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ACCURACY OF REPORTING OF MALARIA RAPID DIAGNOSTIC TESTS IN UGANDA

Nelson Ssewante[1], Jane Namuganga[1], Anne R. Katahoire[1], Jenipher Musoke[1], Noel Mutesi[1], Michael Humes[2], Kevin Griffith[2], Saadjo Sow[3], John Aponte[3], Emily Hilton[3], Natalie Galles[3], Radina Soebiyanto[2], Shawna Cooper[4], Bosco Agaba[5], Jimmy Opigo[5], Kim Lindblade[3], Arthur Mpimbaza[1]

[1]Child Health and Development Centre, College of Health Sciences, Makerere University, Kampala, Uganda, [2]President's Malaria Initiative, USAID, Washington, DC, United States, [3]PMI Insights Project, PATH, Seattle, WA, United States, [4]Audere, Seattle, WA, United States, [5]National Malaria Control Division, Ministry of Health, Kampala, Uganda

To assess the accuracy of malaria rapid diagnostic test (RDT) results recorded in health facility registers, we conducted an observational study in two high-burden regions (Busoga and Lango), Uganda. Two districts in each region were purposively selected. Public health facilities (levels II and III) in each district were considered eligible based on three years of complete data and an average of at least 50 RDTs performed monthly. Facilities were grouped into four strata based on patient volume and test positivity rate (TPR). From each stratum, one facility was randomly sampled, resulting in a total of 16 facilities. At each selected facility, using a smartphone application, study staff captured the image of each RDT administered and the corresponding RDT result and patient data recorded in the register. Cohen's kappa was used to determine the level of agreement between the HCW RDT result and that of a trained, external panel that reviewed all of the RDT images and recorded their interpretation. Between June and November 2023, 45,838 RDTs were reported, of which 40,049 (87%) were recorded by the study and 33,429 (83%) complete records were included in the final analysis. The majority of patients tested by RDT (67%) were female, and 43% were 15 years or older. The TPR based on the outpatient register was 62%. Overall, there was a high level of agreement (kappa 0.82; 95% confidence interval 0.79, 0.84) between HCW and external reader results, with no significant variation observed over the study period. Considering the external result as the gold standard, 7% and 2% of HCWs' results were considered 'false positive' (FP) and 'false negative' (FN), respectively. The proportion of FP RDTs was higher among facilities in Lango (8%) compared with the Busoga region (5.5%), while both FP and FN were higher among persons aged 15 years or older (8.2% and 2.2%, respectively) compared to those aged less than five years (5.8% and 1.3%). These findings suggest that RDT results reported in the registers of Ugandan public facilities are largely accurate. However, reasons for higher rates of disagreement in the Lango region and among older patients need to be investigated.

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SETTING UP A SUSTAINABLE ACTIVE SURVEILLANCE SYSTEM IN SOUTHERN ANGOLA: PROGRESS TOWARDS MALARIA ELIMINATION IN THE SOUTHERN AFRICA REGION.

Fernanda Guimarães[1], Mário Hossi[1], André Domingos[2], José Franco Martins[3], Paulo Máquina[4], Manuel Lando[5], Sérgio Lopes[6], **Teresa Nobrega**[7], Ana Direito[7]

[1]National Malaria Control Programme, Ministry of Health, Luanda, Angola, [2]Provincial Public Health Department, Ondjiva, Angola, [3]National Malaria Control Program, Ministry of Health, Luanda, Angola, [4]SADC Elimination 8, Luanda, Angola, [5]The Mentor Initiative, Ondjiva, Angola, [6]The Mentor Initiative, Haywards Heath, United Kingdom, [7]The Mentor Initiative, Luanda, Angola

Angola has a wide malaria transmission heterogeneity ranging from high transmission in the north and central parts of the country to low and very low transmission in southern bordering areas with Namibia. Since 2017 Angola has been supporting regional elimination efforts through the implementation of robust interventions to eliminate *foci* of transmission in border areas, and as a result, supporting elimination efforts in neighboring Namibia. In the southern provinces of Cunene and Cuando Cubango, new surveillance strategies were developed and piloted such as case line listing, case investigation, reactive case detection, *foci* classification and *foci* investigation. Malaria paper-based case line listing started in November 2022 in 5 health facilities and was later expanded to 53 health facilities. A DHIS2 based malaria case notification tracker system was developed and has been used since September 2023. A total of 7 malaria focal points, 7 statisticians and 53 health workers from selected health facilities were trained. The results showed the variability of transmission across the targeted region. In total, 1137 confirmed cases were notified and classified. A total of 1,074 cases (95%) were classified as Local 1 (sleeping within the same household) and 3 were classified as imported. After conducting entomological capacity building trainings among local focal points, *foci* investigations are currently being implemented to localize vector breeding sites and classify the foci as well as give information for response decision-making. Results highlight the importance of having a robust and integrated active surveillance system to target existing *foci* of transmission in southern Angola. As data becomes more detailed and available, further efforts should be made to implement reactive case surveillance approaches and *foci* management interventions to progress towards malaria elimination.

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INTRODUCTION OF THE RTS,S MALARIA VACCINE IN BURKINA FASO: RESULTS FROM THE FIRST SUPPORTIVE SUPERVISION

René Didace BAKOUAN[1], Christelle Nomwendé Néya/ Ouédraogo[1], Mninmalo Ines Evelyne DA[2]

[1]Ministry of health, Ouagadougou, Burkina Faso, [2]Jhpiego, Ouagadougou, Burkina Faso

Burkina Faso introduced the RTS,S vaccine into its expanded vaccination program on February 5, 2024. Following the recommendations of the World Health Organization, a supervision was conducted to assess the state of readiness. This supervision, which took place a few days before the introduction of the new vaccine, was carried out in all selected districts. This article describes the initial vaccination efforts in Burkina Faso.This is a secondary data analysis conducted from February 2 to 10, 2024, using the Kobo tools during the first supervision of the RTS,S introduction into the expanded vaccination program.The first supervision covered 95 health facilities (HF) across the 27 selected districts. All HFs received the necessary financial resources for preparatory activities of the vaccine introduction. Coordination teams were established, and 99% of HF managers were briefed. Supply replenishment was effective in 99% of HFs, with 84% starting on February 5, 2024. The vaccine was correctly administered by 92% of health workers, registration was well documented by 88% of vaccinators, and 92% reminded mothers of the next visit. Less than a quarter (14%) of HFs had received communication and social mobilization materials before the first vaccinations. There were almost no rumors about the vaccine in the community, and no mothers refused the vaccine. Overall, the main challenges encountered were the unavailability of updated data management tools, limited community mobilization, and insufficient cold chain capacity.The initial on-the-ground results are satisfactory despite the challenges faced during the introduction of the malaria vaccine in Burkina Faso. Future challenges will include monitoring vaccinated children and scaling up to the remaining 43 districts in the country.

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PFS230D1 24- AND 60-COPY SINGLE COMPONENT MALARIA TRANSMISSION BLOCKING NANOPARTICLE VACCINES ELICIT A POTENT AND DURABLE RESPONSE UPON VACCINATION

Nichole D. Salinas, Rui Ma, Thayne H. Dickey, Holly McAleese, Tarik Ouahes, Kazutoyo Miura, Carole A. Long, Lynn E. Lambert, Niraj H. Tolia

National Institutes of Health, Bethesda, MD, United States

Although the number of cases of and deaths associated with malaria had been declining prior to the COVID-19 pandemic, forward progress has since stalled, and there were an estimated 249 million cases and 608,000 deaths

worldwide due to malaria in 2022 according to the WHO's World Malaria Report 2023. Tragically, most of these deaths were children under the age of 5. With the rise in parasite resistance to anti-malarial drugs, a malaria vaccine is desperately needed. Malaria vaccines can be broken down into three major classes: Pre-erythrocytic vaccines, Blood Stage vaccines, and Transmission Blocking vaccines (TBVs). TBVs function by reducing disease transmission by breaking the continuous cycle of infection between the human host and the mosquito vector, specifically by reducing/inhibiting the infection within the mosquito after feeding on an infected human. The gametocyte surface protein Pfs230 is a leading TBV candidate. Pfs230 is a large multi-domain protein and most antibodies with transmission reducing activity (TRA) map to Domain 1 (D1). Here we show that both a 24-copy and 60-copy nanoparticle composed of Pfs230D1 genetically fused to either ferritin or the catalytic domain of dihydrolipoyl acetyltransferase protein (E2p), respectively, result in single-component self-assembling nanoparticles (Pfs230D1-ferritin and Pfs230D1-E2p) that have high stability, homogeneity, and production yields. Pfs230-ferritin and Pfs230D1-E2p nanoparticles also correctly present potent human transmission blocking conformational epitopes within Pfs230D1 as shown by the ability of human mAbs possessing high TRA to bind to the nanoparticles. Both nanoparticles elicited potent and durable antibody responses with high TRA after two vaccinations of New Zealand White rabbits when formulated in two distinct adjuvants suitable for translation to human use (Alhydrogel and AddaS03) that was maintained for 4.5 months post vaccination. These single-component nanoparticle vaccines may play a key role in malaria control and have the potential to improve production pipelines and cost of manufacturing of a potent and durable TBV.

6504

SINGLE IMMUNIZATION WITH GENETICALLY ATTENUATED *PLASMODIUM FALCIPARUM ΔMEI2* (GA2) SPOROZOITES INDUCES HIGH LEVEL PROTECTION AGAINST A CONTROLLED HUMAN MALARIA INFECTION

Geert V.T. Roozen, Roos van Schuijlenburg, Annefleur D.O. Hensen, Jan Pieter R. Koopman, Olivia A.C. Lamers, Fiona J.A. Geurten, Jeroen C. Sijtsma, Els Baalbergen, Jacqueline J. Janse, Séverine C. Chevalley-Maurel, Chanel M. Naar, Sascha Bezemer, Hans Kroeze, Huybert J.F. van de Stadt, Abraham de Visser, Pauline Meij, Mara S. Tihaya, Emil D. Colstrup, Eva Iliopoulou, Helena M. de Bes-Roeleveld, Els Wessels, M.Y. Eileen C. van der Stoep, Chris J. Janse, Rajagopal A. Murugan, Blandine Franke-Fayard, Meta Roestenberg

Leiden University Medical Center, Leiden, Netherlands

Malaria vaccines consisting of metabolically active *Plasmodium falciparum (Pf)* sporozoites have the potential to offer a better and more durable protection than the currently deployed subunit vaccines. Recently, we demonstrated the unequivocal superior protective efficacy of late-arresting genetically attenuated parasites (GA2) as compared to its early-arresting counterpart (GA1) against a controlled human malaria infection (CHMI). We found high level protection accompanied by potent circulating cellular memory responses, presumably against late liver stage antigens. So far, malaria vaccines have always been tested in regimens of three or more immunizations, but the necessity of multiple immunizations in inducing strong cellular response and high protective efficacy remains unknown. Encouraged by the previous results, we explored whether such responses and protection could also be induced after a single immunization. An effective simple regimen will facilitate vaccine implementation and will significantly reduce costs. To address this critical knowledge gap, we investigated the protective efficacy and cellular memory formation upon a single GA2-immunization administered through the bites of 50 GA2-infected mosquitoes in a randomized double-blind placebo-controlled clinical trial in healthy malaria-naive adults. By testing the preliminary efficacy of this simplified regimen with a homologous CHMI six weeks later, we found 9/10 GA2-immunized participants to be sterile protected, as compared to 0/5 mock-immunized participants (infectivity controls). GA2-immunized participants had a significantly higher frequency of *Pf*-specific polyfunctional CD4+ T cells than the controls within both central and effector memory compartments. This unprecedented 90% protective efficacy upon only one GA2-immunization shows the potency of cellular immune memory formed against GA2-derived late liver-stage antigens, further underlining their importance. Moreover, our study provides strong support for the further clinical development of malaria vaccines based on late-arresting genetically attenuated parasites.

6505

CHARACTERIZING THE SEROLOGICAL IGG REPERTOIRE OF TANZANIAN CHILDREN VACCINATED WITH NOVEL MALARIA BLOOD-STAGE CANDIDATE RH5.1/MATRIX-M ADJUVANT

Jeffrey Marchioni[1], Kirsty McHugh[2], Allison Seeger[1], Cassandra Rigby[2], Doris Quinkert[2], Ana Rodrigues[2], Randall S. MacGill[3], George Georgiou[1], Simon J. Draper[2], Jason J. Lavinder[1]

[1]The University of Texas at Austin, Austin, TX, United States, [2]Oxford University, Oxford, United Kingdom, [3]Center for Vaccine Innovation and Access, PATH, Washington, DC, United States

For the first time, malaria blood-stage vaccine antigen Reticulocyte Binding Protein Homologue 5 (RH5), a protein found on the surface of *Plasmodium falciparum* merozoites, has been tested in a Phase 1b clinical trial (NCT04318002). RH5 has the potential to provide superior protection compared to previous blood-stage vaccine candidates due to its low levels of polymorphism and role as an essential component of a non-redundant erythrocyte invasion pathway. Further, previously characterized anti-RH5 antibodies exhibit protective properties, such as the ability to inhibit parasite growth *in vitro*. The vaccine, consisting of an engineered RH5 variant termed RH5.1 (Draper Laboratory, Oxford) with Matrix-M™ adjuvant (Novavax), is designed to induce high, long-lasting, and protective antibody titers. In the trial, n=11 healthy Tanzanian children between 5-17 months old, a population susceptible to *P. falciparum* infection, were administered two monthly doses of 10 µg RH5.1 with 50 µg Matrix-M followed by a delayed booster dose six months following the first dose. The highest anti-RH5.1 titers observed in humans to date (median 723 µg/mL; range: 450-1436 µg/mL) were seen 14 days post-boost (Silk et al. 2024, *medRxiv*). Polyclonal IgG isolated from plasma also showed the highest level of functional GIA observed in humans to date following vaccination; all 11 children exhibited >60% GIA at 2.5 mg/mL (median 88%; range: 73-97%), a benchmark previously witnessed to predict blood-stage protection in *Aotus* monkeys (Douglas et al. 2015, *Cell Host Microbe*). To further examine the robust antibody response seen within this cohort, we completed high-throughput B cell receptor sequencing (BCR-Seq) alongside high-resolution, bottom-up tandem mass spectrometry (Ig-Seq) (n=3 donors). By cross-comparing the BCR- and Ig-Seq data sets, we determined the full-length VH and VL sequences of the most abundant circulating plasma IgG lineages in each individual child. The identified plasma lineages were subsequently expressed as recombinant monoclonal antibodies and functionally characterized for epitope specificity and *in vitro* parasite growth inhibition activity.

6506

VALIDATION OF CIRCULAR RNA VACCINE PLATFORM FOR MALARIA TRANSMISSION BLOCKING VACCINE

Nawapol Kunkeaw[1], Thitipa Thosapornvichai[2], Suradej Hongeng[3], Eizo Takashima[4], Takafumi Tsuboi[4], Patompon Wongtrakoongate[5], Wang Nguitragool[6], Jetsumon Sattabongkot[1]

[1]Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [2]Department of Biochemistry, Faculty of Science, Mahidol UniversityMahidol University, Bangkok, Thailand, [3]Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Rachathewi, Bangkok, Thailand, [4]Division of Malaria Research, Proteo-Science Center, Ehime University, Ehime, Japan, [5]Department of Biochemistry, Faculty of Science, Mahidol University,

Bangkok, Thailand, [6]Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Plasmodium vivax is a major malaria parasite that causes acute illness in millions of people each year. A vaccine that interrupts parasite transmission (transmission-blocking vaccine, TBV) will contribute to the elimination of malaria but no such vaccine has been approved to date. We have recently demonstrated that the nucleoside-modified mRNA formulated with lipid nanoparticle (mRNA-LNP) vaccine targeting a leading transmission blocking antigen of *P. vivax*, Pvs25, has ability to elicit long-lasting transmission-blocking immunity. A new vaccine platform using circular RNAs (circRNAs) to express target protein antigens has demonstrated improved stability, protein expression capacity and several advantages that facilitate its use as cost-effective vaccines. In this study, we developed and evaluated a lipid nanoparticle (LNP)-encapsulated circular Pvs25 RNA vaccine (circPvs25). *In vitro* protein protection and immunogenicity in mice of a circPvs25 vaccine was tested and compared with that of a linear nucleoside-modified Pvs25mRNA-LNP vaccine (linear Pvs25). The direct membrane feeding assay was utilized to assess the capacity of vaccine induced antibodies to block the parasite development in the mosquitoes. We observed similar levels of protein expression of our unpurified circPvs25 and purified linear PVS25 in Western blot, flow cytometry and immunofluorescence assays. Pvs25-reactive antibodies were induced by a single immunization of either circPvs25 or linear Pvs25. A booster immunization with the same vaccine significantly increased the Pvs25-specific antibody titer, and a higher antibody response was observed in circPvs25-circPvs25 homologous vaccination. Both homologous circPvs25 and homologous linear Pvs25 immunization showed strong transmission reducing activity with ability to completely block parasite development in mosquitoes and robust memory B cell and T cell responses. With the ability to induce complete transmission-blocking activity, the circPvs25 RNA vaccine holds a strong promise for further development/testing in non-human primates.

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A WHOLE ORGANISM *PLASMODIUM VIVAX* BLOOD STAGE VACCINE PARTIALLY PROTECTS AOTUS MONKEYS AGAINST A HOMOLOGOUS EXPERIMENTAL INFECTION

Nicanor Obaldia[1], Marlon Nunez[1], Ariel Magallon[1], Santiago Montilla[1], Joao Luiz Da Silva Filho[2], Kanjee Usheer[3], Matthias Marti[4], Manoj Duraisingh[3]

[1]Instituto Conmemorativo Gorgas de Estudios de la Salud, Panama, Panama, [2]Wellcome Centre for Integrative Parasitology, Institute of Infection, Immunity and Inflammation, College of Medical Veterinary & Life Sciences, Glasgow, United Kingdom, [3]Department of Immunology and Infectious Diseases, Harvard University | T.H. Chan, School of Public Health, Boston, MA, United States, [4]Wellcome Centre for Integrative Parasitology, Institute of Infection, Immunity and Inflammation, College of Medical Veterinary & Life Sciences, Glasgow University, United Kingdom

Previous studies achieved sterile immunity in Aotus monkeys following two repeated exposures to Plasmodium vivax blood stages. This pilot study aimed to protect Aotus monkeys using a crude P. vivax whole organism antigen (pvWAg) adjuvanted with Al(OH)3, delivered intramuscularly (i.m.), in a prime-boost immunization scheme against a homologous challenge. Using a 47% Percoll cushion, the band (mostly trophozoites and schizonts) was washed with PBS, subjected to three cycles of freezing and thawing, and adsorbed onto $Al(OH)_3$ to obtain a concentration of 50 µg per 0.1 mL. Five Aotus monkeys were immunized i.m. three times in alternating thigh muscles with 50, 100, and 100 µg of the crude immunogen at 0, 2, and 5 weeks respectively, while one control received the adjuvant alone. Three weeks after the last immunization, all animals including a malaria-naïve infection control, were challenged intravenously (i.v.) with 50,000 parasites of the homologous *P. vivax* AMRU-1 strain. Parasitemias were monitored daily using the Earle & Perez (1932) method, and blood samples were collected pre-immunization and post-challenge to determine the antibody immune response by ELISA. After the challenge, all animals tested positive for infection between days 8 and 9 post-inoculation (PI). Parasitemia peaked in the control animal at 115.9 x 10^3/µL on day 15 PI. In contrast, immunized animals -except for one animal requiring treatment for high parasitemia (120.0 x 10^3/µL on day 14 PI)- exhibited 7-fold lower parasitemias (Mean ± sd = 16.1 x 10^3/µL on day 15 PI; n = 4) compared to the inoculation control. The total parasitemia area under the curve (AUC) excluding the non-responder, was 88.4 in the immunized group (n = 4) compared to 231.8 in the controls (n = 2) ($P<0.0001$; F test). Similarly, survival curves, with the endpoint being rescue treatment, were significantly different in the immunized group compared to the controls ($P=0.0254$; Gehan-Breslow-Wilcoxon test). This pilot study demonstrates that a crude pvWAg adjuvanted with Al(OH)3 provides partial protection in Aotus monkeys against a homologous P. vivax challenge.

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ACCEPTABILITY AND FEASIBILITY OF ADMINISTERING RTS,S/AS01 MALARIA VACCINE TO SCHOOL-AGED CHILDREN IN SOUTHERN MALAWI.

Blessings N. Kaunda-Khangamwa[1], Linda A. Nyondo Mipando[2], Christopher C. Stanley[1], Mark L. Wilson[3], Terrie Taylor[4], Tabither Kaunda[1], Lauren M. Cohee[5], Clarissa Valim[6], Don P. Mathanga[1]

[1]Malaria Alert-Communicable Diseases Action Centre (MAC-CDAC), Kamuzu University of Health Science, Blantyre, Malawi, [2]Department of Health Systems and Policy, School of Public Health and Family Medicine, Kamuzu University of Health Sciences, Blantyre, Malawi, [3]Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, United States, [4]Department of Osteopathic Medical Specialties, College of Osteopathic Medicine, Michigan State University, East Lansing, MI, United States, [5]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [6]Department of Global Health, Boston University, School of Public Health, Boston, MA, United States

School-age children (SAC) in sub-Saharan Africa have a significant malaria burden and are recognized as reservoirs for malaria transmission. We explored whether the RTS,S/AS01 malaria vaccine, which the WHO approved in 2021 for use in children under age five, could be feasibly and acceptably administered through schools to SAC. These data were collected as part of a clinical trial to assess the efficacy of the vaccine in preventing malaria morbidity in SAC. Qualitative data grounded within the Theoretical Framework of Acceptability were gathered and mapped onto seven domains: affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy. Using purposive sampling with maximum variation, we selected 116 participants (ages 10-71 years) to capture diverse perspectives in 16 focus group discussions: SAC (N=44), caregivers (N=40), community health workers (N=12), and Learner Treatment Kit teachers/dispensers (N=20). Framework analysis highlighted and interpreted key patterns within and across groups of participants and themes within the context of implementation. Results indicate that implementing the malaria vaccine in schools is highly acceptable and feasible due to accessibility, other school-based health programmes, and confidence to invite school-going siblings to participate. Most caregivers stated that the vaccine was aligned with their values, as fewer children reported being sick and absent from school. However, community members perceived high opportunity costs due to the deviation from daily routines for caregivers and SAC to access all three doses. Additional barriers affected demand and uptake included competing priorities and limited understanding of the purpose of the vaccine, as some expected it to eliminate malaria. Mixed feelings toward this vaccine also involve persistent misconceptions, misinformation, and conspiracy theories affecting uptake of the 2nd and 3rd doses. Addressing misinformation is important for optimal uptake, requiring multi-sectoral support and coordinated efforts of both Health and Education Ministries.

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IN-SILICO ANALYSIS OF *PLASMODIUM FALCIPARUM* SURFACE PROTEINS AND MONOCLONAL ANTIBODIES TO DESIGN MALARIA VACCINE

Fatoumata Gnine Fofana[1], Mamadou WELE[1], Olaposi Idowu OMOTUYI[2], Seydou Doumbia[3], Mahamadou DIAKITE[4]

[1]University des Sciences, Techniques et des Technologies de Bamako (USTTB)/ African Center of Excellence in Bioinformatics (ACE-B), Bamako, Mali, [2]Adekunle Ajasin University, Akungba-Akoko (AAUA), Akungba-Akoko, Nigeria, [3]University des Sciences, Techniques et des Technologies de Bamako (USTTB)/ University of Clinical Research Center (UCRC), Bamako, Mali, [4]University des Sciences, Techniques et des Technologies de Bamako (USTTB), Bamako, Mali

Efforts to develop effective vaccines against *Plasmodium falciparum*, the deadliest malaria-causing parasite, have intensified with the aid of computational methods. This research focuses on utilizing in-silico analysis to explore the interactions between *Plasmodium falciparum* surface proteins and monoclonal antibodies (mAbs) as potential targets for vaccine development. Through comprehensive literature review and bioinformatics tools, twenty-three (23) key surface proteins of the parasite were identified, and their structural characteristics elucidated, even in instances where experimental structural data was unavailable. Concurrently, mAbs are computationally analyzed to assess their potential in recognizing and neutralizing these surface proteins. The resulting insights into the dynamics and stability of antibody-antigen interactions provide crucial understanding of immune responses essential for vaccine design. Integration of computational findings aids in the identification of promising vaccine candidates, which can subsequently undergo experimental validation for assessment of immunogenicity, safety, and efficacy. This study underscores the significance of computational approaches in accelerating the discovery and development of vaccines against malaria caused by *Plasmodium falciparum*, offering a promising avenue for combating this global health menace.

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ASSESSMENT OF PARENTAL/CAREGIVER PERCEPTION AND ACCEPTANCE OF THE MALARIA VACCINE IN A CONFLICT-AFFECTED REGION IN CAMEROON

Ayuk-Maru Pamela Oben epse Besong

Ministry of Public Health, Buea, Cameroon, Cameroon

Malaria poses a significant challenge to public health in Cameroon, with an annual estimate of 2.7 million infections and 11,000 deaths. The development of the first malaria vaccine (RTS, S) and its subsequent pre-qualification by the WHO has provided an additional tool in the fight against this deadly disease. Consequently, African countries, including Cameroon, have expressed interest in integrating the vaccine into their standard immunization programs. In preparation for this rollout, evaluating the public's comprehension and willingness to accept this vaccine was essential. The Study employed a cross-sectional descriptive design involving 444 caregivers attending Infant Welfare Clinics. Data was collected over one month, and questionnaires were administered to those who consented to the study. Qualitative analysis using SPSS was done to have the most significant variables. Our study revealed that a significant % of caregivers (83.6%) were aware of the malaria vaccine, and half (54.5%) were willing to accept vaccination. It's important to note that caregivers, as key players in the vaccination process, were twice as likely to vaccinate their children in urban areas than their rural counterparts. However, this difference was not statistically significant. The findings underscore the importance of comprehensive information, education, and communication about the malaria vaccine before its implementation. This is particularly crucial in rural areas where vaccine hesitancy is prevalent. By implementing effective communication strategies, we can empower caregivers to make informed decisions for malaria vaccination, to sustainably reduce the malaria burden.

