenital syphilis, whereas for maternal syphilis, the north coast of Peru stood out. This study found that none of the Syphilis MTCT targets proposed by the WHO were met in Peru in 2022. Decentralized strategies are needed to achieve the goals of syphilis screening coverage and reduction of syphilis incidence by 2030.

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BACTERIOLOGICAL PROFILES OF DIABETIC ULCERS IN CASES OF MAJOR LIMB AMPUTATION: INSIGHTS FROM SOLOMON ISLANDS

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Solomon Islands is a Pacific island country with a 19.8% estimated diabetes prevalence. Diabetic patients there face limited access to medical care leading to poor glycemic control and increased risk of diabetic ulceration. This retrospective study describes the microbiota of diabetic ulcers in cases of major limb amputation in Solomon Islands. It is the first report

of microbiological data from diabetic ulcers in the nation. Demographic, microbiological, and outcomes data was collected from the records of patients with diabetes who underwent major limb amputation in Solomon Islands between 2018-2023. Summary and univariate analysis were conducted. Among 338 adults who underwent major limb amputation during the study period, 33% (N=113) had microbiological data available for abstraction. The median age was 53 (range: 22-83) and 58% were male (N=65). A total of 20 species were identified via pus and tissue culture. The most common species were *Pseudomonas aeruginosa* (N=27, 24%), *Enterococcus* spp. (N=25, 23%), and *Klebsiella pneumoniae* (N=18, 16%). MRSA was identified in one patient. 55% (N=62) of cultures demonstrated resistance. Resistance against ampicillin (N=31), amoxycillin (N=31), gentamycin (N=21), and Trimethoprim/sulfamethoxazole (N=21) were most common. On univariate analysis, colonization with *E. coli*, *K. pneumoniae*, and *Enterococcus* spp. was significantly associated with antibiotic resistance. The relative predominance of *Pseudomonas*, *Enterococcus*, and *Klebsiella* species is consistent with prior research on the microbiota of diabetic infections. Despite limited data, cultures from this cohort were diverse, including rarer opportunistic species such as *P. agglomerans* and *P. gergoviae*. The high percentage of resistance is concerning given the limited access to next generation antibiotics in Solomon Islands. Data gaps prevented assessment of the appropriateness of antibiotic selection. Further research is needed to better understand local infection management practices, factors contributing towards resistance, and clinical outcomes from antibiotic-resistant infections in Solomon Islands.

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HANSEN'S DISEASE (LEPROSY) IN THE UNITED STATES OF AMERICA: A SYSTEMATIC REVIEW

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Hansen's disease, also known as leprosy, is a chronic infectious disease that is caused by the bacteria *Mycobacterium leprae* and, more rarely, by *M. lepromatosis*. It is primarily spread through respiratory droplets from person to person but can also be transmitted zoonotically from nine-banded armadillos and some other mammals. The condition commonly affects the skin, peripheral nerves, mucous membranes, and extremities and occasionally impacts internal organs. Patients often face chronic impairments in both their physical and mental health. A systematic review of all published U.S. cases of leprosy has not been undertaken prior. This study's aim was to characterize all scientifically published case reports and case series of leprosy diagnosed in the U.S. Four databases were searched for relevant studies published in English up to 6/2/2023. A total of 133 case reports and series, from 1896 to 2023, met selection criteria. From these, 328 unique cases were identified. Median age was 43 years (range: 3.5 - 87 years). Most were male (79.9%) and White (51.5%), followed by 13.4% Asian and 10.4% Black. One-third presented to the National Hansen's Disease Program (NHDP) in Louisiana. State of residence and state of diagnosis trends aligned. A majority identified the U.S. as their country of origin and resided in regions providing NHDP resources. Prior to 1960, most cases were linked to military service abroad (86.5%); however, mode of transmission was usually unknown. A growing proportion of cases has been linked to zoonoses (22.8%) since 1980. Skin biopsy remained the dominant diagnostic modality (61.6%) through 2023, with PCR utilized more since 2000. By Ridley-Jopling classification, most cases (47.3%) were lepromatous. By WHO classification, when information was reliably available, 21.8% were multibacillary and 8.3% were paucibacillary. Multi-drug regimens have dominated treatment protocols since 1980, but other antibiotics have been increasingly used over the past decade. Studies reporting leprosy in the U.S. are limited overall. This systematic review comprehensively informs on past and present trends of leprosy in the U.S.

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COXBASE GOES WIKI - HOW TO CREATE SUSTAINABILITY FOR GENOMIC Q FEVER DATA.

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Q fever is a wordwide distributed zoonotic disease, caused by the Gram-negative bacterium *Coxiella burnetii*. It primarily affects livestock and animals but can also be transmitted to humans through direct contact with infected animals or contaminated animal derived materials in the environment via aerosols. CoxBase (https://coxbase.q-gaps.de/) is an online platform for epidemiological surveillance, visualization, analysis and typing of Coxiella brunetii genomic sequence and for tracking outbreak. It is maintained and closely monitored by a small team of experts from German Interdisciplinary Program "Q-GAPS - Q fever GermAn Interdisciplinary Program for reSearch" (https://q-gaps.de/). It aims to gather and display information about isolates discovered all around the world. The dataset of CoxBase provides a deep dive into epidemiological information about a bacterium and its distinctive resilience little is known about. Wikibase is a versatile open-source software platform developed by the Wikimedia Foundation. It provides the infrastructure and tools needed to create, manage, modify and query data. The best known instance is Wikidata (https://www.wikidata.org/), which host more than 1 Billion items and is maintained by a large, global community of contributors. Wikibase offers an easy to use web-interface to enter the primary structured data and can be efficiently queried via SPARQL (SPARQL Protocol And RDF Query Language.) and connected to other knowledge graphs.Here we would like to present how the genomic data of CoxBase was integrated into a dedicated Wikibase instance. The resulting resource offers all the benefits of Wikibase including an easy way to curate data collaborativly, querying it with a powerful language and connecting it with other resources. In addition we hope that this would be a model for the future to produce sustainability for genomic data - independent from research projects and their grants.

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ROLE OF ACRAB AND OQXAB EFFLUX PUMPS IN AMIKACIN AND CIPROFLOXACIN RESISTANCE AMONG CLINICAL ISOLATES OF KLEBSIELLA PNEUMONIAE IN LIMA, PERU

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Klebsiella pneumoniae is the most significant pathogen and is associated with one of the highest global mortality rates, with an average pooled mortality. The WHO has designated this bacterium as a top-priority target for research on novel antimicrobials, due to its raising antibiotic resistance. We conducted is study to determine the prevalence of the AcrAB and OqxAB efflux pumps in clinical isolates *K. pneumoniae* and their role in amikacin and ciprofloxacin resistance. The clinical samples identified as *Klebsiella pneumoniae* collected from in patients hospitalized from Lima, Peru. Antimicrobial susceptibility testing was conducted using the microdilution method. The susceptibility to antibiotics was evaluated in the presence and absence of the inhibitor CCCP and PaβN efflux pumps. Efflux pump resistance genes AcrA, AcrB, OqxA, and OqxB were amplified using the polymerase chain reaction amplification technique. We found that 100% of the isolates of *K. pneumoniae* were resistant to amoxicillin-clavulanic acid, cefotaxime, ceftazidime, cefuroxime, ertapenem, gentamicin, imipenem, meropenem and tobramycin. The 93.75% were

resistant to ciprofloxacin and piperacillin/tazobactam; 87.5% were resistant to trimethoprim/sulfamethoxazole; 56.25% were resistant to fosfomycin; 25% were resistant to levofloxacin and 18.75% to amikacin. The exposure to the PaβN inhibitor, an increase in susceptibility was observed in clinically resistant strains to amikacin, and strains resistant to ciprofloxacin show susceptible with both inhibitors. In the case of CCCP addition to ciprofloxacin, 18.75% exhibited a fourfold decrease and 56.25% displayed a threefold decrease in MIC, with 25% remaining unchanged. The prevalence of resistance genes show AcrA gene was detected in 43.75% isolates, the AcrB gene in 56.25%, OqxA in 31.25%, and OqxB in 25.00%. In conclusion, our findings suggest that efflux pumps are major mechanisms for ciprofloxacin and amikacin resistance in *K. pneumoniae*, with the AcrAB and OqxAB systems being significant contributors to this resistance

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PREVENTION AND CONTROL OF HYDATID CYST: STRATEGIES, CHALLENGES, AND FUTURE DIRECTIONS

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Background: Hydatid cyst, caused by the larval stage of Echinococcus tapeworms, is a significant public health concern worldwide but mainly in Africa. Understanding the strategies, challenges, and future directions in hydatid cyst prevention is essential for developing effective interventions and promoting global health.Objective: This abstract aims to provide an overview of the current strategies employed for the prevention and control of hydatid cyst, highlight the challenges faced in implementing these measures, and discuss potential future directions for improved prevention strategies.Methods: A review of the literature was conducted by searching electronic databases including PubMed, Scopus, and Embase. Relevant articles published between 1960 and 2021, including research studies, reviews, and public health reports, were analyzed and synthesized to provide a comprehensive overview.Results: Various prevention strategies have been implemented to combat hydatid cyst, including public health education, surveillance and control programs, veterinary interventions, and improved sanitation and hygiene practices. Future directions for hydatid cyst prevention include the development of novel diagnostic tools, vaccines, and targeted interventions, as well as strengthening collaboration between human and veterinary health sectors.Conclusion: Prevention and control of hydatid cyst necessitate a multi-faceted, integrated approach that addresses the complex interplay between human, animal, and environmental factors. Collaboration between researchers, policymakers, healthcare professionals, and communities is crucial to achieving sustainable prevention and control efforts.Keywords: hydatid cyst, echinococcosis, prevention, control, interventions, strategies, challenges, future directions.

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CLINICAL MANAGEMENT AND RECURRENCE OF HUMAN CYSTIC ECHINOCOCCOSIS IN A SECONDARY HEALTHCARE CENTER OF A HIGHLY ENDEMIC AREA IN THE ANDES OF CUSCO, PERU

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Cystic echinococcosis (CE) management in low- and middle-income countries remains a challenge due to advanced disease at presentation, limited resources and lack of standardization of care. Surgical outcomes including recurrence rates are unknown. Up to 45% CE patients in tertiary hospitals of Cusco City are referred from the Sicuani District. We reviewed medical records of 115 patients with CE admitted to a secondary care hospital in Sicuani from January 2010 to December 2019. The median age was 25 years (IQR, 16-46) and 60.5% were female. Fifty-six patients (48.7%) were referred from primary care centers. Liver cysts were diagnosed in 106 patients (92.2%), lung cysts in 5 (4.3%), and combined liver/lung cysts in 4 (3.5%). The median duration of symptoms was 21 days (IQR, 3-89 days). The median length of stay was 7 days (IQR, 5-10). Pre-surgical complications were documented in 46 cases (40%). One hundred seven patients (93%) had an ultrasound, identifying 134 liver cysts. The median largest liver cyst diameter was 13 cm (IQR, 9.2-15.2). Eighty-four patients (62.7%) had single cysts, 19 had two cysts, and 12 patients had 3 cysts. Eighty-one cysts (58.3%) were staged: 28 (34.6%) were Gharbi I, 31 (38.3%) Gharbi II, 17 (21%) Gharbi III, and 5 (6.2%) Gharbi IV. Of the 102 (88.7%) surgically treated patients, 57 (55.9%) received albendazole (ABZ) after surgery, 27 (26.5%) before and after surgery, 7 (6.9%) did not received it, 6 (5.9%) before surgery, and in 5 the timing was not specified. Anti-spillage measures were documented in 11 (9.6%) patients. Fourteen out of 110 (12.7%) were readmitted to the hospital, 8 for cyst recurrence (new cyst, same site), 4 for complications, 3 for elective two-stage treatment, and 1 for a new cyst (different site). Considering past medical history, readmissions, and follow-up, the recurrence rate was 16/115 (13.9%). The patients admitted to this secondary care hospital in a highly CE endemic area presented advanced disease and complications. Surgery was the main stage-specific treatment implemented. The high recurrence rate created a burden that could be effectively reduced with spillage prevention and peri-operative ABZ.

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SUBARACHNOID NEUROCYSTICERCOSIS: CLINICAL, SEROLOGICAL AND NEUROIMAGING EVOLUTION AFTER ANTIPARASITIC TREATMENT

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Neurocysticercosis (NCC) presenting in the subarachnoid space, represents the most aggressive form of the disease. The cysts' growth within this space tends to be uncontrolled and diffuse, often resulting in mass effects and triggering immune responses in surrounding tissues, that may lead to arachnoiditis or even vasculitis. Data on the efficacy of antiparasitic treatment in subarachnoid NCC remain scarce, leaving healthcare providers and patients without clear guidance on therapeutic outcomes. This cross-sectional study assessed the clinical, serological, and imaging evolution of 80 individuals with a history of subarachnoid NCC who received antiparasitic treatment at least two years before. Seventeen participants (23.6%) continued presenting subarachnoid NCC lesions. From these, 15 (82.35 %) had positive levels of circulating parasite antigen, most of them at high levels (11/15, 73.3%, with rations above 20, and 4 (26.6%) with ratios between 1-3). All cases continued having positive antibody responses on EITB (western blot), with 11 reacting to all 7 diagnostic bands. Univariate analysis showed that individuals with high antigen levels had 43.1 times the OR compared to those who have a negative antigen ratio, individuals with 60 years more have 6.75 the OR of having lesions compared to those age less than 45 years (CI 95% 1.33-34.26, p=0.02), patients with continuous crisis have 3.9 (CI 95% 1.03-15.03, p=0.04) times the OR compared to those who did not have seizure activity per every increase in one reactive antibody band on EITB the OR of having lesions increases by a factor of 2.9 (CI 95% 1.7-4.9, p<0.001). Multivariate analysis showed strong evidence that those who have high antigen ratio have 39.9 times the OR of having lesions compared to those who have a negative result p=0.017, when adjusted by sex, age, clinical symptoms (headache and seizures) and WB. Incomplete cure of subarachnoid NCC occurs in a sizable proportion of

patients, and serological results (in particular very high antigen levels) are strong predictors of treatment failure.

Keywords: subarachnoid, neurocysticercosis, evolution, recurrence

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EXPERIMENTAL INFECTIONS DEMONSTRATE CONCOMITANT IMMUNITY AGAINST *TAENIA SOLIUM* IN PIGS: QUANTIFYING THE IMPACTS OF AGE AND PRIOR INFECTIONS ON THE NUMBER OF CYSTS

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Taenia solium is a major cause of epilepsy in low- and middle-income countries. Important efforts have been made to control and eliminate this parasite but, due to the high costs of large-scale field testing, it is difficult to experimentally validate the optimal strategy. Mathematical models are therefore also used to help design cost-effective strategies, but knowledge gaps around the existence and extent of pig immunity hamper the representation of transmission in endemic settings. In this study, we show that pig immunity constrains cyst development, and we quantify this effect. In a first experiment focusing on the impact of age, six groups of pigs (48 pigs in total) between 4 and 22 weeks old were infected with 20,000 eggs each. In a second experiment focusing on the impact of prior infections, 80 pigs were either infected with 100, 1,000, 5,000 or 20,000 eggs at 4 weeks old and reinfected after 12 weeks with 5,000 or 20,000 eggs, or infected only once, at the time of the first or second infection. To decrease the variability in results, pigs were infected in individual pens with eggs coming from a pool of up to 10 tapeworms with more than 75% of activated oncospheres. The first experiment showed that the ratio of viable cysts to eggs ingested first increased with age at infection, up to approximately 10-16 weeks old, then declined drastically in older pigs (KW test p=0.008). The second experiment showed that first exposure with as few as 100 eggs, almost entirely prevents the development of more cysts at reinfection, even with high re-exposure doses, with no statistical differences between infected and reinfected pigs. Despite extensive efforts to control for variability in infective doses, the number of cysts varied a lot between individual pigs within each group. In conclusion, age at infection and prior exposure affect cyst development in pigs. These factors may explain why low number of cysts are routinely found in endemic regions, usually fewer than 10 per animal, despite high transmission levels. The parameters we have obtained will be incorporated into simulation models to replicate the distribution of cysts found in pigs from endemic settings.

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ECHINOCOCCOSIS: ASSESSING SURVEILLANCE NEEDS FOR AN EMERGING INFECTIOUS DISEASE IN THE UNITED STATES

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Echinococcosis is caused by several species of zoonotic tapeworms and affects dogs and wild canids worldwide; sheep, cervids, and rodents are intermediate hosts. Two main species, *E. granulosus* and *E. multilocularis,* affect humans, who are accidental hosts. Infection causes enlarging lesions in multiple organs; rupture of cystic lesions can lead to anaphylaxis and death. During 1980-2010, no locally acquired human cases were described, but since 2010, nine such human cases have been identified in three states, along with infections in wild canids and domestic dogs. Recently, echinococcosis consultations to CDC increased from 32 in 2022 to 61 in 2023. Echinococcosis is not nationally notifiable and is reportable in only two states: Texas and Washington. Key stakeholders were identified from states where echinococcosis is reportable (n=2) and states with locally acquired human or animal cases (n=6). Stakeholders were interviewed during September-December 2023 using a semi-structured questionnaire and participated in group discussions. Responses were analyzed for thematic patterns around surveillance. The most common themes were desire for multi-state collaboration (n=8), interest in improving surveillance (n=7), and need for a One Health approach (n=6). No states had outreach materials, although the need was recognized (n=4). Surveillance in states where echinococcosis is reportable began in 2016 (Texas) and 2023 (Washington). Clinical criteria differ between these case definitions, and one state noted difficulty applying the criteria. Given the limited number of cases in any state, the need for a coordinated approach was identified. Subsequently, two multi-state working groups were established to develop a standardized case definition and outreach materials for pet owners, hunters, farmers, veterinarians, and public health professionals. Because this emerging disease is rare, aggregating standardized human case data at CDC would help stakeholders understand the risk for transmission in the US and develop prevention strategies. Further, outreach materials would raise awareness around reporting potential cases.

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POVERTY LEVELS ASSOCIATED WITH THE PREVALENCE OF LIVER CYSTIC ECHINOCOCCOSIS IN A PERUVIAN RURAL COMMUNITY

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Human cystic echinococcosis (CE) is a zoonotic parasitic disease categorized among the most neglected diseases. It detrimentally impacts the economy and the quality of life of affected individuals. While associations with poverty-related factors have been observed, these relationships have not been thoroughly assessed using appropriate methods. The current study aims to determine the influence of poverty on the prevalence of CE within the livestock-rearing community of Canchayllo, Peru. For this analysis, a secondary examination was conducted on a convenience sample of 138 individuals selected from a dataset of 232 subjects. The selection criteria included only those who responded to the survey designed to measure the Wealth Index. A generalized binomial regression model with a log link function was used to evaluate the association between the presence of liver CE and levels of poverty. Poverty was classified into two categories: high poverty (1st and 2nd wealth index quintiles) and non-high poverty (3rd to 5th wealth index quintiles). The analysis adjusted for screening coverage and other covariates. The findings indicate a liver CE prevalence of 13.04% (95%CI: 7.42 - 18.66) and a prevalence ratio (PR) of 2.35 (95%CI: 1.17 - 4.73, p=0.016) between groups with high levels of poverty compared to those with non-high levels of poverty, after adjusting for sex, gender, and screening coverage. Some variables like sheep raising were excluded from the model due to multicollinearity with the wealth Index. The results demonstrated a significant correlation between the level of poverty and the prevalence of liver cystic echinococcosis, thereby confirming the influence of poverty on the development of the disease.

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ALVEOLAR ECHINOCOCCOSIS: NOT JUST IN ENDEMIC COUNTRIES

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Alveolar echinococcosis (AE) is a zoonosis caused by the larval form of *Echinococcus multilocularis*, a cestode endemic in Asia, especially China, Turkey and north-eastern European countries. *E. multilocularis* has a sylvatic life cycle, where foxes act as definitive hosts and rodents as intermediated hosts. When the intermediate host ingests eggs of *E. multilocularis* excreted by the definitive host with feces, the larval stage can develop. Humans are accidental intermediate hosts, after ingesting contaminated foods. Until 2023, no cases of AE had ever been reported in Italy, and the first case was reported in February 2024. Here we report a second case of AE diagnosed in Italy. A 87-year-old Swiss woman living in Italy, was seen in a Hospital in northern Italy for a painful epigastric mass ,not dissociable from the gastric wall, pancreas and liver, with peripheral contrast enhancement at CT scan. An esophagogastroduodenoscopy excluded the gastric origin of the mass. The patient was diagnosed with liver neoplasm of unknown origin. Chemotherapy was excluded due to her age and performance status. No biopsy was performed. However, serology for CE returned positive and she was referred to our center. Ultrasound showed a roundish inhomogeneous mass 11 x 7 x 12 cm in diameter, with ill-defined margins, anechoic central areas, calcifications and small cystic images within. While this appearance was not consistent with CE, the Swiss nationality of the patient prompted us to inquire about contact with foxes in her home country, which she reported. AE was therefore suspected and confirmed by serology. The patient was referred to a center for AE in Switzerland where she was staged as P4 N0-1 M1 for the presence of metastatic lesions in the lung. Albendazole at 100 mg/die was started for the presence of biliary tree compression, with of resolution of epigastric pain after few weeks . She is clinically stable and asymptomatic at the time of this writing. AE is a rare but potentially fatal parasitic disease if not diagnosed and left untreated and should be included in the differential of neoplastic lesions in selected cases also in non-endemic areas.

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SURGICAL TECHNIQUES AND COST ANALYSIS OF PULMONARY ECHINOCOCCOSIS: A SINGLE CENTER EXPERIENCE

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Surgery is the established therapy for thoracic echinococcal cysts, but there is no consensus about the optimal surgical method. Options include lobectomy, segmentectomy, or cystostomy with closure of bronchial openings and capitonnage. The choice depends on several factors such as cyst integrity, quantity, location in the lung, associated lung tissue damage, and costs. Each surgical approach carries its own disadvantages and potential benefits, and a careful assessment of the individual patient's condition and the medical team's expertise is crucial. We report our experience with surgical techniques and costs in the treatment of thoracic echinococcosis (TE). We reviewed hospitalization expenses and surgical techniques used in the treatment of 11 patients with TE admitted to the Thoracic Surgery Ward at 'Santi Antonio e Biagio e Cesare Arrigo' Hospital in Alessandria, Italy from May 2023 to March 2024. The total expenditure for a single hospitalization, encompassing both hospital stay and surgical intervention, ranged from €7754.387 to €19160.987. Cystostomy with closure of bronchial openings and capitonnage was the primary surgical approach. Our data indicate that a more conservative approach, such as cystostomy, yields superior surgical outcomes, consistent with the literature. Despite incurring slightly higher costs than with lobectomy, the benefits offered by cystostomy outweigh this marginal expense difference. Given the relatively similar costs between the two procedures, opting for the more conservative surgery appears to be a prudent and therefore best choice.

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FORMALIN INJECTION LEADING TO CHEMICAL CHOLANGITIS IN SURGERY FOR ECHINOCOCCAL CYST: A CASE REPORT

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Cystic echinococcosis (CE) is a debilitating chronic infection predominantly affecting the liver and lungs. Various surgical options, including conservative (endocystectomy) and radical approaches (pericystectomy or segmentectomy), are employed in treatment. However, the intracystic administration of scolicidal agents is contraindicated in cases where connections to the biliary system are present, due to the risk of chemical cholangitis, a severe and feared complication.In this report, we present a case involving an Italian patient who, in 1993, underwent surgical resection of a hepatic CE cyst. The procedure involved the injection of formalin into the cyst cavity, followed by aspiration of its contents and pericystectomy. This outdated method led to the development of chemical cholangitis and multiple biliary strictures, necessitating the placement of several stents over time. The patient's condition progressively deteriorated, culminating in a liver transplant in 2016. Complications from this procedure included embolization of a hepatic artery pseudoaneurysm, ultimately necessitating a second transplant shortly thereafter.While no consensus exists on the optimal surgical technique for treating liver CE—owing to variables such as cyst stage, size, segmental location, and presence of complications—adhering to fundamental safety principles is imperative to prevent dire outcomes.

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A RARE CASE OF NEUROCYSTICERCOSIS WITH THE NORTHERN HEMISPHERE TAPEWORM *TAENIA CRASSICEPS*

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Neurocysticercosis occurs mainly in South America and Sub-Saharan Africa and is usually caused by larvae of *Taenia solium*. In Europe neurocysticercosis is not a common differential diagnosis for intracerebral lesions. In rare cases *Taenia crassiceps*, a tape worm, that is endemic in the northern hemisphere can cause neurocysticercosis. We present a case of *Taenia crassiceps* neurocysticercosis in a 72-year-old immunocompetent male.The patient presented in the emergency room with symptoms, that were suspected to be a stroke. There was no relevant medical history, especially no immunosuppression. A CT scan showed a cerebral lesion with atypical haemorrhage. Neurological symptoms resolved without intervention, hence a follow-up cerebral MRI scan of the lesion was performed after three months. This showed increasing perifocal oedema so that surgery was indicated. Macroscopically it appeared as a lesion with a rough shell and a fluid core. Histopathology showed no malignancy but the remnants of a cystic lesion with signs of chronic inflammation and small calcified bodies. A detailed travel and exposure history made the diagnosis of a parasitic disease highly likely. Neurocysticercosis seemed a potential differential diagnosis, however neither MRI nor histopathological findings were typical. Serology for cysticercosis was negative. A biopsy specimen was sent for a specific cestode PCR. The result showed DNA of the tapeworm species *Taenia crassiceps*. Given the paucity of published clinical case reports, therapy with praziquantel and albendazole was started, prednisolone was added. Therapy was well tolerated. *Taenia crassiceps* tapeworm infections have been described rarely in humans. Diagnosis is difficult on the basis of MRI-imaging and histopathological findings and needs high index of suspicion. Specific serological testing is not available; hence we are depending on molecular diagnostics. An immuncompromised host is not a precondition for infection. Reasons for the increasing number in infections as well as therapy can be discussed and need further investigation.

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PYROPTOSIS CELL DEATH IN RAT BRAIN TISSUE WITH NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is a parasitic disease affecting the central nervous system (CNS), whose infectious agent is the larval form of the parasite *Taenia solium*. The pathology of the disease is not fully understood, as it is a chronic disease affecting humans. Clinical manifestations include headache, dizziness, seizures and memory loss or cognitive deficits. During treatment, the clinical manifestations are exacerbated by the death or degeneration of the parasite. The clinical picture of NCC resembles other neurodegenerative diseases such as Alzheimer's, Parkinson's and multiple sclerosis, clinical manifestations that are associated with pyroptosis processes. Pyroptosis is a type of programmed cell death that plays a protective role against infections, but excessive pyroptosis can cause neuronal damage and be detrimental to normal cells and tissues. Therefore, in this research we determined whether the larval stage of *T. solium* causes pyroptosis cell death in the central nervous system in an animal model of NCC. Brain tissues from rats with NCC, untreated and treated with antiparasitic drugs, and a control group of brain tissues from non-infected rats were used. Immunoreactivity in tissues around the cyst was determined by immunohistochemistry for markers associated with programmed cell death: NLRP3 inflammasome, Caspase-1 (Casp1), Gasdermin D (GSDMD) and IL-1β. The immunoreactivity to GSDMD was elevated in all NCC-infected tissues, being statistically significant compared to brain tissues from non-infected rats. While immuoreactivity to NLRP3, Casp1, GSDMD and IL-1β markers was elevated in 30% of infected brain tissues, being the pattern of immuoreactivity different from the control. Our data suggest that there is pyroptosis-programmed cell death due to immuoreactivity to GSDMD in rat brain tissues with NCC.

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A ONE HEALTH SYSTEMATIC REVIEW OF ECHINOCOCCAL INFECTIONS IN CANADA

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Echinococcus canadensis and *multilocularis* are parasitic agents transmitted among animals, occasionally infecting humans. Despite being classified as neglected tropical diseases, echinococcal infections are believed to be emerging within the ranges of their wild definitive hosts across Canada. This study aims to consolidate and systematically review estimates of parasitic zoonoses frequency available in Canada. Considering that these parasites infect various host species and involve stages in the soil, an integrated One Health approach is imperative for obtaining an accurate epidemiological overview. A systematic review on the frequency of *E. canadensis* and *E. multilocularis* in humans, animals, and soil in Canada is currently underway following the PRISMA guidelines. We have developed a search query encompassing the names of the two parasites, the diseases they cause, and the Canadian provinces and territories. Three databases were searched for relevant articles. Subsequently, articles were imported into Covidence© software for assessment by two independent reviewers in two phases (title and abstract screening, followed by full-text review) following predetermined inclusion and exclusion criteria. These articles will undergo evaluation using modified JBI quality assessment checklists tailored for One Health studies. Data will be extracted on general study characteristics, population demographics, study design, diagnostic tests, and estimates for the outcome variable (prevalence, incidence, count). A total of 1152 unique articles were identified spanning from 1962 to 2023, of which 965 were deemed irrelevant after screening titles and abstracts. The remaining 187 articles are currently undergoing full-text review. This presentation will demonstrate the geographic distribution of the selected articles, the number of case reports for each host group, and where possible, the frequency trends over time for each host group. Additionally, the limitations of the existing JBI tools in addressing frequency measures concerning domestic and wild animals and the environment will be highlighted.