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PHASE 1A CLINICAL TRIAL OF SAFETY AND IMMUNOGENICITY OF RH5.1 AND R78C WITH MATRIX-M™ ADJUVANT IN UK ADULTS - A NOVEL COMBINATION VACCINE CANDIDATE AGAINST THE *PLASMODIUM FALCIPARUM* BLOOD-STAGE RH5-CYRPA-RIPR (RCR) INVASION COMPLEX

Jo Salkeld[1], Dimitra Pipini[1], Andrew DS Duncan[1], Melanie Etti[1], Megan Baker[1], Nicola Greenwood[1], Barnabas G. Williams[1], Lloyd DW King[1], Ababacar Diouf[2], Cassandra A. Rigby[1], Doris Quinkert[1], Cecilia Carnrot[3], Alison M. Lawrie[1], Katherine Skinner[1], Rachel E. Cowan[1], Jee-Sun Cho[1], Carole A. Long[2], Carolyn M. Nielsen[1], Kazutoyo Miura[2], Sarah E. Silk[1], Simon J. Draper[1], Angela M. Minassian[1]

[1]University of Oxford, Oxford, United Kingdom, [2]National Institutes of Health, Bethesda, MD, United States, [3]Novavax AB, Uppsala, Sweden

The *Plasmodium falciparum* RH5-CyRPA-RIPR (RCR) hetero-trimeric invasion complex, part of a larger pentameric complex, is a highly conserved and essential blood-stage malaria vaccine target. A soluble protein vaccine candidate, called "RH5.1", targeting the full-length reticulocyte binding protein homologue 5 (RH5) component of the complex is the most advanced clinically, but RH5-interacting protein (RIPR)- and cysteine-rich protective antigen (CyRPA)-based vaccines have not previously been tested in clinical trials. Here we assessed "R78C", a new soluble protein antigen comprising RIPR EGF domains 7-8 fused to CyRPA, alone and combined with RH5.1, formulated with Matrix-M™ adjuvant, in a first-in-human Phase 1a trial. Healthy, malaria-naïve UK adults (N=32) were recruited into four groups: i) 10 µg RH5.1 alone, or ii) 10 µg R78C alone in a delayed (0-1-6 month) vaccination regimen; iii) the combination of 10 µg R78C admixed with 10 µg RH5.1 in a delayed (0-1-6 month) regimen; or iv) the combination of 10 µg R78C and 10 µg RH5.1 with both proteins admixed for the first two doses (at 0-1 months) and with the third and final doses given separately at 6 and 7 months. All vaccinations were given with 50 µg Matrix-M™ adjuvant. Vaccinations to-date (April 2024) have been well tolerated with no safety concerns. The most commonly reported adverse events (AEs) were injection site pain and fatigue. Solicited AEs were generally mild-moderate in severity and all spontaneously resolved within 7 days. Functional immunogenicity is being assessed via the growth inhibition activity (GIA) assay, and IgG titres to the individual antigens and to the RCR-complex are being assessed by ELISA and these data will be presented. RH5.1 formulated with Matrix-M™ has shown clinically significant efficacy against clinical malaria in a Phase 2b field trial as a standalone blood-stage vaccine. Initial immunogenicity data from this trial suggest that the combination of R78C and RH5.1 may induce a superior antibody response (as compared to RH5.1 alone) and support onward clinical testing. A Phase 1b trial is planned to start in Tanzania in April 2024 with a Phase 2b trial in 2025.

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PRE-CLINICAL AND CLINICAL EFFICACY OF ATTENUATED AND KILLED WHOLE PARASITE MALARIA BLOOD STAGE VACCINES TO LIMIT DISEASE

Danielle I. Stanisic[1], Winter A. Okoth[1], Takashima Eizo[2], Tsuboi Takafumi[2], Mei-Fong Ho[1], Kylie Alcorn[3], James Beeson[4], Moses Lee[5], Terry Spithill[6], James Fink[3], Kim-Lee Sim[7], Steve Hoffman[7], John Gerrard[3], **Michael F. Good**[1]

[1]Griffith University, Gold Coast, Australia, [2]Ehime University, Matsuyama, Ehime, Japan, [3]Gold Coast University Hospital, Southport, Australia, [4]Burnett Institute, Melbourne, Australia, [5]Georgia State University, Atlanta, GA, United States, [6]La Trobe University, Melbourne, Australia, [7]Sanaria Inc., Rockville, MD, United States

Subunit vaccines against the blood stages of malaria have shown limited efficacy. All candidates have aimed to induce antibodies to interfere with merozoite invasion. Polymorphism of B-cell epitopes is the major obstacle. We have championed a different approach, relying on the entire antigenic

composition of the parasite delivered in a way to maximize induction of cellular immunity. Our first candidate consisted of ring-stage parasitized red cells attenuated using seco-cyclopropyl pyrroloindole analogs. These induced strong clinical and parasitological immunity to different rodent parasites. A clinical trial involving malaria-naive adult volunteers vaccinated using chemically attenuated magnet-purified *Plasmodium falciparum*-parasitized red cells was undertaken. We have now shown that vaccination leads to strong cellular responses involving Th1 and Th2 cytokine-secreting T-cells. We screened antibody responses to randomly chosen antigenic fragments of 271 PfEMP1 and 78 other blood stage antigens and observed baseline responses to the vast majority of antigens. Two volunteers were completely protected from a blood stage challenge infection with no parasites detected by PCR. This proof-of-principle study laid the groundwork for a whole parasite vaccine in which the parasite antigens were frozen prior to admixing with a liposomal adjuvant, CAF01. Pre-clinical work using the *P. yoelii* model demonstrated long-lived protection against clinical disease and parasite burden (>9 months in mice) with induction of Th1 and regulatory cytokines. CD4+ T-cells were critical. Infection post-vaccination strongly boosted clinical and parasitological protection. Vaccine-induced protection was also augmented by prior infection. In advance of moving to a clinical trial, we modified this vaccine to block induction of antibodies to human red cells using methoxy polyethylene glycol (mPEG) treatment of *P. falciparum*-parasitized magnet-purified red cells. mPEG treatment did not reduce vaccine efficacy in a *P. yoelii* model. The vaccine has now completed formal toxicological evaluation with no adverse findings. The trial will commence in Q3 2024.

6513

IN SILICO EVALUATION OF PREDICTED *PLASMODIUM FALCIPARUM* EPITOPES IN LEADING VACCINE CANDIDATE ANTIGENS

Alexander John Laurenson, Ryan Scalsky, Jean-Paul Courneya, Matthew Adams, Matthew B. Laurens

University of Maryland School of Medicine, Baltimore, MD, United States

Plasmodium falciparum is the most lethal and common human malaria parasite. Epitope-based vaccines could overcome existing limitations of currently recommended malaria vaccines by targeting conserved and immunogenic regions within multiple discrete antigens presented in pre-erythrocytic, erythrocytic, and sexual stages. We hypothesize that *in silico* tools can incorporate parasite protein diversity and host HLA allele frequency data to identify and rank multiple predicted epitopes. Through literature review, 42 malaria proteins were identified as nonredundant, conserved, and essential for either hepatocyte or erythrocyte invasion or transmission, making them ideal targets for a multistage malaria vaccine. Using leading vaccine candidate protein sequence datasets constructed from *P. falciparum* samples collected in highly endemic areas, we predicted and evaluated epitopes with high affinity for regional HLA alleles. After performing quality control filtering and sequence clustering, we used NetMHCpan to predict CD4+ and CD8+ T-cell epitopes. To score and rank epitopes, we developed a heuristic-based weighting model integrating the following: 1) predicted binding affinities between epitopes and MHC receptors, 2) HLA allele frequency in endemic regions, and 3) sequence conservation. By characterizing predicted epitope distribution across the protein and comparing results to peptide regions with positive or negative immunogenicity and low or high HLA restriction by *in vitro* and *in vivo* assays, we validated weighting model performance in assigning epitope scores. As a proof of principle, we first examined epitopes within the most studied vaccine candidate, circumsporozoite protein (CSP). Our model scored CSP epitopes in multiple conserved and HLA-nonspecific regions as strong candidates with positive immunogenicity, validating the methodology. We plan to refine this model and continue in-depth analyses of predicted and ranked epitopes for the remaining protein candidates to ultimately contribute towards the design of a multistage, multiepitope vaccine for preclinical evaluation.

6514

INNOVATIONS IN MALARIA VACCINE DEVELOPMENT PROGRAM (IMV)

Evangelos Simeonidis[1], Ashley Birkett[1], Simon J. Draper[2], Jenifer Haner[1], Jessica Harkhani[1], Linda Hoang[1], Kerry Laurino[3], Emily Locke[3], Randall S. MacGill[3], Robin Miller[4], Lorraine Soisson[4], Tara Tagmyer[3], Yimin Wu[3], Susan Youll[4]

[1]PATH, Seattle, WA, United States, [2]University of Oxford, Oxford, United Kingdom, [3]PATH, Washington, DC, United States, [4]United States Agency for International Development (USAID), Washington, DC, United States

The Innovations in Malaria Vaccine Development (IMV) contract is designed to solve key underlying challenges in the preclinical development and clinical evaluation of next-generation *Plasmodium falciparum* malaria vaccines. The IMV contract is funded by the U.S. Agency for International Development and implemented by PATH and sub-partners. A core strategy of all IMV projects is to identify and advance next-generation malaria vaccine candidates that will induce more potent and durable immune responses interfering with critical steps in the parasite life cycle—namely, the infection of hepatocytes and progression to asexual blood-stage infection. By focusing on the potency of immune responses, IMV projects aim to increase the durability of protection of future vaccines—an important limitation of the first-generation vaccines RTS,S/AS01 and R21/Matrix-M. The IMV program consists of three workstreams: the circumsporozoite protein (CS) workstream; the blood stage (BS) workstream, focused on RH5 and other antigens in the RH5 complex; and the combination (CS+BS) workstream, exploring the preclinical and clinical challenges and opportunities of combining CS and BS vaccines. With an international consortium, including Johns Hopkins University, Scripps Research, the Statens Serum Institut, the University of Oxford, and the University of Texas at Austin, along with USAID government partners the National Institute of Allergy and Infectious Diseases, the Naval Medical Research Command, and the Walter Reed Army Institute of Research, the IMV program is making progress in all three workstreams. Important milestones include establishing RTS,S as a benchmark in a preclinical model of malaria infection, now available for comparison testing of novel CS-based vaccine candidates, and evaluating a particle-based RH5-based BS vaccine candidate in a Phase 1 clinical trial. We will present an overview of key accomplishments, platforms of interest (such as mRNA-LNP and other nanoparticles), lessons learned, and future directions. We will also highlight IMV-funded work being presented at ASTMH 2024 and in scientific literature.

6515

HEALTH SYSTEMS CAPACITY STRENGTHENING FOR MENINGITIS SURVEILLANCE AND SAFETY SIGNALS MONITORING: LESSONS FROM THE RTSS/AS01 MALARIA VACCINE PILOT EVALUATION IN GHANA

Samuel Ekow Bernard Harrison[1], Thomas Gyan[1], Eliezer Odei-Lartey[1], Justice Sylverkin[2], Dennis Adu-Gyasi[1], Nana Buabeng Yiadom[3], Albert Dornudo-Agordo[3], Lawrence Osei-Tutu[2], Tsiri Agbenyega[3], Daniel Ansong[2], Kwaku Poku-Asante[1]

[1]Kintampo Health Research Centre, Ghana Health Service, Kintampo, Ghana, [2]Kwame Nkrumah University of Science and Technology (KNUST), School of Medical Sciences, Kumasi, Kumasi, Ghana, [3]Agogo Malaria Research Centre, Agogo Presbyterian Hospital, P.O. Box 27 Agogo, Ghana, Agogo, Ghana

Meningitis constitutes a major public health burden and presents a diagnostic challenge for many resource-limited health systems. It accounts for over 5 million new cases and about 300,000 annual deaths mainly among children under 5 years. Survivors may suffer lifelong neurological and hearing impairment. Based on safety signals observed from the pivotal phase III trial of RTSS malaria vaccine, there was the need for enhanced meningitis surveillance and monitoring of these safety signals during the WHO led malaria vaccine implementation (MVIP) in routine health systems in Ghana. Baseline capacity assessment was carried out involving 20 referral Hospitals within 6 regions in Ghana prior to the MVIP. Eight (8)

hospitals serving both vaccine implementing and comparator districts were selected as sentinel hospitals for the safety cohort event monitoring using standardized questionnaire deployed on digital surveillance platform. Trial interventions were implemented based on identified gaps and their impact on meningitis surveillance and cerebral malaria were evaluated. Prior to the MVIP in 2019, baseline lumbar puncture (LP) rate among eligible children was 0.25% across assessed hospitals. The underlying reasons for the low LP rates included limited health worker capacity to perform LPs, few paediatricians and medical officers, inadequate laboratory equipment and reagents to process and analyse cerebrospinal fluid samples and lack of motivation to perform LPs. The interventions instituted included regular refresher trainings on LPs, health worker incentives, supportive supervision and monitoring, supply of reagents and logistics and incorporation of a meningitis alert algorithm into the digital platform for early notification to perform LPs. We observed a significant increase in LP rate from 0.25% at baseline to 78% as at December, 2022 for all eligible children. Sustained health systems strengthening is key for effective meningitis surveillance in routine health facilities. Lessons learnt during the vaccine implementation have implications for future safety events monitoring in health systems in Ghana.

6516

CHARACTERIZATION OF THE IMMUNE RESPONSES INDUCED BY THE *PLASMODIUM FALCIPARUM* BLOOD-STAGE VACCINE CANDIDATE, RH5.1/MATRIX M™, IN A PHASE IIB TRIAL IN BURKINABE 5-17MONTH OLDS

Sarah E. Silk[1], Dimitra Pipini[1], Ousmane Traoré[2], Magloire Natama[2], Jo Salkeld[1], Athanase Somé[2], Seyi Soremekun[3], Ababacar Diouf[4], Toussaint Rouamba[2], Florence Ouedraogo[2], Salou Diallo[2], Massa dit Achille Bonko[2], Hermann Sorgho[2], Umesh Shaligram[5], Jee-Sun Cho[1], Alison M. Lawrie[1], Katherine Skinner[1], Rachel Roberts[1], Carolyn M. Nielsen[1], John Bradley[3], Carole A. Long[4], Kazutoyo Miura[4], Simon J. Draper[1], Angela M. Minassian[1], Halidou Tinto[2]

[1]University of Oxford, Oxford, United Kingdom, [2]Clinical Research Unit of Nanoro, Nanoro, Burkina Faso, [3]LSHTM, London, United Kingdom, [4]National Institutes of Health, Rockville, MD, United States, [5]Serum Institute of India, Pune, India

There are promising advances in vaccines against *Plasmodium falciparum* (*Pf*) malaria, with both R21/Matrix-M™ and RTS,S/AS01 now licenced. However, these vaccines are only partially effective against clinical malaria and induce no blood-stage immunity to neutralise parasites that may emerge from the liver. Development of an effective blood-stage malaria vaccine therefore remains crucial for a future multi-stage vaccine approach. The reticulocyte-binding protein homologue 5 (RH5) is essential for erythrocyte invasion, has limited polymorphism, and antibodies induced by RH5 have demonstrated *in vivo* efficacy against blood-stage malaria challenge in non-human primates (NHPs). This protection has been strongly correlated with anti-RH5 serum IgG antibody concentration and *in vitro* functional growth inhibition activity (GIA), requiring a threshold of >60% GIA at 2.5mg/mL purified total IgG for protection. In a Phase Ib trial in Tanzania (NCT04318002), assessing full-length recombinant protein RH5 (RH5.1) with Matrix-M™ (MM) adjuvant in 5-17month old children, we reported the highest levels of GIA in human participants to date, now above the defined correlate of protection in NHPs. We therefore progressed to a Phase IIb, double-blinded, block randomised, controlled trial (NCT05790889) in Siglé, an area of seasonal transmission, in Burkina Faso, to assess safety, efficacy and immunogenicity of RH5.1/MM. A total of 360 5-17month olds were randomized to receive 3x 10 µg doses of RH5.1 with 50µg MM (2 groups of N=120 children, in a 0-1-2 month or a delayed 0-1-5 month regimen) or 3x doses of the rabies vaccine, Rabivax-S (2 groups of N=60 children, in a 0-1-2 or 0-1-5 month regimen). Type of vaccine delivery system, regimen and demographic characteristics of vaccinees have been shown to have substantial impact on anti-RH5 immune responses in studies to date. Here, we report the effects of monthly vs delayed third dose regimen on humoral response magnitude, quality and durability, as well as functional GIA assessment of antibody responses in the first opportunity for correlation with clinical malaria outcome for RH5-based vaccines.

6517

CREATING SUPERIOR PFSPZ VACCINES FOR MALARIA BY GENETICALLY CROSSING WEST AND EAST AFRICAN *PLASMODIUM FALCIPARUM* TO PRODUCE PFSPZ WITH GREATER ANTIGENIC DIVERSITY AND POTENCY

B. Kim Lee Sim[1], Lucia Pazzagli[2], Bethany Jenkins[1], Ankit Dwivedi[3], Asha Patil[1], Yonas Abebe[1], Ehud Inbar[1], Manuel Llinas[4], Stephen L. Hoffman[1], Joana Carneiro da Silva[3], Ashley M. Vaughan[2]

[1]Sanaria Inc., Rockville, MD, United States, [2]Seattle Children's Research Institute, Seattle, WA, United States, [3]University of Maryland, School of Medicine, Baltimore, MD, United States, [4]Penn State University, University Park, PA, United States

Plasmodium falciparum sporozoite (PfSPZ) vaccines are the only malaria vaccines to have 100% vaccine efficacy (VE) against heterologous CHMI, sustained VE for 2 transmission seasons in Africa without boosting, and VE against highly divergent Pf in Papua, Indonesia. PfSPZ vaccines are based on a W. African isolate, NF54. Their VE is primarily mediated by cellular immunity against potentially 1000's of protective CD8+ T cell epitopes expressed in the Pf liver stage. Target epitopes vary among Pf isolates and genetic divergence from NF54 increases with geographic distance from W. Africa. Furthermore, NF54 SPZ do not invade/develop in hepatocytes as well as other Pf strains, thereby limiting immunogenic potency. To enhance VE against divergent Pf, an approach is to mix PfSPZ from parasites from different geographic regions. However, the 5-10x fewer PfSPZ/mosquito produced by other Pf strains relative to NF54 makes this approach cost prohibitive. We hypothesized that by genetically crossing strains of Pf from E. Africa with NF54, we could produce a hybrid parasite that made as many PfSPZ as NF54, had greater invasion/development in hepatocytes than NF54, and by having critical epitopes from both parental strains, would have better VE against E. African Pf than PfSPZ (NF54) without losing VE against W. African Pf. Thus, we generated pan African hybrids by crossing NF54 with 3 E. African Pf strains (MAL31 Malawi, NF165 Malawi and HL1209 S. Sudan). All 3 crosses gave rise to PfSPZ which transitioned through humanized FRG huHep mice and RBC stage parasites were cloned resulting in 60, 31 and 17 clones respectively. We then selected hybrids that 1) had a balanced representation of a) both parental genomes, b) genes implicated in protective immunity that were highly transcribed in PfSPZ and liver stages; 2) produced high numbers of PfSPZ; and 3) developed in hepatocytes better than NF54. This resulted in identification of 2 pan African recombinant hybrids, AV27 & AVD7, that met all criteria. We are creating late arresting replication competent parasites, PfSPZ-LARC2 (AV27 & AVD7), by deleting genes for *Mei2* and *LINUP*, and plan GMP production and clinical trials.

6518

IMPLEMENTATION COSTS OF A SCHOOL-BASED RTS,S/AS01 MALARIA VACCINATION PROGRAM IN MALAWI

Jobiba Chinkhumba[1], Saviour Mphande[1], Tabitha Kaunda[1], Christopher Stanley[1], Harrison Msuku[1], Clarissa Valim[2], Terrie Taylor[3], Don Mathanga[1]

[1]Kamuzu University of Health Sciences, Blantyre, Malawi, [2]Department of Global Health, Boston University School of Public Health,, Boston, MA, United States, [3]College of Osteopathic Medicine, Michigan State University,, Ann Arbor, MI, United States

Costs are increasingly considered key outcomes in implementation research given their importance in informing health intervention programmatic decisions. We assessed implementation costs of a school-based RTS,S/AS01 vaccination program piggybacked on a trial assessing the effects of vaccinating school-aged children in 5 primary schools in Malawi. In the trial, learners aged 6 to 16 years received 3 doses of RTS,S/AS01 vaccines administered by health workers at monthly intervals. The present study

objectives were to estimate the total start-up and post start-up costs for the school-based RTS,S/AS01 vaccination program, cost per fully vaccinated learner and project total costs of implementing the program at national level. We adopted a provider perspective, combining Ministry of Health and Ministry of Education perspectives. Micro-costing approach was used to identify, quantify and value resources used for the main strategy activities including micro-planning, training of health workers, community mobilization and sensitization, procurement and delivery of RTSS vaccines. Trial related costs were precluded. The total costs for the school-based RTS,S/AS01 vaccination program were $23,141. Of this, $7,846 (34%) were incurred during the start-up phase. During this phase, community mobilization and sensitization, health worker trainings, briefings of health facility and district executive members were the main cost drivers accounting for 52, 27 and 8% of the cost, respectively. For the post-start-up phase, RTSS vaccines and supplies, health worker allowances and supervision were the main cost drivers accounting for 79, 16 and 5% of the costs, respectively. The average costs per learner with 1, 2 and 3 RTS,S/AS01 doses (fully vaccinated) were $11.72, $13.51 and $14.75, respectively. [Work is ongoing to extrapolate costs at national level]. School-based RTSS malaria vaccine delivery strategy appears a low cost intervention to implement and may be affordable at scale. Implementation strategy re-configuration focusing on cost driving activities has the potential to improve efficiencies and further lower implementation costs.

6519

RHESUS MODELS FOR PRE-ERYTHROCYTIC STAGE SPOROZOITE VACCINES AGAINST MALARIA

Sumana Chakravarty[1], Natasha KC[1], Jonathan Herman[2], Brandon Wilder[3], Stephen L. Hoffman[1]

[1]Sanaria Inc., Rockville, MD, United States, [2]The Ragon Institute of Mass General, MIT, and Havard, Cambridge, MA, United States, [3]Oregon Health & Science University, Portland, OR, United States

There are no animal models or *in vitro* assays that indicate a human will be protected against malaria by a pre-erythrocytic stage sporozoite(SPZ) vaccine. Based on murine models, the prevailing hypothesis is that protective immunity is mediated by antigen specific, tissue resident CD8+ T cells in the liver. This hypothesis correlated well when CD8+ T cell responses in the livers of rhesus macaques immunized IV or subcutaneously with *Plasmodium falciparum* (Pf) SPZ were compared with clinical efficacy of PfSPZ Vaccine administered by these routes. We performed protective efficacy studies in rhesus macaques with vialed, cryopreserved *P. knowlesi* (Pk) SPZ administered IV, to develop a reliable model to interrogate protective immunity in the liver that cannot be addressed in humans. In the 1st study with irradiated PkSPZ we achieved 66% (4/6) sterile protection at 8 weeks after last vaccination (3 doses of 10^6 PkSPZ), and a significant difference compared to controls in pre-patent period in non-protected macaques. The 2nd and 3rd studies used infectious PkSPZ co-administered with chloroquine (PkSPZ-CVac [CQ]), that provides increased breadth and magnitude of protective antigens since the parasite replicates in the host, but is arrested in the blood. In these studies, we achieved sterile protection of 50% (3/6) at 13 weeks (3 doses of $2x10^5$ PkSPZ) and 60% (3/5) at 12 weeks (3 doses of $4x10^5$ PkSPZ) after last immunization and a significant delay in pre-patency in unprotected animals. In the 4th study, we immunized with a Pf vaccine, PfSPZ-LARC2 which overcomes the logistic limitations of administering chloroquine with PfSPZ-CVac and there was no cross-species protection against challenge with PkSPZ. These data demonstrate it is more difficult to achieve high-level protection with PkSPZ immunization in rhesus than with PfSPZ Vaccine or PfSPZ-CVac (CQ) in humans, with the latter demonstrating 100% vaccine efficacy at 10-12 weeks with 3 doses of $5x10^4$ to $2x10^5$ PfSPZ. The reasons for this and the results of systems immunology/serology assessments of the sera, PBMCs, and lymphocytes from the liver and spleen will be presented.