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COMPARISON OF THE DIAGNOSTIC ACCURACY OF LIVER ULTRASONOGRAPHY AND COMPUTED TOMOGRAPHY FOR CYSTIC ECHINOCOCCOSIS IN A NATURALLY INFECTED SHEEP MODEL

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Cystic echinococcosis (CE) is a major zoonotic disease in Peru's central highlands, where controlling this disease in animals requires significant interventions. Imaging methods are favored over serological tests for diagnosing CE due to the latter's cross-reactivity with other parasites. To evaluate the diagnostic accuracy of liver ultrasonography (US) and

computed tomography (CT) for detecting cystic lesions in sheep, using necropsy as the gold standard. We assessed the sensitivity and specificity of US and CT in sheep over four years old from an endemic area. Diagnostic criteria for US positivity were defined as any suspicious lesion, lesions ≥20 mm regardless of WHO stage, lesions in early stages (CE1, CE2, CE3) irrespective of size, and lesions ≥20 mm in stages CE1, CE2, and CE3. Necropsy data served as the basis for sensitivity and specificity estimates. Necropsy showed a CE prevalence of 82.3% (79/96). US sensitivity ranged from 18.4% to 84.6%, with specificity from 62.2% to 100%. CT sensitivity was between 26.5% and 92.3%, and specificity ranged from 35.6% to 100%. Concordance between US and CT varied from 41.4% to 89.7%, indicating significant variations depending on diagnostic criteria listed above. This study highlights the variability in the sensitivity and specificity of US and CT depending on the applied criteria. The results underscore the importance of non-invasive imaging in diagnosing CE in sheep and suggest potential applicability in human diagnostics

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STUDY OF THE PREVALENCE OF CYSTIC ECHINOCOCCOSIS IN LIVESTOCK COMMUNITIES OF CUSCO, PERU

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Cystic echinococcosis (CE) poses a significant public health challenge worldwide, particularly in regions where livestock is a major economic activity and human-animal interaction is frequent, such as in Peru. The liver and lungs are the most commonly affected organs, with a previous studies performed in Peru indicating a prevalence ratio of 3:1. This study aimed to analyze the prevalence of liver CE in three endemic communities in the southern highlands of Cusco, Peru—Acopia, Combapata, and Pomacanchi—and to examine the spatial distribution of cases within these communities. We conducted an abdominal ultrasound survey across the three communities, enrolling a total of 811 participants. Epidemiological and clinical data were also collected to identify relevant risk factors. Ultrasound evaluationindicated prevalence levels of 3.4% (95% CI: 0.1% - 6.8%), 7.9% (95% CI: 4.1% - 11.7%), and 6.5% (95% CI: 4.4% - 8.7%) in Acopia, Combapata, and Pomacanchi, respectively. Geospatial analysis revealed that the spatial risk of liver CE was primarily concentrated on the peripheries of each community, where informal slaughter practices are common. The study highlights the ongoing challenge of CE in endemic regions and underscores the importance of spatial analysis in understanding the distribution of health risks. Addressing informal slaughter practices may be key to reducing the prevalence of CE in these communities.

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IMMUNOHISTOCHEMICAL IDENTIFICATION AND SPATIAL DISTRIBUTION OF TWO ANTIGENS IN CEREBRAL PORCINE NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC), invasion of the central nervous system by *Taenia solium*, stands as the predominant cause of acquired epilepsy worldwide. In viable phase, cyst actively produces/releases sets of antigens that stimulate a host immunological response and can induce inflammation. However, the antigen distribution across cyst stages (viable, degenerating, and calcified) is unknown. Using anti-*T.solium* monoclonal antibodies (moabs), targeting total cyst, vesicular fluid and excretory/secretory (E/S) antigens, we explored its localization in brain tissue samples of treated naturally infected-NCC pigs in different cyst stages. We selected two clones of moabs for each antigen type based in our western blots results against well-defined recombinant antigens related to anchoring, scaffold formation, and secretion (rGP50, rT24H and sTsRS2-sTs14/18, respectively). Moabs against total cysts principally targeted rGP50, rT24H and sTsRS2, while the others recognized sTs14/18 and sTsRS2. Four moab-based immunohistochemistry techniques (IHC), two against anchoring antigens (TsW5/TsW8) and two against E/S (TsV3/TsE1) were standardized and tested with viable, degenerating, and calcified cysts from 17 pigs. IHC results determined two distinct antigen patterns: moabs TsW5/TsW8, directed against total cysts were detected in the cyst walls, vesicular fluid, and the spiral canal in viable cysts, while TsV3/TsE1, directed against E/S, in cyst walls and vesicular fluid only. Both were detected in the surrounding tissue. In calcified cysts TsW5/TsW8 recognized antigens within the cyst, while TsV3/TsE1 stained antigens in the surrounding parenchyma (500µM). Residual antigens were detected until 12-months after antiparasitic treatment with a gradual decrease in immunoreactivity percentage (4-months:30.8%, 8-months:7.5%, 12-months:1.8%). These findings demonstrate the dynamic nature of antigen distribution. The presence of antigen in the tissue, even in calcified lesions, suggests an antigen diffusion mechanism from parasite E/S to brain cells that can potentially cause structural alterations.

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EVALUATION OF DAMAGE IN AXONAL TRANSPORT THROUGH THE IMMUNOREACTIVITY OF THE MOTOR PROTEINS KINESIN AND DYNEIN IN BRAIN TISSUE OF RATS WITH NEUROCYSTICERCOSIS

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Neurocysticercosis (NCC) is a parasitic disease of the CNS that causes acquired epilepsy in people from endemic countries in Latin America, Africa and Asia, generated by the larval form of the cestode *Taenia solium*. It is a chronic disease, which in symptomatic patients is characterized by seizures and epilepsy that make it impossible for them to carry out their daily activities. Infection studies in laboratory rats have identified that in NCC there is axonal damage characterized by the accumulation of proteins (neurofilament, amyloid precursor protein) in areas of axonal swelling or axonal spheroids, which could be related to a probable deterioration in the axonal transport and would contribute to the degeneration and death of neuronal cells. Therefore, in this study, the reactivity of the motor proteins kinesin and dynein in brain tissue of rats with NCC treated and not treated with antiparasitics at different post-treatment sacrifice times (up to 12 months) was evaluated by immunohistochemistry. It was identified that rats with NCC present accumulation of kinesin and dynein in the axonal spheroids surrounding the parasite, with no significant difference between the treated and untreated group; with absence of spheroids in the control group. Likewise, there is a greater number of axonal spheroids reactive to these motor proteins in gray matter than in white matter. These results indicate that in NCC there is damage in axonal transport characterized by the pathological accumulation of these proteins that would contribute to the process of neuronal degeneration, and that is maintained over time indicating irreversible axonal damage.

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IDENTIFICATION OF PROTEINS WITH TGF- β FUNCTION IN THE EXCRETORY SECRETORY PRODUCTS OF *TAENIA SOLIUM* LARVAL STAGE

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Helminth parasites have the ability to modulate the host's immune response through their secretory excretory products (ES) that activate TGF-β

signalling. *Taenia solium* is a cestode helminth whose larval stage affects the central nervous system in humans, causing neurocysticercosis which is associated with seizures. The mechanism that this parasite uses to establish itself and remain in its host is not yet known. The aim of this study was to identify proteins with TGF- β function. For these, the ES products were fractionated by ion exchange chromatography, then each fraction was incubated in MFB-11 cells that release alkaline phosphatase enzymes in the presence of TGF-β-like proteins (TGF- β bioassay). Each fraction was also observed using SDS-PAGE and silver stain. Protein fractions positive in the TGF-β bioassay were analyzed by LC-MS/MS. The results showed a total of 12 fractions of the ES products, and 4 fractions were positive in the TGF- β bioassay. In the SDS-PAGE, we observed differences in the banding pattern in each fraction. Besides, we evaluated these fractions by immunoblot using an anti-TGF β antibody, and we observed that no band was recognized by this antibody, suggesting that these proteins have TGB function but are structurally different from TGF β. These positive fractions were evaluated by LC-MS/MS.

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DEFINING THE CELLULAR COMPOSITION OF THE CSF IN SUBARACHNOID NEUROCYSTICERCOSIS THOUGH MULTIDIMENSIONAL SPECTRAL FLOW CYTOMETRY

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The most severe manifestation of neurocysticercosis is subarachnoid disease (SANCC), causing chronic relapsing-remitting inflammation, arachnoiditis, and significant morbidity and mortality if untreated. Improved understanding of the inflammatory milieu in the central nervous system (CNS) may improve targeted immunomodulation as an adjunct to anthelmintic therapy. To characterize the cellular nature of the CNS inflammation, fresh CSF was obtained from patients at their entry to care ("pre-treatment"), prospectively every 3-6 months ("mid-treatment"), and at the time of presumed cure (CSF antigen and qPCR tests for *T. solium* were negative) from 2022-present. Cells were analyzed by multidimensional spectral flow cytometry. In the 7 pre-treatment CSF, each had elevations of leukocytes (GM 10 leukocytes/μL; normal 0-5/μL). Lymphocytes were the primary cells present, with CD3+ T lymphocytes making up 66.4% (GM 2.3/μL, normal 0.15-1.83/μL) and B cells forming the next largest group of cells identified in all specimens at 14.1% (GM 0.43/μL, normal 0-0.03/μL). CSF from untreated SANCC was characterized by expansion of a sizeable effector memory (Tem) CD4+ T population (84.8% of CD4+ cells, GM 1.2/μL, normal 0-0.02/μL), with smaller populations of TEMRA (GM 0.04/μL, normal 0.00-0.02/μL), T regulatory (FoxP3+, GM 0.03, normal 0.00-0.12/μL), T central memory (GM 0.03/μL, normal 0.05-1.6/μL) and naïve T cells (0.3%, 0.003/μL, normal 0.00-0.08/μL). CXCR3+/CD4+ cells (Th1) made up 38.4% of the Tem cells (39.4%). Among B cells, plasmablasts represented 5.4%, naïve B cells 7.5%, and central memory B cells 5.4%. Cluster analysis (FlowSom) identified a CD3+/TCRgd-/CD4-/CD8- population as being notably expanded (GM 6.7% of T cells, range 1.8-35.8%) along with a CD3-/CD19+/CD27-/IgD- population (GM 14.7% of B cells, range 7.9-42.1%), both of which have been shown to be associated with other non-infectious autoimmune inflammatory disease. Post cure analyses are underway using paired samples (n=2) but await additional subjects. Our data help provide a single cell landscape that underlies some of the contributors to pathology seen in SANCC.

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SARS-COV-2 EXPOSURE BEFORE OR AFTER PLASMODIUM VIVAX INFECTION EXACERBATES THE HUMORAL RESPONSE AGAINST THE LATTER

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Loreto is a region of the Peruvian Amazon with a high risk of transmission of malaria whose health system suffered deeply early in the COVID-19 pandemic. Previously it has been shown that a *Plasmodium* infection diminishes the humoral response against respiratory viruses. We hypothesize that symptomatic (Sym) acute malaria and asymptomatic (Asym) malaria reduces pre-existing natural IgG antibody levels against SARS-CoV-2 in people living in the Peruvian Amazon. This study performed a multiplex assay in a Luminex platform to analyze IgG antibody levels against a 11-antigen (Ag) panel of *P. falciparum*, 10-Ag panel of *P. vivax* (*Pv*) and a 6-Ag panel of SARS-CoV-2. The study population was a total of 93 individuals. Samples of healthy endemic controls from Iquitos city (n=9) (no history of malaria in the past 3 years and no confirmed *Plasmodium* infection); Asym (n=24) and Sym (n=34) Amazonian subjects with only a confirmed *Pv*-infection; subjects with a *Pv*-infection first and a latter SARS-CoV-2 exposure (n=20) and the opposite sequence: exposure to SARS-CoV-2 first and a latter Pv-infection (n=6) were evaluated. *Pv*-infection was determined by positive microscopy and/or qPCR and SARS-CoV-2 exposure by positive antigenic, serological, or molecular testing or vaccination against COVID-19 self-reported by the subject. MFI (mean fluorescence intensity) log-transformed data was compared between study groups for each antigen by permutation ANOVA. Individuals with SARS-CoV-2 exposure before or after *Pv* exposure have lower IgG anti-PvEBPII and anti-PfMSP1 and higher IgG anti-PvMSP1-19 and anti-PvMSP8 levels compared to the only *Pv*-infected Asym group. In addition, these individuals have higher IgG anti-Spike, anti-RBD, and anti-NP levels for the Wuhan and Omicron strains compared to the only *Pv*-infected group whether they were Asym or Sym. This analysis shows that SARS-CoV-2 exposure before or after *Pv* exposure has an Ag-dependent effect on the response against *Pv* and that the order of coexposure to *Pv* and SARS-CoV-2 does not affect the response against SARS-CoV-2.

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EVALUATION OF NEUROCYSTICERCOSIS PRESENTATION AND MANAGEMENT IN HOUSTON, TEXAS

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Neurocysticercosis (NCC) is a neglected tropical disease affecting 2-8 million people globally and results in ~30% of epilepsy cases in endemic countries. While the causative agent, Taenia solium, is not endemic in the United States (US), experts estimate 4,000 annual US cases. Data from our health system in Houston, TX, describe >10 new NCC diagnoses yearly. Infectious Disease Society of America (IDSA) guidelines recommend treatment based on location and viability of cysts in the central nervous system (CNS). Here we describe NCC cases presenting to our system serving at-risk patients in Houston, TX between 2017-2021. We retrospectively identified patients ≥18 years old tested for NCC in the Harris Health System [HHS], systematically extracted demographic, clinical, imaging, and treatment variables from the patients' records, and recorded this data via a REDCap instrument. We classified NCC patients by NCC type and performed descriptive statistics. Of the 113 unique patient NCC records found, most were born in Mexico (n=65, 57%) and lived in the US for >5 years prior to NCC diagnosis (n=66, 58%). 67 (59%) initially presented as inpatients. 72 had calcified parenchymal lesions and 57 (50%) had viable cysts (24 with extra-parenchymal NCC [EPN]). Patients with calcified disease frequently reported chronic headaches (n=29, 56%), whereas patients with viable parenchymal NCC (VPN) more often presented with seizures (n=18, 55%). Considering IDSA guideline-directed management, 25 (76%) of patients with VPN cysts received corticosteroids. 16 (66%) of 22 patients with 1-2 VPN cysts received albendazole monotherapy, and 5 (56%) of 13 patients with >2 VPN cysts were treated

with dual anti-parasitic therapy for at least 7-14 days. Regarding patients with EPN, only 15 (63%) received corticosteroids and only 8 (33%) received dual anti-parasitic therapy of which 4 (50%) were treated with shorter duration (7-14 days). In summary, in our healthcare system, management of NCC varied greatly and often did not follow IDSA guidelines. Improving frontline provider education on NCC may enhance adherence to guideline-based treatment and neurologic outcomes.

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ASSOCIATIONS BETWEEN C-REACTIVE PROTEIN, MALARIA, AND MALNUTRITION AMONG CHILDREN WITH FEBRILE ACUTE RESPIRATORY ILLNESS IN UGANDA

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C-reactive protein is a useful biomarker in differentiating bacterial from viral acute respiratory illnesses (ARI) in resource-constrained settings. In malaria endemic regions, however, CRP production may be influenced by malaria infection. The relationship between nutritional status and CRP levels is unclear. We conducted a posthoc analysis of data from the intervention group of a stepped-wedge cluster-randomized controlled trial evaluating the use of a clinical algorithm including a CRP rapid diagnostic test (RDT) to guide antibiotic treatment among children with febrile ARI. We enrolled 1220 children aged 2 months to 5 years old evaluated by a village health worker (VHW) in the Kasese district of western Uganda. CRP was measured by a semi-quantitative rapid test (<10, 10-40, 40-80, 80+ mg/L). Malnutrition status was assessed using MUAC (mid upper arm circumference). Participants were tested for malaria using an antigen RDT specific for *Plasmodium falciparum*. The association between CRP and malaria RDT results was assessed with a Cochran-Mantel-Haenszel chi-squared test. We accounted for the sensitivity and specificity of the CRP RDT. The association between CRP and MUAC was assessed with a Kruskal-Wallis chi-squared test. Of the 632 children evaluated during intervention periods, both CRP and malaria RDT results were available for 629 children. 50.4% tested positive for malaria. Malaria positive children tended to have higher CRP levels compared to those who were malaria negative ($p<0.0001$). Among those with MUAC measurements, 12.7% had severe or moderate malnutrition (MUAC < 13.5 cm). CRP levels were similar between those with severe or moderate malnutrition and those without ($p=0.24$). CRP levels among children with malaria in our study tend to be elevated and may be like those observed with bacterial infection. Additionally, CRP levels among children with severe or moderate malnutrition were like those without malnutrition. The presence of malaria should be considered when designing treatment algorithms to guide antibiotic decisions for febrile children in malaria-endemic regions.

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UNRAVELLING THE ENIGMA: HOW SIMULATION-BASED CLINICAL TRAINING ENHANCES THE DIAGNOSIS OF VIRAL ENCEPHALITIS - INSIGHTS FROM GHANA'S SECOND LARGEST REFERRAL HOSPITAL

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Viral encephalitis poses a significant global health challenge, particularly in developing countries like Ghana. However, accurate diagnosis is hindered by low rates of essential lumbar puncture (LP) and cerebrospinal fluid (CSF) analysis. A 3-year retrospective study at Ghana's second largest tertiary hospital showed that only 26% (15/57) of patients with suspected Central Nervous System infection underwent LP subsequent CSF fluid analysis. To address this, clinical skills training was implemented to enhance healthcare professionals' proficiency in lumbar puncture. Training materials were developed using the Modified Delphi Approach. Pre- and post-training knowledge assessments were conducted using online data collection forms. The training was conducted by expert clinicians and included didactic and hands-on practice sessions. Customized mannequins were used for LP simulation training, with intracranial pressure (ICP) measuring devices utilized to demonstrate proper techniques. All training items were donated to the hospital's skills development and simulation centre for continuous skills enhancement. Twenty-one healthcare professionals participated in the training. The pre-training assessment showed that 85% (18) clinicians encountered more than 3 suspected cases of viral encephalitis monthly but were likely to request LP in only 10% of cases. Barriers to LP performance included contraindications (15, 71%), absence of intracranial pressure (ICP) measuring devices (7, 33%), inadequate tools (6, 29%), and lack of expertise (6, 29%). After the training, participants experienced notable improvements: 90% (19) reported fulfillment of training expectations, 81% (17) gained confidence in LP, and 77% (16) enhanced their LP skills. LP performance surged from 15 to 77 over 3 years, representing a 413% increase. The improved LP proficiency led to identifying viral agents causing encephalitis for the first time in Ghana. This advanced medical knowledge and diagnosis strengthened the healthcare system, and potentially improved patient outcomes.

7402

SEVERE *PLASMODIUM FALCIPARUM* MALARIA WITH SYMMETRIC PERIPHERAL GANGRENE: A REPORT OF TWO CASES

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Malaria remains a leading cause of morbidity and mortality in sub-Saharan Africa, particularly in its severe forms. Symmetric peripheral gangrene (SPG) occurring with disseminated intravascular coagulation (DIC) during severe *Plasmodium falciparum* malaria is a rare and serious event, more commonly reported in Asia than in West Africa. SPG is defined as symmetric distal ischemic lesions on two or more sites without major vessel obstruction. The pathophysiological mechanisms involve complex consumptive coagulopathy, which is increasingly understood.We report two cases from the medical intensive care unit at the Principal Hospital of Dakar, Senegal. The patients, aged 60 and 66, presented with severe malaria evidenced by blood smears showing >10% parasitemia with *P. falciparum*. Both developed DIC with multi-organ failure (neurological, hemodynamic, renal, hematological, hepatic, and metabolic) requiring supportive treatments. They subsequently developed SPG affecting all four limbs, leading to bilateral lower limb amputations for one and disarticulation of fingers for the other. The use of anticoagulants (unfractionated heparin for Case 1 and low molecular weight heparin for Case 2) played a crucial role in managing the coagulation-inflammation cycle. Early diagnosis of infection, prompt antimalarial treatment, intensive care management, and anticoagulation therapy are critical for improving prognosis in patients with severe malaria complicated by SPG.

7403

PERFORMANCE OF QUANTITATIVE POINT-OF-CARE TESTS TO MEASURE G6PD ACTIVITY: A META-ANALYSIS

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the main risk factor for severe haemolysis following treatment with 8-aminoquinolines (8AQ). The WHO recommends G6PD testing prior to 8AQ-based hypnozoitocidal treatment. We undertook an individual level meta-analysis of the performance of commercially available quantitative point of care assays (PoCs) compared to reference spectrophotometry. A systematic literature search identified 588 articles of which 14 (2.4%) fulfilled pre-defined inclusion criteria and were included; 3 unpublished datasets were also included. In total 12,545 paired measurements were included, 10,313 (82.2%) by STANDARD G6PD Test (SD Biosensor, RoK, "SDB"), 2,042 (16.3%) by CareStart G6PD Biosensor (AccessBio, USA, "CSA"), 150 (1.2%) by CareStart Biosensor (WellsBio, RoK "CSW"), and 40 (0.3%) by FINDER (Baebies, USA, "FBA"). The pooled sensitivities of the SDB when diagnosing G6PD activity <30% of normal were 0.82 (95%CI: 0.72-0.89) and 0.93 (95%CI: 0.73-0.98) for capillary and venous blood samples, respectively. The corresponding values for diagnosing <70% G6PD activity were 0.93 (95%CI: 0.67-0.99) and 0.87 (95%CI: 0.70-0.95), respectively. The pooled specificity of the SDB was high (>98%) for all blood samples and thresholds. Irrespective of the blood samples and threshold applied, the sensitivity of the CSA did not exceed 62%, although the specificity remained high at both the 30% and 70% thresholds (>88%). Only one study each from CSW and FBA were included. Sensitivity of the CSW was 0.04 (95%CI: 0.01-0.14) and 0.81 (95%CI: 0.71-0.89) at the 30% and 70% thresholds, respectively (venous blood samples). Sensitivity of the FBA was 1.00 (95%CI: 0.29-1.00) and 0.75 (95%CI: 0.19-0.99) at the 30% and 70% thresholds (venous blood samples). The specificities of the CSW and FBA were consistently high (>90%) at both diagnostic thresholds. The SDB performed significantly better than other tested PoCs except for the FBA. More evidence is available for the performance of the SDB compared to other PoCs, giving higher confidence in its utility in diagnosing G6PD deficiency.

7404

UNBIASED METAGENOMIC SEQUENCING OF ACUTE ENCEPHALITIS AND MENINGOENCEPHALITIS FOR IDENTIFICATION OF INFECTIOUS ETIOLOGIES IN NEPAL

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The burden of acute encephalitis syndrome (AES) and meningoencephalitis is significant in Nepal. Their causative agents mostly remain unknown because of use of conventional approach which fails to identify the etiologies, leading to delays in treatment, causing morbidity and mortality. We hypothesize presence of several organisms, including vaccine preventable etiologies causing AES, meningoencephalitis and febrile illness, when identified directs public health efforts for prevention and surveillance. This study employs unbiased metagenomic sequencing to investigate infectious etiologies causing AES, undiagnosed febrile illness and meningoencephalitis, in 200 subjects (3mth-75yr) from east Nepal. Cerebrospinal fluids (190) were collected, during May-Dec'23, with process controls from skin and procedure area and clinical metadata. Until now, 38 CSF have been sequenced using Illumina iSeq100. The initial clinical diagnoses of the subjects were meningoencephalitis, AES and sepsis with fever, seizure and vomiting. Most of these subjects had elevated WBC (>11×10^9/L) but normal CSF cell-count (≤5WBC/mm^3) indicating infectious etiology, which was confirmed by sequencing: *Enterovirus C* (5), *Pseudomonas putida* (2) and *Elizabethkingia meningoseptica* (2). The *Enterovirus C* was closely related to isolates from outbreaks in Pakistan and northeast India, near to our enrollment site. Other studies have linked these pathogens as etiologies: *E. meningoseptica* reported as emerging hospital-based pathogen causing meningitis and *P. putida* as a rare pathogen causing central nervous system infections. The subject infected with *P. putida* had high CSF glucose indicating early infection and possible disruption of blood-brain barrier due to sepsis. Another subject which had coinfection of all 3 pathogens, showed higher CSF protein, confirming viral etiology. This novel study was able to identify several etiologies, including depiction of co-infection. Further, this study elevates the utilization of unbiased metagenomic sequencing to complement diagnosis, identify coinfections, conduct surveillance and track transmission.

7405

ENVIRONMENTAL ENTERIC DYSFUNCTION IN NON-SLUM-DWELLING WELL-NOURISHED WOMEN IN DHAKA CITY, BANGLADESH

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Environmental Enteric Dysfunction (EED) is a subacute inflammation of the gut mucosa associated with undernutrition and prevalent in regions with inadequate sanitation facilities. Previous investigations indicated a high prevalence of histologically confirmed EED among undernourished women residing in the slums of Dhaka, with over ninety percent exhibiting the condition. However, scant data exist on histology-confirmed EED among well-nourished women residing outside of slum areas. In the present study, we screened normal Body Mass Index (BMI) (20-24.9 kg/m2) non-pregnant non-lactating women (18-45 years), residing in non-slum areas of Dhaka, who presented with functional dyspepsia according to the ROME IV criteria. Participants consenting to the study underwent upper gastrointestinal endoscopy, with mucosal biopsies obtained from the distal duodenum and subsequently subjected to histopathological examination for EED. Diagnosis of EED was established based on the following criteria: Mild EED, characterized by the presence of at least one EED feature (i.e., lymphocyte infiltration); Moderate EED, defined by the presence of two EED features (comprising mild features along with villous atrophy or crypt hyperplasia); Severe EED, identified by the presence of all three aforementioned features. Between October 2, 2022, to March 30, 2024, a total of 888 women were screened for eligibility, among whom 33 participants provided consent for endoscopic evaluation. The mean age of the participants was 28.7±6 years with a mean BMI of 23.2±1.4 kg/m2. Histological examination revealed that 21% (n=7) of the participants exhibited features indicative of EED, whereas the remaining 79% (n=26) exhibited no histological evidence of the condition. Among those diagnosed with EED, five individuals demonstrated mild EED, while two exhibited moderate EED. This study contributes novel insights into the epidemiology of EED, suggesting a lower prevalence among well-nourished women residing in non-slum areas. Furthermore, it underscores the pivotal role of environmental sanitation and nutritional status in the pathogenesis of EED.

7406

ADAPTIVE DENGUE ANTIVIRAL PLATFORM TRIAL (ADAPT): A RANDOMIZED, ADAPTIVE, OPEN LABEL TRIAL FOR ANTIVIRAL SCREENING IN PATIENTS WITH EARLY SYMPTOMATIC DENGUE

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Dengue virus infection is the most abundant and rapidly spreading vector borne disease globally (est. 105million cases/year). Climate change is driving disease emergence in altitudes and latitudes not previously endemic. There are currently no licensed antiviral therapies. Severe manifestations occur between day 4-6 of illness, allowing only a brief window to intervene with a directly acting antiviral drug. There is no consensus pharmacometric approach to evaluate antivirals in early symptomatic dengue. Previous phase 2 trials have used either time to viral clearance or area under the viraemia curve, but these are insensitive measures and generalise poorly. We will present the protocol for our multi-center, phase 2 open label, randomised adaptive platform trial for the rapid screening and dose optimisation of antiviral drugs in early symptomatic dengue. This will be a continuously running adaptive platform, with capacity to add new intervention arms as therapeutic agents become available, and terminate arms if efficacy/futility endpoints are met. We will enrol participants with dengue confirmed by positive NS1 antigen test, and <48hrs of symptoms. Where safety data is available for individual drug candidates, we will recruit children ≥10yrs. Patients will be randomised 1:1 to eligible intervention arms, or the control arm (supportive care, no placebo). Initial therapeutic candidates include a monoclonal antibody (Serum Institute of India), Baricitinib and Molnupiravir. After enrolment, participants will have serial plasma samples collected for viral load measurement every 12 hours for 5 days. The primary virological endpoint will be rate of viral clearance estimated under a hierarchical log-linear model fit to serial viral load measurements. The initial efficacy endpoint will be a ≥10% increase in viral clearance rate in the intervention arm relative to control arm. We anticipate that this trial will provide proof of concept for the rapid assessment of in-vivo antiviral activity for dengue using rate of viral clearance, and provide evidence to justify progression of promising antiviral agents to phase 3 trials.

7407

SURVIVING SNAKEBITE ENVENOMING: DECADES-LONG WAR WITH CHRONIC KIDNEY DISEASE: A CASE SERIES FROM RAJASTHAN, INDIA

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Snakebite envenoming is a neglected tropical disease. Vipers- *Daboia russelii*, *Echis carinatus* and *Hypnale hypnale* are commonly responsible for Acute kidney injury (AKI) that resolves with antivenom and supportive care. However, antivenom ineffectiveness in Rajasthan poses a special challenge. Here, we report 2 young patients who developed CKD decades following probable *Echis carinatus sochureki* envenoming. *Case 1:* A 22-year-old lady with a snakebite at 5y of age, and again at 11y of age presented to us with status epilepticus. She had experienced local swelling on both occasions but developed a superadded infection, requiring incision and drainage during the second bite. She did not receive any antivenom for either event. Her pregnancy (18 y) was complicated by preeclampsia. She had elevated urea, creatinine, bilateral contracted kidneys, hypocalcemia (4.2 mg/dL) and raised PTH (1409 pmol/l). Symptoms resolved with parenteral calcium. She is currently on bi-weekly maintenance haemodialysis (HD) for CKD. *Patient 2*: A 30-year-old lady, CKD on maintenance HD, presented with MRSA central-line associated blood stream infection (CLABSI) complicated by spinal epidural abscess (C7-T1 destruction), cord compression and spastic quadriparesis. She had a snakebite at 18y of age during complicated by bleeding and anuria. She improved with antivenom, 2 HD sessions and remained asymptomatic for 10 years before developing CKD. She further developed *Pseudomonas* CLABSI. She received daptomycin, meropenem and brief empirical anti-tubercular therapy. Despite this and change of HD catheter thrice, she succumbed to septic shock. Throughout her medical journey, CKD was a focal point, significantly impacting her prognosis and contributing to her eventual demise. CKD is reported in 26-37% after Russell's viper bites. Though, AKI occurs in ~20% of *Echis* bites, to our knowledge, this is the first report of CKD after possible *E. c. sochureki* bite. We highlight the long-term productivity loss, financial burden and suffering of snakebite survivors.

7408

PREVALENCE OF *PLASMODIUM FALCIPARUM* INFECTION AMONG CHILDREN HOSPITALIZED WITH ACUTE RESPIRATORY ILLNESS IN WESTERN UGANDA

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Previous studies suggest malaria co-infection with influenza in sub-Saharan Africa is uncommon, but coinfected children are more likely to experience more severe illness. However, the prevalence of malaria in influenza-infected children in sub-Saharan Africa may have changed due to the expanded global efforts to decrease the burden of malaria in the past decade. From July to November 2022, we enrolled 265 children aged 2 months to 18 years admitted to the inpatient departments of one rural (Bugoye Health Centre [BHC]) and one semi-urban (Rukoki Health Center [RHC]) health facility in Kasese District, Uganda with acute respiratory illness defined as onset of documented fever (≥38°C) and respiratory symptoms (i.e., cough, respiratory rate > 30 breaths per minute, and/or oxygen saturation < 90%) in the prior 7 days. All participants were tested for influenza A and B, respiratory syncytial virus (RSV), and SARS-CoV-2 by polymerase chain reaction (Cepheid, Inc., GeneXpert platform). Rapid Plasmodium falciparum malaria HRP-2 antigen testing (mRDT) was performed on capillary blood. A total of 12 participants were excluded because of missing data. Overall, 36% (86/253) of children tested positive for Influenza A (24%) or B (13%), while 42% (106/253) had a positive mRDT. Among influenza-positive children, 48% (41/86) had a positive mRDT, compared to 39% (65/167) of influenza-negative children. Influenza was not significantly associated with a positive malaria RDT, (Unadjusted Prevalence Ratio: 1.2, 95% CI: 0.90, 1.78). When stratifying by study site, 54% (36/67) of influenza-positive children at the rural site had a positive malaria RDT whereas the prevalence of co-infection at the semi-urban site was lower at 26% (5/19). Our findings demonstrate that malaria parasitemia among children hospitalized with acute respiratory illness in western Uganda is frequent, but similar between influenza-positive and influenza-negative children. These results highlight the need for further research assessing the impact of malaria co-infection on the transmission and pathogenesis of influenza.