6520

PFSPZ VACCINE ELICITS PFCSP ANTIBODIES THAT CROSS-REACT WITH OTHER *PLASMODIUM FALCIPARUM* PROTEINS AND CORRELATE WITH PROTECTION FROM MALARIA

Andrea A. Berry[1], Olukemi O. Ifeonu[1], DeAnna J. Friedman-Klabanoff[1], Jozelyn Pablo[2], Andy Teng[2], Adam D. Shandling[1], Sumana Chakravarty[3], Richard S. Pinapati[4], Jigar J. Patel[4], John C. Tan[4], Xiaowu Liang[2], Philip L. Felgner[5], Mark A. Travassos[1], Matthew B. Laurens[1], Christopher V. Plowe[1], Shannon Takala Harrison[1], Azza H. Idris[6], Robert A. Seder[6], Stephen L. Hoffman[1], Kirsten E. Lyke[1], Joseph J. Campo[2]

[1]University of Maryland School of Medicine, Baltimore, MD, United States, [2]Antigen Discovery Inc., Irvine, CA, United States, [3]Sanaria Inc., Rockville, MD, United States, [4]Nimble Therapeutics, Madison, WI, United States, [5]University of California, Irvine, Irvine, CA, United States, [6]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States

Two WHO-approved malaria vaccines, RTS,S and R21, are subunit vaccines containing a fragment of the *Plasmodium falciparum* (Pf) circumsporozoite protein (CSP). Such vaccines mediate protection at the liver stage of infection that wanes over time. Enhancing the breadth of vaccine-induced immunity may improve efficacy and durability of next-generation vaccines. PfSPZ Vaccine is comprised of live, attenuated sporozoites, presents thousands of Pf proteins in addition to PfCSP, and has also been shown to be protective at the liver stage of infection. We conducted parallel seroprofiling studies of PfSPZ Vaccine-induced antibody responses in 3 clinical trials of PfSPZ Vaccine on (1) whole protein and (2) linear peptide microarrays. We tested baseline and post-vaccination sera from a subset of 42 malaria naïve participants: all received 3 or 4 doses of PfSPZ Vaccine followed by controlled human malaria infection (CHMI) three weeks later. Following vaccination and CHMI, 29 vaccinees demonstrated sterile protection. Protein and peptide microarrays identified 22 and 75 immunoreactive proteins respectively and a common subset of 5 proteins for which antibody responses were higher in protected vs. not-protected vaccinees: CLAMP (PF3D7_1030200), MSP5 (PF3D7_0206900), DOC2 (PF3D7_1211200), GSK3 (PF3D7_0312400), and an uncharacterized protein (PF3D7_0720500). Peptide sequences associated with differential antibody responses were found to have sequence homology with PfCSP. Two PfCSP-binding monoclonal antibodies, mAb4 and mAb10, also bound the same 5 proteins and putative epitopes, suggesting that some antibody responses to PfSPZ Vaccine elicited by PfCSP are cross-reactive with multiple other Pf proteins. Hierarchical clustering grouped cross-reactive responses into high and low groups with a higher proportion of protected vaccinees clustering into the high group. This work highlights the importance of considering the possibility of broadly cross-reactive antibodies in seroprofiling studies and demonstrates a correlation between broad seroreactivity and vaccine efficacy.

6521

RESULTS FROM A PHASE III STUDY TO ASSESS THE SAFETY, IMMUNE RESPONSE, AND LOT-TO-LOT CONSISTENCY OF EUTCV SINGLE-DOSE AND MULTI-DOSE FORMULATION COMPARED TO THE COMPARATOR VACCINE TYPBAR-TCV® IN HEALTHY AFRICAN ADULTS AND YOUNG CHILDREN 6 MONTHS TO 45 YEARS OF AGE

Birahim Pierre Ndiaye[1], Lucy Koech[2], Ndeye Sakha Bob[3], Niles Eaton[4], Winnie Keter[2], Siry Diye[1], Badara Cissé[1], Vajra Allan[4], Yeong Ok Baik[5], Chankyu Lee[5], Howard Her[5], Sookyung Kim[5], YoungJin Choi[5], Moussa Dia[6], Emily Locke[7], Gamou Fall[6], John J. Aponte[8], **Patricia Njuguna**[9]

[1]L'Institut de Recherche en Santé, de Surveillance Épidémiologique et de Formations, Dakar, Senegal, [2]Kenya Medical Research Institute -Walter Reed Army Institute of Research, Kericho, Kenya, [3]Institut Pasteur of Dakar,, Dakar, Senegal, [4]PATH, Seattle, WA, United States, [5]Eubiologics, Seoul,

Korea, Republic of, [6]Institut Pasteur of Dakar, Dakar, Senegal, [7]PATH, Washington, DC, United States, [8]PATH, Geneva, Switzerland, [9]PATH, Nairobi, Kenya

Typhoid fever remains an important public health problem, especially in low- and middle-income countries (LMICs). Safe water, sanitation, and hygiene (WASH) interventions alongside vaccines play a vital role in preventing the spread of typhoid. Two conjugate vaccines against *Salmonella enterica* serovar Typhi (*S*. typhi), which have been administered to millions of children and shown to be safely co-administered with other routine childhood vaccines, have been prequalified by the World Health Organization (WHO). Previous studies demonstrated the comparable safety and reasonable immunogenicity of a third vaccine, EuTCV (EuBiologics Co. Ltd.), relative to other typhoid conjugate vaccines when delivered as a single dose. This Phase III study (PACTR202112680671189), conducted at IRESSEF at Sandiara, Senegal, and KEMRI/WRP at Kericho, Kenya, enrolled 3,219 healthy African adults and young children 6 months to 45 years of age to assess the safety, immune responses, and lot-to-lot consistency of EuTCV single-dose and multi-dose presentations. Measles-rubella and yellow fever vaccines were co-administered to infants aged 9 to 12 months (Cohort 3, n=1,012), alongside the typhoid conjugate vaccine. The objectives of the study were to evaluate: i) non-inferiority of single-dose and multi-dose vial formulations of EuTCV compared with Typbar TCV® at 28 days post-vaccination in Cohort 3 and ii) the safety of single-dose and multi-dose vial formulations of EuTCV compared to that of Typbar TCV® in all participants. Throughout the study, all participants were followed for safety, with reporting on local and systemic adverse reactions 7 days post-vaccination, unsolicited adverse events 28 days post-vaccination, and serious adverse events during the entire study period until Day 181. In Cohort 3, immunogenicity assessments included typhoid (anti-Vi polysaccharide geometric mean titer and seroconversion rates 28 days and 6 months post-vaccination) and seroconversion rates following measles, rubella, and yellow fever vaccination. We report the results of this Phase III study which will be submitted as part of the PQ dossier.

6522

MOLECULAR CHARACTERIZATION OF MULTIDRUG RESISTANCE *E.COLI* RECOVERED FROM DIARRHEAGENIC CHILDREN UNDER FIVE YEARS FROM MUKURU INFORMAL SETTLEMENT, NAIROBI, KENYA, BASED ON WGS ANALYSIS

Susan W. Kiiru, Purity Kasiano, John Mwaniki, Samuel Kariuki
Kenya Medical Research Institute, Nairobi, Kenya

High genomic plasticity within *E. coli* enables it to acquire and accumulate genetic material through horizontal gene transfer. In this study, we sought to investigate the virulence genes, phylogroups, antibiotic resistance genes, plasmid replicons, MLST, and cgMLST of multidrug-resistant E.coli recovered from diarrheagenic children under five years from Mukuru Informal Settlement, Nairobi Kenya. A total of 26 MDR strains had their DNA extracted, and Whole Genome Sequencing was done using the Illumina HiSeq 2500 platform. Twenty-six *E.coli* assemblies were analyzed using web-based bioinformatics tools at the Centre for Genomic Epidemiology and EnteroBase. The isolates were categorized into four main phylogroups, where 10/26 (38.5%) belonged to the B2 phylogroup, 4/26 (15.4%) belonged to D, 3/26 (11.5%) belonged to A, 1/26 (3.8%) belonged to B1, while 8/26 (30.8%) were not determined. FimH30 was predominantly found in the most frequent phylogroup B2 and Sequence Type(ST) 131. The most common Beta-lactam resistance genes were $bla_{\text{Tem 1B}}$ and $bla_{\text{CTXM 15}}$, followed by fluoroquinolone resistance genes (*qnrS1* 6/26(23.1%), *qnrB4* 2/26 (7.7%), and *aac(6')-Ib-cr,* 8/26(30.8%)). A total of 40 diverse virulence genes were detected among the isolates. 13 different STs were isolated from the *E. coli* genomes, which included ST 131, ST 3036, ST 38, ST 10, ST 12569, ST 15271, ST 2076, ST 311, ST 3572, ST 394, ST 453, ST 46 and ST 1722. Only two isolates (2/26, 7.7%) from the Municipal City Council (MCC) clinic were genetically related. Additionally, the most abundant plasmid replicon identified belonged to the IncF family followed by the Col family. Of 26 isolates, 15 had at least one nonsynonymous mutation in the housekeeping genes *gyrA (p.S83L), gyrA (p.D87N), parC (p.S80I), parC (p.E84V), parC(p.S57T),* and *parE(p.I529L),* associated with resistance to fluoroquinolones. The study highlighted the first *E.coli* ST46 to harbor the *NDM5* gene encoded in Col(BS512), IncFII(pRSB107), and IncFIB(AP001918) plasmid replicons in Kenya. We further demonstrated the diversity of MDR *E. coli* associated with diarrhea in an endemic setting in Kenya.

6523

ASSOCIATION OF GUT REDOX POTENTIAL WITH SEVERE ACUTE MALNUTRITION AND STUNTING IN HOSPITALIZED CHILDREN

Md. Shabab Hossain
International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh

Redox potential is a composite measurement of factors influencing gut microbiota. Secretion of reactive oxygen species from gut epithelium in response to intestinal injury, chronic infections and inflammation increases gut redox potential. This imposes 'oxidative stress' leading to gut dysbiosis characterized by decline in beneficial microbes like *Bifidobacterium* accompanied by increase in aerotolerant pathogens like *Enterobacteriaceae*, resulting in diarrhea and malnutrition. Furthermore malnutrition, specifically severe acute malnutrition (SAM), is associated with inadequate intake of energy as well as qualitative lack of micronutrients leading to low antioxidant levels, again increasing gut redox potential and oxidative stress. This altered redox dynamics and invasion by aerotolerant bacterial pathogens highlight the need for antibiotics that further promote gut dysbiosis. This creates a vicious cycle of oxidative stress, gut dysbiosis and malnutrition. In this study, we aimed to explore the association of gut redox potential with malnutrition among 6-24 months old hospitalized children. This cross-sectional study was conducted on 200 children aged between 06-24 months getting admitted in icddr,b Dhaka Hospital and Dhaka Shishu Hospital. 50 of these children had weight-for-length Z scores (WLZ) <-3, and were considered as the SAM group. Anthropometric, socio-demographic and food frequency questionnaire data was recorded and 2g of stool was collected for assessing gut redox potential using redox meter. The mean gut redox potential for stunted and SAM children was 183.92±22.36 and 191.68±25.98; while the same for non-stunted and non-SAM children was 178.11±24.75 and 175.91±22.23, respectively. After inclusion of factors affecting malnutrition into the multivariate linear regression model, a statistically significant association was observed between gut redox potential and SAM ($p<0.05$; OR 1.02; 95% CI 1.01-1.05). The mean gut redox potential was higher in stunted children and significantly higher in children suffering from SAM. Increased gut redox potential was found to have a significant association with SAM.

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GENOTYPIC DIVERSITY AND ANTIMICROBIAL RESISTANCE DETERMINANTS *IN SALMONELLA* TYPHI ISOLATED FROM CHILDREN LIVING IN INFORMAL SETTLEMENTS IN NAIROBI, KENYA

Susan K. Kavai[1], Julius Oyugi[2], Cecilia M. Mbae[1], Sylvia Omulo[2], Samuel M. Kariuki[1]
[1]Kenya Medical Research Institute, Nairobi, Kenya, [2]University of Nairobi, Nairobi, Kenya

Whole genome sequencing (WGS) is a tool for disease diagnostics and identification of multi-drug resistant genotypes of enteric pathogens globally. In typhoid-endemic regions, WGS of *Salmonella* Typhi (*S*. Typhi) has identified haplotype 58 as one of the dominant MDR haplogroups. This case-control study reported on AMR and genotypic diversity of *S*. Typhi from children in Mukuru and Kibera informal settlements. From 2013 to 2018, children ≤ 16 years in 4 health facilities in Nairobi County were recruited if they had a fever; $\geq 38^0$C with or without diarrhea. Controls were recruited if they came for vaccinations and presented with non-typhoid-related symptoms. All participants provided stool samples that were

subjected to culture and antimicrobial susceptibility testing for phenotypic analysis of AMR. *S*. Typhi isolates that showed resistance to ampicillin, co-trimoxazole, and chloramphenicol were considered as MDR and subjected to WGS. DNA of 90 *S*. Typhi was extracted for WGS. Sequencing was done using Illumina Nextseq2000 platform. The raw reads were *de novo* assembled and pathogen-watch was used for analysis. Of the sequenced isolates, 60(67%) were confirmed to be *S*. Typhi. All of the *S*. Typhi belonged to the sequence Type 1 and genotype 4.3.1 (Haplotype 58). Out of the 60 *S*. Typhi strains 40(67%) were found to have plasmids, out of which 38(95%) had the IncHI1A/IncHI1B (R27) plasmids. The distribution of *S*. Typhi in cases and controls was; 31(51%) and 30(49%). The 60 *S*. Typhi isolates were observed to have AMR determinants of 6 antibiotics with ampicillin (*bla TEM-1D*) as the most common; 59 (98%) of the isolates. Point mutations conferring reduced susceptibility to quinolones were detected in 42 (70%) of *S*. Typhi isolates, 14(33%) *gyrA_S83Y*, and 28/42 (67%) *gyrB_S464F*.This study reports 4.3.1 (H58) as the most dominant *S*. Typhi genotype. It is evident that H58 is responsible for the spread of MDR phenotypes that carry on IncHI1 plasmids. Circulation of H58 *S*. Typhi genotypes in Mukuru and Kibera informal settlements especially among asymptomatic individuals reiterates the need for mass vaccination as a control and prevention measure of Typhoid fever.

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SEROCONVERSION AND KINETICS OF VIBRIOCIDAL ANTIBODIES DURING THE FIRST 90 DAYS OF RE-VACCINATION WITH ORAL CHOLERA VACCINE IN AN ENDEMIC POPULATION

Caroline C. Chisenga[1], Bernard Phiri[1], Harriet Ngombe[1], Mutinta Muchimba[1], Kalo musukuma Chifulo[1], Suwilanji Silwamba[1], Natasha Makabilo Laban[1], Charlie Luchen[1], Fraser Liswaniso[1], Kennedy Chibesa[1], Cynthia Mubanga[1], Kapambwe Mwape[1], Michelo Simuyandi[1], Adam Cunningham[2], David Sack[3], Samuel Bosomprah[1]

[1]Centre for Infectious Disease Research in Zambia, Lusaka, Zambia, [2]Institute of Immunology and Immunotherapy, University of Birmingham, Edgbaston, Birmingham, B15 2TT, Birmingham, United Kingdom, [3]Johns Hopkins University, Baltimore, MD, United States

Despite the successful introduction of oral cholera vaccines, Zambia continues to experience multiple, sporadic, and protracted cholera outbreaks in various parts of the country. While vaccines have been useful in staying the cholera outbreaks, the ideal window for re-vaccinating individual's resident in cholera hotspot areas remains unclear. Using a prospective cohort study design, 225 individuals were enrolled, re-vaccinated with two doses of Shanchol™ regardless of previous vaccination and followed-up for 90 days. Bloods collected at baseline before re-vaccination, at day 14 prior to second dosing and subsequently on days 28, 60, and 90. Vibriocidal assay was performed on samples collected at all five time points. Our results showed that anti-LPS and vibriocidal antibody titers increased at day 14 after re-vaccination and decreased gradually at 28, 60 and 90 across all the groups. Seroconversion rates were generally comparable in all treatment arms. We therefore conclude that vibriocidal antibody titers generated in response to re-vaccination still wane quickly irrespective of previous vaccination status. However, despite the observed decline, the levels of vibriocidal antibodies remained elevated over baseline values across all groups, an important aspect for Zambia where there is no empirical evidence as to the ideal time for re-vaccination.

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ETIOLOGY OF DIARRHEAL DISEASE CAUSING SEVERE DEHYDRATION IN INFANTS AND YOUNG CHILDREN RESIDING IN LOW AND MIDDLE INCOME COUNTRIES

Anna Jones[1], Sharia M. Ahmed[1], Ashraful I. Khan[2], Karen L. Kotloff[3], James A. Platts-Mills[4], Eric F. Nelson[5], Daniel T. Leung[1]

[1]University of Utah, Salt Lake City, UT, United States, [2]icddb, r, Dhaka, Bangladesh, [3]University of Maryland, Baltimore, MD, United States, [4]University of Virginia, Charlottesville, VA, United States, [5]University of Florida, Gainesville, FL, United States

Acute infectious diarrhea remains a leading cause of death among young children, especially in low- and middle-income countries (LMICs). Given the limitations of available diagnostic testing in LMICs, a clinical syndrome or case definition frequently informs pediatric diarrheal illness management. Diarrhea with severe dehydration is a clinical syndrome with distinct clinical management per the World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) and the Global Task Force on Cholera Control (GTFCC) guidelines. We sought to characterize the pathogens in this group specifically using data from the Global Enteric Multicenter Study (GEMS). GEMS was a three-year prospective, case-control study of children aged 0-59 months with moderate-to-severe diarrhea (MSD) at seven sites in sub-Saharan Africa and South Asia. We used quantitative real-time PCR-based (qPCR) majority attribution models to assign the etiology of diarrhea as well as both IMCI and GTFCC guidelines to define severe dehydration. Among the 5304 cases of MSD with qPCR results, the IMCI or GTFCC guidelines classified 2,284 (43%) of the cases as having severe dehydration. Approximately one third of the cases with severe dehydration did not have any attributable pathogens (33% for the IMCI definition, 35% GTFCC). Pathogens attributed to severely dehydrated cases of diarrhea varied by age group. Rotavirus (30.9%), *Cryptosporidium* (12.0%), and ST-ETEC (10.3%) were the top pathogens for ages 0-11 months compared to *Shigella* (25.8%), rotavirus (19.3%), and ST-ETEC (10.3%) for those ages 12-23 months and *Shigella* (25.9%), *V. cholerae* (10.4%), and rotavirus (9.2%) for those ages 2-5 years. Most of the top pathogens attributed to severe dehydration were similar to those attributed to MSD for each age group. However, several pathogens, notably adenovirus and *H. pylori* were less frequently attributed to severe dehydrating MSD than to MSD overall. Vaccine and treatment advances should be targeted at pathogens associated with severe dehydration, given the potential morbidity caused by severe dehydration.

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ANTIRADICAL SCAVENGING AND UREASE INHIBITION POTENTIALS OF *DICTYOPHLEBA SETOSA* (APOCYNACEAE) AND ISOLATION OF ITS CHEMICAL CONSTITUENTS TOWARDS MANAGEMENT OF GASTRIC AND PEPTIC ULCERS CAUSED BY *HELICOBACTER PYLORI* ACTIVITIES

Akuma Michael Nde[1], Pantaleon Ambassa[1], Bathelemy Ngameni[1], Mehmet Emin Duru[2]

[1]University of Yaounde 1, Yaoundé, Cameroon, [2]Mugla Sitki Kocman University, Yaoundé, Turkey

This study is design to determine the antiradical scavenging and Urease inhibition potentials of *Dictyophleba setosa*, a medicinal liana native to central Africa used traditional as a vermifuge in children, as an alternative to manage peptic and gastric ulcers. The antiradical potentials of the DCM/MeOH crude extracts of the leaves (DSL), stem bark (DSS) and roots (DSR) of *Dictyophleba setosa* were determined by five different complementary methods (DPPH, CUPRAC, $ABTS^{\bullet+}$, metal chelating and β-carotene-linoleic acid assays). DSS showed to be a more powerful antioxidant compared to the standards BHA and α-tocopherol in the $DPPH^{\bullet}$, $ABTS^{\bullet+}$ and CUPRAC assays. That is, DSS (IC_{50} = 7.13 ± 0.21; IC_{50} =5.22 ± 0.53; IC_{50} =5.80 ± 0.12 µg/mL) respectively is at least 5 times more active than α-tocopherol and at least 2 times more active than BHA (IC_{50} = 19.82 ± 0.33; IC_{50} = 12.80 ± 0.08; IC_{50} = 25.50 ± 0.43 µg/mL) respectively. The urease enzyme

inhibition potentials of extracts carried out by determination of the amount of ammonia produced using the Indophenol method displayed IC_{50} values ranging from 30.48 ± 0.62 to 11.23 ± 0.38 µg/mL compared to Thiourea (IC_{50} = 8.15 ± 0.33 µg/mL) as standard among which DSS was the most potent. Purification of DSS using standard chromatographic techniques led to the isolation of fifteen secondary metabolites whose structures were elucidated by analysis of their spectroscopic data, three of which are reported for the first time. The isolates will be further evaluated for their urease enzyme inhibitory activity. These findings clearly indicate that the stem bark extract of *Dictyophleba setosa* can be used in the traditional pharmacopeia to prevent/manage gastric and peptic ulcers by inhibition of urease enzyme produced by *Helicobacter pylori.*

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PREVENTION AND MANAGEMENT OF TRAVELERS' DIARRHEA IN AN INTERNATIONAL WORKER IN GLOBAL OIL AND GAS COMPANY

Candace McAlester, Susan Ngunjiri, Joyce Ighedosa, Elijah Akpomrughe, Jas Dadhra, Patricia Sviech, Valeria Gomez
ExxonMobil Corp, Spring, TX, United States

According to CDC, Travelers' diarrhea (TD) occurs in 30%-70% of travelers during a 2-week travel period, depending on the destination and season of travel. ExxonMobil (EM) has a global workforce with both short and long-term international travelers to areas with varied risks throughout the year. TD interferes with travel itineraries and business prospects, causing loss in productivity from absences. There may be significant medical costs with complications requiring hospitalization. TD results from ingestion of contaminated food and/or water and is defined as 3 or more loose stools in 24-hour period. In 2023 EM had over 61,007 international business trips in over 134 countries with majority of the locations with high-risk for travelers' diarrhea. The company has a robust pre-travel health process, which educates international travelers on disease prevention and health promotion. The pre-travel process includes a country-specific risk assessment, immunizations, medications, and travel education., ExxonMobil's global Emergency Medical Response System (EMERS), a 24-hour medical assistance for business travelers, provides mitigative services ranging from telephone consultation to medical evacuation. Highlight pre-travel health preparation including identifying health risks and education of preventive practices for TD. Retrospective review of annual EMERS calls for medical assistance from 2023, with focus on gastrointestinal related services. In 2023, 30% of travelers visited sites with increased risk for food and water borne diseases. Out of 217 EMERS calls, gastrointestinal illness (20) was the second most common health concern recorded. Over 9% of medical calls made where related to gastrointestinal disease such as gastroenteritis. The pre-travel health consultation is effective in preventing significant cases of TD. EM had only 9% of EMERS calls for gastrointestinal diseases and there was adequate mitigative response from travelers. A comprehensive travel preparation contributes towards achieving minimal cases, and no occurrence of serious illness events from TD cases.

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THE VALIDATION OF A LOW COST STOOL SPECIMEN PRESERVATION METHOD, COMPARING TIME AND TEMPERATURE STORAGE CONDITIONS

Amanda K. Debes[1], Jamie Perin[1], Jie Liu[2], Wensheng Luo[1], David A. Sack[1], Nicola Page[3], Camille Williams[1]
[1]JHSPH, Baltimore, MD, United States, [2]School of Public Health, Qingdao University, Qingdao, China, [3]3Centre for Enteric Diseases, NICD, NHLS, Sandringham, South Africa

Testing the nucleic acid (NA) from dried stool spots (DSS) on filter paper provides a simple method to detect enteric pathogens., especially in low-resource settings where cold-chain transport is not always available. The NA is stable, the samples are easily collected, stored, transported, and processed. We used qPCR to document the stability of NA on DSS samples over various times and temperatures. We prepared DSS samples with stools from patients infected with *Shigella* spp. (double-stranded bacterial DNA), rotavirus (double-stranded RNA virus) and norovirus (single-stranded RNA virus) on Whatman903 filter paper and compared to the gold standard, Qiagen-extracted stool samples. We will compare Qiagen-extracted NA from 200ul of frozen stool and 20ul stool-spotted filter specimens spotted the same day (Time Zero, T0), and stored at room temperature, 4°C, -20°C or -80°C. To date, we have evaluated the samples after 3 - 6 months of storage. The results suggest that NA extracted from *Shigella* spp. DSS had similar CT regardless of temperature of storage compared to Qiagen-extracted NA. Interestingly, rotavirus DSS had a lower CT at all temperatures (Mean CT: 20.62 at T0, 20.10 at RT, 20.49 at 4°C, 20.17 at -20°C, 20.37 at -80°C, $p<0.001$) when compared to Qiagen-extracted NA (mean CT 26.86). In contrast, norovirus DSS showed a significantly higher CT compared to Qiagen-extracted samples (Mean CT: 29.53 at T0, 30.12 at RT, 29.77 at 4°C, 29.44 at -20°C, 29.44 at -80°C versus CT 26.28, $p<0.001$). These results suggest that for a minimum of 3-6 months, NA on DSS samples is stable at RT for *Shigella* spp. and rotavirus detection, but there may be some loss in detection of norovirus when using DSS. However, we observed the loss is stable across all filter paper specimens, including T0. This suggests that degradation may occur during the initial spotting, with subsequent stability across time and temperature, suggesting that norovirus can also be preserved over time. These initial results show that DSS samples stored at room temperature may provide a simple method to enhance stool collection in global surveillance networks for diarrheal diseases.