7409

IMPROVING INFECTION PREVENTION AND CONTROL COMPLIANCE IN CAMEROONIAN HEALTHCARE FACILITIES USING THE WORLD HEALTH ORGANIZATION CORONAVIRUS SCORECARD TOOL

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Infection prevention and control (IPC) is a clinical and practical evidence-based-approach aiming at protecting patients, health workers and visitors from avoidable infections. We conducted a study to determine the baseline level of infection prevention and control and to determine if repeated evaluations of healthcare facilities after prior trainings of healthcare workers could lead to the improvement of IPC. The study took place

from March 2020 to November 2023. Trainings of healthcare workers in selected healthcare facilities were followed by baseline assessments and reassessments. From 2020 to 2023, we evaluated and analyzed 2,188 IPC assessments from 1,358 healthcare facilities during the 3-year period. IPC assessments included 1,358 (62%) at baseline, 485 (2%) IPC first reassessment, 234 (1%) IPC second reassessment, 65 (0.3%) IPC third reassessment, 33 (0.1%) IPC fourth reassessment, 7 (0.03%) IPC fifth reassessment, 5 (0.2%) IPC sixth reassessment and 1 (0.04%) IPC seventh reassessment. Among all the healthcare facilities evaluated, only 497 (36.5%) have been evaluated more at least 2 times. The median IPC score was 52.4% at baseline and increased to 88.1% in some facilities. Between the baseline and reassessments, there were significant differences in the median IPC score between healthcare facilities, translating a better compliance after trainings. These differences were maintained during the multiple reassessments. Our findings are in accordance with previous studies in other sub-Saharan African countries which found a significant association between the ownership status and IPC performance, an improvement in the median IPC score from baseline and higher IPC scores in healthcare facilities dedicated to COVID-19. Our findings could guide policy implications, since there is a recognized low utilization and effectiveness of validated IPC tools in low- and middle-income countries, particularly in Sub-Saharan Africa. Emergencies are opportunities to improve and monitor IPC compliance in LMIC.

7410

COULD EARLY CARE SEEKING AND INCREASED ACCESS TO COMMUNITY-LEVEL HEALTH SERVICES STOP THE INCREASING MALARIA-RELATED DEATHS IN ZIMBABWE?

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Mashonaland Central and East provinces are among the highest malaria burden provinces in Zimbabwe with an average annual incidence of 24/1000 in 2023. During the peak period January to June, there were 42 malaria deaths in 2022 and 94 deaths in 2023; the case fatality rate increased 63% from 0.08% to 0.13%. A retrospective review of deaths reported in Mashonaland Central and East provinces was completed using a structured investigation form to extract patient data from clinical charts, including demographics, reasons for delays in care, appropriate clinical management, and associated complications. Out of 94 malaria-attributed deaths, 88 (94%) had records available and were reviewed. Overall, 14% were <5 years, 24% were aged 5-14 years, 43% were aged 15-59 years, and 19% were ≥60 years. Males accounted for 52% of all deaths. Seventy-seven percent of all deaths obtained care more than 24 hours after the onset of malaria symptoms, and 28% of these delayed reaching a healthcare provider because of a lack of transportation. Most cases (68%) first sought care at a health facility, while 25% sought care first from a community health worker. Seventy-four percent of the cases were diagnosed as severe malaria at the initial presentation. Shortages in diagnostic equipment and consumables for assessing kidney function, blood glucose levels, parasite levels, and temperature were reported in 30% of deaths. Ninety-one percent of deaths occurred at the health facility, while 9% were in the community. The most commonly reported complications requiring specialized care were impaired consciousness (64%), acute respiratory distress (40%), and acute kidney injury (17%). A lack of specialized services and expertise for intensive care and hemodialysis to manage associated complications was reported in 36% of deaths. The clinical courses of individuals dying secondary to malaria infection suggest that use of community health services may play a role in reducing mortality by preventing delays in seeking care. Limited resources and expertise to manage complications of severe malaria disease may be a contributing factor and could represent a target for intervention.

7411

ESTIMATES AND SPATIAL PREVALENCE OF *TRYPANOSOMA CRUZI* INFECTION AMONG CHILDREN IN NEW YORK CITY

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Chagas disease, caused by the protozoa *Trypanosoma cruzi*, is the leading cause of parasitic death in Latin America. Humans are primarily infected when a Triatomine bug defecates while feeding and the feces are scratched into the bite; other modes include vertical transmission, ingestion of contaminated food, transplantation, and blood transfusion. Acute *T cruzi* infection is typically asymptomatic and undiagnosed. If untreated, however, nearly 30% of individuals progress to debilitating chronic Chagas disease decades later after initial infection. In 2023, it is estimated that 37,500 migrants younger than 18 years of age arrived in New York City (NYC) primarily from *T cruzi* endemic countries in Latin America. To date, there has not been a large-scale pediatric prevalence study of *T cruzi* in NYC.*T cruzi* infection in NYC's Latin American pediatric migrant population is highly variable and dependent of socio-demographic factors, country of origin, and built environment. We aim to screen roughly 300 pediatric migrants of Latin American origin for *T cruzi* at Mount Sinai affiliated outpatient pediatric clinics as well as to administer a demographic survey to identify risk factors for exposure. We will develop risk profiles for *T cruzi* infection and create a statistical model to extrapolate prevalence estimates for the five boroughs of NYC using geo-located information on migrant age structure and origin. This work represents an initial step in developing a cost-effective pediatric *T cruzi* screening protocol for NYC.

7412

EPIDEMIOLOGY OF NEUROCYSTICERCOSIS: A 30 YEAR PILOT STUDY OF HOSPITALIZED PATIENTS IN FLORIDA

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Neurocysticercosis (NCC) is a parasitic disease of the CNS caused by the pork tapeworm, *taenia solium*, and is the leading cause of acquired seizure disorder worldwide. Although there have been international and out-of-state studies characterizing the epidemiology of patients presenting with NCC, this study is the first to characterize the burden of NCC in Florida. The inclusion criteria for this retrospective chart review included any patient presenting to UF Health Shands Hospital, Gainesville, FL, with symptomatic NCC (defined as one or more of the following symptoms unexplained by another disorder: seizures, focal neurologic deficits, headaches, hydrocephalus, nucal rigidity, psychiatric disturbances, and altered mental status plus or minus systemic symptoms) between June 1993-June 2023 given an ICD-9 or ICD-10 code of NCC. 34 patients in total met this criteria. Demographic characteristics of these patients included country of origin (76% non-USA, 24% unspecified), sex (59% Male, 41% Female), ethnicity (65% Hispanic, 32% non-Hispanic, 3% unspecified), age (68% 21-50, 18% 51-70, 15% 0-20), race (47% white, 12% black/AA, 9% Asian, 3% AIAAN, 29% unspecified), insurance status (41% uninsured, 21% insured, 38% unspecified), language preferred for medical correspondence (47% Spanish, 38% English, 6% other, 9% unspecified), and per capita income of Florida county of origin (53% bottom 50%, 41% top 50%, 6% unspecified). Selected hospitalization outcomes were also collected and compared between groups. 97% of patients reported NCC symptoms prior to receiving an NCC diagnosis and 72% of patients presented to at least one healthcare facility for similar symptoms without receiving a diagnosis of NCC. 21% of patients were readmitted at least once for NCC symptoms or complications. 18% of patients stayed in the hospital for more than 10 days. Although the power of this study is limited, this research identifies

delays in patient presentation and diagnosis and may aid clinicians in identifying common patient presentations associated with NCC in order to promote prompt diagnosis and close follow-up for these patients.

7413

TARGETED CLINICAL MENTORSHIP IMPROVES PERFORMANCE OF MALARIA SERVICES IN ZIMBABWE

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The PMI-funded Zimbabwe Assistance Program in Malaria II (ZAPIM II) project uses targeted clinical mentorship to improve case management and malaria in pregnancy service provision in health facilities (HFs) with observed service provision gaps. In September 2022, ZAPIM II conducted a malaria quality standards assessment (QSA), using a structured tool, to evaluate facility readiness and 108 health workers' (HWs) clinical performances at 70 HFs in Mashonaland Central and Mashonaland East provinces. The project assessed HF readiness to provide malaria services, including availability of material and human resources trained in malaria case management, HW clinical skills, and use of standard operating procedures (SOPs) for diagnosis, classification, and treatment of malaria cases. Action plans were made for assessed health facilities to address identified gaps through mentorship. Fifty-two health facilities received onsite mentorship, 15 virtual mentorship and 3 onsite supportive supervision between October 2022 and August 2023. In September 2023, ZAPIM II conducted another QSA at the same 70 HFs and 124 HWs were assessed to document the improvements in malaria service delivery after mentorship. There was a 21% significant decrease in the proportion of HWs trained in malaria case management (CI: 17%-24%, p<0.0001) due to newly recruited HWs. Overall, HW clinical skills scores improved by 9.3% (CI: 5.6%-13.1%; p =0.000) despite the decrease in the percentage of providers trained in malaria case management. Use of SOPs during rapid diagnostic testing for malaria increased by 10% (CI: -24.9%-7.5%; p =0.272). Correct classification of malaria cases, documentation of treatment doses and duration, and explanation and advice on malaria prevention given to patients increased by 10.6% (CI: -48.8%-27.6%; p=0.5322). Lack of statistically significant increases in these parameters could be due to the high number of untrained new staff in the second assessment. Findings suggest that targeted mentorship can improve HW malaria case management clinical skills. More analysis is needed to assess the overall impact on malaria services.

7414

A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL PROGNOSTIC MODELS AMONG CHILDREN WITH SEPSIS IN LOW- AND MIDDLE-INCOME COUNTRIES

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Sepsis is the leading cause of child death worldwide, with the majority of these deaths occurring in low- and middle-income countries (LMICs). The aim of this systematic review and meta-analysis was to describe clinical prognostic scores and models for pediatric sepsis outcomes and assess the performance of these scores for predicting mortality in LMICs. Ovid Medline, CINAHL, Cochrane Library, EBSCO Global Health, Web of Science, were searched through September 2022 for citations related to the development or validation of a clinical prognostic score or model among children with sepsis, conducted in an LMIC. Titles, abstracts, and full texts were screened by two independent reviewers and data extracted regarding population characteristics, variables included, outcomes, and model performance. Risk of bias was assessed with the Prediction Model Risk of Bias Assessment Tool (PROBAST). 4,251 titles/abstracts and 315 full-text studies were screened, with 12 studies meeting inclusion criteria. Study countries included India, China, Egypt, Indonesia, Tanzania, and a multi-site study in Latin America. Prognostic scores/models included existing scores such as PELOD-2, pSOFA, PRISM, P-MODS, refractory shock criteria. There was high risk of bias in all studies. Meta-analysis was possible for pSOFA and PELOD-2 with pooled area under the receiver-operator characteristic curve of 0.86 (95%CI 0.78-0.94) and 0.83 (95% CI 0.76-0.91), respectively. Relatively few clinical scores and models have been externally validated for prognostication and risk-stratification among children with sepsis in diverse LMIC settings. Notably there were no studies from low-income countries. Some potentially relevant studies were excluded due to lack of clarity regarding the presence of sepsis in the study populations. More widespread and standardized use of sepsis criteria may aid in better understanding the burden of sepsis and prognostic model performance among children in LMICs. Further research to externally validate, implement and adapt these models is needed to account for challenges in use of these scores at the bedside in resource-limited settings.

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STRONG HEARTS: A NOVEL PRIMARY-CARE BASED DIAGNOSIS AND TREATMENT SUPPORT PROGRAM FOR CHAGAS DISEASE IN EAST BOSTON, MA, USA (2017-2023)

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Chagas disease is a neglected infection of poverty estimated to affect 300,000 people in the US, with a prevalence of 49 per 100,000 in Massachusetts. If left untreated, it progresses to irreversible heart disease and death in 20-30%, but <1% of the infected in the US receive treatment. Strong Hearts is a Chagas disease diagnostics and treatment initiative centered at the East Boston Neighborhood Health Center (EBNHC) in Boston, MA, whose goal is to uphold the preciousness of every person and the human right to healthcare. We present the program structure, diagnostics uptake, local epidemiology, and Chagas care continuum. Following provider and East Boston community information sessions, a protocol for EBNHC was developed and approved by its Board. Confirmed Chagas patients were referred to Boston Medical Center for evaluation and treatment. Our chart reviews identified continuum of care barriers, addressed by Strong Hearts' care navigators. 14,354 patients were screened at EBNHC from Mar 2017-May 2023. 3.4% of screening tests were positive. After confirmation, the overall population prevalence was 0.7% (95% CI: 0.6% - 0.9%) with no sex difference. Steep barriers at most steps of the care continuum would have been insurmountable for most patients without a care navigator. Of 90 patients diagnosed at EBNHC Mar 2017-Sep 2022, 44 (49%) began and 28 (31%) completed antiparasitic therapy. Major barriers to diagnosis and treatment were complexity of the confirmation process for positive screening results, number of steps between referral and initial appointment, challenges for patients taking time from work and traveling for appointments, lack of insurance, and medical bills. While some barriers to care are specific to Chagas disease and its lack of optimal diagnostic and treatment modalities, others exemplify barriers faced by many low-income Latin American community members in accessing medical care in the US. We identified important barriers to care that could be attenuated by medical institutions. We find that motivated primary care clinicians provide Chagas care when support for confirmatory testing and care navigation are in place.

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BURULI ULCER CASE DETECTION AND DIAGNOSIS IN THE OBOM SUB MUNICIPAL IN GA SOUTH MUNICIPALITY OF THE GREATER ACCRA REGION, GHANA.

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Mycobacterium ulcerans is the cause of Buruli Ulcer Disease (BUD), a chronic, debilitating condition that mostly affects the skin and sometimes the bone. Patients who have BUD may have long-term disability, irreversible deformity, and a decline in their quality of life. There is no known way to prevent M. ulcerans, mode of transmission is yet unknown. BUD is still a public health concern in Ghana's endemic communities. Hence, there is the need for periodic assessment in endemic areas to control the diseases. The current study examines Buruli ulcer prevalence, case detection, and diagnosis in the Obom sub municipality of the Ga South Municipality in the Greater Accra Ghana.**A** community-based cross-sectional study was conducted. The Obom community, Konkon Lebene, Nyormishie, was specifically chosen because to its history of Buruli ulcer endemicity. Residents who had resided in the research area for the previous six months and were present throughout the study's duration were the study's potential participants. The survey used simple random sampling to choose participants from houses. Furthermore, health screening was done to look for Buruli ulcer case in the community. Samples from potential participants were taken for laboratory testing. To identify the possible variables linked to Buruli Ulcer case detection, information on demographic traits, awareness of Buruli ulcer, health-seeking behaviour. Tables and figures were used to report the findings.All the 32 suspected buruli ulcer samples tested negative for buruli ulcers using both PCR and microscopy. About 6% of participants had no knowledge about Buruli Ulcer while males are 10 percent less likely to be knowledgeable about the Buruli Ulcer compared to females in the community with an odds ratio of OR = 0.9(95%C. I, -1.2 – 1.3). The study concludes zero prevalence of Buruli ulcer within the study area. The knowledge of Buruli ulcer is high among community members and majority of individuals visits health facilities upon detection of symptoms of Buruli ulcer. The study recommends targeted public health programs that address diverse beliefs and practices related to BU detection in Obom community.

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DENGUE SEVERITY PREDICTION IN A HYPERENDEMIC REGION IN COLOMBIA

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Early detection of severe dengue (SD) warning signs is crucial in preventing life-threatening complications. Despite its importance, comprehensive knowledge about these early indicators is still limited. This study aims to identify predictors of SD in a hyperendemic region of Colombia. A cross-sectional analysis was conducted using data from 2018 to 2022, encompassing 233 patients. Utilizing the 2009 World Health Organization dengue classifications, cases were differentiated between severe dengue (SD) and non-severe dengue (non-SD). Among these, 47 were confirmed as SD. Associations between clinical, demographic, and laboratory data and disease severity were examined using Fisher's exact tests or the Mann-Whitney U test ($p<0.05$). Profiles for SD and non-SD cases were established through multiple correspondence analysis, and a logistic regression-based predictive model was validated using training and test sets. The model's performance was evaluated using the area under the receiver operating characteristic curve (AUC-ROC), accuracy, sensitivity, F1-score, and precision. Differences in place of residence, comorbidities, type of infection, and signs and symptoms were observed between the severe dengue (SD) and non-severe dengue (non-SD) groups. Median levels of platelets, white blood cells (WBC), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were found to be higher in the SD group compared to the non-SD group. Key hematological markers, including neutrophils, leukocytes, platelets, AST, and primary infection, were identified as significant predictors of SD. The model demonstrated an area under the receiver operating characteristic curve (AUC) of 0.91 (95% CI, 0.85-0.96). The developed predictive model significantly assists clinicians in assessing SD risk and optimizing triage, which is particularly crucial during dengue outbreaks.

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ACCIDENTS BY CATERPILLARS IN THE VALLEY OF CARACAS, VENEZUELA: AN OUTBREAK STUDY

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Most accidents by caterpillars are mild, self-limited hypersensitivity reactions and occur in tropical areas with limited access to medical care, making the epidemiology of lepidopterism poorly understood. Several clinically important species are subject to dramatic variations in density, resulting in infestations of large numbers of caterpillars or moths and subsequent outbreaks of coincident cases. In August 2023, an unexpected increase in accidents by caterpillars was observed in the valley of Caracas, Venezuela, including a small group with cardiovascular alterations. This outbreak study describes the clinical cases of accidents and analyzes the geographical behavior of the reported caterpillar sightings during the study period. A total of 32 sighting reports were recorded, with 117 caterpillars observed, including 13 accidents. Most reports occurred in Miranda state (n=115, 98.2%). Most of the caterpillars were identified as belonging to the family *Saturniidae*, genus *Dirphia* (*n*=101; 86.3%) and *Automeris* (*n*=11; 9.4%). Two (1.7%) caterpillars were identified as *Megalopygidae Megalopyge*. More than half of the accidents occurred in children under 9 years of age (53.8%). Accidents occurred more frequently in residential gardens and parks (*n*=7; 53.8%), and public parks and pedestrian paths (*n*=4, 30.7%). In addition to all of them presenting skin lesions, six patients presented systemic symptoms, the most common being fever (n=3) and palpitations (*n*=3). A 9-year-old child showed an EKG with a negative T wave from V1-V4; a 5-year-old boy presented bradycardia, atrial extrasystoles, and CK-MB elevation; another child under 2 years old presented CK-MB elevation; and a 31-year-old girl had T-wave repolarization disorder. All these alterations were resolved in the follow-up control. This study describes a period of occurrence of caterpillar accidents consistent with multiple sightings of different caterpillars in the Valley of Caracas. It describes not only cutaneous alterations but also previously undescribed electrocardiographic and cardiac enzyme alterations.

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POTENTIAL RISK INCURRED BY HEALTH CARE PROVIDERS ATTENDING TO MALARIA PATIENTS ACROSS KENYA

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Management of malaria patients necessitates close monitoring, which exposes healthcare providers (HCPs) to increased risk. In many malaria-endemic regions, effective mosquito control is inadequate. Research shows a higher mosquito affinity for individuals infected with the gametocyte stage of malaria. This situation risks increasing the population of malaria-infected mosquitoes within healthcare facilities. Further, recent changes in mosquito feeding patterns reveal peaked activity during daylight hours—a time that coincides with patient visits. The potential for health facilities to become malaria transmission hotspots due to these combined factors needs further investigation. Understanding the infectiousness of individuals seeking malaria treatment is crucial for assessing the risk to HCPs in Kenyan hospitals. This knowledge helps in formulating guidelines for countermeasures aimed at reducing transmissions within hospitals. Between January 2023 and March 2024, 991 blood samples were collected from individuals with naturally acquired *Plasmodium* species infections presenting with uncomplicated malaria from six different sites countrywide. 295 samples from Busia, 50 from Kericho, 238 from Kisumu, 224 from Kombewa, 51 from Kisii, and 133 from Marigat. These samples were diagnosed for the presence of *Plasmodium species* before downstream screening for *P. falciparum* gametocyte life-cycle stage composition using real-time PCR. About 78.3% (766/991) of individuals tested positive for malaria by PCR. 87.37% (678/766) of these harbored gametocytes lifecycle stage comprising Marigat 93.41% (85/91), Kombewa 88.54% (170/192), Busia 87.39% (194/222), Kisii 86.05% (37/43), Kericho 85% (34/40) and Kisumu 84.04% (158/188). The substantial proportion of gametocytes in infections indicative of potential for patients to infect mosquitoes roosting within the hospital poses a risk of transmission of the disease to health workers. There is need for effective preventative strategies to protect healthcare providers exposed to malaria patients from possible transmission while in the health care facilities.

7420

EXPLORING ACUTE UNDIFFERENTIATED FEVERS AT A TERTIARY CARE HOSPITAL IN INDIA: ETIOLOGICAL PROFILE, CLINICAL CHARACTERISTICS AND BIOMARKERS

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This observational study was conducted at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi to determine the seroprevalence and clinical & laboratory profiles of malaria, scrub typhus, leptospirosis, typhoid, hepatitis A, hepatitis E, chikungunya, and dengue among patients presenting with acute undifferentiated fever (AUF). From July 2022 to November 2023, 18,362 patients with febrile illnesses lasting 2-14 days were included. Blood samples were tested for malarial parasites, dengue NS1 antigen, antibodies against typhoid, dengue IgM, Leptospira IgM, Scrub typhus IgM, Chikungunya IgM, hepatitis A IgM, and hepatitis E IgM antibodies. Additionally, C-Reactive Protein, Procalcitonin levels, and complete blood counts were assessed. Cases were defined according to IDSP, 2019 P and L form criteria. Out of 18,362 febrile patients screened, 4,259 tested positive for at least one of the 8 pathogens studied. Among these cases, 75% had single infections, while 25% had co-infections. Dengue was the most common single infection (2,049 cases), followed by typhoid (667) and chikungunya (353). Symptoms varied by pathogen, but fever was universal. Anaemia was observed in 85% of malaria and 82.5% of scrub typhus cases. Thrombocytopenia was seen in 15.9% of dengue and chikungunya cases. Higher CRP levels (4.8 mg/dl) were predominantly found in bacterial infections, followed by malaria, dengue, and chikungunya. Procalcitonin levels were elevated in scrub typhus, typhoid, malaria, and leptospirosis cases, indicating PCT to be a poor indicator of viral infections Dengue emerged as the most common mono-infection, while dengue-typhoid combination was the most frequent co-infection. This study offers robust epidemiological data on AUF, providing valuable insights for diagnosing single as well as multiple infections. The comprehensive data on clinical and laboratory findings in conjunction with levels of biomarkers presents valuable tools for improved diagnosis, management, and awareness of AUF and its associated aetiologies.

7421

SUBCUTANEOUS MYCOSES: ENDEMIC BUT NEGLECTED AMONG THE NEGLECTED TROPICAL DISEASES IN ETHIOPIA

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Subcutaneous mycoses are a chronic infectious disease of the skin and underlying structures endemic in tropical countries. The disease has serious medical and socioeconomic consequences for patients, communities and health services in endemic areas. The inclusion of mycetoma and other deep fungal infection in the list of Neglected Tropical Diseases by WHO highlights the need to assess the burden of these diseases and establish control programs where necessary. In Ethiopia no strategies can be devised because of a lack of epidemiologic information. To address this evidence gap, we performed a national rapid assessment of the geographic distribution of subcutaneous mycoses. We conducted a rapid retrospective assessment using hospital records to identify all suspected and confirmed cases of subcutaneous mycoses in 13 referral hospitals across the country between 2015 and 2022. In each hospital the logbooks were reviewed for diagnoses of deep fungal infections, as diagnosed per routine practice. Descriptive analysis was done. From 12 hospitals we extracted 85 cases of subcutaneous mycoses, registered from July 2018 to September 2022. 60 (70.6%) patients were diagnosed as mycetoma, 21 (24.5%) as chromoblastomycosis and the remaining 4 (4.7%) as sporotrichosis. The median age of patients was 35 years (IQR=18). 61 (71.8%) patients were male and 80.8% patients were farmers. 30 (36.9%) cases were from the Amhara national regional state. 56 (65.9%) patients had information on diagnostic microscopic evaluation: for mycetoma histopathologic evaluation and fine needle aspiration cytology have a higher positivity rate while for chromoblastomycosis Potassium hydroxide (KOH) staining had abetter yield. The main clinical presentations were nodules, sinuses and infiltrative plaques on the skin. Mycetoma and other subcutaneous mycoses are endemic in Ethiopia, with cases reported from almost all regions albeit with variation in case distribution. A routine program and systems should be developed to identify and document the burdens of subcutaneous fungal infections in the country.

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IMPACT OF INTESTINAL PARASITE INFECTIONS ON HUMAN PAPILLOMA VIRUS INFECTION AND REPRODUCTIVE HEALTH: EXPLORING ALTERATIONS IN INTESTINAL AND CERVICOVAGINAL MICROBIOME

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Intestinal parasite infections (IPIs) pose significant public health risks in areas with limited sanitation and healthcare, like the Peruvian Amazon. As they establish chronicity in the human gut, they downregulate host immunity to ensure survival, potentially facilitating the establishment of other pathogens, like HPV. While helminths clearly impact the gut microbiome, a major regulator of the systemic immune system, their impact on the cervicovaginal (CV) microbiome is uncertain. *Lactobacillus* spp. comprise >70% of CV microbiota in healthy women and promote protective immunity. Severe or prolonged CV dysbiosis, characterized by predominance of non-*Lactobacillus* spp., has been linked to increased HPV risk. This study aims to investigate intestinal and CV microbiome changes among Peruvian women aged 30–50 with and without IPIs, to understand IPI impact on these microbiomes and their association with HPV infection risk. We enrolled 353 women undergoing cervical cancer screening in Iquitos, Peru, between August 2022 and November 2023. Participants provided demographic, clinical, and risk factor information; underwent sexually transmitted infection (STI) and stool ova and parasites testing; and submitted CV and stool specimens for microbiome analysis via 16s rRNA sequencing. We used multiple logistic regression to evaluate IPI risk factors. Of 353 participants, the median age of sexual debut was 17 years [IQR 16-18], 6% were smokers, and 1.7% reported prior STI. CV infection frequencies were: HPV 21% [71/336], HIV 0.5% [2/353], syphilis 0.5% [2/353], chlamydia 0% [0/50], BV 32% [112/345], and TV 3.2% [11/342]. 312 submitted stool specimens. 41% had IPI; 7.4% had helminths (69.5% [16/23] *Ascaris*, 13.04% [3/23] hookworm, 8.69% [2/23] *Enterobius* and 8.69% [2/23] *Hymenolepis*) and 37% had protozoa (99.1% [114/115] *Giardia* and 65% [75/115] *Entamoeba histolytica*). Comparative analysis of CV and intestinal microbiota distributions is ongoing. We expect CV *Lactobacillus* spp. will be less abundant in women with IPIs. Study results will pave the way for a larger longitudinal analysis.

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DOES THE RUN- IN PHASE ADD WHEN ASSESSING SAFETY OF TRYPANOCIDAL THERAPIES? THE EXPERIENCE OF THE EQUITY TRIAL

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The run-in phase is a design tool seeking to select compliant participants in randomized trials. This may be relevant when assessing long-term interventions or those with low tolerance, such as trypanocidal therapy. The EQUITY trial tested a 120 day treatment including Nifurtimox, Benznidazole or placebo (PBO) among *T. cruzi* seropositive young adults with no cardiomyopathy. Treatments were assigned in two consecutive 60 day periods, with participants receiving either active treatments or PBO in a blinded fashion. Before randomization, participants underwent a 10 day run-in phase with PBO. Only those showing acceptable tolerance or adherence (>80% of treatment) were randomized. The treatments assigned over the study periods led to four possible situations after introducing, continuing, or interrupting the active treatment (OFF-ON, OFF-OFF, ON-ON, or ON-OFF). We recorded the occurrence of adverse events (AE) defined as moderate to severe symptoms, including those leading to additional prescriptions, dose reductions or study treatment discontinuation. Participants were assessed in the first 20 days of each study period (day 20 and 80 after the run-in). We computed McNemar's chi square statistics for 2x2 tables of paired observations (appearing/disappearing events) for each situation. After the run-in phase, 44 (12.5%) of 351 candidates were excluded (34 due to diverse complaints). In 307 randomized, when introducing active treatments (the OFF-ON group, n=232) AE appeared/receded in 64/18 participants (X^2 25.8, p <.001). These figures differed by the continuation of PBO (groups OFF-OFF, n=126, 15/10, X^2 1.00, p 0.31) or active treatment (ON-ON, n=110, 16/12 X^2 0.571, p 0.45) and its interruption (ON-OFF, n=44, 6/7, X^2 0.076, p 0.78). Using a run-in period in this trial allowed a better estimation and discrimination of AE after introducing active treatments, suggesting causality. Twenty days may not be enough to notice receding symptoms after stopping active treatment. At the cost of inducing some nocebo effect and excluding some candidates, the run-in improves the risk-benefit assessment of therapies for neglected tropical diseases.