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ANTIMICROBIAL RESISTANCE AND INTESTINAL SHEDDING OF NONTYPHOIDAL *SALMONELLA* AMONG CHILDREN UNDER FIVE YEARS AND CARRIAGE IN ASYMPTOMATIC HOSTS IN KENYA

Kelvin Kimutai Kering[1], Celestine Wairimu[1], Georgina Odityo[1], Kariuki Njaanake[2], Marianne Mureithi[2], Cecilia Mbae[1], Samuel Kariuki[1]
[1]Kenya Medical Research Institute, Nairobi, Kenya, [2]University of Nairobi, Nairobi, Kenya

Nontyphoidal *Salmonella* (NTS) infection is characterized by self-limiting enterocolitis, but can become invasive resulting in bacteremia. *Salmonella enterica* serovars Typhimurium and Enteritidis (*S*. Typhimurium and *S*. Enteritidis) are the most common causes of NTS with the highest incidences reported in sub-Saharan Africa and in children ≤ 5 years. Since intestinal shedding could serve as a potential source of new infections in vulnerable individuals, this study aimed to determine rates of post-convalescent shedding in children under five years of age and corresponding age-matched controls in the community. This was a prospective case-control study in children from the Mukuru Informal settlement in Nairobi, between June 2021 and April 2023. Children presenting with fever for > 24 hours with or without diarrhoea were recruited. Blood and stool were collected, subjected to culture for NTS isolation, and identified through serology and PCR. Disk diffusion method was used to determine the antimicrobial susceptibility to 14 commonly used antibiotics. Fourteen days post-treatment, index cases, their household contacts, and randomly selected controls were followed up for a minimum of one month. Follow-up was stopped after three consecutive negative cultures from the stool. Of the 3,057 participants, 1.5% (46) were NTS-positive with 58.7% (27/46) being male. The positivity rate per age group was: ≤ 12 months (1.7%), 13-24 months (1.7%), 25-36 months (1.1%), 37-48 months (0.7%), and 49-60 months (2.2%). Intestinal shedding was observed in 26.1% (12/46) of the index cases with 66.7% of those being male. The longest duration of intestinal shedding was three months post-treatment. Among the healthy individuals, 3.7% were found to be shedding NTS. Resistance to Azithromycin, the current drug of choice for the treatment of invasive NTS, was observed in 13.8% of *S*. Typhimurium and 8.9% of *S*. Enteritidis with reduced susceptibility in 72.4% of *S*. Typhimurium and 82.2% of *S*. Enteritidis. This study demonstrates the need for vaccine introduction in the prevention of invasive NTS infections especially among young children in endemic settings.

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THE ROLE OF FERMENTED PICKLE CONSUMPTION ON THE GUT MICROBIOME OF WOMEN OF REPRODUCTIVE AGE IN RURAL PAKISTAN

Sumbal Hafeez Haris, Najeeha Iqbal, Aqsa Khalid, Juanid Iqbal, Sheraz Ahmed, Furqan Kabir, Syed Asad Ali

Aga Khan University, Karachi, Pakistan

Gut microbiota-targeted diets can modulate microbial community and immune system, potentially preventing multiple health conditions linked to gut dysbiosis. Fermented foods containing Lactic Acid Bacteria (LAB) benefit the host by enhancing the availability of bioactive compounds and improving the gut microbiome. This study aimed to evaluate the effect of traditional fermented pickle consumption on the gut microbiome of women of reproductive age (WRA). In eight weeks of an intervention trial, a total of 210 healthy WRA were recruited from rural Matiari, Pakistan, and were divided into one control and 6 intervention groups (30 each) provided with fermented onion, radish, carrot, lemon-chili, water-based, and oil-based mango pickles respectively. Pre-intervention (week 0), end-of-intervention (week 8), and post-intervention (week 12) stool samples were collected. Among Onion and Lemon-chili (LC) intervention groups, 16S microbiome analyses showed a significant increase in α diversity [Observed α diversity at 0, 8, and 12 weeks: Onion (p= 0.01), LC (p=0.0005)] and variation in ß diversity [Onion: 0 to 8 weeks (p= 9e-04) and 0 to 12 weeks (p= 0.02), LC: 0 to 8 weeks (p= 0.02) and 0 to 12 weeks (p= 0.01)]. Most of the bacteria detected post-intervention belonged to *Actinobacteria* and *Firmicutes*. The linear discriminant analysis (LDA) at cut-off =2 showed an increase in *Actinobacteriota* (Week 8) and *Olsenella*, *Singui*, and *Intestinobacter* (week 12) among Onion while *Eggerthellaceae*, *Oscillospiraceae, Burkholderiales, Sutterellaceae, Coprococcus, Isoflavoniconvertens, Ruminococcaceae* (week 8) and *Erysipelatoclostridiaceae, Subdoligranulum, Marvinbryantia, and Fusicatenibacter* (week 12) among LC participants. Hence, fermented onion and lemon-chili pickles can be an affordable and socially acceptable microbiota-targeted diet that can potentially improve gut microbiota in WRA belonging to malnourished settings. Further studies will inform about the usefulness of such interventions for alleviating gut disorders.

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MISSED OPPORTUNITIES OF SYNDROME-BASED DIARRHEA MANAGEMENT GUIDELINES TO DETECT NON-DYSENTERIC *SHIGELLA* INFECTIONS IN KENYAN CHILDREN: FINDINGS FROM THE ENTERICS FOR GLOBAL HEALTH -*SHIGELLA* SURVEILLANCE STUDY, 2022-2024

Alex Ondeng Awuor[1], **Alex Ondeng Awuor**[1], Richard O. Omore[1], Billy Ogwel[1], Patricia B. B. Pavlinac[2], Hannah E. Atlas[3], Sharon M. Tennant[4], Karen Kotloff[5], John B. Ochieng[1], Sean R. R. Galagan[6]

[1]KEMRI, KISUMU, Kenya, [2]University of Washington, ,, Seattle, Washington, WA, United States, [3]University of Washington, ,, Seattle, WA, United States, [4]University of Maryland School of Medicine, Baltimore, MD, United States, [5], University of Maryland School of Medicine, , MD, USA, Baltimore, MD, United States, [6]University of Washington, Seattle,, WA, United States

Current World Health Organization (WHO) guidelines recommend empirical use of antibiotics for children with dysentery, a proxy for suspected *Shigella*-attributed diarrhea. However, recent diarrhea etiology studies have highlighted the major contribution of *Shigella* to watery diarrhea, which is not covered by WHO syndromic guidelines. Leveraging data from the Enterics for Global Health (EFGH) Kenyan site, we quantify the burden of *Shigella* among Medically Attended Diarrhea (MAD) cases, outline the proportion missed by WHO guidelines, and characterize antibiotic management. We enrolled children aged 6-35 months with MAD, collected rectal swabs at enrolment, and tested for *Shigella* using the standard culture method. The susceptibility of *Shigella* isolates to a panel of antimicrobial agents was determined by the Kirby-Bauer disk diffusion method and the results were relayed back to clinicians to guide further management. We used logistic regression to estimate the odds of *Shigella* positivity based on dysentery. Between August 2022 to March 2024**,** we enrolled 1,158 MAD cases, of whom 66 (5.7%) had culture-positive *Shigella*. Nearly a quarter (15 of 73, 20.6%) of dysentery cases were *Shigella* positive compared to 51 of 1,084 (4.7%), watery diarrhea (odds ratio=5.24, 95% confidence interval 2.78-9.87). Although all 15 dysenteric cases were treated according to WHO guidelines, 43 of 51 (84.3%) non-dysenteric were not treated as per WHO guidelines. Among these non-dysenteric cases, 33 of 43 (76.7%) were prescribed other antibiotics with the leading antibiotics being metronidazole (34.9%), cotrimoxazole (25.6%), and amoxicillin (23.3%) which are not recommended for treatment of shigellosis. However, treatment of *Shigella* cases was revised based on culture and susceptibility results where appropriate Our data highlighted a substantial proportion of culture-positive *Shigella* cases are missed by WHO dysentery-based guidelines. Majority of children with *Shigella* and no dysentery ended up receiving an ineffective antibiotic. An effective *Shigella* vaccine holds promise for reducing not only diarrhea but also antibiotic use.

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DEVELOPMENT OF A RAPID, PORTABLE PCR ASSAY FOR *SHIGELLA* SEROTYPING

Fahad Khokhar[1], Vignesh Shetty[2], Madhumathi Irulappan[3], Dhivya Murugan[3], Agila Pragasam[3], Jobin J. John[3], Balaji Veeraraghavan[3], Xiaoliang Ba[1], Ankur Mutreja[1], Hilary MacQueen[4], Sushila Rigas[4], Kate S. Baker[1], Mark Holmes[1]

[1]University of Cambridge, Cambridge, United Kingdom, [2]Wellcome Sanger Institute, Hinxton, United Kingdom, [3]Christian Medical College, Vellore, India, [4]The Open University, Milton Keynes, United Kingdom

Shigella species are a major cause of diarrheal disease worldwide, with *S. flexneri* and *S. sonnei* the predominant species in developing countries. Standard serotyping methods alone are expensive, vary in performance and lack the resolution to specific serotypes, which is important for surveillance and vaccine development and evaluation. Here we report the development of a multiplex PCR assay for *Shigella* serotyping, focussing on the proposed vaccine targets of *S. flexneri* 2a, 3a, 6 and *S. sonnei*. A total of 38 DNA samples were included in the initial screening (*S. flexneri* [n=22], *S. sonnei* [n=6], *S. boydii* [n=5] and *S. dysenteriae* [n=5]), and results compared to standard antisera serotyping method. Of the 38 samples tested, 34 (89.5%) had consistent results between phenotypic serotyping and PCR. All serotype 2 (*n=5*) and serotype 3 (*n=3*) samples were further classified as 2a (*gtrII* positive, *gtrX* negative) and 3a (*gtrX+oac* positive) respectively. Additionally, all six serotype 1 samples were initially positive for only the *oac* gene indicating serotype 1b. Intriguingly, of the four samples originally classified as serotype 4, samples 09 and 08 were positive for only *ipaH* (serotype Y) and *ipaH+gtrII* (serotype 2a) respectively, and samples 25 and 26 were positive for *gtrX* only (serotype X). All four samples were negative for the serotype 4 *gtrIV* gene marker. ONT sequencing and genomic *in silico* classification with ShigaPass confirmed the PCR results for samples 08 and 26, and identified the *optII* gene (involved in O-antigen modification) in samples 09 and 25, resulting in a WGS-based serotyping of Yv and Xv respectively. Once optimised, further testing will be performed on additional clinical *Shigella* DNA samples, as well as conducting large scale *in silico* screening. Additionally, amplicon detection will be transferred to dipsticks carrying antitags to tagged primers. We will also optimise our assay to work directly on bacterial cultures and clinical samples, to detect these four type strains in any suspected shigellosis sample during surveillance for vaccination programs or outbreak evaluation.

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ANTIBACTERIAL ACTIVITY OF *CORRYOCACTUS BREVISTYLUS* (SANKY) METHANOL EXTRACT AGAINST *STAPHYLOCOCCUS AUREUS* AND *ENTEROCOCCUS FAECALIS*

Ronald Aquino-Ortega[1], Hugo Carrillo-Ng[1], Luz M. Paucar-Menacho[2], Miguel A. Aguilar-Luis[1], Wilmer Silva-Caso[1], **Juana del Valle-Mendoza**[3]

[1]Universidad Peruana de Ciencias Aplicadas (UPC), Lima, Peru, [2]Universidad Nacional del Santa, Ancash, Peru, [3]Universidad Peruana de Ciencias Aplicadas (UPC), lima, Peru

Staphylococcus aureus and *Enterococcus faecalis* are two important pathogens associated with health-care associated infections. In 2017, the WHO published a list of bacteria for which new antibiotics are urgently needed, which included both bacteria in the highest priority group among gram positive bacteria. *Corryocactus brevistylus* (K. Schum. ex Vaupel) Britton & Rose, commonly referred to as Sanky is a Peruvian Cactaceae grown in the Andean regions with antioxidant properties, however, its antibacterial effect has not been studied yet. To determine the antibacterial effect of *Corryocactus brevistylus* (Sanky) methanol extract, against *Staphylococcus aureus* (ATC®25175) and *Enterococcus faecalis* (ATCC®29212). The methanol extract of *Corryocactus brevistylus* was prepared from freeze-dried fruit pulp. Agar diffusion test was used by preparing wells with the experimental solutions cultivated in aerobic conditions for 24 h at 37 °C. Six independent tests were prepared for each type of bacteria, using penicillin-streptomycin and clorhexidine 12% as positive controls. The MIC was determined using the microdilution method as described by the CLSI. Antibacterial effect of the methanol extract was observed with inhibition halos of 23.33 ± 0.72 mm and 24.34 ± 0.55 mm against *Staphylococcus aureus* and *Enterococcus faecalis*, respectively. Meanwhile, penicillin-streptomycin (10 U) showed an inhibition halo of 28.32 ± 2.6 mm and 22.84 ± 1.2 mm, respectively. Clorhexidine 12% produced halos of 26.8 ± 0.4 mm and 24.3 ± 0.4 mm, respectively. The minimum inhibitory concentration of the fruit extract was 0.83 mg/mL for *Staphylococcus aureus* and 0.21 mg/mL for *Enterococcus faecalis*. The experimental findings showed a favorable *in vitro* antibacterial effect of the methanol extract of *Corryocactus brevistylus* against *Staphylococcus aureus* and *Enterococcus faecalis*.

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THE INTRICATE RELATIONSHIP OF G-QUADRUPLEXES AND PATHOGENICITY ISLANDS

Bo Lyu, Qisheng Song

University of Missouri, Columbia, MO, United States

Guanine-rich and cytosine-rich DNA can form four stranded DNA secondary structures called guanine quadruplex (G4) and i-motif, respectively. These structures widely exist in genomes and play important roles in transcription, replication, translation and protection of telomeres. The dynamic interplay between G4 structures and pathogenicity islands (PAIs) represents a captivating area of research with implications for understanding the molecular mechanisms underlying pathogenicity. This study conducted a comprehensive analysis of a large-scale dataset from reported 89 pathogenic strains of bacteria to investigate the potential interactions between G4 structures and PAIs. G4 structures exhibited an uneven and non-random distribution within the PAIs and were consistently conserved within the same pathogenic strains. Additionally, this investigation identified positive correlations between the number and frequency of G4 structures and the GC content across different genomic features, including the genome, promoters, genes, tRNA, and rRNA regions, indicating a potential relationship between G4 structures and the GC-associated regions of the genome. The observed differences in GC content between PAIs and the core genome further highlight the unique nature of PAIs and underlying factors, such as DNA topology. High-confidence G4 structures within regulatory regions of *Escherichia coli* were identified, modulating the efficiency or specificity of DNA integration events within PAIs. Collectively, these findings pave the way for future research to unravel the intricate molecular mechanisms and functional implications of G4-PAI interactions, thereby advancing our understanding of bacterial pathogenicity and the role of G4 structures in pathogenic diseases.

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WHOLE GENOME SEQUENCING OF A *CRONOBACTER SAKAZAKII* ST8 STRAIN ISOLATED FROM SPICE POWDER

Irshad M. Sulaiman, Nancy Miranda, Steven Simpson, Kevin Karem

U. S. Food and Drug Administration, Atlanta, GA, United States

Cronobacter sakazakii is a Gram-negative, human-pathogenic bacterium that can survive in extreme dry conditions. This emerging opportunistic pathogen is recognized for causing acute meningitis and necrotizing enterocolitis in neonates, ageing, and immunocompromised individuals. It is linked predominantly to contaminated powdered infant formula (PIF) and to cause PIF-related sporadic cases and outbreaks worldwide. However, it has also been isolated from a wide variety of foods. Molecular characterization have indicated a high level of species-level genetic variation, comprising unique clonal complexes and sequence types, often associated with foodborne sickness and outbreaks. At present, application of whole genome sequencing (WGS) has improved bacterial typing and is widely utilized for correct strain identification to understand disease transmission. In this study, a *Cronobacter sakazakii*-like Gram-negative bacterial isolate SRL-104, from spice powder produced in the Caribbean Island nation, was recovered and analyzed. Initial microbial identification was accomplished on VITEK 2, RT-PCR, and MALDI-TOF MS based analysis, following FDA's Bacteriological Analytical Manual and manufacturer's recommended protocols. WGS was completed on an Illumina MiSeq system, using a Nextera XT DNA library preparation kit and a 250-bp paired-end read MiSeq Reagent v2 kit (500-cycle), following manufacturer's instructions. MALDI-TOF MS identified the *Cronobacter sakazakii* SRL-104 isolate as *Cronobacter sakazakii* with a high confidence value (99.9%). WGS analysis revealed the genome sequence of *Cronobacter sakazakii* isolate SRL-104 was 4,494,638 bp in length and distributed in 54 contigs. The analysis further confirmed the genome of *Cronobacter sakazakii* isolate SRL-104 to be Sequence Type 8 (ST8). *Cronobacter sakazakii* ST8 is considered as a highly stable clone with a high susceptibility to cause neonatal meningitis. Thus, MALDI-TOF mass spectrometry and WGS based analysis can be utilized for rapid and precise identification of infectious *Cronobacter sakazakii* strains of public health importance.

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SCREENING OF THE PANDEMIC RESPONSE BOX LIBRARY IDENTIFIED PROMISING COMPOUND CANDIDATES AGAINST EXTENSIVELY DRUG-RESISTANT *ACINETOBACTER BAUMANNII*

Nonlawat Boonyalai, Nattaya Ruamsap, Dutsadee Peerapongpaisarn, Chatchadaporn Thamnurak, Wilawan Oransathid, Nantanat Wongpatcharamongkol, Wirote Oransathid, Woradee Lurchachaiwong, John Griesenbeck, Norman Waters, Samandra Demons, **Brian Andrew Vesely**

WRAIR-AFRIMS, Bangkok, Thailand

Infections caused by antimicrobial-resistant *Acinetobacter baumannii* pose a significant threat to human health, particularly in the context of hospital-acquired infections. As existing antibiotics lose efficacy against Acinetobacter isolates, there is an urgent need for the development of novel antimicrobial agents. In this study, we assessed 400 structurally diverse compounds from the Medicines for Malaria Pandemic Response Box for their activity against two clinical isolates of *A. baumannii: A. baumannii* 5075, known for its extensive drug resistance, and *A. baumannii* QS17-1084, obtained from an infected wound in a Thai patient and displaying resistance to nearly all antimicrobial classes, including tetracycline. Among the compounds tested, seven from the Pathogen box exhibited inhibitory effects on the in vitro growth of *A. baumannii* isolates, with IC50s ≤ 48 μM

for *A. baumannii* QS17-1084 and IC50s ≤ 17 μM for *A. baumannii* 5075. Notably, two of these compounds, MUT056399 and MMV1580854, shared chemical scaffolds resembling triclosan. Further investigations involving drug combinations identified five synergistic drug combinations, suggesting potential avenues for therapeutic development. Our findings highlight gepotidacin, epetraborole, and eravacycline as promising candidates for further evaluation in murine wound infection models against multidrug-resistant *A. baumannii*. These compounds hold potential for addressing the critical need for effective antibiotics in the face of rising antimicrobial resistance.

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BURDEN OF MYCOBACTERIUM TUBERCULOSIS DRUG RESISTANT AMONG PRESUMPTIVE PULMONARY AND EXTRAPULMONARY TUBERCULOSIS PATIENTS AT AMBO GENERAL HOSPITAL WEST ETHIOPIA

Berhanu Seboka Adugna[1], Tasisa melka gutema[2]

[1]St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia, [2]Ambo University, Addis Ababa, Ethiopia

Drug resistant Mycobacterium tuberculosis is one of the serious public enemy out there that deterring progress made in tuberculosis cases and control in several countries including Ethiopia. Rifampicin resistance is an indicator for drug-resistant Mycobacterium tuberculosis, because it disclose the existence of more than 90% Isoniazid resistance. Early detection of drug-resistant tuberculosis is crucial for patient management and infection control. This study was designed to assess Burden of Mycobacterium tuberculosis, its Rifampicin-resistance pattern and associated factors among presumptive Pulmonary and Extra Pulmonary Tuberculosis patients at Ambo General Hospital, West Ethiopia. Hospital based cross-sectional study design was carried out from September 2, 2021 to March 27, 2022. Detection of Mycobacterium tuberculosis and resistance to Rifampicin pattern was determined by using GeneXpert MTB/RIF assay. Data were entered and analyzed by SPSS version 23.0. Bivariate and multivariate analyses were used to examine the relationship between dependent and independent variables. P-value was significant(<0.05) . A total of 322 presumptive tuberculosis patients were included in the study; of these, 52 (16.2%) of them were identified as having Mycobacterium tuberculosis by the GeneXpert MTB/RIF assay, 3/52 (5.8%) were resistant to Rifampicin and 6/52 (11.5%) patients were TB/HIV co-infected. From the total of M. tuberculosis detected 46 (16.1%) were identified in pulmonary and 6 (8.5%) were in extra-pulmonary presumptive patients. Rifampicin-resistant M. tuberculosis was detected in 3 patients who had a history of taking Anti-tuberculosis drugs and no in new patients. Previous history of tuberculosis treatment and having close contact history with tuberculosis patients were found as an important associated factors that enhance the Burden of tuberculosis. This indicates the mandate to make better and oversee the treatment protocol and prevention method to control the burden of tuberculosis.

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ANTIMICROBIAL RESISTANCE AMONG PATHOGENS CAUSING SURGICAL SITE INFECTIONS: TRENDS AND IMPACT OF THE COVID-19 PANDEMIC

Rania Nada[1], Alaa Ismail[2], Noha Assem[3], Hanan El-Mohammady[1], Mohammad AbderRazik[2], Mohamed Elazzay[2], Mohamed Abdelsattar[2], Mostafa Abdelrahman[2], Isabelle Nakhla[1]

[1]U.S. Naval Medical Research Unit – EURAFCENT, Cairo, Egypt, [2]Ain Shams University, Cairo, Egypt, [3]Cairo University, Cairo, Egypt

Surgical site infection (SSI) with antimicrobial resistant (AMR) bacteria is a progressing healthcare burden. This study assessed AMR in SSI cases at two University Hospitals in Egypt. A total of 361 cases were enrolled from March 2018 to September 2023: 154 cases pre-COVID-19 and 207 post-COVID-19. Identification and antibiograms of isolated pathogens were done by VITEK2. Up to four pathogens were isolated from 70% of the cases. ESKAPE-E (*E. faecium*, *S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, Enterobacter spp*., *E. coli*) constituted 88% of isolated pathogens. *E. coli* (30%), *K. pneumonia* (23%), *A. baumannii* (12%), and *P. aeruginosa* (9%) were the most frequently encountered pathogens. High AMR was observed among ESKAPE-E pathogens, with 15% pan-drug resistance (PDR), 43% extensive drug resistance (XDR) and 27% multi-drug resistance (MDR). *K. pneumoniae* (44%) had the highest PDR, and *A. baumannii* (79%) had the highest XDR. *Enterobacteriaceae* isolates showed lowest resistance rates against amikacin (27%) and meropenem (39%), whereas >85% were resistant to 3rd and 4th generation cephalosporins. Resistance of *Enterobacteriaceae* to meropenem, fluoroquinolones and cefoxitin increased post COVID-19, and lead to substantial increase in XDR and PDR in both *K. pneumoniae* and *E. coli*. *A. baumannii* lowest resistance rates were against colistin (7%) and minocycline (33%), whereas resistance against the rest of antibiotics ranged from 71% to 98%. Overall increase in *A. baumannii* resistance was observed post-COVID-19. For *P. aeruginosa*, colistin had the lowest resistance rates (11%), while resistance to the rest of antibiotics ranged from 56% to 82%. Prophylactic antibiotics were administered to almost all cases. Of these, 3rd generation cephalosporins were used in 86% of the cases, which may explain the elevated resistance rates against these antibiotics. Moreover, less restricted use of antibiotics during the pandemic may have contributed to the rise in resistance following the COVID-19 pandemic. This study highlights the significant AMR issue in Egypt, emphasizing need for updating guidelines for prophylaxis and empiric therapy.

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PHYTOACTIVITIES OF THE LEAF OF *VERNONIA AMYGDALINA* (BITTER LEAF) ON BACTERIAL INFECTIONS

Chika M. Ezenwa

Imo State University Owerri, Owerri, Nigeria

Dr Ezenwa C.M, Dr Obum Nnadi C.N, Dr Nwachukwu I.O, Dr. Njoku-Obi T.N, Dr Okechukwu-Ezike Ngozi, Prof, Yongabi A.K, And Prof. Ukaga C.N. Imo State University[1-6] Nigerian University Abuja[2].

Anti-bacterial activities of the leaf of *Vernonia amygdalina* (bitterleaf) were tested on *Escherichia coli* and *Staphylococcus aureus*. Five concentrations 0.5g/ml, 1.0g/ml, 1.5g/m, 2.0g/ml and 2.5g/ml were used and the control experiment was carried out to compare the diameter zones or clearing from the extracts and already standardized antibiotics. Agar well plugs method was used for the tests. The bitter leaf extract was made with cold water. Nutrient agar was prepared and inoculated with the different bacteria strains after which wells were made in the in the media and bitter leaf extracts were poured on them. The cold-water extracts of *V. amygdalina* showed inhibitions on the five organisms according to concentration. The organism susceptibility varied with more inhibition to *E. coli, Pseudomonas aeruginosa, Salmonella typhi, Klebsiella pneumonia* and least to *Staphylococcus aureus*.