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BRUGIA IMPACT SURVEY AS AN ALTERNATIVE METHOD FOR LYMPHATIC FILARIASIS TRANSMISSION ASSESSMENT SURVEY IN INDONESIA

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Indonesia's 236 districts endemic with *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* worms require at least five years of mass drug administration (MDA) to interrupt lymphatic filariasis (LF) transmission. The subsequent transmission assessment surveys (TAS) determine whether an evaluation unit (EU) can safely stop MDA. Indonesia has a current backlog of surveys in districts with *Brugia spp* due to global supply challenges with diagnostic tests. As such, the World Health Organization (WHO) recommended the Brugia impact survey (BIS) as an alternative method to TAS. The traditional TAS employs rapid tests among students in sampled schools, whereas the BIS requires night blood collection from adults for microscopic identification of microfilaria. Indonesia has conducted BIS in 42 EUs in 41 districts since September 2022; 41 EUs used a method-specific complex cluster sampling and 1 smaller EU used systematic sampling. The median sample size in EUs using cluster sampling was 1050 while the smaller EU had a sample size of 794; all surveys met required minimum sample sizes. Microscopists identified microfilaria in 17 EUs (range 1-12 positive samples). The threshold for passing the BIS was 4 or fewer positive samples; 2 EUs were over this threshold and therefore failed. The collection of microfilariae from randomly selected adults in the BIS makes it a robust methodology but challenging to implement. To be used as an assessment survey, the BIS needs to be a reliable proxy indication of low enough transmission to safely stop MDA, and Indonesia's experience has shown feasibility with proper training and supervision. However, the BIS had increased costs and higher refusals due to overnight sampling, required accurate population registers, and relied on a network of 76 skilled lab technicians with prior night blood sample experience. Indonesia's experience may be useful for other settings considering microfilaria testing in combination with rapid tests. The BIS implementation also established a precedent for other emerging methodologies with complex sampling; such novel approaches are essential to maintain momentum towards LF elimination.

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ASSESSMENT OF DISABILITY AND HEALTH-RELATED QUALITY OF LIFE USING WHODAS 2.0 TOOL IN A POPULATION LIVING IN *LOA LOA* ENDEMIC AREAS OF THE REPUBLIC OF CONGO (THE MORLO PROJECT)

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Loa loa filariasis, a parasitic infection endemic to Central Africa, is considered a frequent cause of medical consultation in this region. To evaluate the quality of life (QoL) of individuals living in loiasis endemic areas, we enrolled 991 subjects (one-third being microfilaremic) in the general population of a rural area of the Republic of Congo. WHODAS 12-items and information on the number of eye worm (Ew) and Calabar swellings episodes experienced throughout their lives, were collected. We analyzed the overall WHODAS score and its six domains (mobility, self-care, cognition, life activities, social activities, and participation). Nested analyses of baseline data showed that individuals with more than 10 Ew episodes had significantly higher scores than those without such history, which was particularly significant in the domains of mobility, cognition, and social participation. These individuals had also an increased risk of experiencing moderate (score >25/100) and severe impairment (score > 50/100) by nearly 3-fold (adjusted OR = 3.13, 95% CI 1.28-7.64, P = 0.012) and 2.69-fold (95% CI 1.41-5.13, P = 0.003), respectively, compared to individuals without any history of Ew. No other variable related to loiasis (Calabar swelling frequency, *L. loa* microfilaremia, and positivity to *L. loa* antibody rapid test) was associated with the various scores. Assuming that the frequency of Ew episodes throughout life could be a suitable proxy for overall exposure to the infection and/or the number of adult worms present in the individuals, the impact of loiasis on daily QoL appears to be primarily attributable to adult worms rather than to the microfilarial density. Adult worms would primarily affect everyday activity through peripheral symptoms, such as joint-related discomfort (with notable mobility impairment), while microfilariae would primarily induce organ dysfunction. Further studies are needed to better understand the respective clinical impacts of adult worms and *L. loa* microfilariae.

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BASELINE EVALUATION OF ONCHOCERCIASIS TRANSMISSION IN FIVE DISTRICTS OF BENIN

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Onchocerciasis, or river blindness, is a disease caused by the filarial parasite, *Onchocerca volvulus*. Achieving the World Health Organization (WHO) recommended Ov16 seroprevalence threshold of <0.1% in children under 10 to stop mass drug administration (MDA) is a major challenge for most endemic countries. Modeling studies suggest that the seroprevalence threshold could be increased to ≤2%. To evaluate the 2% threshold, Benin conducted serological and entomological surveys in five onchocerciasis-endemic districts where seroprevalence by Ov16 rapid diagnostic test (RDT) in 2020 was ≤2%. If the baseline survey shows an Ov16 seroprevalence ≤2% in children 5–9 years and blackfly infectivity by O150 PCR meets the WHO threshold, MDA will be stopped, and the area monitored for recrudescence. Results from the entomologic survey are not available and will not be discussed here. Samples were collected from children aged 5–9 years in the districts of Ouaké, Tchaourou, Bassila, Bante and Savè in 2023. Villages were selected by probability proportional to estimated size method, plus one additional first-line village. In villages, a multi-stage random sample of children was enrolled with parental authorization. Dried blood spots (DBS) were prepared from venipuncture samples, then eluted for analysis using the DBS Ov16 RDT method. From the 5 districts, 51 villages were selected and 1,884 children were enrolled: 53% were girls and 47% boys. In Bantè, no children had positive RDT results. Seroprevalence by RDT was 0.41% [95%CI: 0.00–1.21] in Ouaké, 0.54% [95%CI: 0.01–1.07] in Tchaourou, 0.98% [95%CI: 0.02–1.95] in Bassila, and 3.26% [95%CI: 0.88–5.63] in Savè. Overall seroprevalence was 0.9% [95%CI: 0.5%–1.4%]. The results in Savè might suggest an increase in seroprevalence between the 2020 and 2023 studies. These results need to be confirmed by Ov16m ELISA and analyzed with the results of the blackfly qPCR analysis to decide whether to discontinue MDA in the districts that have met the serological criteria. Demonstrating that transmission is interrupted at a higher serological threshold would facilitate progress towards the WHO targets for 2030.

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SUBSTANTIAL PROGRESS TOWARDS ENDING LYMPHATIC FILARIASIS AS A PUBLIC HEALTH PROBLEM IN DELTA STATE, NIGERIA

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Lymphatic filariasis (LF) is a neglected tropical disease endemic in Nigeria. In Delta state, in southern Nigeria, 16 of 25 districts were found to be LF-endemic with prevalence of circulating filarial antigen (CFA) by immunochromatographic test ranging from 1- 4% in baseline mapping (2005-2011). Annual mass drug administration (MDA) with ivermectin and albendazole delivered by community directed distributors (CDDs) started in 2014 in the 16 districts. Pre-transmission assessment surveys (Pre-TAS) were conducted in 16 districts in 2022 using filariasis test strips (FTS) among 22,400 people ≥ 5 years in each of 32 sites (one sentinel and one spot-check per district). Among 9,251 people tested, 9,246 (99.9%) were negative, and all 16 districts had <2% positive by FTS meaning they passed Pre-TAS and progressed to TAS-1 in 2023. The 16 districts were grouped into 11 evaluation units (EUs) based on geographic and epidemiological similarity. An average of 45 schools per EU were randomly selected for sampling from a list of registered schools. Students were sampled according to WHO guidance using survey sample builder. Refusal rate was low (0.6%), likely the result of a multi-pronged approach that engaged Parent Teachers Association (PTA) meetings in every selected school to obtain consent and dispel rumors and radio and television jingles to combat misinformation in addition to typical community mobilization for surveys. Valid FTS results were available for 16,887 children from 497 schools; only 6 children (0.04%) were CFA-positive. No EU had more than 2 positives, less than the critical threshold in each EU (range 14-18). Thus, all 11 EUs passed TAS-1, stopped MDA, and entered post-treatment surveillance for LF. Over 2.9 million people in the 16 districts no longer require LF MDA, representing a significant achievement toward national LF elimination. The national LF elimination program and partners should sustain the involvement of health workers and stakeholders like PTAs in subsequent TAS to support high participation in these surveys.

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MIXED TREATMENT STRATEGIES ARE AN EFFECTIVE HEALTH CAMPAIGN TO IMPROVE DRUG COVERAGE FOR RIVER BLINDNESS ELIMINATION IN INSECURE AREAS OF EDO STATE, NIGERIA.

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The region of Edo state, Nigeria along the Osse River has ongoing transmission of onchocerciasis and perennially low coverage of semi-annual mass drug administration (MDA) treatments. To improve MDA coverage, a health campaign involving mixed treatment strategies was deployed between November and December 2023 in six districts in Edo, bordering Ondo state. Methods consisted of integrating traditional house-to-house community-directed treatment with ivermectin (CDTI) with the immunization program's outbreak response (OBR), use of mobile health teams, providing medicines house-to-house, at fixed locations, and special teams of health workers, along with indigenous residents with security operatives to treat insecure areas termed "hit and run". This special strategy included identifying safe periods when intervention teams could travel to the security-compromised areas. A total of 990,813 treatments were distributed in the mixed strategy approach in the 6 districts November-December 2023—an 8.5% increase over the 913,367 treatments distributed in the prior June 2023 CDTI-only MDA. Correspondingly, the reported coverage increased from 65% overall in June 2023 (districts ranged from 54 – 70%) to 71% in December 2023 (districts ranged from 68 – 74%). Independent coverage surveys across all 6 districts confirmed this increase with significantly higher coverage in December 2023 than in the prior round (76.2% vs. 66.8%, $p<0.001$). Mixed treatment strategies were an effective health campaign that enhanced MDA coverage over CDTI alone in this area of Nigeria with persistently low coverage and offer a way to hasten disease elimination in other areas where terrain and insecurity pose challenges to house-to-house CDTI.

7429

POST-TREATMENT SURVEILLANCE FOR LYMPHATIC FILARIASIS SUPPORTS CESSATION OF TRANSMISSION IN HISTORICALLY CLASSIFIED ENDEMIC FOCI IN THE DOMINICAN REPUBLIC

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The Dominican Republic aims to eliminate lymphatic filariasis (LF) as a public health problem by 2025. Nationwide baseline mapping using lot-quality assurance sampling identified 3 endemic foci in need of mass drug administration (MDA) - Southwest, La Ciénaga, and East. By 2018, prevalence of circulating filarial antigen (CFA) was < 2% in all foci, meeting the criteria to stop MDA and begin post-treatment surveillance (PTS). The World Health Organization (WHO) recommends a minimum 4-year period of PTS to confirm that LF prevalence remains significantly below sustainable transmission levels. A community-based transmission assessment survey (TAS-3) was conducted in the East focus from December 2023-February 2024, six years after the halt of MDA in 2018 and two years after a TAS-2. In total, 154 bateyes (agricultural settlement villages targeted for MDA in the East region) were visited to exceed the target population of 909 children ages 6-7 years to test for CFA by Filariasis Test Strip. The threshold to pass TAS was 11. CFA was not detected among any of the 933 children tested with valid results, and the TAS passed. Similarly, CFA was not detected among 811 "adults" (85% female; age range [15-93 years], mean: 37 years) also invited for testing in the same household with valid results. WHO criteria to validate a country as having eliminated LF as a public health problem includes alleviating suffering through morbidity management and disability prevention (MMDP). A morbidity assessment was concurrently conducted in these bateyes where 4 members of 3 HHs self-reported lymphedema, all from the same province. These results, combined with finding no CFA-positive children or adults in the most recent PTS surveys conducted in the Southwest (2020) and La Ciénaga (2021) foci, indicate that LF transmission has been eliminated in all historically-classified endemic foci in the Dominican Republic. Remaining steps include scaling up MMDP services, dossier submission to WHO for validating elimination of LF as a public health problem, and maintaining post-validation surveillance until LF transmission is interrupted across Hispaniola.

7430

COMORBIDITY BETWEEN LYMPHATIC FILARIASIS AND HYPERTENSION AND DIABETES: A PROSPECTIVE CASE-COHORT STUDY IN KENYA

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Lymphatic Filariasis (LF) can lead to unilateral or bilateral swelling (Lymphoedema) in the legs, which in its advanced stage is known as elephantiasis, one of the world's leading causes of permanent and long-term disability. Due to its disfiguring nature, LF may directly or indirectly interfere with a person's mobility, predisposing a patient to a sedentary lifestyle and thus increasing the risk of non-communicable diseases like Type 2 diabetes and hypertension. A prospective case-cohort study was conducted in Kwale County in Kenya among 123 lymphoedema patients to screen them for type-2 diabetes and hypertension. Socio-demographic data, nutrition status, tobacco use, and physical activity (PA) levels were collected. Blood pressure and diabetes assessment was done over two subsequent days. PA assessment followed the Global Physical Activity Questionnaire (GPAQ) guidelines, with metabolic equivalent (MET) scores calculated based on frequency and type of exercise. Participants were grouped into diabetic/non-diabetic and hypertensive/normotensive categories. Those with either disease were treated as cases, while the rest were controls. Most of the study participants were female (60.2%), with the majority aged above 60 (61.8%). All of them were either minimally active, 19.5% (95% CI: 13.1 - 27.8), or moderately active, 80.5% (95% CI: 72.2% - 86.9%), with none classified as health-efficient physically active. The prevalence of hypertension was 79.7% (95% CI: 71.3 - 86.2), while 17.1% (95% CI: 11.1% - 25.1%) were diabetic, with hypertension higher among women and diabetes higher among men. Linear model revealed significant association between lower MET scores and presence of disease (hypertension and diabetes) (Estimate: -264.4; 95% CI: -437.8 to -91.0; $p=0.003$) among lymphoedema patients. This study demonstrates that lymphedema patients need to be enrolled in PA under the guidance of physiotherapists to improve their MET scores and prevent them from secondary diseases like type 2 diabetes and hypertension. If already diagnosed with both conditions, they should be targeted for glycaemic and blood pressure control, respectively.

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ONCHOCERCIASIS SEROPREVALENCE IN BIÉ PROVINCE, ANGOLA: A CROSS-SECTIONAL SURVEY TO GUIDE EFFORTS TOWARDS ELIMINATION

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Despite intensive control efforts in many countries, it is estimated that onchocerciasis still affects over 19 million people globally and continues to be a cause of considerable morbidity including blindness. Recently, a program of mass drug administration (MDA) with ivermectin was introduced to areas of Angola including Bié province that had been determined to be endemic through surveys conducted between 2003 and 2015 using either nodule palpation or microscopy of blood specimens. In Bié, prior to the initiation of MDA, we conducted a cross-sectional survey across three areas to determine suitability for a planned cluster-randomised trial of moxidectin versus ivermectin MDA. We randomly selected 10 villages in each area, with 10-12 households randomly selected per village, aiming to enrol 50 participants aged one year and above with informed consent per village; to reach a total of 500 participants in each study area. Finger-prick blood samples were collected from consenting participants for dry blood spots (DBS) and thick blood smears for onchocerciasis and *Loa loa* diagnosis, respectively. The Ov-16 rapid diagnostic test was conducted on the DBS eluates, with results read 24 hours later. Thick blood smears were stained with Giemsa and examined under light microscopes for *Loa loa* detection. Additionally, participants aged 15 years and above were invited to respond to a questionnaire on black fly exposure. We also conducted an exploratory entomological survey, assessing blackfly breeding sites along rivers in the study areas and collected blackfly larvae for subsequent laboratory analysis. Preliminary findings of Ov-16 seroprevalence adjusted for clustering at village and household level revealed it varied across the three study areas, ranging from 8.2% to 46.6%. Older age groups had higher Ov-16 prevalence. One *Loa loa* case was detected. The breeding site assessments confirmed the presence of blackfly larvae in all three study areas. Our findings confirm the urgent need for MDA against onchocerciasis in this province.

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POST-TREATMENT SURVEILLANCE FOR LYMPHATIC FILARIASIS IN HAITI: RESULTS FROM TRANSMISSION ASSESSMENT SURVEY (TAS-3) IN NIPPES AND SOUTH-EAST.

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Lymphatic filariasis (LF) is a leading cause of permanent disability globally with over 882 million people in 44 countries at risk for infection. Haiti is one of 4 remaining LF-endemic countries in the Americas. Baseline mapping determined that 88% of Haiti's districts were endemic, however, the Haitian Ministry of Public Health and Population decided to implement nationwide annual mass drug administration (MDA) of diethylcarbamazine and albendazole. The World Health Organization recommends transmission assessment surveys (TAS) to determine whether the prevalence of circulating filarial antigen (CFA) is below 2%--the putative threshold for interrupting *Wuchereria bancrofti* in *Culex* or *Anopheles* transmission areas. Repeated TAS are recommended at 2-3-year intervals during 4-5 years of post-treatment surveillance (PTS). Nippes and Sud-Est *departments* (regions) of Haiti's southern peninsula halted MDA after passing TAS-1 in 2014-2015. Following successful TAS-2 surveys in 2017, TAS-3 was conducted in November and December of 2023 in 21 districts grouped into 3 evaluation units (EUs): Miragoane (a single district in Nippes), Nippes (the remaining 10 districts), and Sud-Est (10 districts). A total of 4,610 children aged 6-7 years old were tested for CFA by filariasis test strips in community-based TAS: 1,416 children in 30 localities in Miragoane, 1,607 children in 39 localities in Nippes, and 1,587 in 64 localities in Sud-Est. Among these, 3 (0.21%), 1 (0.06%), and 0 (0%) were CFA-positive—all beneath the critical cut-off values (range 16-18) for each EU. All 4 CFA-positive individuals were microfilaria-negative in follow-up night blood testing. Children were also tested for malaria by rapid diagnostic test, with prevalence estimates of 0.07% (1/1,414), 0.44% (7/1,608), and 0.13% (2/1,587) in Miragoane, Nippes, and Sud-Est, respectively. Results indicate that LF and malaria are rare in these areas. Passing TAS-3 fulfills the epidemiological criteria for eliminating LF as a public health problem, yet follow-up is needed to investigate persistent CFA-positive signals and to maintain PTS given displacement and insecurity in Haiti.

7433

HIGH MORTALITY AMONG PERSONS WITH SUSPECTED EPILEPSY: A FOCUS ON ONCHOCERCIASIS-ENDEMIC COUNTIES OF SOUTH SUDAN

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Onchocerciasis, a neglected tropical disease, has been consistently associated with epilepsy. We investigated epilepsy prevalence and mortality in four onchocerciasis-endemic counties in South Sudan: Maridi, Mvolo, Mundri and Wulu. House-to-house cross-sectional surveys from 2021 to 2024 identified suspected persons with epilepsy (sPWE) and ascertained deaths among sPWE and individuals without epilepsy (IWE). Epilepsy diagnoses were confirmed by trained clinicians. Epilepsy prevalence ranged from 3.3% in Mundri (86/2588) to 4.5% in Mvolo (672/15092), with Maridi (586/14402) and Wulu (55/1355) having a rate of 4.1%. In Maridi and Mundri, with access to free antiseizure medication (ASM) at a treatment centre, ASM adherence was 91% and 95%, respectively, compared to Wulu (9%) and Mvolo (23%) without such access. The median age of death for sPWE varied from 19 years in Maridi to 22 years in Mundri. sPWE mortality rates per 1,000 person-years were 44 in Maridi (95%CI: 36-55), 46 in Mvolo (95%CI: 38-56), 66 in Mundri (95%CI: 37-113) and 70 in Wulu (95%CI: 34-133). In comparison, IWE mortality rates per 1,000 person-years were significantly lower, ranging from 5 in Mvolo (95%CI: 4-5) and Mundri (95%CI: 4-8) to 10 in Wulu (95%CI: 7-15) and Maridi (95%CI: 9-11). The resulting mortality rate ratios indicated that sPWE were 4-12 times more likely to die than IWE. Limitations include potential recall bias on mortality data and the cross-sectional design preventing confirmation of epilepsy diagnoses among deceased sPWE. Additionally, self-reported ASM access may be inflated in the counties with treatment centres due to social desirability bias. Our study highlights a significant mortality burden among PWE in onchocerciasis-endemic areas. The observed high mortality burden may be explained by the combination of high epilepsy prevalence and related mortality, exacerbated by a substantial epilepsy treatment gap. Thus, more advocacy is needed to strengthen onchocerciasis elimination programmes associated with decreased epilepsy incidence in endemic areas and ensure uninterrupted free access to ASM in primary healthcare settings for all PWE.

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INTEGRATED LYMPHATIC FILARIASIS, SCHISTOSOMIASIS AND SOIL TRANSMITTED HELMINTHIASIS IMPACT ASSESSMENT IN OHAUKWU, EBONYI STATE, NIGERIA

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Lymphatic filariasis (LF), Schistosomiasis (SCH), and soil-transmitted helminthiasis (STH) are co-endemic in Ohaukwu local government area of Ebonyi State and have been treated by mass drug administration (MDA) since 2014, 2015, and 2014, respectively. Impact assessments for SCH/STH are recommended every 2-3 years, but none have occurred since baseline surveys in 2013 due to funding constraints. We integrated an SCH/STH assessment into a planned LF transmission assessment survey (TAS-1) in Ohaukwu to attempt cost-effective impact assessment. LF TAS-1 was conducted in January 2024 according to standard WHO protocol, with filariasis test strips (FTS) used for all children from classes 1 and 2 (~age 6-7 years) in 40 systematically selected schools from the LGA. The target sample was 1,380 with a critical cut-off of 16 positives. We randomly included 10 selected schools in the SCH/STH survey, and purposively added the 5 still-extant schools from the 2013 baseline survey. Urine and stool samples were collected from a target of 50 school-aged children (SAC) aged 5-14 years in each school and 50 adults in each surrounding community and microscopically examined with urine filtration and Kato-Katz methods. None of 1,473 SAC had positive FTS results, meaning that Ohaukwu passed TAS-1 and qualifies to stop LF MDA. Of 701 adults, 36 (5.1%) were positive for any STH and 12 (1.7%) for SCH. Of 736 SAC, 64 (8.7%) were positive for any STH and 68 (9.2%) for SCH. The prevalence in SAC reflects a reduction in SCH from 19.7% in 2013 and in STH from 58.4%. In the 5 resurveyed villages, SCH prevalence reduced in 4 and increased in 1, while STH reduced in all 5. We estimate that the integrated survey reduced costs by approximately 19% compared to the costs of conducting the TAS and SCH/STH surveys separately. We conclude that integrating SCH/STH impact assessment into an LF TAS is feasible and reduces costs, and that SCH/STH control and LF elimination efforts in Ohaukwu have been successful.

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COMPREHENSIVE ASSESSMENT OF ONCHOCERCIASIS TRANSMISSION DYNAMICS AND COMMUNITY PERCEPTIONS: A CASE STUDY IN HYPO-ENDEMIC COMMUNITIES OF OGUN STATE, NIGERIA

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Onchocerciasis persists as a significant neglected tropical disease in Africa, causing notable morbidity and socioeconomic strain, leading to a rise in disability-adjusted life years. Control efforts have mainly focused on preventive chemotherapy (PC) in moderate to high endemic areas. However, extending PC to hypo-endemic regions is crucial for meeting 2030 elimination targets. An epidemiological and entomological survey was conducted in hypo-endemic areas of Ogun State to assess onchocerciasis prevalence, associated risk factors, and blackfly vectors' abundance and infectivity over 12 months. 230 participants aged 5-70 were recruited from three communities within hypo-endemic implementation units (IUs). Parasitological and entomological surveys, along with questionnaires, were employed, and findings revealed a 10.04% and 15.79% prevalence microscopically and via O-150 screen pool analysis, respectively. Visual impairment (4%), Onchodermatitis (6.27%), and nodules (10.45%) were observed among adults aged 50 and above, with no significant gender difference. 418 blackflies were collected, with higher numbers during the rainy season (27% wet, 56% dry), notably in November and December. Larvae were absent upon dissection. Biting rates surged during early rainfall (April-June 2023) and continued rising till December, paralleled by an increase in blackflies' parous level. Participant interviews highlighted symptoms caused by microfilariae, but a lack of knowledge regarding blackfly breeding sites (69%) and prevention methods (87%). Traditional remedies were commonly used post-bites, while anti-malarial drugs, herbs, and local concoctions were mentioned for treatment. This study underscores the onchocerciasis status in hypo-endemic communities, stressing the need for intensified control efforts aligned with WHO objectives.

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INTESTINAL HELMINTHIASIS IS NOT ASSOCIATED WITH CLINICAL AND THERAPEUTIC ASPECTS OF DISSEMINATED LEISHMANIASIS CAUSED BY *LEISHMANIA BRAZILIENSIS* IN AN ENDEMIC AREA OF BRAZIL

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Disseminated leishmaniasis (DL) is an emerging but poorly characterized form of cutaneous leishmaniasis (CL) caused by metastatic infection with *Leishmania braziliensis*. We recruited participants with PCR-confirmed CL (n=99) and DL (n=20) between January and December 2017 at a dedicated leishmaniasis center in Bahia, Brazil. At enrollment, participants provided a stool sample, which was evaluated for presence of intestinal helminth infection and the number of helminth ova per gram of stool was quantified. Initial clinical examination consisted of an evaluation of the size and number of cutaneous lesions. Upon 60- and 90-day follow-up, participants were evaluated for the appearance of new lesions and response to treatment of existing lesions. Participants were considered cured by the presence of complete re-epithelialization of all lesions after the initiation of antimonial treatment. The median age of participants was 26 years (13-69) and 76.5% were male. Individuals with DL were significantly older than those with CL (42 vs 24 years; p=0.02), though univariate analysis among individuals with DL did not demonstrate a correlation between age and time to cure (R^2 0.06, p=0.5). The cure rate after 90 days of treatment was significantly lower in individuals with DL compared to those with CL (30% vs 65.9%; p=0.003), and the median time to cure was significantly longer (154.5 vs 65 days; p<0.001). There was no significant difference in the median number of lesions, median area of largest lesion, cure rate at 90 days, or median time to cure between DL patients with or without intestinal helminthiasis. The prevalence of intestinal helminthiasis was 40.3% (48/119), with no difference between the CL and DL populations. The most commonly identified organisms were *Necator americanus* (23/119), *Trichuris trichiuris* (19/119), and *Ascaris lumbricoides* (14/119). Coinfection with *L. braziliensis* and intestinal helminths does not affect clinical aspects or response to therapy in DL. Compared to individuals with localized cutaneous leishmaniasis, those with DL are significantly older.

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AN INVESTIGATION OF MUCOSAL LEISHMANIASIS IN THE U.S. MILITARY HEALTH SYSTEM

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Leishmaniasis is a protozoal infection with an increased risk of transmission to those serving in the United States (U.S.)military due to theaters of

operation in endemic regions.There has, in recent decades, been robust experience with old-world leishmaniasis in the MilitaryHealth System (MHS); however, new-world leishmaniasis, which may result in mucosal leishmaniasis, has been less studied. A total of 88 patients from 2012-2022 with diagnosis codes for "mucocutaneous leishmaniasis"or "leishmaniasis, unspecified"were identified in the Military Data Repository and reviewed. Within this cohort, there were two validated cases of mucosal leishmaniasis. Case one was a 28-year-old Active Duty (AD) male with recent travel to Belize who presented with a mucosal lip lesion that was biopsied and had inconclusive species confirmation, but was thought to be either *L. braziliensis* or *L. mexicana*. The second case involved a 30-year-old AD male with a history of travel to French Guyana who had a cutaneous lesion on his left hand that was identified as *L. guyanensis*, a causative species for mucosal leishmaniasis. Neither had evidence of any further mucosal involvement on otolaryngologic evaluation, and both subsequently received systemic therapy with a good clinical response. Although only two cases were identified over this period, this disease remains an important medical consideration when conducting military operations within endemic regions as both cases had recent military-specific travel to these areas.

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FIRST DETECTION OF *LEISHMANIA MAJOR* IN DOGS LIVING IN AN ENDEMIC AREA OF ZOONOTIC CUTANEOUS LEISHMANIASIS IN TUNISIA

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Dogs are considered the main domestic animals reservoir for *Leishmania infantum* parasite, the agent of Zoonotic Visceral Leishmaniasis (ZVL) in several Countries of the World. Dog may host other *Leishmania species* but its epidemiological role in the maintaining and spreading of these parasites is not completely elucidated. Zoonotic Cutaneous Leishmaniasis (ZCL) caused by *Leishmania major* affects thousands of people every year in North Africa. In ZCL endemic Countries few reports of *Leishmania major* positive dogs have been reported, probably because most human cases occur in poor rural areas where the social role of the dog and its medical management is not well considered. The aim of the present study is to add information on the possible involvement of domestic dog in the epidemiology of ZCL. Our research focused on a well-established endemic focus of ZCL, in the area of Echrarda, Kairouan Governorate, Central Tunisia. Fifty-one dogs with no apparent clinical signs of vector borne diseases were selected in small villages where human cases of ZCL are yearly present. Most of them appeared not well managed and were infested by ticks and fleas. All dogs were sampled for the *Leishmania spp*. diagnosis, by using the following procedures: blood sample for serology and buffy coat qPCR, popliteal fine needle aspiration and cutaneous biopsy punch for lymph node and skin qPCR. The results demonstrated a high percentage (21.56%) of dogs positive at least at one or more test, the most sensitive technique was the lymph node qPCR that detected 8/11 positive dogs. Nine, out of the eleven positive dogs, resulted infected by *Leishmania infantum*; ITS1-PCR-sequencing allowed *Leishmania major* identification in the remaining 2 cases, both from the popliteal lymph node samples that can suggest a possible visceral spread of a cutaneous *Leishmania* species in dog. Interestingly, one of the two *Leishmania major* positive dogs was living in the same house where 6-year-old children showed cutaneous lesions referred to ZCL. To our knowledge, this is the first report of *Leishmania major* positive dogs in Tunisia, the epidemiological role of which remains under investigation.

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SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF LIPOSOMAL AMPHOTERICIN B (AMBISOME) EFFECTIVENESS DATA FROM CLINICAL TRIALS FOR THE TREATMENT OF VISCERAL LEISHMANIASIS IN SOUTHEAST ASIA

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Leishmaniasis is transmitted by sandflies and caused by obligate intracellular protozoa of genus *Leishmania*. Visceral leishmaniasis (VL) is a neglected tropical disease, lethal if untreated, with 50 000- 90 000 cases/ year, caused by *L. donovani* in South-East (SE) Asia and East Africa, and *L. infantum* in Latin America and Mediterranean regions. The regimen of AmBisome approved by FDA in 1997 for VL is intravenous (IV) 3 mg/ kg, on D1-5, 14, and 21 (total: 21 mg/kg). This currently recommended regimen was based on studies with VL patients with *L. infantum* infection where AmBisome was administered in various regimens. Since then, in SE Asia, multiple studies have been run to optimize the treatment regimen in patients with *L. donovani*. Since 2014 in India, the treatment of choice for primary, immunocompetent patients with VL by the national elimination program has been IV 10mg/kg single dose AmBisome (SDA), in line with WHO recommendation. Systematic literature review and meta-analysis were conducted to review efficacy of 10mg/kg SDA. The estimate of clinical efficacy of 10mg/kg SDA obtained from this meta-analysis will inform future phase 3 studies. Following the systematic literature review, the meta-analysis limited inclusion to those studies conducted in the last 37 years on primary VL patients treated with AmBisome in SE Asia. Analysis of all 13 studies, totaling 3563 patients, based on Intent to Treat (ITT) set was conducted. These studies included treatment of patients at various doses and regimens of AmBisome and revealed cure rate of 92% at six months (CI 91-93%). A subsequent analysis of six of the 13 studies including 2768 patients treated with the SE Asia current treatment of choice, SDA 10mg/ kg, revealed cure rate of 93% at six months (CI 92-94%). The systematic literature review identified a significant number of studies conducted in the region, with over 3000 VL patients treated with AmBisome. The meta-analysis showed consistently high effectiveness of 10mg/kg SDA (>90%), which is the treatment of choice for VL patients in SE Asia, and is in the same range as multiple dose regimens of AmBisome that have been tested.

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GENOTYPING OF *BLASTOCYSTIS* SP. ISOLATES FROM FECAL SAMPLES FROM CHILDREN OF THE EDUCATIONAL INSTITUTION "128 LA LIBERTAD" (SAN JUAN LURIGANCHO), LIMA, PERU

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Diseases caused by intestinal parasites are among the most common public health problems, mainly in developing countries. *Blastocystis* sp. It is a single-celled, cosmopolitan intestinal protozoan that affects the intestinal tract of humans and various animals. *Blastocystis* sp. is considered commensal and is currently recognized as an emerging, opportunistic, zoonotic agent with broad genetic diversity. Its extensive diversity is evidenced by the 39 subtypes identified to date, whose assignment depends on the sequence analysis of the RNA gene (*SSU-rRNA*). This study aimed to genotype and characterize the subtypes of *Blastocystis* sp. from isolates of fecal samples from children in Lima, Peru. Seventy-two fecal samples from school-age children were analyzed, corresponding to 53% (38/72) and 47% (34/72), respectively, with age ranges ranging from 6 to 11 years. Four diagnostic techniques were used: direct examination,

culture in Jones medium, spontaneous sedimentation, and staining with Gomoris Trichromic. The 72 stool samples were cultured in Jones culture medium, from these samples, 35 positive cultures were obtained for *Blastocystis* sp.; likewise, DNA extraction was carried out using the commercial kit "High pure PCR Template Preparation". *Blastocystis* sp. was identified through PCR- SSU-rRNA gene. The genotypes of *Blastocystis* sp. were identified by RFLP using the restriction enzymes AluI and HinfI. For the identification of subtypes, specific primers. By direct observation and culture of Jones, *Blastocystis* sp. was the most prevalent species with 36% (26/72) and 48.6% (35/72) in the positive samples, respectively. An 1800 bp band evidenced the presence of *Blastocystis* sp. The RFLP with the two restriction enzymes (*Alu*I and *Hinf*I) showed varied band patterns; the ST3 subtype was the most predominant. *Blastocystis* sp., the RFLP allowed the identification of genotypes, and the ST1, ST3, and ST5 subtypes were also identified; these results suggest a genetic diversity associated with pathogenesis and zoonosis of the parasite.

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EPIDEMIOLOGICAL DYNAMICS OF LEISHMANIASIS IN THE SOUSS-MASSA REGION, MOROCCO (2017-2022)

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Leishmaniasis, identified as the second leading cause of mortality among global parasitic diseases, represents a significant public health challenge in Morocco, particularly in the Souss-Massa region. This study aims to elucidate the epidemiological dynamics of leishmaniasis within this region. We analyzed data from 1,103 cases across the six provinces of Souss Massa recorded between 2017 and 2022, using Jamovi software version 2.3.2.1 for statistical analysis. The vast majority of these cases were cutaneous leishmaniasis, accounting for 98% (1,084 cases) of the infections, with visceral leishmaniasis making up only 1.7% (19 cases). A notable 88% of the cases occurred in rural areas. The leading causative agent was *Leishmania major*, responsible for 56% (619 cases) of the infections, followed by *Leishmania tropica* at 42%, and *Leishmania infantum* at 2%. The average age of the affected individuals was 15.6 years, with a standard deviation of 16.4 years, indicating a wide age range among patients. The median age was 11 years. Males showed a statistically significant higher incidence, representing 56.1% of cases, compared to 43.9% in females ($p < 0.05$). Peaks in the number of cases were observed in May and January, while lower case numbers were typically seen in October and November. Tata province was identified as the main hotspot, contributing 57% of the cases, primarily due to *Leishmania major*, with an epidemic center in Akka. In Agadir province, accounting for 20% of all cases, 52% were attributed to *Leishmania tropica*, with a new epidemic focus in Drarga. These findings suggest a potential correlation with climate change and highlight the need for targeted public health interventions sensitive to the region's demographic and environmental factors influencing the spread of leishmaniasis. Alongside climate change, urbanization also emerges as a significant factor affecting disease dynamics. Passive screening played a crucial role, detecting 66.4% of the cases and proving essential for effective disease surveillance.

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THE EFFECTS OF ADVERSE ENVIRONMENTAL EXPOSURES ON RISK FOR CONGENITAL CHAGAS TRANSMISSION AND ADVERSE BIRTH OUTCOMES IN SANTA CRUZ, BOLIVIA

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Nearly 8 million people in Latin America are infected with *Trypanosoma cruzi* (*Tc*), the parasite causing Chagas disease, and most infections are initially asymptomatic and go undiagnosed. Chagas results in ~12,000 deaths annually, which is ten-times the number of deaths caused by Malaria in this region, making it the leading cause of parasitic death in the Americas. While treatable if diagnosed early, left untreated, *Tc* evades the immune system and decades later becomes a chronic cardiac, gastrointestinal, and/or neurological disease. *Tc* is also known to cause adverse birth outcomes in infants born to infected mothers, and congenital transmission occurs in about 5% of these births and can result in delayed childhood development. How *Tc* evades the immune system to traverse the placental barrier and establish congenital infection isn't well known. One theory is that a complex interaction between parasite, placenta, and inflammatory and oxidative stressors weakens the placental barrier from repeated activation of the innate immune system allowing the parasite to cross the placental barrier. Similarly, it is known that environmental exposures during pregnancy can have deleterious effects on birth outcomes. Repeated gestational exposure to ambient PM2.5 has been shown to result in adverse birth outcomes due to oxidative and inflammatory stress and PM2.5 can cross the placental barrier resulting in placental maladaptation. Extreme heat exposure can also have negative effects on pregnancy. Studies indicate that a 1°C increase in temperature correlates to double the risk for both pre-term and stillbirths. This ongoing study leverages two existing congenital chagas cohorts with ~10,000 mother-child dyads with a maternal *Tc* prevalence of 23.7% combined with freely available girded remote sensing environmental data to identify the effect of environmental exposures on congenital Chagas transmission and negative birth outcomes in Santa Cruz, Bolivia. This is a status update on an ongoing pilot-study and to our knowledge this is the first study to investigate the effects of environmental exposures on congenital Chagas transmission.

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MODELING CLIMATE DRIVERS OF CUTANEOUS LEISHMANIASIS INCIDENCE IN NORTHERN SYRIA

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Modeling climate drivers of cutaneous leishmaniasis incidence in northern SyriaLeishmaniasis is a Neglected Tropical Disease of global epidemiological importance caused by *Leishmania* parasites. Leishmaniasis is associated with high morbidity and impacts on quality of life, as it results in large open wounds during infection, which are associated with severe social stigmatization. In northern Syria, cutaneous leishmaniasis (CL) is endemic and its incidence exhibits significant geographic and temporal variation. Furthermore, CL incidence in northern Syria is dependent on the presence of the dipteran vector, which displays high variation in relation to environmental factors and public health vector control interventions. This study examines historical associations between CL due to *Leishmania tropica* and *Leishmania major* and environmental variables including rainfall, temperature, humidity, and vegetation cover in 63 subdistricts in 21 districts in the Al-Hasakeh, Aleppo, Raqqa, Deir-ez-Zor, and Idlib Governorates of northern Syria. Specifically, this study employs a time-lag generalized linear model to examine the relationship between the environmental variables and CL incidence over 479 weeks between December 2014 and March 2024. Weekly case counts varied from zero cases per week in many subdistricts to 2185 cases per week in the Ras Al Ain subdistrict in the 45th week of 2021. On the governorate level, over the study period, CL cases were highest in Al-Hasakeh governorate, peaking at 2216 cases in the 45th week of 2021. Seasonal trends were particularly apparent in Deir-ez-Zor governorate, where cases peaked in January every year between 2018 and 2022. This study found significant intra-governate and intra-district variability

in weekly case counts. Variations in temperature, rainfall patterns, humidity, and vegetation cover associated with climate change are likely to have a significant impact on future CL transmission patterns in endemic regions. These models suggest that climate monitoring is an important tool in the control and prediction of future CL incidence.

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SPECIES IDENTIFICATION OF CUTANEOUS LEISHMANIASIS CAUSING PARASITES IN NEPAL

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The ongoing Kala-azar elimination programme in Nepal is based on anthroponotic transmission of Kala-azar caused by the protozoan parasite *Leishmania donovani*. In recent years, a shift of reported cases from classical lowland foci in the east to hilly and mountainous areas of the western and far western regions of Nepal was well documented by the national control programme. In addition, cutaneous leishmaniasis cases are increasingly being reported, mainly from the west of the country, though the causative parasite species is not yet fully elucidated. Hence, to support of the ongoing country disease programme and to generate further evidence on the causative parasite species for cutaneous leishmaniasis in Nepal, a study was set up, in which we collected detailed patient information as well as skin biopsies from several hospitals located in the western and far western regions of Nepal. Altogether, 24 skin samples were collected and subjected to PCR and sequencing to determine the infecting parasite at species level. Samples were obtained from 11 different hilly districts, all from patients who didn't have a travel history outside of the country. Out of 24 skin samples, PCR detected *Leishmania* infection in 13 samples. Further molecular analysis confirmed the presence of *L. donovani* in 12 of them. Although these findings do not exclude other causative species to be involved in cutaneous leishmaniasis in Nepal as well, the confirmation of *L. donovani* in these cutaneous leishmaniasis patients could have important implications for the Kala-azar elimination programme. Furthermore, there is no evidence yet that this particular *L. donovani* strain could also cause visceral leishmaniasis, there is a clear need for genomic surveillance of visceral and cutaneous leishmaniasis cases in Nepal to rule out any potential threat to the Kala-azar elimination initiative in the region.

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BLASTOCYSTOSIS INFECTIONS AMONG CHILDREN ATTENDING FOUR HOSPITALS IN WESTERN KENYA

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Blastocystis spp, is a common intestinal parasite affecting both humans and animals worldwide. Although the role of Blastocystis *spp* as an enteric pathogen is disputed, it has been associated with infections including gastrointestinal discomfort. *Blastocystis spp* is thought to have harmful functions in the presence of certain enteric pathogens, in addition, having a potential pathogenic role in the gut, affecting growth and development in children. This study determined the prevalence of *Blastocystis spp* infection or carriage in children 15years and below, characteristic symptoms and association of infection with water source and water treatment. Faecal microscopy was conducted on 976 stool samples (488 symptomatic, 488 asymptomatic) from children enrolled in a case-control study in four County Hospitals in western Kenya. The samples were processed using Mini Parasep SF Faecal Parasite concentrator. Blastocystis *spp* was detected in 73/ 976 (7.5%) of the stool samples from both symptomatic and asymptomatic subjects with a distribution of 36/488 (7.4%) infections in cases and 37/488 (7.6%) in controls. Among the 73 infections, 56 /73 (76.7%) were Mono-infections while 17/73 (23.3%) were co-infections. Of the 73, 34/73 (46.6%) were females while 39/73 (53.4%) were males. General gastrointestinal symptoms reported were mainly; abdominal pain/ cramps (42.5%), diarrhea (15.1%), and loss of appetite/vomiting (12.3%). Additionally, cough (15.0%) and fever (12.3%) were reported as secondary symptoms, while headache (6.8%) was less frequently reported. The highest number of infection 35/73(47.9%) was among subjects who used municipal/tap water, followed by 30/73 (41.1%), 28/73 (38.4%) and 7/73 (9.6%) among those who used water from the river/springs, rainwater and borehole/well respectively. 50/73 (68.5%) of the *Blastocystis spp* were found in subjects who did not treat water. However, 23/73 (31.5%) infections were found in those who treated water. There is asymptomatic carriage of *Blastocystis spp* in children of up to 15years of age is 7.5%, however, no follow-up was done to see if the participant got diarrhea or not.

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THE GROWING PROBLEM OF LEISHMANIASIS IN TUSCANY, ITALY: AN INVESTIGATION OF UNDERREPORTED HUMAN CASES AND COMPARISON WITH CANINE INCIDENCE USING A MULTIDISCIPLINARY APPROACH.

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The Mediterranean basin, including Italy, hosts endemic areas for leishmaniasis, mainly attributable to the presence of sand flies. Leishmaniasis has gained importance in Europe, fuelled by factors such as climate change, globalisation and migration. For at least 10 years in Tuscany (Italy) there has been an important discrepancy between official notifications on reports of human visceral and cutaneous leishmaniasis cases and the number of hospital admissions, highlighting an important underreporting, despite the Italian reporting obligation. Moreover, official reports have increased alarmingly over the last three years. Human leishmaniasis is a disease that does not always require hospitalisation: it often presents cutaneous manifestations, whereas in the immunocompetent individual it may not manifest itself at all. For this reason, it is reasonable to assume that the number of cases is higher than the number of hospitalisations. The project aims to investigate the underreporting of human leishmaniasis cases from 2014 to 2023 by analysing laboratory diagnoses (considering any laboratory test that according to the guidelines of the Italian Ministry of Health is useful in identifying a 'confirmed case', thus serological tests; parasitological tests; culture tests; PCR). To estimate the extent of the underreporting, the capture-recapture method will be used, taking into account laboratory data, official reports and hospital data. Subsequently, a comparison will be made with the incidence, in the same territory, of veterinary cases, particularly in dogs, using data obtained from the Lazio-Tuscany Zooprophylactic Institute, to compare the trend of human and canine cases over time. Analyses are in progress and currently confirm a significant underreporting of up to five times the official number of notifications. The results will be presented at the conference. Poor surveillance leads to ineffective prevention policies. The impact of the project is to strengthen the leishmaniasis surveillance system in Tuscany in order to reinforce prevention systems and face emergencies.

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UNTANGLING THE LEISHMANIASIS THREAT: A MULTIFACETED ANALYSIS OF TRANSMISSION NETWORKS, ECOLOGICAL FACTORS, AND GEOGRAPHIC IMPLICATIONS IN A LEISHMANIASIS ENDEMIC REGION IN THE EASTERN MEDITERRANEAN

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The Leishmaniases, a group of neglected tropical diseases exhibiting significant anthropo-zoonotic transmission, are experiencing a worrying upsurge across the Mediterranean and Middle East, particularly in Israel. This review delves into the multifaceted factors driving this concerning trend.Israel, a Leishmaniasis hotspot within the Middle East, presents a unique case study. Four Leishmania species (*Leishmania major*, *Leishmania tropica*, *Leishmania infantum*, and the recently identified *Leishmania donovani*) co-exist, each engaged in intricate zoonotic cycles involving specific sandfly vectors and mammalian reservoirs. This intricate interplay between specific Phlebotominae sand flies of the genus *Phlebotoums*, diverse mammalian reservoirs, and Israel's varied ecological landscapes results in a spectrum of clinical presentations in both humans and animals. This complex transmission web underscores the critical need for in-depth research to develop effective control strategies.Factors such as cross-border transmission, the detection of novel transmission cycles, local conflicts, and evolving transmission dynamics all contribute to the escalating risk. Climate change adds another layer of complexity by potentially altering sandfly distribution and parasite development.This work emphasizes the urgent need for further investigation into the dynamic interplay between Leishmania parasites, sandfly vectors, animal reservoirs, and environmental factors. Only through a comprehensive approach can effectively combat the growing threat of Leishmaniasis in the Middle East and beyond.

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ASSESSING *TOXOPLASMA GONDII* SEROPREVALENCE AMONG IMMUNOCOMPETENT AND IMMUNOCOMPROMISED INDIVIDUALS LIVING IN PERU: A COMPARATIVE STUDY BETWEEN LIMA AND IQUITOS

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Toxoplasmosis, caused by *Toxoplasma gondii*, is a disease that may produce severe consequences among immunocompromised individuals. The seroprevalence of Toxoplasmosis among immunocompromised patients has not been well studied in Peru. Our study aimed to: 1) evaluate the performance of an in-house ELISA using the commercially available Vircell ELISA kit as a reference; 2) estimate the seroprevalence of Toxoplasmosis among individuals living in Lima, located in the coastal region of Peru, and Iquitos, in the Peruvian Amazon basin; and 3) evaluate factors associated with *T. gondii* seropositivity. We enrolled HIV positive individuals with neurological signs in hospitals in Lima (n=50) and Iquitos (n=50), and healthy individuals working at a university from Lima (n=73) and from houses randomly selected in Iquitos (n=108). We processed 90 randomly selected samples for performance evaluation of our in-house ELISA. Our ELISA showed 98.3% and 100% positive and negative percent agreements, with the Vircell ELISA kit. In Iquitos, individuals had a median age of 38.5 (IQR 27-51), with 77 (48.7%) males and 50 (31.65%) HIV positive. In Lima, individuals had a median age of 26 (IQR 23-34), with 70 (56.9%) males and 50 (40.65%) HIV positive. Toxoplasmosis seroprevalence was 88% in Iquitos (139/158) and 29.3% in Lima (36/123). In Lima, older individuals (PR 1.04, [95% CI 1.03-1.06]) and in Iquitos, males (PR 1.13, [95% CI 1.01-1.27]) showed higher seropositivity rates. HIV positive individuals from both study sites were more likely to be seropositive (PR 2.29, [95% CI 1.30-4.05] for Lima; and 1.18, [95% CI 1.07-1.29] for Iquitos). Our in-house ELISA presented a high performance. Future studies should determine the performance of this in-house test with other human and animal samples. Our results highlight important seroprevalence levels of Toxoplasmosis in Iquitos, Peru. Although this seroprevalence was not low among HIV negative persons living in Lima (14/73, 19.2%) and Iquitos (90/108, 83.3%), it was even higher among HIV individuals (22/50, 44%; and 49/50, 98% in Iquitos), which represents a risk for neurological complications among these patients.

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DEFORESTATION, LAND REVERSION, AND *TRYPANOSOMA CRUZI* INFECTION IN DOGS LIVING IN RURAL COMMUNITIES IN CENTRAL PANAMA

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Given dogs' roles as sentinels and reservoirs for *Trypanosoma cruzi*, the etiologic agent of Chagas disease, it is important to understand host and environmental factors associated with *T. cruzi* infection in dogs. The objective of our study is to measure *T. cruzi* infection in dogs from 12 rural communities and to evaluate intrinsic (e.g., sex, age, body condition, hemogram) and environmental (e.g., land cover) relationships between *T. cruzi* infection in dogs. We hypothesized that deforestation and land reversion influence *T. cruzi* infection rates in dogs and that *T. cruzi* infection will be higher in areas dominated by secondary forest growth. We performed physical examinations and sampled blood from 483 dogs from 203 households. We collected epidemiological variables (e.g., age, sex, body condition score) and performed rapid immunochromatographic tests, western blot, indirect immunofluorescence, and multiplex microsphere immunoassay to evaluate previous *T. cruzi* exposure. Additionally, we evaluated *T. cruzi* parasitemia by conventional PCR using S35/S36 targeting the 330bp region of the kinetoplast. Dogs positive for two or more serological tests or PCR were considered positive. Preliminary results show that across the communities,15.21% (95% CI, 11.89-19.04) (63/414) of dogs were positive for two or more *T. cruzi* serological tests. In addition, 3.54% (95% CI, 1.63-6.62) (9/254) had *T. cruzi* parasitemia confirmed by PCR. Overall, there were no significant associations between *T. cruzi* infection in relation to dog sex, body condition, and age. However, there were community level differences in *T. cruzi* infection/exposure in dogs- communities surrounded by secondary forest growth had positive associations with *T. cruzi* prevalence. Preliminary results suggest that complex interactions between land cover types around communities and households influence *T. cruzi* infection in dogs.

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KNOWLEDGE ABOUT CHAGAS DISEASE AMONG HEALTHCARE PROFESSIONALS

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The knowledge of health professionals about Chagas disease among health professionals is essential for controlling this Public Health problem. We aimed to identify the knowledge about this public health problem among these Primary Health Care professionals. We performed a cross-sectional, exploratory study, with 257 professionals between April and September 2023 in Irecê city, Brazil. Data were collected using a standardized questionnaire and data were analyzed descriptively. From the total number of professionals, 87.9% recognized the etiological agent is a protozoan, and identified the following forms of transmission: vector (100%), blood transfusion (55.3%), and oral (61.9%); the main organs affected were: heart (99.2%) and spleen (58.4%). The signs/symptoms identified in the acute phase were fever (76.6%), adenomegaly (59.4%), edema (85.2%), splenomegaly (68.0%), hepatomegaly (65.2%), Romaña sign (50.4%); at chronic cases, it was recognized that it may occur asymptomatically, but electrocardiographic changes (99.2%), megacolon (64.6%), megaesophagus (59.1%), congestive heart failure (99.2%) may be present.), thromboembolic phenomena (58.4%), and respiratory distress (80.9%). Regarding etiological treatment, 72.0% recognized its existence, but 47.5% were unable to inform which medication was recommended; and for 73.5% of participants, the disease is incurable. Regarding the insect vector, 81.7% recognized it. When asked about the service where triatomines should be sent, 65.7% recognized the Zoonosis Control Center. The care to be taken when handling triatomines was to use gloves or protect your hands with a plastic bag (92.2%); the guidance to be given when faced with an insect bite in humans was to carry out serological tests (91.8%) and personal access to information occurred informally in everyday daily work (30.0%) or during the training course in the health area (28.8%). It is of fundamental importance that health professionals are trained on Chagas disease for early recognition and specific treatment, and that health surveillance and vector control actions are effective.

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IMPACT OF *BLASTOCYSTIS* SUBTYPES ON POLYPARASITISM IN COLOMBIAN CHILDREN

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Polyparasitism is prevalent in developing communities and peri-urban areas of large cities. Factors contributing to persistent polyparasitism include recurrent environmental exposure and reinfection. Identifying the primary risk factors is crucial for effective intervention. *Blastocystis* is a common intestinal protozoan with a contested role as a human pathogen, with pathogenicity dependent on the *Blastocystis* subtype. In a peri-urban area of Medellín, Colombia, stool samples were taken from 202 children under five years old, and we conducted stool-based multi-parallel real-time quantitative PCR. Preliminary results revealed that 57.9% of children tested positive for *Blastocystis* DNA, 20.3% *Cryptosporidium*, 20.3% *Giardia intestinalis,* 9.4% *Necator americanus,*1.9% *Trichuris trichiura,*1.9% *Entamoeba histolytica*, and 1.5% *Ascaris lumbricoides*. No positive samples were found for *Ancylostoma duodenale* and *Strongyloides stercoralis.* We found varying degrees of polyparasitism, with 57.2% of children testing for one parasite, 34.9% for two, and 7.9% for three. The children infected with *Blastocystis* and a helminth had a significantly different burden of *N. americanus*, *T. trichiura*, and *A. lumbricoides* (0.011 vs 0.12 vs 0.59, p = 0.0018). There is a greater burden of *G. intestinalis* within *Blastocystis* negative children than *Blastocystis* positive children (1.36 versus 0.26 fg/µl, p = 0.0340). Also, a significant positive correlation was identified between *Blastocystis* and *G. intestinalis* with Spearman R = 0.37898, p = 0.0385. These findings suggest *Blastocystis* is a valuable indicator of GI parasite exposure rates. Given its reported transmission through fecal-oral contamination and cyst-infected water sources, further studies will explore *Blastocystis* subtypes and their associations with helminth/protozoan infections.

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IMPACT OF EDUCATIONAL ACTIVITIES AND AN ELECTRONIC MEDICAL RECORD TEMPLATE ON CHAGAS DISEASE SCREENING

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Given a lack of comprehensive screening programs or standardized screening recommendations for clinicians, the estimated prevalence of 300,000 people with Chagas disease in the United States (US) is likely an underestimate. In 2021, clinicians and public health experts began the Implementing Novel Strategies for Education and Chagas Testing (INSECT) study at Boston Medical Center (BMC) to improve awareness and knowledge of Chagas disease and enhance healthcare provider screening. As a quality improvement initiative, we examined the influence of educational activities and implementation of an electronic medical record (EMR) template on changes in screening rates at BMC. Educational sessions were conducted in the BMC departments of internal medicine, obstetrics/gynecology, pediatrics, and family medicine and sections of nephrology, transplant nephrology, cardiology and infectious diseases. Audience members included medical students, resident, fellow and attending physicians, nurses, midwives and public health experts. From 2014 to the start of BMC educational activities in 2021, 729 tests were ordered, including screening and confirmatory testing at the Centers for Disease Control and Prevention. The top five ordering departments were obstetrics/gynecology (OB/GYN) (152, 21%), adult inpatient medicine (123, 17%), transplant surgery (92,13%), cardiology (80, 11%), and infectious diseases (60, 8%). From 2021-2024, INSECT study members conducted 23 Grand Rounds and lectures to approximately 870 individuals at BMC. Since INSECT implementation, 3,731 tests were ordered (2021-April 17, 2024), displaying increased testing overall and a shift towards more primary care testing. Top ordering departments included OB/GYN (1802, 48%), transplant surgery (844, 23%), adult outpatient primary care (407, 11%), adult inpatient medicine (159, 4%), and family medicine (116, 3%). With the implementation of educational programming for providers and an EMR template for ordering ease, we increased testing for Chagas disease at BMC. We anticipate that other sites with at-risk patients may benefit from similar activities.

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BIBLIOMETRIC META-ANALYSIS OF CHAGAS DISEASE AND EQUITABLE ACCESS TO HEALTH CARE

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Chagas disease, transmitted by *Trypanosoma cruzi*, has been historically reported in endemic areas of Latin America. However, an increasing

presence of this disease is currently observed in urban habitats with domestic transmission cycles and adapted to different ecological environments. Currently, the total burden of Chagas disease is approximately 7 million cases worldwide. The objective of the study was to investigate the vertical transmission of *Trypanosoma cruzi*, its presence in blood banks and donors, its epidemiological distribution in urban areas, and its appearance in non-endemic regions. We conducted a bibliometric meta-analysis through searches in Scientific Technical Health Literature of Latin America and the Caribbean (LILACS), PubMed, multilingual collaborative health evidence database (epistemonikos), Cochrane, and Scopus. The search for scientific articles was conducted in English, Portuguese, and Spanish, with a cutoff date of December 27, 2022. The data network was constructed using VOSviewer software to: a) visualize any possible overlapping between the analyses by applying the association strength normalization technique, and b) analyze the information by a clustering technique, with relevant co-authorship publications between countries. The distance from one country to another reflects the strength of co-authorship each country exerts. The obtained results highlighted trends and patterns on Chagas disease research, its transmission, and epidemiology in the context of current knowledge and its implications for public health, especially in urban areas and non-endemic regions. In conclusion, this analysis focused on the infection of the parasite *T. cruzi* and its association in urban environments of both endemic and non-endemic countries, based on data collected from various studies published in scientific journals. The results underscore the need to strengthen disease surveillance and control programs in urban settings, and to implement strategies for early detection and timely treatment.

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CAPACITY-BUILDING IN MOLECULAR SURVEILLANCE OF INFECTIOUS DISEASES: PROGRESS AND ACHIEVEMENTS OF THE INSTITUTE OF RESEARCH IN TROPICAL DISEASES IN AMAZONAS, PERU

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Amazonas is a northeastern region located between the Andean mountains and the Amazon plain with a population of 429 483 inhabitants. This region has seven provinces with areas where native communities do not have access to public services such as electricity, drinking water or sewage. Amazonas is affected by several infectious and tropical diseases such as malaria, leishmania, Chagas, HIV, dengue and other arbovirus. The UNTRM was the first university in Amazonas to implement, in collaboration with the Regional Direction of Health, molecular tools for the research of infectious diseases that constitute a severe burden to the region. By January 2020th, the IET was created with three main laboratories: molecular epidemiology and genomics, cell culture and advanced therapies, and biosensors and biomedical devices. Molecular confirmation tests for the previously mentioned diseases were implemented and by September 2020th the COVID-19 laboratory for molecular diagnosis and genome sequencing received its operating license, becoming the first in the region. Additionally, we made major progress in implementing a surveillance platform for parasitic diseases such as malaria, reporting an outbreak of *Plasmodium falciparum* and a recent clonal expansion in the district of Rio Santiago, with its vector *Anopheles benarrochi*. We also managed to implement a reader device for electronic differential measurement to detect nucleic acid of Plasmodium in blood samples to be used in the field. On the other hand, the immunomodulatory cytokine profile of the secretome of mesenchymal stem cells cultured in the presence of Leishmania antigens was characterized. As a result of these investigations, over 15 papers have been published so far and several undergraduate and graduate students have participated and benefited by performing their thesis and dissertations. In conclusion, the UNTRM in collaboration with partner institutions was successful in building an institute with the latest technology in a hard-to-reach area, transferring capabilities to improve the diagnostic capacity of infectious diseases in Amazonas.

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TSLP UPREGULATES IFN-GAMMA PRODUCTION IN CUTANEOUS LEISHMANIASIS PATIENTS

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Patients with cutaneous leishmaniasis (CL) due to *Leishmania braziliensis* infection develop ulcerative skin lesions that are associated with inflammatory response. Activation of macrophages by IFN-gamma is the main mechanism of *Leishmania* parasite killing, whereas Th2 environment with IL-5 production is associated with parasite replication. Our previous results show intense inflammatory infiltrate with high production of TNF and IL-1-beta in lesions from CL patients. Thymic stromal lymphopoietin (TSLP) is an epithelial cell-derived cytokine expressed in skin, gut, lungs, and thymus that induce Th2 cytokines and is produced during helminth infection and atopy. Our aim was to assess the production and effect of TSLP in cells from CL patients. By analyzing single-cell RNAseq we found that TSLP is not significantly expressed in lesion C57BL/6 mice upon infection with *L. major*, or in lesion from CL patients due to *L. braziliensis* infection. To assess the effect of TSLP on CL patients we added recombinant (r) TSLP to Soluble *Leishmania* Antigen (SLA)-stimulated peripheral blood mononuclear cells (PBMC) from CL patients. Surprisingly, addition of rTSLP increased IFN-gamma in SLA-stimulated PBMC culture supernatants without affecting the production of TNF, IL-5 and IL-10. Our data suggest that presence of TSLP may benefit CL patients by increasing IFN-gamma production, thus contributing to parasite killing.