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FIVE-YEAR SURVEILLANCE OF ANTIMICROBIAL RESISTANCE IN ESKAPE PATHOGENS OF NOSOCOMIAL ORIGIN IN LIMA, PERU

Jesus D. Rojas[1], Enrique Canal[2], Manuela Bernal[2], Tyler D. Moeller[2], Paul Rios[2]

[1]Vysnova Partners LLC, Alexandria, VA, United States, [2]U.S Naval Medical Research Unit SOUTH, Callao, Peru

The increasing trend of antimicrobial resistance (AMR) among bacterial pathogens in nosocomial settings (NS) presents a global threat. Continuous surveillance of pathogens from NS is crucial due to their potential impact on patient outcomes, particularly in regions with limited resources. We conducted a prospective surveillance study of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter spp*. (ESKAPE) in six hospitals in Lima, Peru, from 2017 to 2021. Bacterial pathogens were isolated and identified in these hospitals and then transported under refrigerated conditions to the U.S. Naval Medical Research Unit SOUTH

for further analysis, including pathogen re-identification and antimicrobial susceptibility testing. A total of 1,465 bacterial isolates were recovered with *K. pneumoniae* (35.4%) being the most prevalent pathogen, followed by *P. aeruginosa* (31.4%), *A. baumannii* (15.4%), *S. aureus* (12.4%), and *E. coli* (5.4%). Overall, these pathogens exhibited resistance to between one and 12 different antimicrobial families (AFs). We found high rates of multidrug resistance (MDR, non-susceptible to ≥ 1 agent in ≥ 3 antimicrobial categories) in 474 (91.5%) *K. pneumoniae*, 458 (99.1%) *P. aeruginosa*, 224 (99.6%) *A. baumannii*, 130 (71.08%) *S. aureus*, and 76 (96.2%) *E. coli* isolates. Furthermore, we observed significant differences between the means of the number of AFs from 2017-2019 compared to 2021 for *P. aeruginosa* (7.9 vs. 6.8, p<0.001) and *A. baumannii* (7.6 vs. 4.8, p<0.001). No significant changes in AMR trends over time were found for any antimicrobial category tested. The differences in AF resistance underscore the critical need for ongoing surveillance of antimicrobial resistance.

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RICKETTSIOSES AMONG HOSPITALIZED ACUTE FEBRILE ILLNESS ADMISSIONS, WESTERN AND CENTRAL PROVINCES, SRI LANKA

Hua-Wei Chen[1], Neesha Rockwood[2], Kalpa Kariyawasam[2], Senevirathne Mudiyanselage Priyantha Senevirathne[2], Enoka Corea[3], Sarah Jenkins[1], Allen Richards[1]

[1]Naval Medical Research Command, Silver Spring, MD, United States, [2]University of Colombo, Colombo, Sri Lanka, [3]Univeristy of Colombo, Colombo, Sri Lanka

Diagnostics for acute undifferentiated febrile illness (AUFI) are limited in lesser developed countries, such as Sri Lanka. Patient management is mainly based upon clinical case definitions. We aimed to determine the seroprevalence and importance of typhus group (TGR) and spotted fever group (SFGR) rickettsiae as AUFI pathogens during a study to determine the epidemiology and diagnostics for AUFI in Western and Central Provinces, Sri Lanka. Total of 800 patients (≥14years) hospitalized with AUFI (<7days) were recruited from 3 district general hospitals. Pan-*Rickettsia* qPCR assay (Rick17b) was performed on all study participants blood and/or eschar DNA samples. Cases were confirmed as *Rickettsia* spp. based upon positive triplicate qPCR results. In-house IgG (*Rickettsia typhi* for TGR and *Rickettsia conorii* for SFGR) enzyme-linked immunosorbent assays (ELISA) were performed on a sub-cohort with paired acute and convalescent (≥2 weeks) sera. Screening assays were performed on paired samples at 1:100 dilution to determine seroconversion. In the overall AUFI study cohort, there were 25/800 (3%) rickettsial infections diagnosed by qPCR (Rick17b). In the sub-cohort of participants with paired serology (n=492), the etiology of AUFI was determined as TGR and SFGR in 10 (2%) and 17 (3%), respectively. Overall seroprevalence (combined acute and previous infections) of SFGR (27/162, 17%) was higher in Central Province compared with SFGR (21/330, 6%) in Western Province. Seroprevalence of TGR in Central Province (13/162, 8%) was comparable with TGR (23/330, 7%) in Western Province. Only 11/42 (26%) of the acute rickettsioses diagnosed by PCR and/or ELISA, were clinically diagnosed rickettsial infection by the medical team on admission. Our results showed that rickettsioses represent an important under recognized differential diagnoses for AUFI in Sri Lanka. A combination of PCR and ELISA diagnostics will optimize management of patients and improve surveillance of rickettsioses.

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IDENTIFICATION AND ANTIMICROBIAL SUSCEPTIBILITY OF MILK PATHOGENS ISOLATED FROM MASTITIS INFECTED COW'S MILK IN ADO EKITI, NIGERIA

Ayodele Oluwayemisi Ogunlade[1], Oluwatoyin Modupe Aladejana[2]

[1]The Federal Polytechnic, Ado-Ekiti, Nigeria, [2]Redeemer's University, Ede, Nigeria

Mastitis is the most common and economically significant disease affecting dairy cattle. It is the most important cause of economic losses to the dairy industry throughout the world. This study aimed to evaluate the profile of resistance pathogens isolated from mastitis infected cow milk in Ado-Ekiti. Different bacteria were isolated using standard Microbiological techniques and further characterized using biochemical methods and identified using API Kit. A total of 80 Milk samples from cows diagnosed with subclinical mastitis were collected from four dairy farms in Ado-Ekiti (Aba Erifun, Aba baba Medinat, Afao road and Irasa). Antibiotic susceptibility testing was conducted using the Kirby-Bauer disk diffusion method. The study revealed that highest prevalent pathogen was *Streptococcus agalactiae* 25/80 (31.25%) and *Staphylococcus aureus* 18/80 (22.5%) followed by *E. coli* 15/80 (18.75%). Antibiotic sensitivity test revealed that *S. agalactiae* revealed the highest sensitivity to ofloxacin, ciprofloxacin, gentamicin and resistance to amoxicillin and doxycycline; *S. aureus* revealed the highest sensitivity to ciprofloxacin, doxycycline and azithromycin and resistance to amoxycillin and gentamicin. *E. coli* revealed the highest sensitivity to azithromycin and chloramphenicol and resistance to amoxicillin and ciprofloxacin. Results indicate a need to educate the dairy farmers about mastitis (particularly subclinical), proper hygiene methods in milking and the public health implications of consuming contaminated raw milk.

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PREVALENCE AND RISK FACTORS FOR COLONIZATION DURING THE FIRST THREE MONTHS OF LIFE WITH THREE CRITICAL ANTIBIOTIC-RESISTANT PATHOGENS IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW, META-ANALYSIS, AND META-REGRESSION STUDY

Anne-Lise Beaumont[1], Elsa Kermovant-Duchemin[2], Sébastien Breurec[3], Bich-Tram Huynh[1]

[1]Institut Pasteur, Université de Versailles-Saint Quentin, INSERM, Paris, France, [2]Assistance Publique - Hôpitaux de Paris, Hôpital Necker-Enfants malades, Department of Neonatal medicine, Paris, France, [3]Faculté de médecine, Université des Antilles, Laboratoire de Microbiologie clinique, CHUG-CIC Antilles Guyane CIC 1424 Inserm, Institut Pasteur de Guadeloupe, Pointe-à-Pitre, France

In low- and middle-income countries (LMICs), neonatal bacterial infections are mainly caused by *Enterobacterales* and *Staphylococcus aureus*, both significant contributors to mortality attributable to antimicrobial resistance. However, obtaining blood cultures in neonates, particularly in these settings, presents challenges, leaving a significant gap in our understanding. Given that bacterial colonization often precedes infection, we conducted a systematic review and meta-analysis to provide a comprehensive overview of the prevalence and risk factors for colonization with third generation-cephalosporin-resistant (3GC-R-E), carbapenem-resistant (CRE) *Enterobacterales*, and methicillin-resistant *S. aureus* (MRSA) during the first three months of life. Four databases were searched from January 1, 2000, to June 1, 2023, for cohort and cross-sectional studies conducted within LMICs that reported prevalence rates or risk factors for colonization with 3GC-R-E, CRE, or MRSA in infants up to 3 months of age. A random-effects model was used to compute the pooled prevalences. Out of the 2869 articles identified, 53 studies were eligible (N=40 for 3GC-R-E and CRE and N=13 for MRSA). The pooled prevalence of 3GC-R-E colonization was 31.1% (95%CI 20-45, τ^2 = 1.8), varying from 8.5% in the community to 54.3% in hospitalized patients. The risk of colonization with 3GC-R-E was found to increase with hospital birth, prior neonatal antibiotic intake, and prolonged rupture of membranes. *Klebsiella pneumoniae* was the most frequently identified species in newborns colonized with 3GC-R-E, before *E. coli*. The prevalence of carbapenem-R *Enterobacterales* colonization was 3.3% (1-11, τ^2= 7.1), and increased significantly other time, from 1.6% before 2018 to 23.9% afterward. The prevalence of MRSA colonization was 3.0% (1-9, τ^2 = 3.1). The prevalence of antibiotic-resistant pathogens colonization among neonates is high in LMICs, comparable to that reported in adults despite a limited exposure period. This highlights the need for additional research to identify transmission routes and to design targeted and effective preventive measures.

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INVESTIGATING THE ANTIPHAGE DEFENSE SYSTEMS IN STAPHYLOCOCCAL PHAGE SATELLITE

Adaeze Doris Ojiogu
University of Glasgow, Glasgow, United Kingdom

Phage satellites are one of the mobile genetic elements encoded into the bacterial chromosome and rely on their helper phages (viruses that infect bacteria) to promote their horizontal transfer in a recipient bacterial host. Among these phage satellites are the phage inducible chromosomal islands (PICIs) with the size of genome typically around 12 - 15 kb, significantly contributing to bacterial adaptation and pathogenesis. PICIs are found in Gram-positive or Gram-negative, with the prototypical and best-characterised family being the *Staphylococcus aureus* pathogenicity islands (SaPIs), which include SaPI1 and SaPIbov1. SaPIs exploit the life cycle of their 'helper' phages upon prophage induction or phage infection. Once excised, the SaPI-encoded genes are packaged into phage-encoded structural components, interfering with phage packaging and reducing phage reproduction. Most SaPIs are packaged using helper phage machinery through a headful (*pac*) packaging mechanism. SaPIs interfere with *pac* phage reproduction through a variety of strategies, including the redirection of phage capsid assembly to form small capsids, which can accommodate the smaller SaPI genome. This process depends on the expression of the SaPI-encoded *cpm*A and *cpm*B genes encoded in operon 1 of the SaPI genome. However, another SaPI subfamily, including SaPIpT1028, can remodel helper phage capsids into small capsids without encoding *cpm*AB homologs. It opens new avenues for research, as the basis for this phage interference remains to be deciphered. The interference mechanism by SaPIpT1028 is dependent on a new SaPI-encoded gene, *rcp* (redirecting capsid packaging), encoding a protein involved in remodelling the phage capsid into a small capsid to package the SaPI genome. This study has also identified a novel interference strategy involving an accessory gene, *sma* (single-protein MazF-like antiphage system), encoded at the 5' region of the island genome, that offers protection to its recipient host and the SaPI-inducing phages from other phage infection, shedding light on PICI evolution and the mutual relationship between PICIs and their helper phages.

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IMPROVING SYPHILIS MOLECULAR DIAGNOSTICS: GENOME MINING-BASED IDENTIFICATION OF IDENTICAL MULTI-REPEAT SEQUENCES (IMRS) IN *TREPONEMA PALLIDUM* GENOME

Clement Shiluli[1], Shwetha Kamath[2], Bernard N. Kanoi[1], Rachael Kimani[1], Michael Maina[1], Harrison Waweru[1], Moses Kamita[1], Ibrahim Ndirangu[1], Hussein M. Abkallo[3], Bernard Oduor[3], Nicole Pamme[4], Joshua Dupaty[5], Catherine M. Klapperich[5], Srinivasa Raju Lolabattu[6], Jesse Gitaka[1]
[1]Mount Kenya University, Thika, Kenya, [2]Jigsaw Bio solutions, Bangalore, India, [3]International Livestock Research Institute, Nairobi, Kenya, [4]Stockholm University, Stockholm, Sweden, [5]Boston University, Boston, MA, United States, [6]Jigsaw Bio Solutions, India, India

According to the World Health Organization (WHO) more than 7 million new *Treponema pallidum* infections were reported among people aged 15 – 49 years in 2020 globally, the majority of them in developing countries. Syphilis, which is caused by *T. pallidum* is transmitted through contact with active lesions of a sexual partner or from an infected pregnant woman to her foetus. Gold standard *T. pallidum* laboratory diagnosis methods include dark-field microscopy, silver staining, direct fluorescence immunoassays and the rabbit infectivity test. However, these tests are associated with false positive or negative results. The gold standard 16S ribosomal (rRNA) gene polymerase chain reaction (PCR) is used for routine amplification of *T. pallidum* conserved genes. Here we report on an ultrasensitive syphilis diagnostic method, based on de *novo* genome mining of the *T. pallidum* DNA to identify identical multi repeat sequences (IMRS) as amplification primers. We used genome-mining approaches to find IMRS distributed throughout the *T. pallidum* genome to design a primer pair that target four repeat sequences. Genomic *T. pallidum* DNA was diluted from 8.14×10^{4} to 8.14×10^{-2} genome copies/μ;l and used as template in the IMRS-based amplification assay. For performance comparison, 16S rRNA PCR assay was employed. Probit analysis was used to calculate the lower limit of detection of the *T. pallidum*-IMRS PCR and the conventional 16S rRNA PCR assays. Probit analysis confirmed that the *T. pallidum*-IMRS primers offered higher test sensitivity of 0.03 fg/μ;L compared to the 16S rRNA PCR (0.714 pg/μ;L). Using the *T. pallidum*-IMRS primers, we were able to observe considerable isothermal amplification of genomic DNA at a starting concentration of 0.01 pg/µL. *De novo* genome mining of *T. pallidum* IMRS as amplification primers can serve as a platform for developing ultrasensitive diagnostics for Syphilis and potentially a wide range of infectious pathogens.

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COMPARISON OF COMMERCIAL KITS FOR DNA EXTRACTION AND PRE-TREATMENTS OF SPUTUM SAMPLES FROM PATIENTS WITH TUBERCULOSIS FOR SEQUENCING

Jimena Ráez, Sonia Huamán, Candy León, Patricia Sheen
Universidad Peruana Cayetano Heredia, Lima, Peru

Mycobacterium tuberculosis (MTB), a pathogen of global concern, causes one of the infectious diseases with the highest rates of morbidity and mortality. The challenge of incomplete treatment adherence leads to antibiotics worldwide. This is due to failure to comply with all doses, generating resistance, underscoring the necessity for timely and effective individualized diagnosis and treatment. Whole-genome sequencing (WGS) is pivotal for elucidating the complete DNA sequence of an organism, offering insights into the full spectrum of multidrug resistance, thus positioning it as a critical diagnostic tool. Our study focused on optimizing MTB DNA extraction from sputum samples for sequencing, comparing the efficacy of different commercial DNA extraction kits (n=39) and pre-treatments: NAOH-NALC and saponin (n=32). The comparative analysis revealed that the Quick-DNA Fungal/Bacterial Miniprep and Quick-DNA Miniprep Plus Kits outperformed the ZymoBIOMICS DNA Miniprep Kit in terms of DNA yield (91.19 ng and 77.87 ng, respectively, versus 50.06 ng). Quality assessment based on the 260/280 and 260/230 ratios favored the Quick-DNA Miniprep Plus kit (1.77 and 0.46). Additionally, sputum sample treatment evaluations indicated that saponin treatment yielded higher DNA quantities and better quality metrics (876 ng, 1.83, 0.98) compared to the NaOH-NALC treatment (54 ng, 1.56, 0.29). Quantitative PCR analysis to assess the proportions of human and MTB DNA demonstrated a reduction in human DNA with NaOH-NALC treatment followed by saponin, while the MTB DNA levels were similar across both treatments. In conclusion, for sequencing clinical sputum samples from MTB patients, the combination of DNA extraction using the Quick DNA Miniprep Plus kit and sample pre-treatment with saponin emerged as the most effective strategy.

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SEROPREVALENCE OF LEPTOSPIROSIS IN HORSE KEEPERS IN A REGION OF THE COLOMBIAN CARIBBEAN

Virginia C. Rodríguez-Rodríguez, Andrea C. Osorio-Vargas, Ana M. Castro-Cordero, Omar Y. Ceballos-Atencia, Jose M. Rosero-Mercado, Alfonso Calderón-Rangel
Universidad de Córdoba, Monteria, Colombia

Leptospirosis is an endemic zoonotic disease with high distribution and worldwide prevalence. An analytical observational study was carried out with a cross-sectional approach that determined the seroprevalence and risk factors associated with occupational leptospirosis in horse keepers in the department of Córdoba, 2022-2023. After signing the informed consent, 112 blood samples were taken. to horse caretakers in 33 properties in the department of Córdoba to determine the seroprevalence of leptospirosis through the Microagglutination technique. An epidemiological survey was implemented to carry out the socio-demographic

characterization of the population under study and an association was established between risk factors and the presentation of occupational leptospirosis in equine caregivers through descriptive and inferential statistical analyses. The seroprevalence was 59.8% (n=67). Of the 67 horse keepers with antibody titers against Leptospira spp, 82.1% were associated with a serogroup, the most frequent being Australis. 17.9% were mixed and the most frequent association was with the Australis serogroup. Dairy work (p:0.041, CI:1.02-6.472, OR: 2.57) and frequenting dam-type water sources (p:0.026, CI:1.08-6.843, OR: 2.75) were established as risk factors. Research on horse keepers in Córdoba highlights the correlation between occupational and environmental factors with the prevalence of leptospirosis. There are occupational and environmental risks that deserve to be taken into account for the design of prevention and control strategies for the event by health authorities.

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UNDERSTANDING THE IMPACT OF MONOCULAR SEVERE VISION IMPAIRMENT AND BLINDNESS CAUSED BY FUNGAL KERATITIS IN TANZANIA

Zoha Mian

University of Louisville, Louisville, KY, United States

A majority of current eye care surveys focus on the better-seeing eye, overlooking individuals with monocular problems, and underestimating the extent of eye conditions and the services required to treat them. Therefore, most current definitions and targets for monitoring ophthalmic services are unlikely to recognize the true burden of monocular blindness. There is very little data regarding the quality of life in individuals who are unilaterally blind or have severe visual impairment due to fungal keratitis, both in sub-saharan Africa and worldwide. This project will examine the impact of monocular visual impairment and monocular blindness due to fungal keratitis on people in Tanzania. A mixed-methods study will be conducted at Kilimanjaro Christian Medical Centre Hospital (KCMC) in Tanzania over six weeks. This study will constitute a quality-of-life survey and cross-sectional, semi-structured in-depth interviews. This study is an extension of a previous parent trial. A randomized control trial took place at KCMC starting September 2021 and set out to recruit patients with fungal keratitis to determine if topical chlorhexidine 0.2% in combination with topical natamycin 5% is superior to topical natamycin 5% alone. Participants will be organized into two groups based on World Health Organization visual acuity criteria: those with severe visual impairment or Blindness in the affected eye after treatment: (≤6/60 in the worse eye, presenting ≥6/18 in the better eye), and those with mild to no visual impairment in the affected eye after treatment: (presenting ≥6/18 in both eyes). Only those in the blind or severe visual impairment group will be eligible for interviews. Quality-of-life survey responses for the two groups will be compared to previous surveys completed by participants at the beginning of the clinical trial and 90 days after. Survey responses will also be compared between those who now have monocular blindness/visual impairment and those who do not. Using thematic analysis, interview transcripts will be coded and analyzed to identify common themes between interviews.

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ANTIBIOTIC PRESCRIBING PATTERNS AT OUTPATIENT CLINICS IN WESTERN AND COASTAL KENYA

Melanie Kiener[1], Caroline Ichura[1], Bryson A. Ndenga[2], Francis M. Mutuku[3], Christabel A. Winter[2], Victoria Okuta[4], Laura Mwambingu[2], Kevin Ogamba[2], Karren N. Shaita[2], Charles Ronga[2], Philip Chebii[5], Jael Amugongo[3], Said Malumbo[5], Omar Godana[5], Zainab Jembe[6], Charles Ng'ang'a[5], Mwangosho Mazera[5], A. Desiree LaBeaud[1]

[1]Stanford University, Stanford, CA, United States, [2]Kenya Medical Research Institute, Kisumu, Kenya, [3]Technical University of Mombasa, Mombasa, Kenya, [4]Obama Children's Hospital, Jaramogi Oginga Odinga Referral Hospital, Kisumu, Kenya, [5]Msambweni County Referral Hospital, Msambweni, Kenya, [6]Diani Health Center, Ukunda, Kenya

Antimicrobial resistant pathogens are a leading cause of morbidity and mortality worldwide, particularly in low- and middle-income countries, and the overuse and misuse of antimicrobials are key contributors. We aimed to identify factors associated with antibiotic prescriptions among persons presenting to clinics in Kenya. We performed a retrospective, descriptive cohort study of adults and children presenting to outpatient clinics in Western and Coastal Kenya, including reported symptoms, physical exam findings, clinician assessments, laboratory results and prescriptions. Data analysis was performed using R studio software. We reviewed 1,526 visits among 1,059 people who sought care from December 2019-February 2022. Enrollment was continuous apart from April-June 2020, when the study was paused due to the COVID-19 pandemic. Median age was 16 years (IQR 6-35) and 22% were under 5 years. All persons endorsed fever, and 44% reported onset within 48 hours of presentation. At least one provisional diagnosis was provided for 89% of encounters, and upper respiratory infection was the most common diagnosis (48%). 30% of malaria RDTs were positive and 3% of dengue RT-qPCRs were positive. Antibiotics were prescribed in 73% of encounters overall and in 84% among children under 5. In 48% of visits antibiotics were prescribed without a provisional bacterial diagnosis. In the multivariable model, factors associated with increased odds of an antibiotic prescription were the clinic in Western Kenya (OR 5.1, 95% CI 3.0-8.8), age less than or equal to 18 years (OR 2.1, 95% CI 1.4-3.2), endorsement of cardiorespiratory symptoms (OR 5.2, 95% CI 3.2-8.3), a negative malaria RDT (OR 4.0, 95% CI 2.5-6.8), and a provisional diagnosis that could be bacterial in etiology (OR 5.9, 95% CI 3.5-10.3). High rates of antibiotic prescriptions are common even when associated diagnoses are not bacterial. Compared to our 2014-2017 cohort, we found higher rates of antibiotic prescriptions among children. Improved diagnostics to rule in alternative diagnoses as well as stewardship programs are needed.

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SEVERE INFECTION AMONG YOUNG INFANTS IN DHAKA, BANGLADESH: EFFECT OF CASE DEFINITION ON INCIDENCE ESTIMATES

Alastair Fung[1], Cole Heasley[1], Lisa G. Pell[1], Diego G. Bassani[1], Prakesh S. Shah[2], Shaun K. Morris[1], Davidson H. Hamer[3], Mohammad Shahidul Islam[4], Abdullah Mahmud[5], Eleanor Pullenayegum[1], Samir K. Saha[4], Rashidul Haque[6], Iqbal Hossain[6], Chun-Yuan Chen[1], Abby Emdin[7], Karen M. O'Callaghan[8], Miranda G. Loutet[1], Shamima Sultana[6], S. M. Masum Billah[6], S. M. Abdul Gaffar[6], Enamul Karim[6], Sharika Sayed[6], Shafiqul A. Sarker[6], Daniel E. Roth[1]

[1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Mount Sinai Hospital, Toronto, ON, Canada, [3]Boston University School of Medicine, Boston, MA, United States, [4]Child Health Research Foundation, Dhaka, Bangladesh, [5]Shield Pharmaceuticals Corp., Hauppauge, NY, United States, [6]International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh, [7]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, [8]King's College London, London, United Kingdom

Multiple definitions are used to denote severe infection (SI) in young infants including sepsis and serious bacterial infection (SBI). Heterogeneity in these definitions limits comparability of randomized controlled trials (RCTs) of infant SI prevention interventions. To inform the design of young infant SI prevention RCTs in low-resource settings, we estimated the incidence of SI in Bangladeshi infants aged 0-60 days and examined the effect of variations in SI definitions on incidence estimates. From 2020-2022, generally healthy newborns were recruited at two hospitals in Dhaka, Bangladesh. SI cases were identified through active surveillance at up to 12 scheduled community health worker home visits from ages 0-60 days or through caregiver self-referral. The primary SI case definition combined physician documentation of clinical signs and/or diagnosis of sepsis/SBI and either a positive blood culture or parenteral antibiotic treatment for ≥5 days. Incidence rates were estimated for the primary SI definition, the World Health Organization (WHO)

definition of possible SBI based on seven clinical signs, culture-confirmed SI, and five other alternative SI definitions. Among 1939 infants, the SI incidence rate using the primary definition was 1.1 (95% CI 0.93-1.4) per 1000 infant-days at risk, whereas the incidence using the WHO definition of possible SBI was 0.84 (0.69-1.0) per 1000 infant-days at risk. Culture-confirmed SI incidence was 0.026 (0.0085-0.081) per 1000 infant-days at risk. One third of primary SI definition cases met criteria through a physician diagnosis of sepsis/SBI rather than documentation of clinical signs. Of primary SI definition cases, 85% were identified following caregiver self-referral. The incidence of SI in young infants varied considerably by case definition. Using a clinical sign-based SI definition may result in missing a substantial proportion of cases identified by physician diagnosis of sepsis/SBI. If health facilities are accessible and caregivers seek care for infant illness, frequent scheduled home assessments by study personnel to identify infants requiring referral may not be warranted.