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FOLLICULAR T HELPER (TFH) VERSUS HYBRID TH1/TFH CELLS AND THE OUTCOME B CELL RESPONSE IN *TRYPANOSOMA CRUZI* INFECTION OF SUSCEPTIBLE AND RESISTANT MICE

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Trypanosoma cruzi is the etiologic agent of Chagas disease (CD). Endemic to Latin America, CD affects 6 to 7 million people worldwide and is responsible for over 800,000 disability-adjusted life-years due to digestive and cardiac manifestations. Immune response studies in the context of *T. cruzi* infection are mostly focused on T cells, due to their well-known role associated with better outcomes by the generation of a CD4$^+$ T helper Th1 profile and a strong CD8$^+$ T response that is, however, unable to resolve the infection. Contrarily, B cell response in CD models has been overall under investigated. It's known that *T. cruzi* infection induces a polyclonal B lymphocyte proliferation with unspecific antibody response unable to clear the parasites, resulting in chronic infection. In this work, we performed a thorough characterization of the B cell immune response and Follicular T helper (Tfh) cells, a subset of CD4$^+$ T cells required for the T-dependent germinal center (GC) response, in *T. cruzi* infection. Comparing two different mouse models: C57BL/6 mice described as a resistant model to *T. cruzi* infection, and BALB/c mice, susceptible. Female mice of both strains were infected with 5000 blood form trypomastigotes of the bioluminescent H1 *T. cruzi* strain. Flow cytometry analysis showed that C57BL/6 mice model, associated with type I immunity, produced hybrid Th1/Tfh cells with reduced expression of the transcription factor Bcl6 and increased expression of IFN-γ. Comparatively, BALB/c mouse model, associated with type 2 immunity, produced mainly classic Tfh cells with increased Bcl6 expression leading to IgG 1 hypergammaglobulinemia and an exacerbated expansion of germinal center B cells. In both models, the expression of Bcl6 in germinal center B cells, associated with the production of high-quality antibodies, is delayed appearing only 28 dpi. These results point to the development of different evasion mechanisms by the parasite with the late production of specific high-affinity antibodies.

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GALNAC AND GLCNAC CARBOHYDRATES INCREASE THE PRESENCE AND ACTIVITY OF THE MYELOPEROXIDASE ENZYME DURING *ENTAMOEBA HISTOLYTICA* AND NEUTROPHIL INTERACTIONS, POSSIBLY BY BLOCKING AMEBIC ADHESION

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The present study analyzes the effect of the presence of carbohydrates N-acetyl-D-galactosamine (GalNAc) and N-acetyl-D-glucosamine (GlcNAc) on the myeloperoxidase (MPO) activity of neutrophils during their interaction (mouse model of resistance to amebiasis) with trophozoites of *Entamoeba histolytica* (*E. histolytica*). GalNAc and GlcNAc block the amoebic 260 kDa and 220 kDa lectins, respectively. *E. histolytica* trophozoites (5×10^4 amebas/ml) were interacted with mouse neutrophils (1×10^6 cells/mL) in presence of the carbohydrates at 25 mM and the effect was evaluated at 20, 40, 60, and 90 min. MPO activity was explored with the addition of TMB (chlorhydrate of 3,3', 5,5'-tetramethylbenzidine) and hydrogen peroxide solution. The microscopy analysis was carried out with an anti-ameba polyclonal rabbit IgG antibody, which was detected with a secondary donkey anti-rabbit IgG (H + L) antibody Alexa Fluor-647. MPO was detected with an anti-MPO polyclonal rabbit IgG conjugated to the Alexa Fluor-350 antibody. The samples were counterstained with SYTOX green to observe the DNA and images were collected and analyzed with confocal fluorescence microscopy. A significant increase was observed in the activity and presence of MPO at the different times of the interactions in presence of the carbohydrates compared with the interactions in absence of the carbohydrates. The greatest increase in MPO activity was found in the presence of GalNAc. The increase in the activity and presence of MPO in ameba/neutrophil interactions in the presence of carbohydrates suggests that MPO could be involved in amoebic damage by blocking amebic adhesion, thus making it possible for the MPO of neutrophils to be activated.

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LACK OF INFORMATION AS A REASON FOR NON-PARTICIPATION IN MASS DRUG ADMINISTRATION TARGETING ONCHOCERCIASIS: A MIXED METHOD STUDY

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The World Health Organization recommends mass ivermectin administration to eliminate onchocerciasis as a public health problem. However, despite efforts to achieve sufficient coverage over time, some targeted individuals report never receiving information about the mass drug administration (MDA) campaigns. Our study aimed to understand why some individuals in endemic areas did not receive information about the MDA campaign over multiple rounds in KA-05, one transmission zone in Mali. We conducted a mixed method study, combining community surveys with qualitative and participatory methods. Data collection took place in February 2023 in the health districts of Sagabari, Kita, and Kenieba. We interviewed participants aged 18 years and above using a pre-established questionnaire to collect sociodemographic characteristics and the reasons associated with the lack of information, such as the main source of income, health districts, the travel history, and level of knowledge of the disease. We also conducted individual interviews and focus group discussions using an interview guide. Finally, we performed a thematic analysis for qualitative data using NVIVO v14. We used SPSS v26 to conduct a binary logistic regression for quantitative data to identify factors associated with the lack of information about the MDA campaign. Lack of information was the most frequently reported reason for non-participation in onchocerciasis targeted MDA [20% (187/921)]. People who knew nothing about onchocerciasis were 1.93 times more likely to be unaware of the campaign as compared to those who had heard of onchocerciasis (CI: 1.18 - 3.14). Qualitative study revealed that this lack of information can be attributed to various factors, such as the lack of awareness, education, seasonal movements, rumors, and available communication channels. Despite many years of MDA for onchocerciasis in this location, some people remain unaware about the disease and the MDA. As programs reach the endgame of elimination, new approaches are needed to reach the unreached.

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EVALUATION OF SOIL-TRANSMITTED HELMINTHIASIS AND SCHISTOSOMIASIS COVERAGE FOLLOWING SIX YEARS OF MASS DRUG ADMINISTRATION IN FIVE NIGERIA STATES

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Achieving the WHO recommended treatment threshold during every round of preventive chemotherapy (PC) is essential to reach elimination of parasitic worm infections as public health problems. Reported administrative coverage data, though essential for program monitoring, can sometimes vary from the actual treatment coverage due to weaknesses in health information systems (use of outdated population census data, inaccurate count of persons treated etc). WHO recommends Coverage Evaluation Surveys (CES) to understand reporting accuracy and to determine if there are data reporting problems. This study evaluates CES conducted post-PC in 55 implementing units (IUs) across five Nigerian states for soil transmitted helminths (STH; 38 IUs) and schistosomiasis (SCH; 17 IUs), from 2018 - 2023. Following the WHO CES protocol, households and schools in 1,650 communities were visited and 62,683 individuals surveyed to estimate treatment coverage over six years. The surveyed coverage showed that 45.5% (25; STH- 16, SCH-9) of IUs met/exceeded the 75% target treatment threshold with 95% CI ranging from 75% - 97%, an adequate marker for a well-functioning programme and successful MDA. Only 3% (1,894) of individuals did not swallow the medicines when offered, indicating high compliance. The reported administrative coverage ranged from 42% - 133% in the 55 IUs, but were similar to the surveyed coverage in only 13% (7) and validated in 7% (4) of the IUs, evidence of critical data reporting issues across board. A significant 23% (14,457) reported they were not offered medicines during the PC round; predominant reasons include absence on deworming day (26.4%); school did not participate or receive medicines (20%); and lack of awareness of the PC (11.5%). Data quality assessment post-PC is recommended to check issues around the variances between the survey and reported coverage and strengthen PC reporting. Additionally, strengthening community engagement and sensitization, as well as proper program planning to address medicine quantification and positioning will be necessary to improve awareness and boost participation in PC.

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CHALLENGES IN MEASURING AND DISCUSSING ELIMINATION GOALS: FROM MODELLING TO POLICY

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The World Health Organisation (WHO) have targeted *gambiense* human African trypanosomiasis (*g*HAT) for elimination of transmission (EoT) by 2030. Unfortunately, it is not possible to directly observe new infections, so a proxy indicator is needed to be able to measure progress towards this target. The WHO HAT elimination Technical Advisory Group have recently defined the indicator for EoT as five years of no cases, along with a sufficient level of surveillance. To support programs in achieving this goal, mathematical modelling is being used to predict and quantitively evaluate the effectiveness of interventions and measure progress towards elimination. Unlike in the real world, modelling can find the exact point at which transmission ceases in the model and many papers have been published using this modelled point of EoT to predict when real-world EoT will be reached. Unfortunately, despite sharing a name, these two definitions of EoT are not the same, and in fact can differ very significantly. In this presentation we discuss the difference between these indicators and show with some examples how severely these indicators can disagree. Similarly, models can predict the exact point at which there is no more infection in the population – Elimination of Infection (EoI), an even stronger criterion than EoT, and also not directly measurable in the real world. The difference between EoT and EoI is particularly pertinent for *g*HAT, which has a very long infection time (often multiple years, sometimes over a decade) meaning that cases can be found substantially after infection was first transmitted to the patient. While this presentation focuses specifically on these three benchmarks for *g*HAT, the general points made here about seemingly trivial differences in the definition of elimination and its indicators could have significant consequences on decision making for any infections approaching the endgame. Modellers and policymakers, both in *g*HAT and beyond, need to work closely together and communicate clearly to ensure that they are in alignment when discussing elimination.

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COVERAGE EVALUATION SURVEY OF LYMPHATIC FILARIASIS RE- MASS DRUG ADMINISTRATION AFTER PRE-TAS FAILURE IN 4 DISTRICTS OF MOZAMBIQUE, 2023

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The Department of Disease Prevention and Control conducted a post-lymphatic filariasis (LF) MDA coverage evaluation survey (CES) from August to September 2023 in Cuamba, Murrupula, Mulevala & Ile. The survey aimed to validate the reported coverage and explore factors affecting MDA implementation. The CES is a community-based cross-sectional survey where 30 clusters are randomly selected using probability proportionate to estimate size (PPES), segmented, and then households are selected for interviews based on a numbered list. Surveyed coverage ranged from 64.1% to 83.5% across the four districts, with only Mulevala failing to meet the WHO coverage threshold of 65%. Across all districts, the main reasons for not consuming drugs were “not being at home during distribution”, “unaware of the MDA”, or “distributors did not visit their house, school, or distribution point”. Respondents that were unaware of the MDA ranged from 23% to 44% across districts and 48% to 90% of participants indicated drugs were received during a household visit. Those that had never participated in an LF MDA ranged from 10% to 26%, and despite upwards of 10 years of treatment in some districts, 52% to 87% indicated that they participated only once. Of the 120 clusters surveyed, 32 failed to meet the coverage threshold, suggesting a more focal issue. When cluster coverage data was compared to daily monitoring reports from the MDA, it revealed potential implementation and data quality issues at the community level. Despite sufficient coverage at the district level, low surveyed coverage in some clusters underscores the need for a more targeted, community-based approach. Future MDAs should focus on community preparation & sensitization, engaging community leaders in planning and pre-MDA meetings, ensuring robust IEC, and implementing innovative strategies to reach the absent people. Enhancing CDD training, conducting daily data monitoring at the community level, and planning for post-MDA mop-up in low coverage communities will ensure more uniform coverage across the districts, as missed populations may sustain LF transmission despite achieving recommended thresholds.

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COMPLETING THE TRACHOMA MAP IN SOUTH SUDAN: RESULTS OF THREE BASELINE PREVALENCE SURVEYS IN EASTERN EQUATORIA STATE, 2023-2024

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Estimating the baseline prevalence of trachoma is required for trachoma control programs to determine a district’s eligibility to receive SAFE (Surgery, Antibiotics, Facial cleanliness, and Environmental improvement) interventions. The Ministry of Health of the Republic of South Sudan (MoH-RSS) is dedicated to eliminating trachoma as a public health problem and since 2001 has implemented aspects of the SAFE strategy in parts of the country. However, as of 2022, three counties (districts) in Eastern Equatoria State (EES) had not completed baseline mapping. From 2023-2024, the three counties of Torit, Magwi, and Ikotos were surveyed by the MoH-RSS Trachoma Control Program using a multistage cluster-randomized sampling design. Trained and certified graders examined participants for trachoma clinical signs and county level prevalence was estimated. Dried blood spot (DBS) specimens were collected from individuals one year of age or older in all three counties. In addition, ocular swabs for *Chlamydia trachomatis* (*Ct*) infections were collected from children ages 1-9 years in Torit. During the 2023 surveys of Torit and Magwi, a total of 59 clusters with 6,222 individuals from 1,577 households were examined for trachoma, with 6,213 DBS and 1,346 swabs collected. Prevalence of trachomatous inflammation—follicular (TF) among children ages 1-9 years was 0.8% (95% confidence interval [CI]: 0.4-1.7%) in Magwi and 7.3% (95% CI: 3.3-15.7%) in Torit. Trachomatous trichiasis (TT) in adults 15 years and older was 1.05% (95% CI: 0.59-1.86%) in Magwi and 1.41% (95% CI: 0.81-2.44%) in Torit. The analysis of the 2024 Ikotos survey results, and the results of the infection and serological analysis, will be complete by summer 2024. Based on these results, Torit is slightly above the World Health Organization elimination thresholds of TF<5% and TT<0.2% and will require all SAFE interventions, whereas Magwi will only require S, F, and E interventions until TT levels are <0.2%. With the completion of baseline surveys for all counties in EES, the MoH-RSS has the data needed to drive progress towards the elimination of trachoma.

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ANALYSIS OF THE SITUATION OF LEPROSY CASES IN CHILDREN AGED FROM 5 TO 14 YEARS FROM 2022 TO 2023 IN CONAKRY (GUINEA)

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Depuis 2010, la Guinée a atteint le seuil d’élimination de la lèpre comme problème de santé publique, avec moins d’un cas pour 10 000 habitants dans toutes les préfectures du pays. Malgré les efforts du Ministère de la Santé et de l’Hygiène Publique à travers le Programme National de

Lutte contre les Maladies Tropicales Négligées avec Prise en Charge des Cas (PNLMTN-PCC) en collaboration avec les partenaires techniques et financiers, il y a eu une sous-déclaration ces dernières années dans tous les centres de prise en charge des cas du pays. pays. Plusieurs facteurs peuvent expliquer cette sous-déclaration, notamment un dépistage retardé entraînant une proportion élevée de cas multibacillaires (MB), un nombre important d'invalidités de grade 2, un financement insuffisant pour une surveillance solide de ces maladies et le départ à la retraite du personnel qualifié. Fin 2022, 185 nouveaux cas ont été recensés, dont 4 cas chez les enfants (2,2%). En 2023, 244 nouveaux cas ont été détectés, dont 6 cas chez des enfants, tous scolarisés (1,8%). La moitié de ces enfants résident à Conakry. Plusieurs indicateurs clés mettent en évidence les défis rencontrés pour mettre en œuvre la stratégie de l'Organisation mondiale de la santé visant à interrompre la transmission. Le pourcentage d'enfants supérieur à 1% constitue un indicateur crucial signalant la présence persistante de la maladie dans la population, notamment dans la région de Conakry et ses deux villes du nord. La proportion croissante de cas multibacillaires (80 % et 88 % en 2022 et 2023, respectivement) parmi les nouveaux cas signifie un risque accru de transmission de la maladie au sein de la population, notamment dans les milieux éducatifs où les étudiants interagissent étroitement pendant des périodes prolongées. Seize de ces cas provenaient de Conakry, dont 3 cas impliquant des enfants (19%). Une évaluation de la situation indique une résurgence potentielle de la lèpre en Guinée. Face à ce scénario, il est essentiel d'intensifier les efforts de détection précoce de la lèpre.

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ADDRESSING "LEAVING NO ONE BEHIND" IN AN NTD PROGRAMMATIC CONTEXT: EXPERIENCE FROM THE DEWORMING INNOVATION FUND

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As NTD endemic countries implement the World Health Organization Sustainability Framework for Action Against NTDs 2021-2030, the need to ensure all at risk populations are reached has become urgent. Kenya is implementing interventions on Schistosomiasis (SCH) and soil transmitted helminthiasis (STH) in the Western Region with a view to reaching affected communities with information and services and influence adoption of positive behaviors by prioritizing inclusivity, equity and social justice. One aim of the Kenya NTD Master Plan 2023 -2027 is to interrupt transmission of SCH and STH through adopting comprehensive approaches, one being, leaving no one behind (LNOB). Under the Deworming Innovation Fund, a community consultative process was applied to identify people at risk of infection and the their social networks, while survey data were used to determine effective channels of communication. Key groups identified as needing special attention included street families, prisoners, people in remote areas, persons with disabilities, older persons and minority groups. Tailor-made strategies were implemented including: identifying and sensitizing influencers and change agents; developing culturally acceptable sensitization materials with NTD messages such as religious training manuals with Muslim and Christian groups; collaborating with other sectors such as prisons and social services departments; holding community dialogue forums; working closely with community-based organizations and private sector in implementing social behavior change and social mobilization initiatives. These actions resulted in improved access to information, treatment and increased avenues for structured in-depth conversations triggering behavior change. Quarterly monitoring reports in 2022/23 show increased levels of knowledge and a consistent high uptake of treatment (over 80%). Success stories have been documented in the intervention sites to demonstrate how the program is positively changing lives. Implementing targeted social mobilization and treatment interventions are key strategies to leaving no one behind.

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FACTORS ASSOCIATED WITH PERSISTENT AND RECRUDESCENT ACTIVE TRACHOMA: RESULTS FROM ADAPTIVE COVERAGE EVALUATION SURVEYS IN UGANDA

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Through implementation of the surgery, antibiotics, facial cleanliness, and environmental change (SAFE) strategy, Uganda has made progress towards elimination of trachoma with 59 of 61 previously endemic districts having stopped mass drug administration (MDA). Moroto and Nabilatuk have persistent and recrudescent active trachoma. The population in these districts are predominantly nomadic pastoralists where coverage of water, sanitation, and hygiene (WASH) is low and hard to reach, making MDA campaigns challenging. We investigated the factors associated with trachomatous inflammation-follicular (TF) in children aged 1–9 years following completion of MDA. Trachoma examination was added onto a routine coverage evaluation survey conducted one month after MDA. A two-stage sampling design was used to select 30 clusters and 10 to 12 households per cluster. MDA coverage was assessed in all eligible household members using standard WHO tools while trachoma examination was undertaken by graders certified using Tropical Data standards. Univariate and multivariate logistic regression analysis was used to explore association of TF and explanatory variables. A total 1806 children were included in the analysis and majority (51%) were male. In the univariate analysis, factors associated with increased odds of TF were residing in Moroto district, odds ratio (OR)=6.0 (95% confidence interval [CI] 2.3-16.1); not attending school, OR=9.6 (95% CI=1.3-71.2); not treated during MDA, OR=12.9 (95%CI=5.8-25.5); and low access to water source (p-value<0.001). Adjusting for age and gender, factors independently associated with TF were: residing in Moroto, OR=3.6 (95% CI1.1-9.2); not treated during MDA, OR=8.4 (95%CI=3.1-23.2); and low access to water source (p-value=0.002). The results showed lack of participation in MDA was an important driver of persistent trachoma, especially in Moroto district. The findings also suggest that low access to WASH remains an important driver of trachoma in these mobile and migrant pastoralist populations. Enhanced MDA and WASH interventions are needed to eliminate trachoma in Moroto and Nabilatuk.

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DETERMINANTS FOR UPTAKE OF MASS DRUG ADMINISTRATION FOR SCHISTOSOMIASIS CONTROL IN BUTIABA, UGANDA

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Schistosomiasis is targeted for elimination in Uganda by 2025 through Mass Drug Administration (MDA) using praziquantel. To achieve this, WHO estimates indicate that MDA coverage and uptake of 75% is required. However, coverage remains suboptimal. There is need to add to the body of knowledge to enable more robust mitigation measures. This study aimed to assess the uptake of praziquantel for MDA and associated factors in Butiaba sub-county along the shores of Lake Albert in Uganda. A cross-sectional study was conducted in five randomly selected villages between July and September 2021 using quantitative and qualitative approaches. Semi-structured questionnaires were administered to 450 adults, with two

Focus Group Discussions and Key Informant interviews held with village and district leaders. Self-reported uptake of praziquantel within twelve months of the most recent MDA exercise was 71.56% (95% CI: 67.14 - 75.68). Of all the participants, 5.78% reported having never swallowed praziquantel in their lifetime and 75% (96/128) of participants who didn't swallow praziquantel in the last twelve months reported having at least swallowed the drug in the last ten years. Respondents were less likely to have swallowed praziquantel if they had no knowledge about schistosomiasis signs (AOR= 0.18, 95% CI: 0.08-0.39) and more likely if they were between the ages 30-39years (AOR= 2.31, 95% CI: 1.35-3.95) or 40 years and above (AOR= 2.86, 95% CI: 1.45 - 4.95). Operational challenges such as inadequate supply of praziquantel and financial constraints also influence uptake of praziquantel during MDA in Butiaba sub-county. Uptake of praziquantel was high but still below the WHO target of 75%. People with limited knowledge on schistosomiasis symptoms and those aged 18 - 29 years were less likely to take Praziquantel. Irregular drug supply was also a key challenge. Rigorous health education and ensuring continuous supply of Praziquantel are key in improving MDA uptake.

7467

FORECASTING OF ONCHOCERCIASIS PREVALENCE IN WEST AFRICA THROUGH TIME SERIES MODELING

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Act to End NTDs | West is a five-year USAID-funded program that aims to eliminate or control five Neglected Tropical Diseases across 11 West African countries. WHO's roadmap for NTD elimination targets five diseases for preventive chemotherapy: Lymphatic Filariasis (LF), Trachoma, Onchocerciasis (OV), Schistosomiasis, and Soil-Transmitted Helminth. Disease prevalence is assessed by population-based surveys.As LF and Trachoma are near elimination in several West African countries, the focus of funders and governments is increasingly shifting to eliminating OV. Therefore, this paper sets out to forecast OV prevalence using forecasts through modeling. Utilizing ESPEN site-level prevalence data spanning from 1975 to 2018, we focused on seven countries: Burkina Faso, Benin, Cote d'Ivoire, Ghana, Guinea, Mali, and Togo. Maximum prevalence at the site level was utilized to summarize the data for each year across the selected countries. In instances of missing data, prevalence from the preceding year was used.Various time series modeling techniques, including Autoregressive Integrated Moving Average (ARIMA), Generalized additive model (GAM), Generalized linear model (GLM), and Facebook's Prophet models, were employed using RStudio (version 3.3.0). For these models, we set a calibration period of 43 years and a forecasting horizon from 2019 to 2030 (12 years). Data management was facilitated through MS Excel pivot tables. Despite ARIMA and GAM models showing a minimal decline in prevalence, GLM and Prophet model forecasts suggest that by 2030, OV prevalence will decline to 0% (with a 95% prediction interval of 0% to 2.8%) across the seven countries, indicating the achievement of onchocerciasis elimination by 2030. The Prophet model demonstrated the best fit based on fit statistics, including average Mean Absolute Error (MAE), Prediction Interval Coverage, and Weighted Interval Score (WIS).This talk will additionally explore more complex models, such as the n-sub epidemic and spatial wave framework, for future analyses to forecast OV prevalence. Finally, we aim to expand our analysis to provide country-specific forecasts.

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MIND THE GAP: GENDER DIFFERENCES IN PREVENTATIVE TREATMENT OF SEVEN NEGLECTED TROPICAL DISEASES

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Ensuring gender equity is a core goal of USAID as well as of Act to End NTDs | West, a USAID-funded program supporting Ministries of Health in 11 West African countries to manage seven neglected tropical diseases (NTDs). A key strategy of NTD management is mass drug administration (MDA) of preventative chemotherapy (PC) to populations at risk. Determining the presence and magnitude of gender disparities in MDA is crucial both to ensuring health equity, and to identifying pathways of ongoing NTD transmission. This study assessed 3,832 USAID-funded MDA events covering the seven PC-NTDs across 792 districts in 11 countries from 2019 to 2023, disaggregated by sex. We estimated sex-disaggregated program coverage rates for each MDA by dividing reported male and female treatment data by estimated male and female target populations, respectively. The distributions of, and differences between, male and female coverage rates were analyzed by country and targeted disease. Broadly, NTD programs appear to achieve high MDA coverage, but differences between males and females do exist. Average coverage across all MDA events was 92.8% for females and 85.1% for males. However, 355 MDA events (9.3%) had differences of at least 20 percentage points, and 41 (5.2%) of the 792 districts studied had differences of at least 20 percentage points in three or more MDA held during the study period. Coverage differences vary by the disease being treated, and across countries. MDA treating schistosomiasis had the smallest differences (female coverage exceeded that of males by 6.5 percentage points) while those treating lymphatic filariasis had the largest (female coverage exceeded that of males by 10.6 percentage points). The lowest country-level average difference was 3.3 percentage points, while the highest was 15.2 percentage points. This study will explore country- and disease-specific context to interpretate the drivers of coverage differences that must be addressed to improve gender equity in future MDA programming.

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TRACHOMA ZONES OF CONCERN: IDENTIFYING AREAS OF TRACHOMA RISK BEFORE AND AFTER ELIMINATION USING NOVEL GEOSPATIAL ANALYSIS

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Enhanced analysis methods can help identify areas at high risk for persistent and/or recrudescent active trachoma within and between trachoma endemic Evaluation Units (EUs). Geospatial analysis could identify "zones of concern" likely to have above-threshold trachomatous inflammation—follicular prevalence in children aged 1-9 years (TF1-9) within and between EUs, including within and between countries. This study is a secondary data analysis using trachoma baseline, impact (TIS), and surveillance (TSS) survey data collected with Global Trachoma Mapping Project (GTMP) and Tropical Data support from 2012 to 2022 in Uganda, Kenya, and neighboring countries. Previous work has explored the spatial distribution of trachoma and the spatial relationship of trachoma to spatial covariates in these countries. Leveraging these results and an understanding of trachoma geospatial dynamics, a new analysis approach was developed. The approach borrows information from nearby survey clusters within a certain distance or buffer of a survey cluster and uses these data to estimate a zonal mean TF1-9 prevalence for each survey cluster area. This approach was piloted in several areas of Uganda with different epidemiological and survey profiles. Data from the most recent survey in one area of was used to identify a "zone of concern" with several overlapping 10-kilometer cluster buffers of more than 5% TF1-9 across several districts in the study area. In another area, the results show several zones of concern, including a large zone overlapping international borders. Trachoma is highly focal in distribution, and spatial models need to be tailored to each area of interest. The spatial scale of analysis, including

considering the use of data beyond the borders of a single EU or even country, could be important in some areas. Simple geospatial analysis, such as this "zone of concern" approach, may provide initial information for programs to target interventions in areas at risk of persistent and/or recrudescent trachoma or for post-validation surveillance activities.

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IMPROVING THE QUALITY OF MASS DRUG ADMINISTRATION IN GHANA USING ELECTRONIC DATA CAPTURE.

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Ghana has conducted Mass Drug Administration (MDAs) as a means of controlling neglected tropical diseases for over two decades. These MDAs have used traditional community registers and community drug distributors (CDD) as a channel to distribute essential MDA medicines to community members. Data from these MDAs are sometimes not reported in a manner that is timely, complete, inaccurate and hence NTD programs have challenges making informed decisions timely for improved or quality MDA. This shortcoming leads to even dire consequences as the deficiencies are only discovered a few months after implementation making introduction of strategies to improve MDA during the period impossible. At the implementation level supervisors are constrained in identifying areas with low coverage whiles MDA is ongoing because data does not get to them in real time. The Ghana NTD program is piloting the use of the Lymph App's MDA module for the annual integrated Lymphatic Filariasis (LF) and Onchocerciasis (OV) MDA. The main objective of the study is to demonstrate how the Lymph App MDA module can help improve MDA data accuracy, completeness and timeliness and provide adequate data to support supervisors with the identification of underserved areas. There will also be a rapid assessment of the acceptability and convenience of the app to CDDs and health workers. Five LF and OV endemic sub districts will be purposively selected for this pilot. Supervisors and CDDs in these sub districts will be trained on the use of the app. After training and pretesting, there will be an initial registration of all community members in all study sites. This registration will capture the bio data of all household members and household's geo coordinates. This data which forms the registration for the communities will be cleaned thoroughly and will be used as the community register. MDA medicines given will also be recorded as part of this register. Data from the app will be downloaded, cleaned, analyzed, and presented as maps and tables daily and shared with supervisors to facilitate the identification of areas with poor coverage and address MDA issues immediately to ensure maximum coverage.

7471

OCULAR *CHLAMYDIAL TRACHOMATIS* INFECTION IMMEDIATELY FOLLOWING AN ENHANCED MASS DRUG ADMINISTRATION STRATEGY FOR TRACHOMA IN AMHARA, ETHIOPIA: THE CHILD MDA PILOT STUDY

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The Ministry of Health of Ethiopia has recently recommended an enhanced mass drug administration (MDA) strategy, "Child MDA" for trachoma, consisting of a standard community-wide round of MDA followed by a child only round (ages 6 months to 9 years) 4 weeks later. Child MDA was piloted in the Amhara region in 2023 in 2 districts, Lasta and Wadilla. As of 2022, the trachomatous inflammation-follicular (TF) prevalence among children ages 1-9 years was 30.0% in both districts, and the *Chlamydia trachomatis* (*Ct*) infection prevalence among children ages 1-5 years was 15.5% in Lasta and 9.4% in Wadilla. This study's aim was to determine the prevalence of *Ct* infection 3 weeks post-Child MDA intervention by embedding conjunctival swabbing within MDA coverage surveys. A period of 3 weeks was chosen to allow for enough time for infection to clear and to be recent enough to minimize recall bias. The surveys used multi-level sampling, selecting 30 communities and 30 households within each community. Following household and individual level MDA questionnaires, one swab was collected per child ages 1-9 years. All swabs were tested for *Ct* infection in Amhara. The July 2023 coverage surveys interviewed 1,752 children ages 1-9 years across the 2 districts to assess self-reported MDA coverage for both rounds, and 1,632 (93%) children were swabbed. The MDA coverage among children was >82% at all rounds in both districts. The district-level prevalence of *Ct* infection was 3.5% (CI: 1.7-7.3%) among children ages 1-9 years and 4.6% (CI: 2.3-8.9%) among children ages 1-5 years in Lasta. In Wadilla, the *Ct* prevalence among children ages 1-9 years and children ages 1-5 years was 1.7% (CI: 0.5-5.7%) and 1.3% (CI: 0.4-3.9%) respectively. Across both districts, the *Ct* prevalence among children who reported not taking either dose of MDA (n=95) was 15.9% (CI: 8.0-29.2%), and among those who reported taking both doses (n=1,343), it was 1.2% (CI: 0.7-2.2%). The *Ct* infection prevalence was lower after the Child MDA treatment, however, considerable infection remained 3 weeks post-treatment. One year of Child MDA treatment is likely not sufficient in highly endemic settings.