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CLINICAL PRESENTATION AND MANAGEMENT OF ECHINOCOCCUS INFECTION: A CASE REPORT

Sangeeta Nair-Collins, Julio Mendez, Juan Cardenas, Jane Hata, Diana Villegas

Mayo Clinic Jax, Jacksonville, FL, United States

We report the case of a 51-year-old male from Ecuador who presented to the Mayo Clinic Florida (MCF) for evaluation of an incidentally found hepatic lesion during evaluation of midepigastric pain that started in June 2023 after two days of riding his bicycle. He used over the counter antacids and proton pump inhibitors for a few days without any improvement of his symptoms and when the pain became debilitating, he sought care at a hospital in Ecuador. MRI abdomen from the outside facility was significant for focal hepatic lesions . He denied any pets or animal exposure including visits to farmland, sheep or other cattle. He has lived within the Ecuadorian city of Quito for his entire life except for a 5 year period during which he lived in Egypt. He does not have any exposure to rural areas and works as a consultant for an oil company. He is a meat eater and denies consuming undercooked or uncooked meat products. Our patient underwent sonographically guided needle aspiration of the 6.4 x 4.9 cm hepatic cyst with installation of 20 cc of 23.5% hypertonic saline. No fluid was aspirated from the smaller 3.2 x 2.8 cm cyst but it was injected with 3 cc of absolute ethanol with scolicidal intent. He was started on a three month course of 400 mg PO BID of Albendazole. Our patient underwent surveillance imaging at 3 months which showed stable hepatic cysts. He will continue to have 3 month surveillance followed by yearly imaging.

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ACTIVE MELIOIDOSIS SURVEILLANCE AMONG HOSPITALIZED PATIENTS WITH DIABETES MELLITUS IN BANGLADESH, JUNE 2021-MARCH 2024

Sukanta Chowdhury[1], Lovely Barai[2], Muhammad Abdur Rahim[2], Mindy Elrod[3], Maria Negron[3], Zach Weiner[3], Samira Rahat Afroze[2], Caroline Schrodt[3], Farhana Afroz[2], Julia K. Petras[3], Muhammad Belal Hossain[1], Ayesha Jamal Ananna[1], Mahmudur Rahman[1], Mohammed Ziaur Rahman[1], Jay Gee[3], William A. Bower[3]

[1]International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, [2]Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh, Dhaka, Bangladesh, [3]Centers for Disease Control and Prevention, Atlanta, Georgia, USA, Atlanta, GA, United States

Melioidosis is an infectious disease predominantly found in tropical regions, caused by soil-borne bacterium *Burkholderia pseudomallei*. Melioidosis remains a neglected disease in Bangladesh. From 1961-2021, Bangladesh has documented around 85 cases. The incidence of melioidosis is believed to be much higher. To determine a more accurate incidence of melioidosis in Bangladesh, we initiated surveillance in June 2021 to detect *B. pseudomallei* infection in hospitalized patients at BIRDEM General Hospital. BIRDEM General Hospital is the largest diabetes hospital in Bangladesh which has 715 in-patient beds and more than 3500 out-patient visits daily. Adult patients with diabetes mellitus having clinical suspicions for melioidosis as per case definition were enrolled. As of 20 March 2024, a total of 693 were enrolled; 53% (n= 365) were male and the mean age of all patients was 58 years (range: 18-105). Of the 693 patients, 28 (4%) were culture confirmed for *B. pseudomallei*, 7 (25%) of whom died. The mean age of cases was 54 years (range: 25-70); male was predominant (82%), most patients (96%) had diabetes; 23 (82%) had fever; 7 (25%) had sepsis syndrome; 13 (46%) had skin abscess; 10 (36%) had pneumonia; 4 (14%) had organ abscess; 17 (61%) had urinary tract infection (UTI) and 13 (46%) had chronic Kidney disease (CKD). Most of the cases (n=22, 79%) were detected during June-November; 18 (64%) cases lived in rural areas and all cases originated from 17 districts. Patients with melioidosis were more likely to have soil exposure within the prior 30 days compared to those that did not (OR 2.6, 95% CI: 1.21-5.47). *B. pseudomallei* showed highest sensitivity to meropenem (100%), amoxicillin-clavulanate (100%), ceftazidime (100%), piperacillin (100%) followed by tetracycline (73%), cotrimoxazole (57%), and ciprofloxacin (35%). This hospital-based active surveillance provides evidence that the burden of melioidosis is higher in Bangladesh than previously documented. Active surveillance should be expanded with diagnostic facilities to understand the true country-wide melioidosis burden.

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TROPICAL SPASTIC PARAPARESIS AND ADULT T CELL LEUKEMIA-LYMPHOMA CO-PRESENTATION IN AN HTLV-1 PATIENT

Malika Madhava[1], Jorge C. F. Nakazaki[2], Martin Montes[2]

[1]University of Alabama-Birmingham, Birmingham, AL, United States, [2]Instituto de Medicina Tropical 'Alexander von Humboldt' and Facultad de Medicina Alberto Hurtado, Universidad Peruana Cayetano Heredia, Lima, Peru

Human T-lymphotropic virus type 1 (HTLV-1) affects between 5 to 10 million people globally. In most patients the infection remains clinically inapparent. It carries a 5% lifetime risk of adult T-cell leukemia/lymphoma (ATLL) and a 2% lifetime risk of tropical spastic paraparesis (TSP), which are the most commonly described conditions associated with HTLV-1. Here we report a case of HTLV-1 infection in a patient presenting with both TSP and ATLL. A 53 year old woman from Lima, Peru presented for a 2 year history of facial erythema and skin changes on her legs. She also noted weakness and involuntary movements of her lower extremities for the past year, which had led to falls on three occasions, in addition to urinary retention in the last month. On skin examination, the patient was noted to have erythematous patches on her face, and scaly plaques on bilateral lower extremities. A dermal punch biopsy of the facial erythema was performed, which showed "moderate inflammatory infiltrate on the dermis with lymphocytes and histiocytes, which stained positive for the following: CD4/CD8 3:1; CD3+, CD7+, Ki-67 5-10%, suggestive of mycosis fungoides." A HTLV-1 test was performed via electrochemiluminescence immunoassay, which returned positive, confirming the diagnosis of adult T-cell leukemia/lymphoma. On neurologic exam, she was noted to have decreased tone of both lower extremities, and 4/5 strength in both upper extremities, and 3/5 strength in both lower extremities. She was additionally noted to have hyperreflexia of both patellar and achilles reflexes, positive bilateral Hoffman, Babinski, and Chaddock signs, and spasticity of both lower extremities, leading to a diagnosis of tropical spastic paraparesis in the context of HTLV-1 positivity. There has been only one other case of this co-presentation in the literature, in 1996. Given the rarity of HTLV-1 and its clinical manifestations, the co-presentations of these conditions represents a unique clinical entity and indicates the importance of evaluating patients with one manifestation of HTLV-1 for other conditions associated with the infection.

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PARASITES IN HISTOPATHOLOGY: A TEACHING HOSPITAL EXPERIENCE

Delphine Nyirahabimana[1], Alvaro Laga Canales[2], Thomas Habanabakize[1], Delphine Uwamariya[3], Emmanuel Bizimana[4]

[1]King Faisal Hospital Rwanda, Kigali, Rwanda, [2]Brigham and Women's Hospital, Boston, MA, United States, [3]University Teaching Hospital of Kigali, Kigali, Rwanda, [4]University of Rwanda, College of Medicine and Health Sciences, Kigali, Rwanda

Accurately diagnosing parasitic infectious diseases is essential to ensure those diseases are appropriately treated. The diagnosis of parasitic infectious diseases is achieved in many parts of the world especially in the resource-limited regions, by the observation of parasite life-cycle stages on microscopy of biological samples like urine, stool, sputum, aspirates, and tissue biopsies. This study was done to evaluate the role of histopathology, which is the analysis of tissue biopsies, in the diagnosis of parasitic infectious diseases. This is a retrospective descriptive study that reviewed the clinical and pathological features of cases of parasitic infections diagnosed on tissue biopsies, from January 2014 to December 2019 in the Anatomical pathology department of the laboratory of University Teaching Hospital of Kigali. In total 23 cases of parasitic infections were diagnosed on tissue biopsy. The age of the patients ranged from 1.5 years old to 84 years old. The symptoms and their severity varied according to affected organs. The cases consisted of 14 cases of cysticercosis, 4 cases of schistosomiasis, 3 cases of echinococcosis, 1 case of genital filariasis, and 1 case of arthropod bite larva migrans. The cases of cysticercosis consisted of 7 cases of neurocysticercosis, 1 case of disseminated cysticercosis, and 6 cases of skin and intramuscular cysticercosis. The cases of schistosomiasis consisted of 1 case of intramedullary spinal schistosomiasis, 2 cases of female genital schistosomiasis, and 1 case of intestinal schistosomiasis. The cases of echinococcosis consisted of splenic, liver, and pancreatic cystic echinococcosis. Most of the parasitic infections that are diagnosed on tissue biopsy consist of parasitic infections of the central nervous system, those of the skin and soft tissues, and those of the female genital tract. Histopathology is very useful in diagnosing parasitic infectious diseases, some of which can be life threatening notably those affecting the central nervous system.

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FREQUENCY OF FEVER AMONG CHILDREN AGED 0 TO 15 AT BAMAKO COMMUNE IV DISTRICT HOSPITAL IN 2023, MALI

Bourama Keita, Naman KEITA, Salif Coulibaly, Drissa Konaté, Karim Traoré, Mariam Goita, Abdouramane Traoré, Rouhoulahi Bah, Korotoumou Mallé, Korotoumou Mallé, karamoko Tangara, Salimata Kanté, Sidi Bane, Ibrahim Sanogo, Sory Diawara, Seidina Diakité, Abdoul Razakou Dicko, Mahamadou Diakité

USTTB, Bamako, Mali

Despite progress in the fight against malaria in recent years in Mali and the sub-region, fever remains the most frequent reason for consultations in health facilities. The aim of this study was to identify the current causes of fever in children in Mali. A prospective cross-sectional study was conducted from February to November 2023 at the pediatric ward at the district hospital of the commune IV of Bamako. The study population concerned all patients received in routine consultation aged 0 to 15 years. A paper questionnaire was used for data collection. The entry was made in EPI data and the SPSS 25 software was used for data analysis.A total, we included 501 patients including 308 cases of fever, a frequency of 61.5%. Among the febrile cases, the male sex increased with 54.6%, the age group under 5 years represented 59.4% of the cases. The majority of patients lived in rural areas with 53.9%. Malaria was the leading cause of fever with (69.5%) followed by acute respiratory infections (26.6%) of Gastroenteritis (4.5%) of Salmonellosis (3.6%), oral candidiasis (2.9%) and malnutrition (0.6%). Most cases of fever were recorded in the months of (July August September) during the rainy season and in the months of (February and March) during the dry season. No significant variation between fever and age range was observed. However a significant variation between fever seasonality was observed during this study (p=0.000).Our results suggest that malaria remains the leading cause of fever in children and it was especially common in the under-5 age group. Further studies will be needed to better identify the different causes of fever in children in this health district.

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DEVELOPMENT OF FUNCTIONAL BOWEL DISORDERS AFTER TRAVEL IN DEPARTMENT OF DEFENSE BENEFICIARIES

Tahaniyat Lalani[1], Adam Maier[2], Claire Kuo[1], Derek Larson[2], David Tribble[1]

[1]Infectious Disease Clinical Research Program, Bethesda, MD, United States, [2]Navy Medicine Readiness and Training Command, San Diego, San Diego, CA, United States

Post-infectious irritable bowel syndrome (IBS) has been associated with travelers' diarrhea (TD) in previous studies. We evaluated the association between TD and functional bowel disorders (FBD), based on the Rome IV criteria, in a prospective cohort of US Department of Defense (DoD) beneficiaries (TravMil), traveling to locations with risk of TD for ≤ 6.5 months between 2010-2019. 4787 US active duty servicemembers and adult civilian travelers were prospectively enrolled prior to travel or within 8 weeks following return. 1438 subjects completed a baseline FBD survey (documenting symptoms prior to travel), a post-travel survey (for symptoms and treatment during travel) and a 3-month follow-up FBD survey after return and were included in the analysis. The primary end point was new-onset FBD at 3 months post-travel, based on Rome IV criteria. The relative risk (RR) of FBD associated with TD was computed after adjusting for demographic and trip characteristics. The median age of enrollees was 45 years (IQR: 18-86y); 57% were male, 44% were active-duty personnel and 71% reported travel to a developing country within 5 years prior to enrollment. The median trip duration was 21 days (IQR: 13-61 days), 25% experienced TD and 9% used antibiotics. 15% of subjects reported FBD symptoms prior to travel. 10% (95%CI: 8-12%) reported new-onset FBD at 3 months post-travel. Functional diarrhea was the most common subset of FBD (38%) and 12% met criteria for IBS. TD (RR: 1.7 [95%CI: 1.2-2.6]), active-duty status (RR: 3.1 [95%CI:1.7-5.4]) and post-deployment enrollment (1.7 [95%CI:1.0-2.8]) were associated with new-onset FBD on multivariate analysis. The overall proportion of US DoD beneficiaries with FBD prior to and following travel in our cohort was lower than estimates for the US population (29-32%) possibly due to the older median age in our cohort. Our findings add to the existing post-infectious IBS literature by demonstrating an association between TD and FBD using the Rome IV criteria. Additional studies are needed to understand the increased risk of travel associated FBD in deployed servicemembers including the impact of TD severity and antibiotic use.

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EVALUATING THE IMPACT OF A LAO LANGUAGE MOBILE PHONE APPLICATION ON ADHERENCE TO ANTIMICROBIAL PRESCRIBING GUIDELINES IN LAO PDR

Vilada Chansamouth[1], Danoy Chommanam[1], Mayfong Mayxay[2], Sue Lee[3], Pimnara Peerawaranum[3], Mavuto Mukaka[3], Manivanh Vongsouvath[1], Susath Vongphachanh[4], Sommay Keomany[5], Khamla Silavanh[6], Nunthakone Sihapanya[7], Phouvieng Duangmala[8], Khamsai Detleuxay[9], Valy Keoluangkhot[10], Sommana Rattana[9], Nick Day[3], H. Rogier van Doorn[11], Paul Turner[12], Paul Newton[13], Elizabeth Ashley[1]

[1]Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit, Vientiane, Lao People's Democratic Republic, [2]Institute of Research and Education Development (IRED), University of Health Sciences, Ministry of Health, Vientiane, Lao PDR, Vientiane, Lao People's Democratic Republic, [3]Mahidol Oxford Tropical Medicine Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, Bangkok, Thailand, [4]Mahosot Hospital, Ministry of Health, Vientiane, Lao People's Democratic Republic, [5]Salavan Provincial Hospital, Ministry of Health, Salavan, Lao

People's Democratic Republic, [6]Xiengkhuang Provincial Hospital, Ministry of Health, Xiengkhuang, Lao People's Democratic Republic, [7]Vientiane Provincial Hospital, Ministry of Health, Vientiane Province, Lao People's Democratic Republic, [8]Luangnamthan provincial Hospital, Ministry of Health, Luangnamtha Province, Lao People's Democratic Republic, [9]Department of Healthcare and Rehabilitation, Ministry of health, Vientiane, Lao People's Democratic Republic, [10]Lao Infectious Disease Society, Vientiane, Lao People's Democratic Republic, [11]Oxford University Clinical Research Unit, Hanoi, Vietnam, [12]Cambodia Oxford Medical Research Unit, Angkor Hospital for Children, Siem Reap, Cambodia, [13]Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom

Laos has one of the highest rates of antimicrobial usage among hospitalized patients in Asia. New antimicrobial prescribing guidelines were approved in 2020. An open cohort stepped-wedge cluster randomized 3-step controlled trial was conducted from 2021-2022 (16 months). The intervention was an antimicrobial prescribing guideline smartphone application with antimicrobial stewardship training at the time of introduction. The reference was a paper-based version of the same guidelines. Adherence with the guidelines was defined as prescriptions using the correct antimicrobial agent(s) and correct dose based on the provided guidelines. Primary outcome measurement was done by regular point prevalence surveys of hospital antimicrobial use (4-month intervals). A mixed-effects regression model, adjusting for the effect of time, clusters and possible confounders, was used to analyse the data. At month 0, 413/482 (86%; 82-87%-95%CI) of prescribers across six hospitals had access to paper-based guidelines. By the end of the study 382/498 (77%; 73-80%-95%CI) of prescribers had access to the intervention. Among inpatients, overall adherence to the guidelines was 17% (15-19%-95%CI; n=231/1,360) in the reference group and 26% (23-28%-95%CI; n=285/1,112) in the intervention groups (p<0.0001). Among outpatients, adherence was 22% (19-24%-95%CI; n= 263/1,212) and 23% (21-25%-95%CI; n=346/1,507) in the reference and intervention groups (p=0.433), respectively. The adjusted model showed that odds ratio (OR) for adherence to the guidelines in the intervention group compared to the reference group was 0.6 (0.36-1; 95%CI; p-value=0.06) among inpatients, and 0.9 (0.61-1.29; 95%CI; p-value=0.54) among outpatients. Adherence to the guidelines adherence was similar whether delivered in book format or by mobile phone application in Laos. While guidelines provide useful recommendations, adherence cannot be assumed, and the appropriate use of antimicrobials relies on multiple factors.

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VACCINE-INDUCED ANTIBODY LEVELS IN A PEDIATRIC POPULATION WITH WIDESPREAD ANTIBIOTIC USE

Sarah B. Kohl[1], Dorothy Dickson[2], Masud Alam[3], E. Ross Colgate[2], William A. Petri, Jr.[4], Rashidul Haque[3], Fiona van der Klis[5], Beth D. Kirkpatrick[2], Benjamin Lee[2]

[1]University of Vermont Larner College of Medicine, Burlington, VT, United States, [2]Larner College of Medicine, Translational Global Infectious Disease Research Center, Burlington, VT, United States, [3]International Centre for Diarrhoeal Disease Research, Division of Infectious Disease, Parasitology and Emerging Infections Laboratory, Dhaka, Bangladesh, [4]UVA School of Medicine, Division of Infectious Diseases & International Health, Charlottesville, VA, United States, [5]Netherlands National Institute for Public Health and the Environment, Bilthoven, Netherlands

Children in low- and middle-income countries (LMIC) frequently receive antibiotic treatment in their first year of life due to high rates of respiratory and diarrheal diseases. However, the impact of antibiotics on parenteral vaccine immunogenicity remains underexplored, especially in LMICs with high antibiotic use. Therefore, we conducted a retrospective cohort study using data from the Performance of Rotavirus and Oral Polio Vaccines in Developing Countries (PROVIDE) birth cohort study in Dhaka, Bangladesh. Antibiotic use was categorized based on duration of exposure and spectrum of activity. Vaccine-induced antibody levels against measles, pertussis toxin, pertussis pertactin, filamentous hemagglutinin, diphtheria toxoid, tetanus toxin, and *Haemophilus influenzae* type B (Hib) were measured at 53 weeks. Data from 582 evaluable infants were analyzed. Children in this cohort had high rates of antibiotic exposure, with a median of 80 days of use in the first year, 80% of which were broad-spectrum. Despite this, they were well-protected against measles, tetanus, and Hib, with 96%, 88%, and 91% respectively having antibody levels above protective thresholds. Neither duration nor spectrum of antibiotic exposure in the first 14 weeks of life significantly affected antibody titers at 53 weeks against pertussis, diphtheria, tetanus, or Hib, with two exceptions. We found lower anti-pertussis toxin titers in children with high broad-spectrum antibiotic exposure (>21 days) in the first 14 weeks of life (p = 0.049). Additionally, anti-measles titers in children with high broad-spectrum antibiotic exposure in the first 40 weeks of life were significantly higher than the low-exposure group (p = 0.015). Differences in measles and pertussis toxin antibodies between high- and low-exposure to broad-spectrum antibiotics were of limited clinical significance. Despite very high rates of antibiotic use in this cohort, no substantial impacts on vaccine-induced antibody titers were observed, suggesting the robustness of parenteral vaccine responses among children from LMIC with similar rates of antibiotic use.

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DISCORDANT DATING OF PREGNANCY BY LAST MENSTRUAL PERIOD VERSUS ULTRASOUND AND ASSOCIATED BIRTH OUTCOMES IN RURAL UGANDA

Jimmy Kizza[1], Anju Ranjit[2], Abel Kakuru[1], Miriam Nakalembe[3], Tonny Rachkara[1], Miriam Aguti[1], Timothy Ssemukuye[1], James Bwire[1], Tamara D. Clark[2], Philip J. Rosenthal[2], Prasanna Jagannathan[4], Michele E. Roh[5], Moses R. Kamya[6], Grant Dorsey[2], Stephanie Gaw[2]

[1]Infectious Diseases research Collaboration, BUSIA, Uganda, [2]University of California San Francisco, San Francisco, CA, United States, [3]Makerere University, Kampala, Uganda, [4]Stanford University, California, CA, United States, [5]University of california San Francisco, San Francisco, CA, United States, [6]Infectious Diseases research Collaboration, KAMPALA, Uganda

Estimation of gestational age (GA) is most reliably achieved from the last menstrual period (LMP) confirmed by ultrasound (US) in early pregnancy. However, in resource-poor areas with limited access to US, pregnancy dating may rely only on LMP, which is often unknown. Inaccurate estimation of GA misinforms the true prevalence of population-level indicators such as preterm birth (PTB) and small-for-gestational-age (SGA). We evaluated the accuracy of estimated due date (EDD) via LMP (LMP-EDD) compared to Final EDD (where the LMP-EDD is corroborated by US) and compared the effect on the prevalence of PTB and SGA. In a cohort of 2757 pregnant women from Busia, Uganda enrolled in a randomized controlled trial evaluating intermittent preventive treatment of malaria in pregnancy, all participants received an US at the time of enrollment to confirm that GA was between 12-21 weeks. To determine the Final EDD, LMP-EDD was replaced with the US-determined EDD when the difference between the estimated GA was >7d (for GA <16 weeks) and >10 days (for GA between 16 and 20 weeks). The prevalence of PTB and SGA using LMP-EDD vs. Final EDD was compared among participants. Over half of the participants (56.8%) did not know their LMP and their GA was based solely on US. Among participants with known LMP, 253 (21.2%) had a change in EDD based on US. Overall, 7.6% of live births would have been classified as PTB if using LMP-EDD, compared to a PTB rate of 5.4% when using Final EDD (p=0.04). The overall rates of SGA were similar between the two methods (LMP-EDD 21.2% vs. Final EDD 22.4%, p=0.51). In the subset of patients with known LMP that were redated by US, the PTB rate was 16.0% vs. 3.5%, using LMP-EDD compared to Final EDD, respectively (p=0.01); the SGA rate was not significantly different (18.0% vs 23.6%, p=0.25). In summary, US was needed to determine the GA in the majority of our population. Use of LMP-EDD without US confirmation skews the true prevalence of PTB, an important maternal-child health metric. This study underscores the need for incorporation of US scans in antenatal care in low and middle-income countries.

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CLINICAL PRESENTATION, TREATMENT, AND OUTCOMES OF NEUROCYSTICERCOSIS AT AN ACADEMIC MEDICAL CENTER IN THE STATE OF FLORIDA, USA

Waverly Leonard[1], Maggie Zawoy[1], Norman Beatty[2]

[1]University of Florida College of Medicine, Gainesville, FL, United States, [2]Department of Medicine, Division of Infectious Diseases and Global Medicine, University of Florida College of Medicine; Emerging Pathogens Institute, Gainesville, FL, United States

Neurocysticercosis (NCC) is a parasitic disease of the nervous system caused by the pork tapeworm, Taenia solium. Though NCC is the leading cause of seizures worldwide, it is under characterized in the US. In the US, NCC primarily occurs in patients who are immigrants and travelers to endemic countries. Characterizing the presentation, course, and outcomes of NCC patients will help clinicians improve diagnosis and treatment. A retrospective analysis was conducted from hospital records between 6/1/1993 until 6/1/2023 using ICD-9 and ICD-10 codes for NCC. Inclusion criteria for this study included those presenting to UF Health Shands Hospital (Gainesville, Florida) with asymptomatic or symptomatic NCC. Diagnostic criteria for NCC consisted of radiologic features, serologic evidence of T. solium infection, or pathological tissue confirmation. 34 patients met inclusion criteria. We collected epidemiological characteristics, hospitalization course, and clinical outcomes for each case. 97% of patients reported symptoms (seizures, neurologic deficits, headaches, hydrocephalus, nuchal rigidity, psychiatric disturbances, and altered mental status) prior to receiving an NCC diagnosis. 25% of patients presented with headaches, 20% presented with seizures, 15% presented with systemic symptoms such as fever, chills, and malaise, and 10% presented with CNS deficits such as cranial nerve deficits and tremors. 69% of patients had presented to another healthcare facility for these symptoms without receiving the correct diagnosis. 52% of patients' cysts were staged. Out of the 52% who were staged, 56% received incorrect medical management; these patients either received medications for inactive infection (18%) or did not receive proper medication for active infection (38%). 21% of patients were readmitted at least once for NCC symptoms or complications. Patients presenting with neurologic symptoms who have a history of travel to endemic areas need to be evaluated for neurocysticercosis. When patients are diagnosed with neurocysticercosis, it is essential that the stage of the infection is determined to properly treat the infection.

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IMPACT OF SULFADOXINE-PYRIMETHAMINE FOR MALARIA PREVENTION IN PREGNANCY ON THE RISK OF REPRODUCTIVE TRACT INFECTIONS: A RANDOMIZED CLINICAL TRIAL

Harriet Ochokoru Adrama, Abel Kakuru, Jimmy Kizza, Mirriam Aguti

Infectious Diseases Research Collaboration, Uganda, Kampala, Uganda

Pathogens responsible for treatable reproductive tract infections (RTIs), notably *Chlamydia trachomatis, Neisseria gonorrhoea*, and *Trichomonas vaginalis*, are estimated to cause >350 million infections annually and are associated with adverse birth outcomes, including abortion, stillbirth, preterm birth (PTB), low birth weight (LBW), small-for-gestational age (SGA), and neonatal death. Sulfadoxine-pyrimethamine (SP), the recommended drug for intermittent preventive treatment of malaria in pregnancy (IPTp), has activity against several bacterial pathogens, including *N. gonorrhea*, and in prior studies increasing doses of IPTp were associated with a decreasing risk of RTIs and adverse birth outcomes. However, there are limited data from randomized controlled trials (RCT) on the impact of IPTp-SP on RTIs and adverse birth outcomes. We are conducting a double-blinded RCT of monthly IPTp with SP vs dihydroartemisinin-piperaquine (DP) vs SP+DP (1:1:1) in HIV uninfected pregnant women residing in Busia District, Uganda. GeneXpert testing for RTIs (*C. trachomatis, N. gonorrhea, T. vaginalis, and Group B Streptoccus)* is performed on vaginal swabs collected during labor or within 28 days after delivery. To evaluate the impact of IPTp on the risk of adverse birth outcomes, we are performing a sub-study to evaluate relationships between IPTp arm, detection of RTIs, and adverse birth outcomes. Enrollment of 2757 women was completed between December 2020-December 2023. Based on preliminary findings through January 2024, 2192 women had delivered and the prevalence of RTIs at delivery was 6.0% for *C. trachomatis*, 2.6% for *N. gonorrhea*, 7.3% for *T. vaginalis*, and 9.7 % for Group B *Streptococcus*. The risk of a composite of adverse birth outcomes (abortion, stillbirth, LBW, PTB, SGA, or neonatal death) was 28.7%. Detection of *T. vaginalis*, but not the other studied pathogens, was associated with a significantly increased risk of having any adverse birth outcome (relative risk = 1.35, 95% CI 1.07-1.69, p=0.02). All women are expected to have delivered by August 2024, followed by unblinding, and unblinded results of the study will be presented.

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EPIDEMIOLOGY, CLINICAL PRESENTATION, AND MANAGEMENT OF SNAKEBITES IN GHANA: INSIGHTS FROM A RETROSPECTIVE STUDY AT A DISTRICT-LEVEL HOSPITAL

Melvin K. Agbogbatey[1], Benno Kreuels[2], Kwaku I. Duah[1], Leslie M. Aglanu[1], Jacqueline G. Asibey[3], Jade Rae[2], Jurgen May[2], John H. Amuasi[1]

[1]Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi, Ghana, [2]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, [3]Holy Family Hospital, Techiman, Ghana

Over 9,600 hospital visits due to snakebites are recorded annually in Ghana with a fatality rate of 3%. However, the epidemiology, clinical presentation, management, and outcomes have not been adequately studied. This retrospective observational study used clinical data on snakebites recorded from 2019 to 2023 at the Techiman Holy Family Hospital, a district-level facility in the Bono East Region of Ghana. The Ghana Health Service Ethics Review Committee approved the study protocol. Sociodemographic and clinical characteristics, as well as treatment and outcomes, were described. Data were obtained from clinical records of 587 snakebite victims. There were 366 (62.3%) male patients, with 50% being farmers. Most were bitten on the lower limb (81.2%), and presented with swelling 347 (63.8%), pain 342 (63.6%), and bleeding 126 (23.3%). Over one in five patients (22.3%) used a herbal remedy before reporting to the hospital. Initial whole blood clotting test (WBCT) was done for 480 patients and 111 (23.1%) of them had an abnormal result (greater than 20 minutes). A median of 5 vials each (IQR 2, 5) was used for the 430 patients (73.3%) who received antivenom. No anaphylaxis or other major side effects were recorded following antivenom administration. Other treatments included analgesia (87.5%), antibiotics (83.2%), anti-tetanus (70.3%), and steroids (59.3%). The commonest complications of the bites were cellulitis (39.2%), coagulopathy (17.9%), and anemia (6.6%), with a median hospital stay of 2 days (IQR 1, 4) and overall case-fatality of 2.4%. The study revealed a predominance of male patients, particularly farmers, highlighting the occupational risk in farming settings, a tendency for lower limb bites, and a high prevalence of hemotoxic envenoming. These can inform prevention efforts and appropriate antivenom stocking to address the specific characteristics of snakebite envenoming in the municipality and mitigate associated morbidity and mortality.

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MPOX INFECTION IN A POSTPARTUM PATIENT: A CASE REPORT FROM GHANA

Gordon Kwasi Ampomah Amoh[1], Beatrice S. Omidiji[2], Joyce O. Inoni[1], Priscilla N. E. W. Vandyck-Sey[1]

[1]Family Medicine Department, Korle-Bu Teaching Hospital, Accra, Ghana, [2]Nsuaem Polyclinic, Nsuaem, Tarkwa, Ghana

Monkeypox is a viral zoonotic disease caused by the monkeypox virus. The diagnosis can be easily mistaken for other differential diagnosis such as Chickenpox. In this paper, we discuss the case of a postpartum patient whose diagnosis of Monkeypox infection was missed on two occasions

before eventually being diagnosed and successfully managed remotely. A 42-year-old female had Caesarean section on account of severe pre-eclampsia and prolonged pregnancy. Three days after the surgery, she noticed a rash around the surgical wound which was misdiagnosed as a reaction due to adhesive allergy from the plaster. On discharge from the health facility, she noticed a spread of the similar rash to her face and reported back to the health facility where she was told she had developed Chickenpox and managed as an outpatient. Patient's condition however worsened over the next couple of days with the rash spreading to her arms, hands, legs, feet, and groin. She also subsequently developed low-grade fever, general malaise, fatigue, headache and vomited twice, leading to her coming to our emergency department. Significant examination findings included cervical and inguinal lymphadenopathy, and mostly papular skin rash with a few areas with vesicular skin eruptions. The labs were unremarkable. Her monkey-pox virus PCR swab result returned positive. Our health facility did not have in-patient isolation facilities. We decided to continue the management of the patient remotely after initial resuscitation, leveraging on telemedicine and scheduled out-patient visits. Through this innovative approach, patient recovered fully without the baby or any household member contracting the disease. This case presented clinical diagnostic problems. The first was with the location of the initial rash leading to the misdiagnosis of adhesive (plaster) allergy. The second was that Monkeypox was wrongly diagnosed as Chickenpox. This makes healthcare worker education very necessary, especially at the primary care level. The use of the telemedicine-based patient-centred care approach could help in the management of carefully selected patients in similar settings.

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TYPHOID CONJUGATE VACCINE DURATION OF IMMUNITY AND BOOSTER RESPONSE IN MALAWIAN CHILDREN

Nginache Nampota-Nkomba[1], Osward M. Nyirenda[2], Victoria Mapemba[2], Priyanka D. Patel[3], Happy C. Banda[3], Felistas Mwakiseghile[3], Theresa Misiri[3], Richard Wachepa[3], John Ndaferankhande[3], Bright Lipenga[3], Robert S. Heyderman[4], Marcela Pasetti[1], Leslie P. Jamka[1], Shrimati Datta[1], Melita A. Gordon[3], Matthew B. Laurens[1], Kathleen M. Neuzil[1]

[1]University of Maryland School of Medicine, Baltimore, MD, United States, [2]Blantyre Malaria Project, Blantyre, Malawi, [3]Malawi Liverpool Wellcome Programme, Blantyre, Malawi, [4]University College London, London, United Kingdom

A single dose of typhoid conjugate vaccine (TCV) given to children is safe, immunogenic, and efficacious in preventing typhoid fever for at least four years. A phase 3 trial of a Vi polysaccharide conjugated to a tetanus toxoid vaccine (Vi-TT) in Malawi, randomized children 1:1 to receive Vi-TT or meningococcal capsular group A conjugate vaccine. From this study population, we recruited children vaccinated at 9-11 months of age into a booster substudy to receive a first Vi-TT (1st-TCV) or booster (Booster-TCV) dose at approximately five years of age. Serum was collected before and 28 days after vaccination and tested for anti-Vi immunoglobulin (Ig) G and IgA antibodies by enzyme-linked immunosorbent assay (ELISA). Seroconversion was defined as ≥4-fold rise in antibody titers from day 0 to day 28 post-vaccination. We enrolled 136 children: 64 1st-TCV and 72 Booster-TCV. At baseline, a higher proportion of Booster-TCV (85.9% and 40.9%) compared to 1st-TCV children (26.6% and 3.1%) had detectable (≥7.4 ELISA Units (EU)/mL and ≥3.125 EU/mL) anti-Vi IgG and IgA titers, respectively. Geometric mean titers (GMT) rose significantly between day 0 and day 28 in both groups but were significantly higher in Booster-TCV children at 6794.2 EU/ml (95% CI 5738.2-8044.6) compared to 1st-TCV children at 2837.2 (2360.9-3409.6). Similar results were seen with IgA; 117.7 EU/ml (93.0-148.9) in Booster-TCV and 95.0 EU/ml (78.5-115.0) in 1st-TCV children. On day 28, all Booster-TCV children and all but one 1st-TCV child seroconverted for IgG. For IgA, a similar proportion of Booster-TCV [95.7% (88.0-99.1)] and 1st-TCV [98.4 (91.3-100.0)] children seroconverted at day 28. The geometric mean fold rise was lower in Booster-TCV [370.1 (289.4-473.4) and 56.7(44.1-73.0)] compared to 1st-TCV [(501.5 (373.5-673.4) and 42.7, (31.6-57.7)] children for both IgG and IgA, respectively, likely because 1st-TCV children started with lower titers. Our study shows a detectable Vi-TT immune response in most children at four years post-vaccination and a robust booster dose immune response at five years of age.

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SUCCESSFUL CHAGAS SCREENING PROGRAM IN OBSTETRIC PATIENTS IN A FEDERALLY QUALIFIED HEALTH CENTER IN NEW YORK

Nancy Piper Jenks[1], Quratulain Zeeshan[1], Vasanthi Arumugan[1], Aarathi Nagaraja[1], Iris Arzu[1], Sristi Shrestha[1], Christina Coyle[2]

[1]Sun River Health, Peekskill, NY, United States, [2]Albert Einstein College of Medicine, New York City, NY, United States

Sun River Health (SRH) is the largest not-for-profit network of federally qualified health centers (FQHC) in NY State (NYS), with a visit volume of 250,000; 41% of patients were born outside of the USA and are predominantly from Central and South America. Chagas disease is underappreciated in the United States, reportable in only 8 states. Many providers are not familiar with the disease, epidemiology or the methods of screening and treatment. SRH began a formal screening program in our OB/GYN clinic in Brentwood, Long Island, in July 2023. A multidisciplinary team was engaged including nursing, infectious disease (ID), OB/Gyn, with strong support from administration. After intensive internal education, all patients seen in antenatal visits had country of birth recorded, and if born in endemic areas had Chagas serology performed. For those who tested positive, confirmatory testing was performed at the NYS Wadsworth Lab. Those who were confirmed positive, with a negative cardiology workup, were offered treatment post-delivery and after breast feeding. Babies of confirmed mothers, along with their siblings and spouses, were also tested. To date, 492 obstetric patients have been screened. Six patients were screened positive, 2 are confirmed, and 4 are pending confirmation. The ages of the women who screened positive ranged from 28 to 39 years. Four from El Salvador and 2 from Honduras. The 2 confirmed positive patients have begun treatment with benznidazole. One child has tested positive, but is awaiting confirmatory results. The success of this program is due to a multi-disciplinary group approach with OB/Gyn as a primary driver. Some of the challenges were the logistics of confirmatory testing and identifying patients for screening. Larger healthcare systems such as FQHCs serving these populations are perfectly positioned to develop screening programs to identify and treat those to with Chagas disease.

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IDENTIFYING BLOOD-BRAIN BARRIER SIGNATURES IN CEREBRAL MALARIA AND CENTRAL NERVOUS SYSTEM INFECTIONS TO INFORM TREATMENT TARGETS AND PATIENT STRATIFICATION

Carla Johnson[1], Brenda Karumbo[1], Dagmara McGuinness[1], Yoana Doncheva[1], Andrew Cameron[1], Kevin Couper[2], Peter Bankhead[3], Nigel Jamieson[1], Christopher Moxon[1]

[1]University of Glasgow, Glasgow, United Kingdom, [2]University of Manchester, Manchester, United Kingdom, [3]University of Edinburgh, Edinburgh, United Kingdom

Cerebral malaria (CM) is a leading cause of death and neurodevelopmental complications in African children. Post-mortem, in vivo retinal imaging, and magnetic resonance imaging studies have implicated blood-brain barrier (BBB) breakdown. BBB breakdown is driven by the adherence of *P. falciparum*-infected red blood cells to the endothelial surface of brain microvessels. Targeting cellular response pathways driving BBB breakdown in CM is key to improving patient outcomes, but the specific pathways involved are not well characterised. Existing models, while important, have limitations. Murine models of CM use a different parasite, and the pathology differs from human disease. In vitro BBB models, while manipulatable, are necessarily reductive. Therefore, it is important to identify their relevance. Post-mortem studies provide the only means to investigate the brain directly in human CM; however, investigating the cellular processes in the brain is complex. Rapid advances in spatial biology have enabled a step-change in

understanding such complex biological processes. We performed spatial transcriptomics and multiparameter imaging techniques on post-mortem brain tissue from fatal Malawian paediatric CM (n=51) and non-malaria central nervous system (CNS) infection cases (n=14). Histology, GeoMx Digital Spatial Profiling, and imaging mass cytometry (40-antibody panel) were used to characterise the cell interactions and phenotypes associated with BBB breakdown. Our data provides a spatially resolved atlas of cells in CM and CNS infection and a wealth of information about vascular and brain-associated changes. A focused analysis found that osteopontin and heme oxygenase-1 are significantly upregulated in vessels with BBB breakdown. These are linked to the downregulation of tight junction proteins. Notably, osteopontin has been associated with BBB breakdown in stroke patients. Additional experiments are in place to validate this dataset using orthogonal methods and in vitro mechanistic studies. Our data will help identify specific pathological CM endotypes and stratify patients to improve outcomes.

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EVALUATION OF A SCALABLE DESIGN FOR A PEDIATRIC TELEMEDICINE AND MEDICATION DELIVERY SERVICE: A PROSPECTIVE COHORT STUDY IN HAITI

Molly B. Klarman[1], Xiaofei Chi[1], Youseline Cajusma[1], Katelyn E. Flaherty[1], Jude Ronald Beausejour[1], Lerby Exantus[2], Valery M. Beau de Rochars[1], Torben K. Becker[1], Chantale Baril[2], Matthew J. Gurka[3], Eric J. Nelson[1]

[1]University of Florida, Gainesville, FL, United States, [2]Université d'État d'Haiti- Faculté de Médecine et de Pharmacie, Port au Prince, Haiti, [3]University of Virginia, Charlottesville, VA, United States

Early access to healthcare is essential to avert morbidity and mortality. A telemedicine and medication delivery service (TMDS) is an innovative solution to address this need, however pathways to scalability are unclear. Our objective was to evaluate a scalable design for a pediatric TMDS for low-resource settings that triages severe cases to hospital-level care, reserves in-person exams at households for moderate cases and provides virtual exams with medication delivery for mild cases.A prospective cohort study was conducted of pediatric patients (≤10 years) who were managed at the scalable TMDS (in-person exams reserved). Safety and feasibility metrics were compared to a prior TMDS mode in which all non-severe patients received both virtual and in-person exams (reference cohort). The primary outcome was rate of improvement (better/recovered) at 10-days. Among 1043 cases (41 severe; 1002 non-severe) enrolled at the scalable TMDS, 19% (190) of the non-severe cases received an in-person exam. Among the 382 cases (24 severe, 358 non-severe) enrolled in the reference cohort, 94% (338) of non-severe cases received an in-person exam. The rate of improvement at 10-days was similar between the scalable (97%, 897) and reference (95%, 329) modes. In the context of a five-fold reduction of in-person exams, the scalable TMDS mode that provides virtual exams with medication delivery for most mild cases had a non-inferior rate of improvement at 10-days. These findings provide a scalable pathway to improve healthcare access through a TMDS care model without compromising safety.

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QUALITY OF LIFE AND FATIGUE AFTER SEVEN YEARS OF CHIKUNGUNYA VIRUS INFECTION: RESULTS FROM A STUDY IN PIEDECUESTA, COLOMBIA

Anyela Lozano-Parra[1], Víctor Herrera[2], Elsa Marina Rojas[3], Carlos Andrés Calderón[3], Reynaldo Badillo[4], Rosa Margarita Gélvez Ramírez[3], María Isabel Estupiñán Cárdenas[3], José Fernando Lozano[3], Luis Ángel Villar[5]

[1]Grupo Epidemiología Clínica, Universidad Industrial de Santander, Bucaramanga, Colombia, [2]Departamento de Salud Pública, Universidad Industrial de Santander, Bucaramanga, Colombia, [3]Centro de Atención y Diagnóstico de Enfermedades Infecciosas-CDI, Fundación INFOVIDA, Bucaramanga, Colombia, [4]Director Departamento Medicina Interna. Universidad de Santander-UDES, Bucaramanga, Colombia, [5]Centro deAtención y Diagnóstico de Enfermedades Infecciosas-CDI, Fundación INFOVIDA, Bucaramanga, Colombia

Chikungunya virus (CHIKV) infection is associated with chronic sequelae whose burden has not been fully characterized. The study aimed to evaluate the quality of life (QoL) and the prevalence of fatigue in a cohort of adults exposed to CHIKV between 2014 and 2015 in Piedecuesta, Colombia. We evaluated 79 subjects (median age: 30 years, IQR: 21 years; women: 60.8%) with confirmed CHIKV infection (RT-qPCR or IgG/IgM ELISA) diagnosed during the outbreak (2014-2015) in Colombia. In 2022, patients completed the 36-item short form (SF-36) and the fatigue severity scale (FSS) surveys and underwent a physical examination that included the gait, arms, legs, and spine examination (GALS) conducted by trained physicians. A rheumatologist evaluated all patients with an abnormal, non-trauma-related GALS examination. We defined chronic fatigue (CF) as an FSS≥36 that persisted for >6 months. We assessed the association of QoL and CF with clinical outcomes by estimating age, sex, and comorbidities-adjusted OR (aOR) using multiple logistic regression. After a mean follow-up of 7.5 years, 11 patients (13.9%) were classified as cases of post-CHIK chronic inflammatory rheumatism (pCHIK-CIR), 32 (40.5%) as non-inflammatory pain likely degenerative (NIP-LD), and 36 (45.6%) as recovered from acute articular symptoms. Patients with pCHIK-CIR and NIP-LD had similar and significantly worse QoL (SF-36's physical and mental components) than those who recovered; however, CF's prevalence showed a gradient across groups, being significantly higher among pCHIK-CIR compared to recovered individuals: 54.6% (aOR=19.0, p<0.01), 25.0% (aOR=2.9, p=0.174) and, 8.6% (reference), respectively. Our results show that about one out of ten CHIKV infections develop chronic articular inflammatory sequelae. These are associated with worse QoL and a higher prevalence of CF. This profile might guide physicians in assessing the disease burden and differentiating pCHIK-CIR from NIP-LD.

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EXPLORING THE IMPACT OF HELMINTH CO-INFECTIONS ON SARS-COV-2 INFECTION DYNAMICS AND IMMUNE RESPONSE: A RETROSPECTIVE COHORT STUDY IN AN AFRICAN POPULATION

Brice Armel Nembot Fogang[1], Linda Batsa Debrah[1], Michael Owusu[2], Adjobimey Tomabu[3], Achim Hoerauf[3], Alexander Yaw debrah[4]

[1]Kwame Nkrumah University of Science and Technology, Department of Clinical Microbiology, Kumasi, Ghana, [2]Kwame Nkrumah University of Science and Technology, Department of Medical Diagnostics, Kumasi, Ghana, [3]Bonn University Hospital, Institute of medical Microbiology, Immunology and Parasitology, Bonn, Germany, [4]Kwame Nkrumah University of Science and Technology, Faculty of Allied health Sciences, Kumasi, Ghana

The spectrum of clinical manifestations resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection varies widely. Despite the global halt of the COVID-19 pandemic, the reasons for Africa's comparatively limited exponential spread remain unclear. Helminth co-infections are suspected to have influenced the pandemic's trajectory in Africa. This study employs a retrospective cohort approach to investigate the interplay between SARS-CoV-2 and helminth infections. Blood plasma samples were analyzed from 104 participants using ELISA and Luminex assays, along with in vitro cell culture and stimulation. Our preliminary findings reveal an overall helminth seropositivity of 41.3% and a SARS-CoV-2 seropositivity of 52.9%, with a significant proportion co-infected. Interestingly, among asymptomatic SARS-CoV-2 infected individuals, the majority had helminth infections (61.5%, CI: 52.3 - 67.0). However, this proportion decreased as the severity of SARS-CoV-2 increased, suggesting a potential relationship between co-infection and milder symptoms. Coinfection and elevated levels of helminth-specific IgG were significantly linked to reduced odds of severe SARS-CoV-2 outcomes alongside decreased levels of SARS-CoV-2-specific IgA and IgG, as well as reduced neutralization potential against both wild type and variants. Moreover, individuals with co-infections showed altered cytokine expression

profiles favoring Th2 responses over Th1 and Th17 responses, whereas those with SARS-CoV-2 mono-infection tended to exhibit more Th1 and Th17 responses than Th2 responses. These initial findings indicate that while co-infection may influence adaptive immunity to SARS-CoV-2, it also helps to alleviate hyperinflammation linked to COVID-19 severity, ultimately enhancing overall health outcomes associated with SARS-CoV-2 infection.

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MULTIPLE PELVIC CONDYLOMATOUS MASSES IN AN AFRICAN CHILD

Sanjai Nagendra[1], Anastasia Furtak[2], Farrrukh Azmi[1], Ketan Patel[1]
[1]Labcorp, Burlington, NC, United States, [2]Baptist Medical Center, Nalerigu, Ghana

Human herpes virus 8-associated malignancies cause significant mortality, mainly due to Kaposi Sarcoma (KS). While most patients with KS present with HIV infection, significant literature on the African endemic HIV-negative subtype is lacking. A twelve-year-old girl from North Ghana presented to a medical facility with rapidly increasing masses on the lateral lower pelvis. Physical examination revealed multiple fungating masses in the lateral side of the trunk suprapubic region, external genitalia, and generalized lymphadenopathy. The patient was negative for HIV antibody and VDRL. Biopsy of the pelvic mass was performed and sent to Labcorp. Histopathologic evaluation revealed a spindled cell vascular tumor positive for HHV8 immunohistochemical stain, consistent with KS, African endemic type. Adapalene, 0.1% cream, was prescribed, and the smallest 0.5 cm masses were entirely resolved after several weeks. Although HHV8 is the causative agent of Kaposi sarcoma and the most common cause of malignancy in HIV-positive individuals, the disease also occurs across sub-Saharan Africa in HIV-negative young adults and prepubescent children. This patient's disseminated lesions, generalized lymphadenopathy, and hepatomegaly suggest an aggressive form of endemic KS. While most cases of endemic KS have been described in Central and Southern Africa, her presentation in northern Ghana is somewhat unusual. While treatment for aggressive forms of KS with paclitaxel and liposomal doxorubicin is the first-line therapy, due to unaffordability, a third-generation retinoid was prescribed. However, retinoids have been successfully used to treat cutaneous KS. However, because of the aggressive and systemic nature of the patient's disease, it is unlikely that the patient will achieve remission from this drug alone. African Endemic KS is often a forgotten subtype that garners little attention and manifests with significant morbidity and mortality. It is hoped that governments can collaborate with pharmaceutical companies to make chemotherapeutic drugs available at low or no cost to treat this often fatal malignancy.

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NOT ALL SEVERE MALARIA CASES ARE SEVERE: IS IT TIME TO REDEFINE SEVERITY CRITERIA FOR MALARIA IN NON-ENDEMIC REGIONS?