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ANTIBODY-OMICS REVEALS BIOMARKERS OF SCHISTOSOMIASIS AND CROSS-TALK WITH TUBERCULOSIS.

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Lack of accurate accessible diagnostics for Schistosomiasis (schisto) is a critical bottleneck in its elimination. In the absence of microscopic evidence of parasite, antibody (Ab) tests cannot distinguish past from current infection. Recently developed antigen detection tests (CAA) are promising for detection of current infection but not widely available. Additionally, schisto is associated with higher risk for Tuberculosis (TB), although the mechanism for this is not clear. We have developed a multiplexed 'Ab-omics' platform for deep characterization of a broad set of antigen-specific Abs (isotype, subclass, glycosylation and Fc receptor binding). Machine-learning applied to these data can reveal unique Ab signatures predictive of disease state and outcome. Here, sera from subjects (n=41, from Kenya), previously screened using a CAA test, were characterized with the Ab-omics workflow, using multiple *S. mansoni* (SEA, Sm25, Sm29, MEG, CD63, Calumenin), *M. tuberculosis* (PPD, Ag85A, ESAT6, CFP10 HspX, PstS1, LAM) and other helminth and non-helminth antigens. Antigen-coated barcoded beads were incubated with serum and probed. With a total of 270 measured Ab features from each subject LASSO-based feature selection led to a unique biomarker to differentiate CAA+ from CAA- individuals accurately (AUC>0.9). These findings suggest that a purely Ab-based biomarker, including Sm-29 specific IgG2, Ab galactosylation and Sm25-specific Ab FcR2b binding can achieve accurate diagnosis of current schistosome infection in endemic areas. Further, this approach was also able to distinguish early, late and past infection. Mtb-specific Abs also showed different Ab Fc profiles between CAA+ and CAA- individual's, specifically higher Ab sialylation, galactosylation and Fc2b binding. This is indicative of an anti-inflammatory tuning of the Fc profiles of Mtb-specific

Abs in Schisto patients, which has been earlier shown to be correlated with reduced Ab function and higher risk of reactivation of TB infection to active TB.

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IMMUNOLOGICAL BIOMARKERS FOR DETECTING SUBCLINICAL LEPROSY INFECTION: CROSS-TALK BETWEEN LID-1 AND PGL-1 IN INDIVIDUAL IMMUNE RESPONSES

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Brazil ranks second globally in the number of annual new leprosy cases. Active surveillance is ideal for early detection and interruption of the transmission chain. In this context, identifying immunological biomarkers for the detection of subclinical infection represents a strategy to achieve this goal. A random sampling strategy was utilized to select 1315 asymptomatic individuals residing in hyperendemic municipalities in eastern Minas Gerais. Blood samples were collected and tested to detect antibodies against the *Myocbacterium leprae* protein (LID-1) on a multiplexed beaded assay. Following categorization into anti-LID1+ or anti-LID- groups, individuals were paired based on age and sex, resulting in a total of 160 participants. Immunological assays assessed chemokines (CXCL8, CCL2, CXCL9, CCL5, and CXCL10) and cytokines (IL-6, TNF, IFN-ϒ, IL-17, IL-4, IL-10, and IL-2) using PBMC culture supernatants stimulated by M. leprae antigens. Participants were evaluated for clinical disease, with 14 diagnosed, and an additional serological test for anti-phenoglycolipid-1 (PGL1) was performed. IFN-γ was able to identify LID1+ well (AUC= 0.73, p= 0.01, sensitivity= 71.79%, specificity = 86.30%) indicating its potential as a biomarker for subclinical infection. Conversely, the chemokine CCL2 demonstrated superior characterization of the LID1- group (AUC= 0.61, p= 0.02, sensitivity= 34.18%, specificity = 88.31%), albeit with low sensitivity. The analysis of PGL-1 showed that anti-PGL-1(-) subjects had higher CXCL10 levels. Also, the network correlation between the biomarkers, showed a specific pattern in the IFN-γ, TNF and IL-17 correlation among the subgroups [LID(-)PLG1(-), LID(-)PLG1(+), LID(+)PLG1(-) and LID(+)PLG1(+)]. Overall, the differential biomarker profile and correlation between the groups suggest a promising avenue for developing future diagnostic tests for subclinical infection. Despite being asymptomatic, the participants in this study reside in regions with high endemicity, underscoring the critical need for early leprosy diagnosis. Financial support: CNPq, FAPEMIG, NIH.

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EXPLORING THE IMPACT OF DECENTRALIZATION IN IN THE LEPROSY ENDEMIC REGION OF EASTERN MINAS GERAIS USING GEOSPATIAL AND QPCR TECHNIQUES

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Many studies have explored the qPCR technique for leprosy diagnosis, having successfully identified undiagnosed cases or sites of disease outbreaks. In parallel, the techniques of spatial epidemiology have also been making significant contributions to leprosy control, highlighting differences in the spatial distribution of the disease between regions, states, and municipalities, where places of greater social inequality and accessibility to health services can impact local epidemiology. This study aimed to map asymptomatic individuals examined at the reference center - CREDEN/PES (spontaneous demand or referral) with skin smears positive for the RLEP gene of *M. leprae* in Governador Valadares. Additionally, through a network analysis using point interpolation algorithms, an estimation of the coverage areas of primary health units (ESF/UBS) was conducted in the census sectors of the municipality. Using quantum GIS 3.14 Pi software, maps were created using shape files of census sectors, streets, and sociodemographic data sourced from the Brazilian Institute of Geography and Statistics (IBGE). Individuals' qPCR+ were heterogeneously distributed across census sectors, with a higher proportion of female individuals ($p = 0.0451$), predominating literate individuals ($p = 0.0405$), black ($p = 0.0072$) and mixed race ($p = 0.0020$). Around 70% of the urban area of GV is covered by a health unit. However, only 41.2% of qPCR+ individuals lived in these areas. The remaining 58.8% of qPCR+ individuals lived in areas without coverage by a Health Unit. The estimated average distance traveled by participants to the nearest ESF/UBS was 0.515 km, while the distance to CREDEN-PES (reference center) was 3.77 km. In conclusion, combined molecular and geoprocessing techniques proved effective in identifying critical areas for disease control in Governador Valadares. This study highlighted the importance of expanding ESF/UBS and potentially decentralizing leprosy care, particularly in regions inhabited by individuals from lower socioeconomic strata.

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MYCOBACTERIUM LEPRAE AND *SCHISTOSOMA MANSONI* CO-INFECTION IN COMMUNITIES OF EASTERN MINAS GERAIS, BRAZIL

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Leprosy, caused by *Mycobacterium leprae*, exhibits varied clinical forms depending on the immune response, Th1 or Th2. The coexistence of infections by parasites, particularly *Schistosoma mansoni*, and micronutrient deficiencies with leprosy is observed in endemic regions of Brazil. S. mansoni infection is known to negatively modulate the Th1 response, favoring M. leprae infection and progression to severe clinical forms. In this sense, the identification of risk factors associated with leprosy includes socio-demographic, immunological, and parasitological factors. A random sampling strategy was utilized to select 1315 asymptomatic individuals residing in hyperendemic municipalities in eastern Minas Gerais. IgG reactivity tests to Leprosy IDRI diagnostic antigen 1 (LID-1) and anti-PGL-1 IgM were conducted to identify individuals potentially infected by M. leprae without clinical manifestations. Tests for presumptive detection of schistosomiasis, including Detection of Circulating Cathodic Antigen (CCA) in urine and detection of anti-SEA and anti-SWAP antibodies in serum, were performed. Preliminary results showed 79 participants had anti-LID IgG, designated LID+. Among 156 sera evaluated for anti-PGL-1, 47 were positive (30.12%). ELISA assays revealed 28 sera (17.72%) reactive for SEA and 27 (17.0%) for SWAP. Using the rapid CCA test, 83 urine samples were collected, revealing co-infection in ten cases (12.05%), where patients tested positive for both LID+ (leprosy) and CCA (schistosomiasis). Notably,

14 new cases of leprosy were confirmed among LID+ individuals. Ongoing clinical evaluation and monitoring of participants are crucial for immediate treatment of newly diagnosed cases.

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MODEL-BASED GEOSTATISTICS TO SELECT SITES FOR MONITORING LYMPHATIC FILARIASIS TRANSMISSION INTERRUPTION FOLLOWING MASS DRUG ADMINISTRATION WITH IVERMECTIN, DIETHYLCARBAMAZINE AND ALBENDAZOLE IN EAST NEW BRITAIN, PAPUA NEW GUINEA

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After two rounds of mass drug administration (MDA) with ivermectin, diethylcarbamazine, and albendazole (IDA) for lymphatic filariasis (LF) elimination, the World Health Organization (WHO) recommends the IDA Impact Survey (IIS) to assess if LF transmission has ceased. This involves population proportional sampling (PPS) of 30 sentinel sites to assess LF infection parameters in those ≥20 years. Model-based geostatistics (MBS) is also recommended if capacity exists, but only some countries have used MBS for IIS. Here we used MBS for IIS sentinel site selection in East New Britain province (ENB), Papua New Guinea (PNG). ENB completed two rounds of IDA MDA in 2019 and 2022, with 82% and 67% epidemiological coverage, respectively. We conducted IIS from June 2023 - February 2024 and examined the impact of MDA on sites (villages) with known high LF infection before MDA. Subsequent selection with MBS prioritized sites whose LF infection probability was most uncertain based on prior data. In selected sites we sampled approximately 110 adults ≥20 years with filarial test strips (FTS) followed by night blood smears for microfilaria (Mf) if FTS positive. We tested 4,164 individuals in 42 sites across ENB. Sites were selected based on prior LF infections (N=10), MBS (N=26), and convenience where MBS villages became inaccessible (e.g. weather, security, etc, N=6). The sampled individuals averaged 38 years old, and 42.8% were male. 193 individuals were FTS positive, with a mean of 4.5%, (95% CI 1.8, 7.2). Fourteen of the 26 MBS sites contained FTS-positive individuals, with two containing Mf positives. Overall, ten Mf positives were identified with a mean Mf positivity across ENB of 0.24%, (95% CI 0.02, 0.45). Two sites exceeded 1% Mf positivity. Thus, MBS selected unrecognized sites of FTS and Mf positivity, mainly in remote areas where LF transmission and poor MDA coverage are more likely. We showed that LF transmission has been interrupted across most of ENB. PPS IIS is now underway, and results can be compared to MBS. We will work with the provincial health authority to administer additional MDA in smaller evaluation units encompassing sites with >1% Mf positivity.

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LONGITUDINAL ANALYSIS OF THE PREVALENCE OF MINOR *PLASMODIUM* SPP. INFECTING HUMANS THROUGH SEQUENTIAL INTERVENTIONS IN NORTHERN GHANA

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Current interventions targeting malaria control are focused on *Plasmodium falciparum*, the major species infecting humans. Despite renewed efforts for malaria elimination in sub-Saharan Africa, little attention has been paid to the neglected parasites, *P. vivax, P. malariae,* and *P. ovale* spp. and the impact of interventions, like indoor residual spraying (IRS), and/or seasonal malaria chemoprevention (SMC) on these minor *Plasmodium* spp. To address this research gap, this study was undertaken to assess the efficacy of IRS and SMC combined with long-lasting insecticidal nets (LLINs), on minor *Plasmodium* spp. infections in an area characterized by high seasonal transmission in northern Ghana. Using an interrupted time-series study, five age-stratified surveys, each of ~2,000 participants, were undertaken at the end of the wet seasons between 2012 and 2022. Across this 10-year study period infections with *P. malariae* and *P. ovale* spp. were detected using a species-specific PCR targeting the *18S rRNA* gene, while no *P. vivax* was detected. In 2015, following IRS, the prevalence of the minor *Plasmodium* spp. declined in all ages, with participants being significantly less likely to be infected with *P. malariae* (1.4% vs. 13.7%) and *P. ovale* spp. (0.4% vs. 5.7%) compared to 2012. Despite this decline, in 2017, 2-years after IRS was withdrawn and SMC was introduced, the prevalence of *P. malariae* (2.9%) and *P. ovale* spp. (4.0%), rebounded 2- and 10-fold, respectively. Finally, when we examined this population in 2020 and 2022 after sustained use of SMC, the prevalence of *P. malariae* continued to increase (7.4% and 5.8%), while the prevalence for *P. ovale* spp. declined (2.6% and 1.3%). The rebound in the minor species was observed in all age groups, except for the younger children (1-5 years) targeted by SMC where no *P. malariae* or *P. ovale* spp. infections were detected in 2017 to 2022. Results show that the transmission of *P. malariae,* and to a lesser extent *P. ovale* spp., were affected by the interventions deployed in Bongo District. However, infections with minor species rebounded following the discontinuation of IRS in the age groups not targeted by SMC.

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OPTIMIZING DRUG DISTRIBUTOR PERFORMANCE IN NEGLECTED TROPICAL DISEASE MASS DRUG ADMINISTRATION PROGRAMS; RESULTS FROM A MULTI-COUNTRY EVALUATION

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Community drug distributors (CDDs) and other similar cadres of lay and professional staff are the backbone of neglected tropical disease (NTD) mass drug administration (MDA) programs. These personnel often volunteer time or receive minimal financial incentive for their work. These individuals are often selected to serve their own communities and are asked to participate in periodic trainings to deliver health promotion and counseling, drug distribution, and adverse event monitoring services. There is minimal information available about the characteristics of CDDs associated with program performance, defined as the proportion of individuals accepting treatment from a CDD when offered. We tracked this information in the DeWorm3 project, a large cluster randomized trial testing the feasibility of interrupting transmission of soil-transmitted helminths (STH) in Benin, Malawi, and India. We documented CDD attributes during six rounds of biannual community-wide MDA and, using electronic data collection, linked CDD attributes to treatment coverage for households assigned to a given CDD. We conducted multivariate logistic regression with an interaction term to determine if treatment refusal varied by gender of participants and

CDDs. We engaged 444 CDDs total (113 in Benin, 57 in Malawi, and 274 in India). CDDs were 35% (Benin), 63% (Malawi), and 87% (India) female. In Malawi, CDDs were professional Health Surveillance Assistants while in Benin the majority (21%) worked in agriculture and in India 41% identified as housewives. In Benin and India, the majority of CDDs were ages 18-29 while in Malawi the majority were older (30-39 years). CDDs were able to reach a range of 15.3 (median) households per day in urban areas of Benin and up to 30.4 (median) in rural areas of Malawi. In Benin, women were more likely to refuse treatment from male CDDs as compared to female CDDs (p=0.03). In Malawi, both men and women were more likely to refuse treatment from male CDDs (p<0.001) as compared to female CDDs. These findings are useful for other NTD programs as they consider opportunities to recruit, finance and plan for CDD engagement and to optimize CDD performance.

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ASSESSMENT OF QUALITY OF ONCHOCERCIASIS MASS DRUG ADMINISTRATION, INSIGHTS FROM A COVERAGE SURVEY IN NINE DISTRICTS OF OROMIA REGION, ETHIOPIA

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Onchocerciasis control with community distributed treatment with ivermectin started in 2001 in Ethiopia, with mass drug administration (MDA) expanding to new endemic districts as they are identified until recently. MDA began in nine newly identified districts from 2019 to 2022. Cross-sectional community-based coverage surveys were conducted in the nine districts one month after MDA in 2023 to validate reported MDA coverage, assess service quality, and identify factors affecting ivermectin intake in these new program areas. Two-stage random sampling was used, starting with the random selection of 8 villages per district (72 villages in total). Then, within each selected village, at least 16 households (1,431 households in total) were chosen using systematic random sampling. All household residents were asked whether they took ivermectin during MDA. Overall, surveyed ivermectin coverage was 78% (95% CI 77-79%), with districts ranging from 56% to 86.9%. Three districts reported coverage that was higher than that surveyed by 11% to 26% and 6 districts reported coverage lower than that surveyed by 6% to 7%. Six districts from East and West Hararge zones met the acceptable coverage threshold of ≥80%, but 3 (Girar Jarso and Aleltu of North Shoa zone and Digalona Tijo of Arsi zone) did not. There were high rates of underdosing in Digaluna Tijo (16%) and Aleltu (12%) and high rates of overdosing in Oda Bultum (17%) and Habro (14%) and Melka Belo (13%). Individuals who received health education had 7.6 times the odds of swallowing ivermectin as those who did not (95% CI: 6.6-8.8). In summary, underdosing and overdosing were identified in specific districts, highlighting the importance of quality assurance during MDA campaigns. Health education was strongly associated with ivermectin intake. Based on the observed discrepancies, enhanced training on dosing and reporting for drug distributors is required. Areas of North Shoa and Arsi zones with sub-standard coverage require improvements in both coverage and quality through increased community engagement and empowerment of Community Drug Distributors.

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PRODUCTIVITY RETURNS FROM TEN YEARS OF THE KENYAN NATIONAL SCHOOL BASED DEWORMING PROGRAM

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Many areas of Kenya are endemic for soil-transmitted helminths (STH) and schistosomiasis (SCH). Preventive chemotherapy (PC) among school-aged children (SAC) has been applied to endemic counties since 2012 as part of the National School Based Deworming Program (NSBDP). Providing PC to endemic children results in long-term productivity gains. Previous evaluations of PC my underestimate impact of intestinal helminths, as they often only focus on short-term morbidity without addressing productivity. We aim to quantify total productivity gains from the NSBDP and compare them to estimated program cost for a return on investment from 10 years of the NSBDP's operation. We first constructed a deterministic epidemiological model using a series of ordered differential equations to estimate child time-months spent in different intensity classes of STH/SCH, when subject to different levels of PC. The model was calibrated to national prevalence and coverage data with parameters derived from existing literature. An annual 2022 productivity gain range was estimated and assigned to each class of infection. Total cumulative lifetime productivity gains were estimated for averted child-years of infection from the assumed beginning of a dewormed child's productive life to 20 years in the future. Detailed program costing records were consulted to estimate total costs of the program implementation over 10 years. Overall, $1,100,000,000 2023 USD cumulative productivity returns are estimated to be realized 2012 to 2042 due to 10 years of operation (2012-2022) of the Kenyan NSBDP. The total spend on the program was estimated at $27,000,000 2023 USD suggesting a $30 return on investment for every $1. These results are conservative due to a limited time frame, do not include infections averted through reduced environmental contamination, and do not include other avoided costs such as to the health system. They highlight substantial impact which can be achieved through preventing STH/SCH infections in SAC. Deworming in Kenya and in other endemic countries remains a sound investment due to very high returns comparable to many other health and development programs.

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MORBIDITY MANAGEMENT OF LYMPHATIC FILARIASIS: STRENGTHENING SURGICAL APPROACHES TO FILARIAL HYDROCELES IN KENYA

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Lymphatic Filariasis (LF) is prevalent in Kenya's coastal region, where hydrocele cases have been documented. Due to inadequate local capacity to manage hydroceles, the Ministry of Health Neglected Tropical Disease program partnered with Amref Health Africa, the University of Nairobi Department of Surgery, and the African Filariasis Morbidity Project (AFMP) to train local surgeons and medical officers on a new technique involving total excision of the tunica. We sought to evaluate the impact of the training camp and surgical outcomes of treated patients. Community Health Promoters screened and referred patients with scrotal swelling from LF-endemic counties in May and October 2023. Health workers from endemic

counties underwent training modelled on the AFMP protocol. The training incorporated didactic sessions, selecting eligible patients, and practical theatre sessions in 8 health facilities. Follow-up was done upon discharge on day 3 and in the subsequent training camp. Data collected included the number of cases performed, intraoperative findings, and post-operative complications. Descriptive statistics was used to summarize the findings. Overall, 105 health workers underwent training, including 3 urologists, 5 general surgeons, and 33 medical officers. Furthermore, 22 clinical officer anaesthetists and 42 theatre nurses were trained in perioperative management of hydrocele patients. Of 166 referred patients, 111/166 (66.9%) underwent surgery, 70/111 (63.3%) in May, and 41/111(36.9%) in October 2023 respectively. The median age was 58 years (IQR 52.5 years), with 45 (40.5%) having bilateral hydrocele and 30 (27%) presenting with both hernia and hydrocele. All patients with hernias underwent repair in addition to hydrocelectomy. No post-operative complications were noted upon discharge; minimal complications were noted in 2/37(5.4%) followed up after 5 months. All follow up patients self-reported improvement in psychosocial and overall health status. The training camps increased the local capacity of healthcare workers to manage hydroceles. We recommend continued use of the new technique to manage hydroceles.

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FACTORS ASSOCIATED WITH FAILING ASSESSMENTS TO STOP MASS DRUG ADMINISTRATION FOR ONCHOCERCIASIS IN KONTA SPECIAL WOREDA, SOUTHWEST ETHIOPIA PEOPLE'S REGION

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Mass drug administration (MDA) with ivermectin is the key strategy in the elimination of onchocerciasis in Ethiopia. Community ownership and health education through community drug distributors (CDDs) and community supervisors play a vital role in achieving quality MDA and high coverage. Mapping data from 2000 reported a baseline nodule prevalence of 14.4% in Konta Special Woreda, classifying it as hypoendemic. MDA began in 2015. This district is surrounded by endemic districts of Kaffa, Jimma and Dawuro zones, all bordering the Gojeb river. An impact assessment in 2020 found 1% prevalence of Ov16 antibodies by ELISA, prompting a full stop-MDA evaluation in 2022. The stop MDA survey tested 3,200 children 10 years of age and under. With 23 Ov16 positives (0.7%), the woreda failed to meet the stop-MDA threshold of <0.1%. While MDA continued, the program conducted a retrospective investigation into factors that might have contributed to the failure by evaluating data from MDA coverage surveys conducted in the woreda in 2019 and 2022. Two-stage cross-sectional community-based surveys were done to assess MDA coverage and other CDTI activities. In 2019, from the total 697 participants, 535 were treated with therapeutic coverage of 76% (95% confidence limits [CL] 73-79%), which was lower than the recommended 80%. Of untreated eligible people, 78 (46%) participants in 2019 and 25 (28%) of participants in 2022 were not treated due to absenteeism. From total 127 household (HH) participants in 2022, 22 (14%) of the HH heads participated in MDA site selection. Community participation in CDD selection declined from 2019 (24%) to 2022 (15%). Of those treated in 2019 and 2022, 50 (9%) and 72 (15%) of participants, respectively, did not have their height measured for dosing, and 144 (16%) and 155 (31%) did not get the right dose. The program should work on strengthening community participation in MDA activities as well as focus on overall program quality and responsiveness. Since the district has high density of *Simulium damnosum* along the Gojeb river, further epidemiological and entomological investigation could identify hotspots for special intervention.

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OPTIMIZATION APPROACHES FOR INTEGRATION OF NEGLECTED TROPICAL DISEASES INTO HEALTHCARE SYSTEMS IN KENYA

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Kenya strategy for incorporating Neglected Tropical Diseases (NTDs) into its healthcare systems reflects a notable departure from previous practices, aiming for sustainability and self-reliance in combating these ailments. By adhering to WHO guidelines and aligning with Kenya's health agenda, the country has taken proactive measures to ensure that NTD programs are efficiently managed and seamlessly integrated into existing healthcare structures. A crucial aspect of this integration involves transitioning from isolated approaches to a more comprehensive one. Through the utilization of WHO's health system building blocks and alignment with Kenya's Bottom-up Economic Transformation Agenda (BETA), the Ministry of Health – NTD Programme has facilitated the provision of comprehensive NTD treatment and care by integrating it into the Social Health Insurance Fund (SHIF). This was by engaging the health financing and SHIF team in an NTD costing workshops. This transition not only secures sustainable funding but also underscores the importance of embedding NTD interventions within broader healthcare frameworks. Furthermore, involving implementing and development partners in integrating NTD indicators into Kenya Health Information Systems (KHIS) exemplifies a commitment to evidence-based decision-making and transparency. To improve the timely referral of suspected NTD cases by Community Health Promoters (CHPs) and to ensure efficiency, accountability, and effective supervision during mass drug administration, the NTD program has integrated essential indicators into electronic Community Health Information System (eCHIS) platform which feeds into KHIS. This integration facilitates better monitoring and evaluation of NTD interventions while ensuring efficient resource allocation. Additionally, integrating NTD components into the country's community health strategy training modules and formulating a draft integrated vector management strategy showcases a multifaceted approach to disease control. By bolstering vector surveillance and control in collaboration with other health programs like the National Malaria Program, Kenya is optimizing resources and addressing the interconnected nature of vector-borne diseases. The accomplishments described above have been made possible through the strict adherence to a well-designed NTD coordination framework, which serves as a guiding document for the coordination of NTD integration efforts throughout Kenya.In summary, Kenya's integration approach serves as a model for other nations seeking to incorporate NTD interventions into their healthcare systems. By prioritizing sustainability, efficiency, and collaboration, Kenya is well-positioned to accelerate progress toward NTD elimination and eradication goals, all while alleviating strain on health systems, especially amidst reduced external financing.

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EMPOWERING WOMEN IN BIHAR, INDIA TO ELIMINATE LYMPHATIC FILARIASIS

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Lymphatic Filariasis (LF) poses a significant threat to Bihar, India, affecting over 130 million individuals across its 38 districts. Administering anti-LF drugs through Directly Observed Therapy (DOT) to the eligible 120 million population is a formidable task. Leveraging the State Rural Livelihood Mission's (SRLM) network of 11.6 million women's collectives (Self-Help Groups - SHGs), which touch every other household in rural Bihar, presents a promising solution. A pilot study in 2023 demonstrated the efficacy of SHG platforms, with SHG members exhibiting a 74% DOT compared with 45% among non-SHG members. Building on this success, in February 2024, 24 districts with 6.3 million SHG members were targeted for Mass Drug Administration (MDA). Prior to MDA, SHG members were educated on LF and MDA during their weekly meetings, to disseminate information

to their families and communities. The SHGs were engaged in various awareness activities, including discussions, oath-taking ceremonies, slogan competitions, and community rallies, fostering preparedness for anti-filarial drugs at the household level. Post-MDA, SRLM reported a 66% drug consumption rate among SHG members, contributing to a 6% increase in DOT overall. Further assessment of the intervention revealed that SHG households exhibited a 40% higher unadjusted DOT compared to non-SHG households. Within the SHG network, community mobilizers played a crucial role, increasing the odds of DOT compliance by 12 times (OR: 12.07, p: 0.00, 95% CI: 3.4-42.7) when promoting MDA activities. Moreover, timely information delivery (received 10-20 days before MDA), doubled the odds of DOT (OR: 2.52, p: 0.04, 95% CI: 1.2-2.1). This success underscores the potential of SHGs in enhancing anti-filarial drug compliance and aiding LF elimination efforts. Leveraging millions of women's networks could serve as a model for other endemic regions, amplifying outreach and impact. To mainstream women's involvement in LF elimination, capacity-building initiatives for SRLM staff and cadre could be implemented by health departments.

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STATUS OF LYMPHATIC FILARIASIS TRANSMISSION IN PASTORALIST AREAS OF SOUTH AND SOUTHWEST ETHIOPIA

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Lymphatic filariasis (LF) is targeted for global elimination through treatment of endemic populations with annual mass drug administration (MDA). WHO guidelines call for a transmission assessment survey (TAS) after at least five effective MDA rounds to determine if MDA can be stopped. LF commonly affects pastoralist areas and tends to be persistent since these areas are often hard to reach and have low access to and coverage of MDA. Five rounds of MDA were conducted in pastoralist areas of South and West Omo zones in Ethiopia between 2018 and 2022 with reported average coverage of >81% in all districts, achieved through close follow-up, monitoring, and support with expanded house-to-house attention by community directed distributors (CDDs) given the nomadic nature of the populations. Pre-TAS and TAS1 were conducted in 2023 in pastoralist communities of eligible districts of South and Southwest Ethiopia regional states. Pre-TAS involved sampling ~300 people aged 5 and older in each of sentinel and spot-check communities per evaluation unit (EU) in Hammer, Turmi, and Selamago districts. TAS-1 involved community-based surveys to sample children aged 6-7 years cluster sampled in 322 villages from 570 total villages in pastoralist woredas in South Ari, Surma, Hammer, Turmi, and Selamago districts. Samples were tested for LF antigen by Filarial Test Strips (FTS), and survey data were collected electronically with open data kit software. Pre-TAS included 1,939 FTS results, of which there was one positive from Hammer and one from Selamago. The prevalences in Hammer (0.15%), Selamago (0.15%), and Turmi (0%) were all less than the WHO threshold of 1%, and the EUs proceeded to TAS-1. TAS-1 included FTS results for 4,164 children, of which all were negative. LF transmission has been successfully reduced below sustainable levels such that MDA can be stopped in South Ari, Surma, Hammer, Turmi, and Selamago districts, with ~339,206 people at risk. This reflects the success of program implementation for these hard-to-reach pastoralist populations, though strong post-treatment surveillance is required to ensure that transmission does not recrudesce.

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OUTCOME OF SNAKEBITE VICTIMS MANAGED BY TRAINED HEALTH ASSISTANTS AT A SNAKEBITE TREATMENT CENTER IN NEPAL

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Snakebite envenoming is a neglected tropical disease. The World Health Organization (WHO) roadmap on snakebite envenoming targets snakebite related death reduction to 50% by 2030. Strengthening the health system is one of the four pillars of WHO snakebite strategy for snakebite prevention and control. Unfortunately, skilled physicians are scarce in the areas where snakebite is prevalent. Empowering health assistants (HA) for task sharing to manage snakebite may help prompt management of snakebite and reduce mortality. The aim of this study is to evaluate the outcome of snakebite cases managed by trained HAs at a snakebite treatment center. The study is a fifteen years (2008 AD to 2023 AD) retrospective audit of outcome of snakebite victims from a snakebite treatment center, Damak Red Cross, Damak, Nepal. A six-week training course organized for Health Assistant, to identify the features of envenomation, management, early identification of adverse reactions to anti-venom and need of referral were the focus of the training. Management of snakebite cases were done as per protocol provided by Ministry of Health and Population, Nepal. Anti-venom and other essential medicines were made available by the center itself. Six HA received training in 1998. Two to four days reinforcement of training was provided in subsequent years. HA had access to telephonic consultation with a faculty of medicine at B.P. Koirala Institute of Health Sciences. All records were kept in a structured case record and outcomes were analyzed using SPSS Version 26. A total of 30 HAs were trained. A total of 15,513 snakebite cases were managed in the center. Among the envenomation cases, neurotoxicity was the predominant manifestation. Majority of snakebite victims improved (98.4%), with a low referral rate (0.6%), and case fatality rate (1.2%). Mortality was found to be lower in comparison to national figures and other centers managing snakebite. Structured training and task sharing with paramedics may contribute to reduction in snakebite-related death.

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GENDER AND AGE MODULATING THE HEMATOLOGICAL PROFILES OF LEPROSY PATIENTS: ADISCURSIVE ANALYSIS

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Leprosy is a chronic infectious disease characterized by slow progression. Theobjective of this study was to analyze how age and sex can modify hematological data,as well as plasma levels of Vitamin A and D in patients with leprosy. The study groupcomprised 77 patients, being 44 (57,14%) males, diagnosed at the Reference Centerfor Endemic Diseases and Special Programs (CREDEN-PES/SMS/GV) in GovernadorValadares, eastern Minas Gerais, Brazil, age between 5 to 86 years old and exhibitingclinical forms classified as Paucibacillary (PB) and Multibacillary (MB) according to theWHO's operational classification. Mean values, standard deviations, and confidencelimits were stratified by age group and by gender. Significant differences were observedin the global leukocyte count in both genders (males - p=0.047 and females p=0.043),with higher values observed between 5-30 years old, with significant differences forglobal lymphocyte count (p-0.025) and basophils (p=0.028) only in males, with highervalues between 2-20 years and lower values between

31-40 years. Hematologicalvalues for RBC, hemoglobin and hematocrit were significantly higher in males (p<0.001)than in females. Age significantly modulated only the hematocrit (p=0.033) in males,while it significantly modulated the values for Hgb (p=0.041), HCT (p=0.037), MCV(p=0.015) and MCH (p=0.007) in females. Age significantly modulated the absoluteplatelet count only in males, with higher values between 21-30 and lower valuesbetween 41-50 years. Age significantly modulated only vitamin A values, this beingsignificant only in females (0.016), with the lowest levels between 5-20 years old. Thesefindings underscore the importance of considering variables such as age and gender inthe interpretation of hematological results in leprosy patients. However, further studiesare needed to better understand these differences and their clinical impact on diseaseprogression and management.

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SPATIOTEMPORAL DISTRIBUTION AND DIVERSITY OF AIRBORNE RESISTANT BACTERIA: AN EXPLORATORY ONE HEALTH STUDY IN THE URBAN AND RURAL ENVIRONMENTS OF BANGLADESH

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Antimicrobial resistance (AMR) is a widespread One health issue with planetary impacts. However, there is dearth of knowledge and scientific evidence on the magnitude of resistant bacteria in air and their transmission pathway. Therefore, an exploratory observational study in Bangladesh was conducted to quantify the clinically significant drug resistant bacteria in air with their spatial diversity. This study employed the collection of air samples from both urban and rural settings in four distinct environments – i) Urban live bird markets (LBM) ii) Urban residential area (URA) iii) Commercial poultry farms(CPF) and iv) Rural households (RHH). MacConkey agar supplemented with 3rd generation cephalosporin (3GC) and meropenem respectively was used to obtain 3GC resistant (3GCr) and carbapenem resistant *Enterobacteriaceae* (CRE). Mannitol Salt agar supplemented with oxacillin and Slanetz-Bartley medium supplemented with vancomycin were utilized to obtain Methicillin (Oxacillin) resistant Staphylococci (MRS) and Vancomycin resistant Enterococci (VRE). The bacterial identification and susceptibility testing were conducted by VITEK 2 system. The presence of 3GCr, CRE, MRS and VRE in 85%, 60%, 100% and 80% air samples was observed respectively. 3GCr, CRE and MRS were highest in CPFs and VRE in LBMs. The abundance (>90%) of MRS, VRE and 3GCr in URA is alarming whereas the air samples from RHHs were heavily burdened with 3GCr and MRS (60-100%). The CRE in poultry environment also establishes the threat added by current farm practice. The diversity and richness of resistant organisms were measured by Shannon diversity index, which was higher in both seasons at LBMs and CPFs (H-2.17-2.21 and H-1.99-2.03 respectively). Considering the organism family, the major bacteria were Staphylococcaceae (35%), Pseudomonadaceae (20%), Enterobacteriaceae (15%), Moraxellaceae (10%), Lactobacillaceae (7%) and Enterococcaceae (6%). This study findings emphasize on the inclusion of air in the system approach and surveillance to tackle AMR due to its high potential for acting as both reservoir and medium of spread of resistance.

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FINDINGS FROM A SIMULATION EXERCISE UTILIZING THE ONE HEALTH TRANSBOUNDARY ASSESSMENT FOR PRIORITY ZOONOSES (OHTAPZ) TOOL TO MEASURE HEALTH SECURITY PREPAREDNESS, DETECTION, AND RESPONSE CAPACITIES AT THE JORDAN-IRAQ BORDER

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Strengthening global health security efforts for the prevention, detection, and response to transboundary zoonotic diseases (TZDs) within and between nations requires multisectoral and multilateral approaches. The One Health Transboundary Assessment for Priority Zoonoses (OHTAPZ) tool is a published methodology that engages human, animal, environmental, and border health stakeholders at various levels to assess and prioritize One Health (OH) capacities at points of entry (POEs), where the exchange of people, livestock, goods, and infectious diseases often takes place. The OHTAPZ tool, which encourages bilateral collaboration between two neighboring nations; includes the development of an agreed joint list of priority TZDs; stakeholder mapping through an interactive tabletop exercise; and completing a POE self-assessment which provides a baseline of the current OH capacities at the POEs assessed. Through implementation of the methodology in Jordan and Iraq, our team at Johns Hopkins University then conducted a simulation exercise (SimEx) that tested the self-evaluated OH capacities at each POE. The SimEx assessed current preparedness and response communication and coordination mechanisms within and between the formal land border POEs for during a TZD event, resulting in not only the first bilateral assessment of OH capacities across formal land borders in Jordan and Iraq, but also demonstrating this methodology fills an important role in the global health security research and practice spheres.

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PHARMACOKINETIC PROPERTIES AND MOSQUITO-LETHAL EFFECTS OF A NOVEL LONG-LASTING FORMULATION OF IVERMECTIN IN CATTLE

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Ivermectin is an antiparasitic drug, used in human and animals for decades. It has recently been developed as a novel vector control tool for malaria as ivermectin-treated humans and animals are lethal to blood-feeding *Anopheles* mosquitoes. The aim of this work was to characterise the population pharmacokinetic (PK) and pharmacodynamic (PD) properties of a newly developed long-acting ivermectin formulation (BEPO® technology) in cattle. Two PK studies were conducted in Burkina Faso (Study 1: n=20 and Study 2: n=24). Plasma samples were shipped to Thailand for drug quantification by LC-MS/MS and for membrane feeding mosquito-killing evaluations. Plasma samples were mixed with fresh red blood cells obtained from cattle for mosquito feeding experiments. Only ivermectin and one major human metabolite (M1) were detectable in plasma samples and combined with mosquito mortality data, and evaluated using population PK/

PD modelling (i.e. nonlinear mixed-effects modelling; NONMEM). Specific emphasis was placed on characterising the absorption properties of this novel formulation. Mosquito mortality was modelled using a sigmoidal Emax model. A three-compartment disposition model for ivermectin and a two-compartment disposition model for M1 were used to describe the observed drug concentration data. The final population PK model adequately described the dual absorption processes of fast and slow first-order absorption after subcutaneous injection. The estimated IC_{50} of ivermectin and its metabolite was 12.9 nmol/L for *Anopheles dirus* mortality and 1.48 nmol/L for *Anopheles minimus*. The developed novel formulation demonstrated sustained mosquito mortality after a single injection. Translational simulations were also conducted to inform a prospective first-in-human clinical study. Body weight-scaled doses used in cattle (0.6, 1, 1.5 mg/kg) were predicted to result in sustained ivermectin exposure and sustained *dirus* and *minimus* killing for >35 days and >90 days, respectively, after a single injection. This could be a promising novel tool for transmission blocking of malaria and for the treatment of NTDs in humans.

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MOLECULAR CHARACTERIZATION AND PHYLOGENETIC ANALYSIS OF BOVINE *FASCIOLOSIS* IN UPPER EAST REGION, GHANA

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Fascioliasis, a disease transmitted between animals and humans, is caused by liver flukes. The primary cause of this ailment are two species: *Fasciola gigantica* and *F. hepatica*. These parasites can have a severe impact on both public health and the livestock industry due to their prevalence. To understand the occurrence and genetic properties of these *Fasciola* parasites in the Upper East Region of Ghana, a study was conducted. The research involved examining 246 cattle from this region to determine the presence of *Fasciola* infections. The scientists utilized the polymerase chain reaction (PCR) technique and sequenced a specific portion (290 bp) of the nad5 gene. The findings revealed that around 23.58% (58 out of 246) of the cattle were infected with Fasciola. However, after analyzing the data, no significant correlation (with a p-value greater than 0.05) was found between Fasciola infection and the animals' gender or age. Interestingly, a noteworthy and statistically significant relationship (with a p-value of less than 0.001) was discovered between Fasciola infection and the animals' body condition scores (BCS). When the obtained DNA sequences were compared using the BLAST tool, it was confirmed that the isolated *Fasciola* specimens belonged to the *F. gigantica* species. Five distinct haplotypes were identified, with one haplotype showing similarities to those found in Niger's haplogroups. Notably, two of these haplotypes were previously undocumented.

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POSITIVE ASSOCIATION OF ORAL INFECTION BY *TRICHOMONAS TENAX* WITH PERIODONTITIS IN THE DOMESTIC DOG

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Trichomonas tenax, an anaerobic protozoan, colonizes the oral cavities of humans and animals, particularly in individuals with compromised oral hygiene and periodontal disease. Transmission occurs through droplet spray, kissing, or exposure to contaminated utensils and water. The established association between *T. tenax* and periodontal disease in humans is noteworthy, given the global prevalence of this inflammatory condition leading to tooth loss, impaired chewing function, aesthetic concerns, social disparities, and reduced quality of life. In humans, periodontal disease ranges from 1-57%, while in domestic dogs, it varies from 15-25%. Recognized as a parasite and potential zoonotic agent, *T. tenax* raises concerns about cross-species transmission between humans and their pet dogs. This study aims to correlate *T. tenax* infection with periodontal disease in domestic dogs by comparing its prevalence in dogs with periodontitis to that in healthy dogs. Oral swabs were collected from the gumline of dogs on St. Kitts between October 2023 and January 2024. A total of 50 samples underwent microscopy for *T. tenax* detection. The dogs were categorized into healthy (Stage 0-1, with or without gingivitis) and diseased (Stage 2-4, with periodontitis) groups based on periodontal disease severity. Three swabs were obtained from each dog: two for culture using the classic Diamond media and a newly modified Diamonds media, and one in alcohol for LAMP. *T. tenax* was detected in 14% of all dogs (7/50), specifically, 33% prevalence in the diseased group (7/21) compared to 0% in the healthy group (0/29). Statistical analysis revealed a significant association between *T. tenax* presence and diseased dogs (P=0.0008). The newly modified media exhibited greater sensitivity, detecting 14% of samples (7/50), compared to the classis Diamonds media, which detected only 2% of samples (1/50, P=0.0270). Subsequent LAMP analysis of alcohol-preserved samples will further compare the prevalence and sensitivity of the two detection methods, contributing valuable insights to the observed statistical significance between periodontitis and *T. tenax* infection in mouth.

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BEHAVIORAL AND BIOLOGICAL SURVEILLANCE OF EMERGING INFECTIOUS DISEASES AT THE HIGH-RISK HUMAN-ANIMAL INTERFACE IN BANGLADESH

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Human-animal interactions are the key drivers of zoonotic spillover, highlighting the better understanding of human behaviors to mitigate disease emergence at high-risk communities. Hence, we conducted an integrated biological and behavioral surveillance to detect novel and known zoonotic viruses in potential high-risk populations and identify risk factors for viral spillover in Bangladesh. Between 2017 and 2019, we enrolled a total of 1106 participants for behavioral interviews at three communities and one hospital site. We obtained biological specimens (throat swab, rectal swab, urine, and blood) from 862 participants and tested for coronaviruses, filoviruses, flaviviruses, influenza viruses, and paramyxoviruses using pan (consensus) RNA Virus assays. Overall, 64/862 (7.4%) tested positive for viral families including influenza viruses (51.6%), coronaviruses (20.3%), flaviviruses (12.5%), and paramyxoviruses (15.6%). Participants reported highly contact with poultry (92.4%) and domestic animals (74.6%) comprising raising, handling, slaughtering, scratched or bitten. A significant percentage of participants also reported consuming sick animals' meat (44.3%) and raw meat (5.9%). In case of wild animal, participants had high level of rodent contact (92.5%) and having rodent feces near their food (75.9%), followed by 6.3% contact with bat hunting and processing. Moreover, 17.5% of participants kept the bitten or scratched wound open. Lasso regression model revealed that most salient risk factors of self-reported influenza-like illness (ILI) in the past year were slaughtering animals, had contact with poultry, scratched or bitten by animals and most prominent protective factors were living in urban areas having a smaller family (less than 5 person). The findings underscore the significant level of interaction between humans, livestock, and wildlife in communities, which might lead to transmit emerging pathogens in Bangladesh. We recommend One health surveillance and to develop targeted interventions to mitigate the risk of zoonotic disease spillover at animal-human interface in Bangladesh.

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MYCOBACTERIUM AVIUM SUBSP. *PARATUBERCULOSIS* AND MICROBIOME: A ONE HEALTH CONCERN

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Mycobacterium avium subsp. *paratuberculosis* (MAP) causes the notifiable disease in ruminants, Johne's disease, or paratuberculosis (PTB). Besides, it is a potential zoonotic pathogen as it is implicated in inflammatory bowel disease and many other chronic conditions in humans. Also, MAP is thought to change the gut microbiome, which in turn is connected to some MAP- linked diseases. Animal health and welfare, economic impacts and public health concern are key drivers of PTB control; however, such programmes are costly and hindered by lack of sensitive diagnostics. Microbiome could serve as footprint for MAP infection and/disease; indeed, it could be targeted to control MAP- attributed inflammation. A dairy cattle herd with history of clinical PTB was investigated by serology and molecular detection of MAP in the faeces for 10 months. Also, 103 faecal samples were obtained from patients with chronic gastrointestinal conditions after they consented to participate. Faecal metagenomic analysis was performed using Oxford Nanopore Sequencing Technology. All animals were positive in MAP test(s) except two, while in humans, MAP DNA was detected in 8.7% and MAP was isolated from 28.2%. Most species were depleted from faecal microbiome of MAP positive subjects. In MAP- positive patients, firmicutes and proteobacteria dominated and the colitogenic bacteria, *Klebsiella pneumoniae*, was enriched. In animals, firmicutes and bacteroidetes were highly enriched with a small contribution of proteobacteria. Furthermore, animals with increasing frequency of MAP positivity showed comparable microbial content. Overall, richness and evenness indices decreased with increasing MAP positivity rate. These findings reflect a potential influence of MAP on faecal microbiome, also, demonstrated the unique microbiome of the animals progressively shed MAP in their faeces, the highly infectious animals. This of significance in control such zoonotic pathogen, thus remains for further investigations.

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ONE HEALTH AWARENESS, INTERPRETATION AND PRIORITIZATION IN THE GAMBIA: A PARTICIPATORY SITUATIONAL ANALYSIS OF NATIONAL STAKEHOLDERS ACROSS GOVERNMENT, ACADEMIA AND CIVIL SOCIETY

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The Gambia currently lacks active and coordinated One Health (OH) institutional frameworks or a national strategic plan. Despite the formation of multisectoral task forces *ad hoc* in response to national health emergencies, OH activities remain siloed within a group of governmental and academic bodies, and have lacked the momentum, resources, cross-sectoral engagement and political will to operationalise OH in a sustainable and equitable manner. At the community level, OH beneficiaries are mostly excluded from stakeholder exercises. This study identified national OH stakeholders across government, academia, health agencies and civil society. Semi-structured interviews and focus group discussions were conducted with engaged stakeholders at national and regional levels. Inductive thematic analysis was conducted to identify themes relating to OH interpretation, awareness, prioritisation and operationalisation in The Gambia. Study outcomes were rapidly disseminated to stakeholders at an in-person meeting and in a policy briefing document. Interconnected themes were identified relating to: awareness of the OH concept; OH definition in the context of the participants' working, study or community environment; national activities or frameworks related to OH; community, regional and national level collaborations between OH stakeholders; OH priority areas; and barriers and solutions to OH operationalisation. Awareness levels of the term OH were variable between stakeholder groups, with overall low awareness demonstrated by community and student groups. Upon explanation of OH, the majority of stakeholders successfully related the concept to their diverse working, study or community environments. Between sectors and disciplines, and varying levels of society, shared and diverging OH interpretations, awareness levels, priority areas and challenges were demonstrated. This study provided novel evidence of OH awareness and prioritisation in The Gambia, which could be used to inform OH participatory research activities, policies and national frameworks.

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BRUCELLOSIS SEROPREVALENCE AND RISK FACTORS AMONG HIGH-RISK GROUPS AT TWO URBAN SITES IN KENYA

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Brucellosis is a zoonotic bacterial disease that can affect humans and animals. It is often transmitted to humans through the consumption of contaminated animal products or by direct contact with infected animals. In Kenya, data on human and animal brucellosis are limited. To investigate the seroprevalence of human brucellosis in Kenya, we randomly selected from the participants had possible animal exposure and tested 348 out of 2,779 human blood samples, from a longitudinal cohort study of dengue and chikungunya exposure in western (Kisumu) and coastal (Ukunda) Kenya. The inclusion criteria consisted of those who demonstrated positive responses to any of the following risk factors: ownership of livestock or ruminants, usage of raw animal blood, consumption of raw milk (either fresh or fermented), involvement in animal butchering, and providing of animal care. Our study included 126 males (36%), 222 females (64%) in

different age categories, and 61 children aged 16 years and younger (18%), with an overall median age of 29.5 years [2 -75-year age range]. Samples were tested by Abnova Brucella IgG ELISA Kit (KA0954). Of the tested individuals, anti-Brucella IgG antibodies were detected in 96 (28%) in 348 randomly selected participants. Brucella exposure was not associated with study site, gender, age, socioeconomic status, specific livestock ownership (cattle, goats, and sheep), or consumption of raw animal products. Highly educated individuals were more likely to have brucella exposure (OR = 2.02, 1.20-3.41, *P = 0.01)*. In comparison to previous seroprevalence-based studies conducted in non-pastoral Kenyan communities, our study revealed significantly higher seropositivity. This study highlights the neglected significance of brucellosis exposure among urban human populations in Kenya, which could serve as a baseline to guide future research on brucellosis in humans.

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THE HIGHEST MPOX OUTBREAK EVER REPORTED IN CAMEROON; THE CASE OF MBONGE HEALTH DISTRICT OF THE SOUTH WEST REGION: A CROSS SECTIONAL ANALYTICAL STUDY, JUNE 2023.

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Human mpox is a viral zoonotic disease endemic in Central and West Africa. On May 10th 2023, a laboratory confirmed case was notified in the South West Region. We conducted an investigation to assess the outbreak. We carried out a cross-sectional analytical study in Mbonge District from May 15th to June 3rd 2023. Community-health-workers and leaders were engaged after being trained on simplified case definitions, active case search and sensitization. We reviewed registers in five major hospitals. A suspected case was anybody in Mbonge District between April 19th and May 14th 2023 with acute fever >38.3°C, headache, lymphadenopathy, followed after one to three days by maculopapular rash. Swabs and blood samples were collected from suspected cases. A line-list for all suspected and confirmed cases was analyzed for descriptive epidemiology and binary logistic regression for associated factors. We identified 48 suspected cases of which 15(31,2%) were confirmed positive, 8(53,3%) were Clade-II. Amongst confirmed cases, 7(46,6%) were females and median age was 33 years, [3-52]. Persons who spent at least two-weeks in the bush had four times the likelihood of getting mpox (P:0,007, C.I [0,006 - 0,443]). Sensitization on preventive measures while in the bush and engagement of community actors in a crisis zone remains vital.

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SURVEILLANCE AND HOME RANGE ANALYSIS OF OLIVE BABOONS TO INFORM PROGRAMMATIC DECISIONS FOR GUINEA WORM ERADICATION IN GAMBELLA, ETHIOPIA

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The first Guinea worm infection in Olive baboons (*Papio anubis*) in Ethiopia was reported in 2013. Since then, questions have been raised about the role of Olive baboons in ongoing Guinea worm transmission among both humans and domestic dogs in Ethiopia. In support of eradication and to better understand transmission risks, the Ethiopia Dracunculiasis Eradication Program (EDEP) conducts active surveillance activities among Olive baboon troops in the Gambella region considered high risk for Guinea worm due to previous infections or proximity to human or other animal infections. Surveillance includes weekly tracking of baboon movement and water source use, as well as trapping and sedation of baboons to physically check for emerged worms or signs of Guinea worm. Since 2021, EDEP has screened more than 200 baboons for Guinea worm through active surveillance. During trapping in March 2024, we screened 68 baboons for Guinea worm among nine troops, with no Guinea worm detected. In response to the 2023 animal infection detected in Ethiopia, EDEP is expanding the number of baboon troops under surveillance, with additional trapping sessions planned for July and October 2024. In March, we placed GPS collars on baboons from five troops, and plan to place more collars on baboons during the July trapping. Data from GPS collars, captured year-round, will clarify baboon movement, and troop overlap with both nearby baboon troops and water sources used by communities. Preliminary results indicate variation in total troop home ranges between 2.2 and 7.9 kilometers squared. Daily averages for the troop with the largest total home range during the peak dry season varies from 0.2 to 2.0 kilometers squared. These results are programmatically meaningful given baboon home ranges encompass water sources used by humans and domestic dogs, which could have implications for Guinea worm transmission. EDEP is leveraging findings from baboon surveillance activities to inform programmatic implementation strategies, including surveillance intensity, community mobilization, and water treatment to prevent Guinea worm transmission.

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(UN)SUSTAINABLE SCIENCE: ENVIRONMENTAL FOOTPRINT OF RESEARCH, CLINICAL MICROBIOLOGY AND VETERINARY LABORATORIES LOCALLY AND GLOBALLY

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Recently, the scientific and healthcare research communities have increased their efforts to study the causes, implications, adaptation, and mitigation strategies for climate change. It is also important to address our fields' contributions to climate pollution. In this review, we present the scale of the problem, potential interventions, and a case study on waste management from hospitals in Kenya to give a global perspective. Research laboratories produce 12 billion pounds of plastic waste each year and use up to 70% of their institutions' energy despite occupying a significantly smaller proportion of their institutions' total space. –80°C freezers and fume hoods alone use energy that is equivalent to a single and 3.5 households, respectively, and a single laboratory can have multiple freezers and hoods. Clinical microbiology laboratories have significant carbon footprints that can be reduced through diagnostic stewardship, a process focused on ensuring the collection of the right test from the right patient at the right time. Opportunities exist for reducing reagent waste in frequently ordered clinical tests such as complete metabolic panels. Veterinary laboratories also contribute significant carbon emissions from excessive waste from phlebotomy supplies, packaging, animal carcasses, and other biohazardous waste. Green initiatives have been shown to decrease the carbon footprint of laboratories, provide cost savings, and do not have to be resource- or time-intensive. Reducing waste production by purchasing reusable and refillable materials, autoclaving for reuse whenever possible, participating in recycling programs, using low-faucet valves to reduce water use, shutting off hoods and other equipment when not in use, and increasing freezer temperature from –80°C to –70°C are some eco-friendly practices laboratories might adopt. In addition to reducing carbon footprint and saving costs, these practices can also help advance health equity as waste is often disposed of in areas proximal to marginalized communities causing human morbidity and mortality.

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AVIAN VACCINATION VIA RECOMBINANT *LACTOBACILLUS*-BOUND BIRDSEED TO CURB THE SPREAD OF WEST NILE VIRUS

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West Nile virus (WNV) is the leading cause of domestically acquired mosquito-borne disease in the United States. Despite significant investment, no effective human WNV vaccines have been developed, so current mitigation efforts remain limited to environmentally toxic insecticidal sprays. While humans and other animals can develop disease, they are dead-end hosts because they do not develop high enough viremia to infect other mosquitoes. Rather, propagation of WNV is primarily maintained between mosquitoes and birds. We hypothesize that immunizing WNV-susceptible birds will reduce WNV transmission to mosquitoes, protecting both people and animals from infectious bites and disease. To this end, we are genetically modifying strains of the probiotic *Lactobacillus acidophilus* (LA) to express WNV antigenic proteins premembrane (prM), envelope (E), and non-structural protein 1 (NS1). The bacteria will be administered orally to deliver intact viral protein to mucosal immune inductive sites in birds. Immunogenicity is enhanced by the addition of a dendritic cell targeting peptide (DCpep). Protein expression by the LA-based vaccine (rLA-WNV) will be assessed by Western blot and flow cytometry. Immunogenicity will be measured by vaccinating chickens and assessing development of anti-WNV antibodies via ELISA-based techniques and plaque-reduction neutralization assays. We will lyophilize rLA-WNV and bind it to seed to assess its environmental stability and immunogenicity. We selected this strategy because 1. it is only practical to immunize wild birds orally with food baits in WNV endemic areas, and 2. LA can be lyophilized, allowing for preservation and binding to bird seed. The strategy, if successful, will result in an innovative and cost-effective strategy for control of vector-borne disease.

7501

THE FINANCIAL IMPACT OF LIVESTOCK SCHISTOSOMIASIS AND UNDERSTANDING THE IMPORTANCE OF POLICY BUY-IN ON INTERVENTION SUCCESS

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Schistosomiasis is a neglected parasitic disease that poses major threats to human and animal health, as well as the economy, especially in sub-Saharan Africa. It is second only to malaria in its socioeconomic and public health importance with an estimated 1.864 million disability-adjusted life-years (DALYs) lost, 240 million people infected globally and estimated productivity losses due to human schistosomiasis at $11.9 billion/year for 2021-2030. It also has debilitating effects on animals. However, knowledge about the impact of the disease on economic livelihoods and how policy buy-in at various stakeholder levels affects interventions and economic outcomes is limited. A One Health financial analysis of livestock schistosomiasis was conducted to estimate the financial impact of the disease in northern Senegal. Stochastic partial budget models were developed for traditional ruminant farmers in 12 villages. These models were parameterised using data from a cross-sectional survey, focus group discussions (FGDs), scientific literature, and available statistics. Two scenarios were defined: scenario 1 modelled farmers who tested and treated their livestock for schistosomiasis, while scenario 2 modelled no tests or treatment. Sensitivity analyses were conducted to assess the impact of uncertain variables on disease costs. Results revealed that livestock schistosomiasis has a substantial impact on farmers. Schistosomiasis in a herd reduces the farmers' livelihood and may lead to an inability to meet basic needs. Therefore, treating livestock schistosomiasis has the potential to generate considerable benefits for farmers and their families. These findings will be discussed in the context of policy buy-in across stakeholders. They will be presented alongside work on a literature review and community surveys, where we are identifying current interventions in affected communities; measuring the impacts, accessibility, and cost-effectiveness of these interventions through empirical research; and assessing barriers and facilitators to policy buy-in for intervention uptake and success through FGDs and in-depth interviews.

7502

COMPARATIVE ANALYSIS OF STEROID-RDV COMBINATION THERAPY VERSUS STEROIDS ALONE IN HOSPITALIZED COVID-19 PATIENTS: A SARS-COV-2 VIRAL LOAD DYNAMICS STUDY

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Treatment with steroids and/or remdesivir (RDV) are standard treatments in hospitalized COVID-19 patients. Studies with conflicting findings have investigated how steroids and/or RDV affected SARS-CoV-2 viral load (VL) dynamics in the upper respiratory tract (URT). Our studies in hospitalized patients showed that elevated SARS-CoV-2 in peripheral blood (PB), but not the URT, are predictors of severe disease. To investigate the influence of standard treatments on PB and URT VL dynamics, we examined the impact of steroids alone or in combination with RDV in hospitalized COVID-19 patients (n=475) recruited between 4/2020-12/2021 at the University of New Mexico Hospital. To account for the influence of disease severity, only severe COVID-19 patients (n=190), defined by ICU requirements and/or death, were included in the study. Severe patients were stratified into those who received steroids alone (n=37, 19.5%) or steroids/RDV (n=130, 68.4%). Patients (12.1%) who did not receive treatment due to RDV unavailability, contraindications to steroids and/or RDV, completion of prior therapies, or undergoing alternative treatments were excluded. PB and URT VLs at enrollment and cumulative VLs across 14 days were similar between treatment groups. Refined analyses with linear mixed-effects models were employed to analyze the general trend and individual variations in VL changes over time. VLs in PB (P=4.40E^{-9}) and URT (P=9.00E^{-10}) decreased in both groups across 14 days. Patients who received steroids/RDV had higher initial PB VLs (P=0.049) that decreased at a faster rate (P=0.0019). In contrast, patients treated with steroids/RDV had comparable initial URT VLs (P=0.31) and similar decreases across time to those treated with steroids alone (P=0.406). Importantly, patients receiving combination therapy had a shorter average length of stay (20 vs. 23 days) vs. steroids alone (P=0.041). Collectively, findings presented here indicate that severe COVID-19 is defined by higher PB VLs across time and that combination therapy (steroids/RDV) is more effective than steroids alone for reducing SARS-CoV-2 in blood, as well as length of hospitalization.