Leire Balerdi Sarasola[1], Muñoz Jose[1], Pedro Fleitas[2], Natalia Rodriguez-Valero[1], Alex Almuedo-Riera[1], Alba Antequera[1], Carme Subira[1], Ignacio Grafia[1], Maria Ortiz-Fernandez[1], Teresa De Alba[1], Miriam Martinez-Alvarez[1], Maria Eugenia Valls[1], Claudio Parolo[3], Pedro Castro[1], Daniel Camprubí-Ferrer[1]
[1]Clinic Hospital, Barcelona, Spain, [2]isglobal, Hospital Clínic - Universitat De Barcelona, Barcelona, Spain, [3]isglobal, Barcelona, Spain

Management of malaria in non-endemic regions differs significantly from that in endemic regions. Despite this, the current definition of severe malaria in non-endemic areas follows WHO criteria, mainly targeting children in malaria-endemic areas, potentially misclassifying cases. We assessed the performance of a modified severe malaria classification criteria within our patient cohort. A retrospective cohort study of patients diagnosed and managed for malaria in a non-endemic hospital (2005-2023) was analyzed. Patients were classified into severe malaria (SM) and uncomplicated malaria (UM) according to WHO 2013 severity criteria with the exception of parasitemia. SM cases were re-classified into two new categories, named "very severe malaria" (VSM) and "less severe malaria" (LSM). A composite outcome called "life-threatening conditions", was defined, which integrated death and the need for life-saving interventions such as mechanical or non-mechanical ventilation, use of vasoactive drugs, hemodialysis and automated red blood cell exchange. Secondary outcomes included co-infections. The frequency of the outcomes was compared between groups (SM *vs.* UM and VSM *vs.* LSM). Among 506 malaria patients 176 (34.8%) presented with SM, according to WHO severity criteria. Regarding severity, 37(7.3%) patients developed a life-threatening condition, namely death (n=4) and/or the need for life-saving interventions (n=34). All fatalities and 33 of the 34 life-saving interventions occurred in the VSM group. Patients in LSM group did not develop any life-threatening conditions. As to co-infections, 28(5.5%) patients had a community-acquired co-infection, with no differences between groups (p=0.763). Severity criteria definitions would benefit from a review when assessing patients with malaria in non-endemic areas. Within the spectrum of severe malaria, patients reclassified as LSM have a low risk of developing a life-threatening condition, and could benefit from a less intensive monitorization unit and a restrictive use of empirical antibiotics.

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FIELD EVALUATION OF A NOVEL SEMI-QUANTITATIVE POINT-OF-CARE DIAGNOSTIC FOR G6PD DEFICIENCY IN INDONESIA

Arkasha Sadhewa[1], Lydia V. Panggalo[2], Illene Nanine[2], Ric N. Price[1], Kamala Thriemer[1], Ari W. Satyagraha[3], Benedikt Ley[1]
[1]Menzies School of Health Research and Charles Darwin University, Global and Tropical Health Division, Darwin, Australia, [2]EXEINS Health Initiative, Jakarta, Indonesia, [3]Eijkman Research Center for Molecular Biology, National Research and Innovation Agency, Jakarta, Indonesia

The WHO recommends routine testing of G6PD activity to guide radical cure in patients with *Plasmodium vivax* malaria. Females can have intermediate G6PD enzyme activity, and to date, only complex quantitative diagnostics have been able to reliably identify them. The semi-quantitative G6PD diagnostic "One Step G6PD Test" (Humasis, RoK; "RDT") is a lateral flow assay that offers a simpler diagnostic alternative capable of distinguishing deficient, intermediate, and normal G6PD individuals. G6PD status of participants enrolled in Malinau and Nunukan Regencies and the capital Jakarta was assessed with the RDT, and their G6PD activity was measured in duplicate by reference spectrophotometry. The adjusted male median (AMM) of the spectrophotometry measurements was defined as 100% activity; 70% and 30% of the AMM were defined as thresholds for intermediate and deficient G6PD status, respectively. Results were compared to those derived from spectrophotometry at both of these clinically relevant thresholds. Of the 161 participants enrolled, 10 (6.2%) were G6PD deficient and 12 (7.5%) had intermediate G6PD activity by spectrophotometry. At the 30% threshold, the sensitivity of the RDT was 10.0% (95%CI: 0.3-44.5%) with a specificity of 99.3% (95%CI: 96.4-100.0%); the positive predictive value was 50.0% (95%CI: 1.3-98.7%) and the negative predictive value 94.3% (95%CI: 89.5-97.4%). The corresponding figures at the 70% threshold were 22.7% (95%CI: 7.8-45.4%), 100.0% (95%CI: 97.4-100.0%), 100.0% (95%CI: 47.8-100.0%) and 89.1% (95%CI: 83.1-93.5%), respectively. Although there is an urgent need for an easy-to-use, affordable, semi-quantitative point of care diagnostic for G6PD deficiency, the observed performance of the "One Step G6PD Test" in its current form was insufficient to guide antimalarial treatment.

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CHARACTERIZATION OF MORTALITY AMONG CHILDREN ADMITTED TO A RURAL MOZAMBICAN DISTRICT HOSPITAL: TWENTY-TWO YEARS OF CONTINUOUS HOSPITAL-BASED MORBIDITY SURVEILLANCE

Rosauro Varo[1], Antonio Sitoe[2], Jaime Fanjul[1], Sara Ajanovic[1], Sozinho Acacio[3], Charfudin Sacoor[4], Elisio Xerinda[4], Marcelino Garrine[4], Lola Madrid[5], Inácio Mandomando[4], Quique Bassat[1]

[1]Barcelona Institute for Global Health, Barcelona, Spain, [2]Manhiça Health Research Center, Barcelona, Spain, [3]Manhiça Health Research Center, Manhiça, Spain, [4]Manhiça Health Research Center, Manhiça, Mozambique, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom

Hospitalized children in rural Sub-Saharan Africa often present an unacceptably high risk of mortality. Detailed descriptions of causes of death and in-hospital mortality trends provide valuable data to design targeted interventions for child mortality prevention. However, previous studies are often derived from unreliable and unspecific methods or focus solely on a particular disease. This study aimed to describe the main causes and trends of mortality across time, identifying risk factors independently associated to mortality during admission. Combining demographic and morbidity surveillance databases from the Manhiça district, Mozambique, admissions of children under 15 years to the Manhiça district Hospital from 2000 to 2021 were analysed. Over a total of 62200 paediatric hospital admissions, 2244 in-hospital deaths were identified (in hospital case fatality rate (CFR): 3.6%), with an additional 525 deaths within the first 7 days post-discharge (short-term mortality CFR: 4.45%) potentially linked to the same disease leading to the initial hospitalization. CFRs were significantly higher among neonates up to 28 days of age, and no clear decreasing trends were observed throughout the years. During our study period, malaria was the major contributor to overall mortality, closely followed by pneumonia. However, the proportion of deaths attributed to malaria declined, whereas conditions arising during the perinatal period increased. Variables related with respiratory distress, decreased consciousness status, malnutrition and diarrhea-associated symptomatology showed a higher prognostic value for death across all age groups and were found to be major independent risk factors for death. Other variables such as timing of admission (night or weekend admissions, or certain months during the cold season) also posed a higher risk of death for the admitted patient. This study highlights opportunities for clinicians and policy makers to target specific signs and symptoms, conditions, time periods, and geographical areas in measures aimed at improving child survival.

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ANTIBODY-OMICS REVEALS DISTINCT IMMUNOLOGICAL SIGNATURES IN LEPROSY PATIENTS AND THEIR HOUSEHOLD CONTACTS

Pedro Marcal[1], Anushka Saha[1], Trirupa Chakraborty[2], Priyamvada Guha Roy[2], Jishnu Das[2], Lorena Oliveira[3], Joaquim P. Brito-de-Sousa[4], Olindo A. Martins-Filho[4], Lucia A.O Fraga[5], Jessica K. Fairley[6], Aniruddh Sarkar[1]

[1]Georgia Institute of Technology, Atlanta, GA, United States, [2]University of Pittsburgh, Pittsburgh, PA, United States, [3]Universidade Vale do Rio Doce - Univale, Governador Valadares, Brazil, [4]Grupo Integrado de Pesquisas em Biomarcadores, Instituto René Rachou, FIOCRUZ-Minas, Belo Horizonte, Brazil, [5]Universidade Federal de Juiz de Fora, campus GV, Governador Valadares, Brazil, [6]Emory University, Atlanta, GA, United States

Leprosy diagnosis is often complex, requiring assessment of clinical and laboratory parameters. Lack of tests for an unequivocal early diagnosis has limited control and elimination efforts. Current antibody (Ab) tests (e.g. anti-LID-1 IgG, anti-PGL-1 IgM), offer limited and variable sensitivity. We have developed a multiplexed 'Ab-omics' platform for deep characterization of a diverse array of antigen-specific Abs (isotype, glycosylation, and Fc receptor binding). Applying the Ab-omics pipeline to sera from clinically confirmed leprosy patients, their household contacts (HHC) and endemic controls (EC) (n=92, from Minas Gerais, Brazil), using multiple M. leprae and other antigens uncovered distinct biomarkers indicative of leprosy. With a total of 221 measured features for each sample, LASSO-based feature selection identified an Ab signature, accurately distinguishing Leprosy patients and HHC (AuC>0.9). This included: IgA-PGL1, IgG3-PGL1, RCA-CFP10, FcR1-ML2567. Further we applied SLIDE, a novel interpretable machine learning method, to this high-dimensional dataset to identify latent factors that moves beyond individual biomarkers and provide insights into the pathophysiology of leprosy-infected patients as well as HHC and EC subjects. This identified modules with unique humoral signatures of active disease, including a module highlighting hallmark signatures of infection such as elevated IgG, IgG1, and IgM. However, we also captured previously uncharacterized humoral responses including elevated FcR binding and reduced sialylation and galactosylation in actively infected patients, helping distinguish them from HHCs. Furthermore, analysis of cytokines and chemokines obtained in culture stimulated with crude ML antigen demonstrated an inflammatory profile (IFN-g, TNF and IL-10) in leprosy patients. Overall, we unveil both novel biomarkers for Ab-based diagnostics and latent factors underlying the pathogenesis of Leprosy infection. Our results suggest selective antigen and Fc receptor targeting could be the key to early detection and controlling infection severity.

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DISSECTING THE DIAGNOSTIC PERFORMANCE OF THE ALERE FILARIASIS TEST STRIP FOR THE DETECTION OF ACTIVE *WUCHERERIA BANCROFTI* INFECTION AND TREATMENT SUCCESS

John Opoku[1], Linda Batsa Debrah[2], Stefan Schlabe[3], Jubin Osei-Mensah[2], Vera Serwaa Opoku[1], Derrick Adu Mensah[1], Kenneth Pfarr[3], Patricia Jebett Korir[3], Achim Hoerauf[3], Ute Klarmann-Schulz[3], Alexander Yaw Debrah[2]

[1]Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi, Ghana, [2]Kwame Nkrumah University of Science and Technology, KNUST, Kumasi, Ghana, [3]Institute of Medical Microbiology, Immunology, and Parasitology - University Hospital of Bonn, Bonn, Germany

Accurate and reliable diagnostic tools are critical in achieving the 2030 elimination targets for Lymphatic filariasis (LF), mostly caused by the *Wuchereria bancrofti* parasite. However, there are several concerns regarding the accuracy of the endpoint infection thresholds reported using the Alere Filariasis Test Strip (FTS), recommended for LF assessment surveys and treatment monitoring. This study sought to investigate the diagnostic performance, particularly sensitivity and specificity, of the FTS in providing precise endpoint infection thresholds. Plasma samples obtained from the same cohort of individuals (n = 143) with known adult worm and microfilariae (Mf) burdens at pre-treatment and 24 months post-treatment were used. The sensitivity of the FTS was evaluated in microfilaremic and amicrofilaremic subgroups of adult worm-infected individuals at both time points. Its specificity was assessed in those who cleared adult worm and Mf burdens two years after doxycycline macrofilaricidal treatment. Additionally, samples from 71 uninfected individuals living in the same endemic area were also analyzed for comparison. The FTS showed significantly greater sensitivity in detecting microfilaremic adult worm-infected individuals (pre-treatment = 100%; 24 months post-treatment = 95.8%) compared to their amicrofilaremic counterparts (pre-treatment = 65.8%; 24 months post-treatment = 52.2%). The specificity of the FTS in confirming treatment success among those who cleared both adult worm and Mf burdens at 24 months post-treatment was 73.0% (CI = 62.58-81.90). This was significantly lower compared to its specificity for uninfected individuals (95.8%, CI = 88.14-99.12). Overall, our findings reveal the subpar diagnostic performance of the FTS in detecting amicrofilaremic adult worm-infected individuals and confirming treatment success in individuals who clear adult worm and Mf two years after treatment. Hence, there is a need for alternative diagnostic approaches with improved performance characteristics, particularly in post-treatment contexts, to expedite the realization of the 2030 elimination targets for LF.

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COMPARATIVE ANALYSIS OF THE OV16 ENZYME LINKED IMMUNOSORBENT ASSAY AND THE OV16 RAPID DIAGNOSTIC TEST FOR THE MAPPING OF ONCHOCERCIASIS AND THE DISCONTINUATION OF MASS DRUG ADMINISTRATION

André Domche[1], Linda Djune-Yemeli[1], Hugues C. Nana-Djeunga[2], Flobert Njiokou[1], Flobert Njiokou[1], Joseph Kamgno[2]

[1]University of Yaoundé I, Yaoundé, Cameroon, [2]Higher Institute for Scientific and Medical Research, Yaoundé, Cameroon

Various tools have been evaluated for the diagnosis of onchocerciasis, including the standard diagnostic (SD) Bioline ELISA and the rapid diagnostic test (RDT), but their performance has been inconsistent. Sensitivity, specificity, and standardization of these tools are major challenges. We conducted a study to compare the sensitivity and specificity of the Ov16 ELISA and Ov16 RDT in detecting onchocerciasis infection in dried blood spots from individuals aged 1-10 years in two first-line villages in Central Cameroon. The Ov16 IgG4 ELISA kit and the Ov16 RDT were used to detect antibodies. Spearman correlation and kappa statistics were used to assess relationships and agreement between tests. A total of 158 samples (seroprevalence: 28.2%) were positive for Ov16 antibodies by ELISA and 104 (seroprevalence: 18.6%) by Ov16 RDT ($p<0.0001$). Median IgG4 levels were significantly higher in RDT-positive samples ($p<0.0001$). The agreement between the two tests was good, with high sensitivity (96.4%) and specificity (88.6%). Spearman correlation showed a positive correlation between RDT grade and antibody level, with the higher antibody rate observed in grade 2 and 3 tests ($r = 0.654$, $p<0.0001$). Although there was overall agreement between the Ov16 RDT and the Ov16 ELISA, with good concordance between the two tests, the Ov16 ELISA was able to detect more Onchocerca volvulus infections than the Ov16 RDT. Further studies in other populations and settings may be needed for a more thorough evaluation.

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FOCAL SPLEEN LESIONS IN LOIASIS: THE SPLOA PILOT STUDY IN GABON

Federico Giovanni Gobbi[1], Bayode Adegbite[2], Fabrice M'Baidiguim[2], Anita Lumeka[2], Andrea Obele Ndong[2], Cristina Mazzi[1], Jean Ronald Edoa[2], Yabo Honkpehedji[2], Jeannot Zinsou[2], Jean Claude Dejon-Agobé[2], Zoleko-Manego Rella[2], Michael Ramharter[2], Ayola Akim Adegnika[2], Francesca Tamarozzi[1]

[1]IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Italy, [2]Centre de Reserches Medicales de Lambarene, Lambarene, Gabon

Infection with the filarial nematode *Loa loa*, has been associated with increased morbidity and mortality. A number of reports described the presence of spleen nodules, originating from degradation of microfilariae, in humans and animals infected with *L. loa*. The long-term consequences of this process on individuals chronically exposed to infection in terms of spleen function and possible link with excess mortality are unknown. The aim of this study was to evaluate the prevalence of focal spleen lesions, their evolution over time, and markers of spleen function, in individuals with *L. loa* infection living in highly endemic areas of Gabon. This was a cross-sectional study followed by a longitudinal study of subjects with spleen nodules. 216 participants from Ngounié and Moyen-Ogooué provinces of Gabon, reporting a history of eyeworm migration and/or Calabar swelling, were included. Participants were categorized into infected microfilaraemic with low (N=74) and high (N=10) microfilaraemia, and symptomatic amicrofilaraemic (N=132), based on evaluation of microfilaraemia by microscopy. Howell-Jolly bodies in erythrocytes, as indirect marker of spleen functional impairment, were not observed. On ultrasound, no evident signs of spleen fibrosis or hypotrophy were observed. Multiple spleen hypoechoic centimetric macronodules were observed in 3/216 participants (1.4%), all with patent *L. loa* infection (3.4% of microfilaraemics); macrondules disappeared at the 6-months follow-up examination in 2/3 individuals. Spleen hypoechoic micronodules, persisting at the 6-months follow-up, were detected in all 3/216 participants (1.4%), who became all amicrofilaraemic. Transitory spleen macronodules are present in a small but consistent proportion of individuals with patent loiasis, appearing a rather benign phenomenon in terms of impact on spleen morphology and function. Their occurrence should be taken into consideration to avoid misdiagnosis and mistreatment. Prevalence and significance of spleen micronodular ultrasound patterns in the general population would be also worth evaluating.

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ELIMINATION GOALS FOR ONCHOCERCIASIS CAN BE PROGRESSED FASTER BY INCORPORATING TREATMENT WITH REPURPOSED DRUGS THAT TARGET VARIOUS STAGES OF FILARIAL WORMS

Sara Lustigman[1], James W. Janetka[2], Denis Voronin[3], Judy A. Sakanari[4], Makedonka Mitreva[5]

[1]Laboratory of Molecular Parasitology, Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY, United States, [2]Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, St. Louis, MO, United States, [3]Systems Genomics Section, Laboratory of Parasitic Diseases, Division of Intramural Research, NIAID, NIH, Bathesda, MD, United States, [4]Department of Pharmaceutical Chemistry, University of California San Francisco, San Francisco, CA, United States, [5]Department of Medicine, Washington University School of Medicine, St. Louis, MO, United States

The Current Preventive Chemotherapy and Transmission Control strategy for onchocerciasis aims to interrupt transmission through annual or bi-annual mass drug administration with ivermectin (IVM). Without available macrofilaricides, however, the adult worms producing microfilariae will survive, underscoring the urgent need for developing macrofilaricides. Importantly, transmission model simulations indicate that the combined use of a hypothetical macrofilaricide (with ~60% efficacy) with IVM would substantially increase the probability of elimination compared with the independent use of each, highlighting a need for alternative integrated treatment regimens. Using phenotypic screenings of drugs approved for clinical use, we have identified several drugs that can be repurposed for use as therapeutic macrofilaricidal (targeting adult worms and/or embryos) as well as prophylactic drugs (targeting the establishment of early infections in the host that would have otherwise developed into adult fertile worms). We demonstrated that, 1) Nelfinavir (anti-HIV drug that targets aspartic proteases) significantly inhibited motility of *Brugia pahangi* female worms *in vitro* and reduced survival of adult worms as well as their fecundity *in vivo*; 2) Niclosamide and Rottlerin (autophagy inducing drugs) significantly reduced *Wolbachia* levels *in vitro* and *in vivo*, as well as embryogenesis and fecundity in treated female *B. pahangi* worms *in vivo*; and 3) Emodepside (repurposed macrofilaricide under clinical development), when used as a prophylactic drug, inhibits molting and motility of *O. volvulus* and *B. pahangi* early stages of the parasite *in vitro* with IC_{50}s in the nanomolar range. Our findings indicate that a major programmatic shift that incorporates integrated control strategies, aimed at reducing both the overall adult worm burden and transmission, is needed to achieve the 2030 WHO elimination of transmission goals for onchocerciasis.

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EVALUATION OF A NOVEL BIPLEX RAPID DIAGNOSTIC TEST FOR ANTIBODY RESPONSES TO *LOA LOA* AND *ONCHOCERCA VOLVULUS* INFECTIONS

Jeremy T. Campillo[1], Marco Biamonte[2], Marlhand C. Hemilembolo[3], Francois Missamou[3], Michel Boussinesq[4], Sebastien D S Pion[4], Cédric B. Chesnais[4]

[1]Inserm, Montpellier, France, [2]Drugs & Diagnostics for Tropical Diseases, San Diego, CA, United States, [3]Programme National de Lutte contre l'Onchocercose, Brazzaville, Congo, Republic of the, [4]Institut de recherche pour le développement, Montpellier, France

Loiasis, caused by the filarial worm *Loa loa*, affects approximately 10 million individuals. Clinical manifestations include Calabar swellings, eye-

worm, and less specific general symptoms. Loiasis presents a significant public health challenge because *L. loa*-infected individuals can develop serious adverse events after taking ivermectin, the drug used to combat onchocerciasis. In this context, alternative interventions and rigorous diagnostic approaches are needed. Diagnosing loiasis is challenging due to sporadic and non-specific clinical symptoms. The definitive diagnosis relies on identifying adult worms migrating beneath the conjunctiva, or microfilariae (embryos) in blood smears. However, "occult loiasis" (infection without blood microfilariae) is frequent. Serological rapid antibody diagnostic tests (ARTs) can provide an alternative diagnostic method. We compared a novel ART simultaneously targeting onchocerciasis (IgG4 to Ov-16 and OvOC3261, test line 1) and loiasis (IgG4 to L1-SXP-1, test line 2), called IgG4-SXP-1 biplex test, to the already established *Loa*-ART (all IgG isotypes to LI-SXP-1, called pan-IgG-SXP-1 test). Sensitivity was similar for both ARTs when using eye-worm or Calabar swelling history as references, but diagnostic performance varied based on microfilaremia levels and occult loiasis. Overall, IgG4-SXP-1 biplex test demonstrated a sensitivity of 84.1% and specificity of 47.6% for loiasis compared to the pan-IgG-SXP-1 test, leading to a Kappa coefficient estimated at 0.27 ± 0.03 for the qualitative results of the 2 ARTs. In the group that tested positive with the Pan-IgG test but negative with the IgG4-specific test, there was a lower prevalence of STH infection (p=0.008) and elevated eosinophilia (p<0.001) compared to the general tested population. The diagnostic agreement between the two ARTs was poor, suggesting that IgG and IgG4 antibody responses should be interpreted differently. The assessment of the innovative IgG4-SXP-1 biplex test, designed for onchocerciasis and loiasis, shows encouraging sensitivity but underscores the necessity for further in vitro assessment.

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RANDOMIZED, DOUBLE-BLIND TRIAL EVALUATING THE SAFETY AND EFFICACY OF A 3- OR 5-DAY COURSE OF LEVAMISOLE (2.5 MG/KG) IN SUBJECTS WITH *LOA LOA* MICROFILARAEMIA

Jérémy T. Campillo[1], Cédric B. Chesnais[2], Bachiratou Sahm[2], Marlhand C. Hemilembolo[3], Sébastien D S Pion[2], Francois Missamou[3], Michel Boussinesq[2]

[1]Inserm, Montpellier, France, [2]Institut de recherche pour le développement, Montpellier, France, [3]Programme National de Lutte contre l'Onchocercose, Brazzaville, Congo, Republic of the

Onchocerciasis elimination programs are based on repeated mass administration of ivermectin to the entire population living in endemic areas, without prior diagnosis. However, these programs face challenges in loiasis co-endemic areas due to the risk of serious adverse reactions caused by ivermectin in individuals with high *Loa loa* microfilarial density (MFD). This research aims to evaluate a pre-treatment strategy based on levamisole (LEV) to reduce the *L. loa* MFD, enabling subsequent safe mass treatment with ivermectin in onchocerciasis-loiasis coendemic areas. This study represents the second trial of LEV in *L. loa*-infected subjects. In 2021, we conducted the first double-blind, randomized, placebo-controlled clinical trial in the Republic of Congo, evaluating the safety and efficacy of single doses (escalating dosages) of LEV on *L. loa* MFD. This trial demonstrated the safety of LEV in managing *L. loa* MFD and showed that a single dose of 2.5 mg/kg of LEV induced a transient but still insufficient reduction in MFD. The objective of the present trial is to evaluate the safety and efficacy of 3-day or 5-day regimens of LEV at 2.5 mg/kg. This trial is also a double-blind, randomized, placebo-controlled trial and will involve individuals with high *L. loa* MFD. It will be conducted from June 2024 in a rural area of Congo (Lékoumou department). A total of 99 subjects will be included in one of three study arms: 3 days of LEV (2.5 mg/kg), 5 days of LEV (2.5 mg/kg), or placebo. The goal is to recruit as many individuals as possible with at least 10,000 microfilariae/mL during the screening campaign, but all patients with microfilaremia can be included. Included individuals will be followed for 1 month (15 days of close follow-up for safety and 30 days to assess efficacy on *L. loa* MFD). The main evaluation criteria are assessment of adverse effects during the 15 days following treatment, and assessment of *L. loa* MFD reduction rates at one month.

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PROVIDING EVIDENCE ON THE STATUS OF TRANSMISSION OF ONCHOCERCIASIS IN FIVE COUNTIES IN LIBERIA

Sonnie Ziama Gbewo

Ministry of Health, Paynesville, Liberia

In 2018, Liberia conducted its first programmatic Ov16 serological survey (pre-stop) to provide evidence on the status of transmission of Onchocerciasis in the Southwest Regions (five counties: Bomi, Cape Mount, Margibi, Grand Bassa and River Cess). These five counties had received 14th years of MDA with ivermectin. Specifically, the objective was to determine the village level sero-prevalence of Ov16 in children 5-9 years old. A target convenience sample size of 100 children from each of 30 frontline communities within 5km of a blackfly breeding site or onchocerciasis river basin was selected in line with WHO onchocerciasis technical subcommittee guidelines. All enrolled consented children were tested for Ov16 using RDT in the field, and DBS were collected to allow subsequent ELISA testing. Of children testing negative for rapid test, 10% was randomly selected for confirmatory testing using SD Ov16 ELISA (Abbott, South Korea). Out of the target sample size of 3,000, a sample size of 2,468 was achieved. 91 of these children tested positive for Ov16 via RDT in the field. Out of 30 communities tested with RDT, 19 communities had positive cases while 11 reported all negative tests. The overall seroprevalence rate of 3.7% (91/2432) was found in five counties (Bomi, Grand Bassa, Grand Cape Mount, Margibi and Rivercess) with rate of 3.7% (21/572) in onchocerciasis endemic county only. In addition, rates of 3.2% (10/314), 0.5% (3/595), 0.7% (3/455) was observed in onchocerciasis and lymphatic Filariasis co-endemic counties with a high rate of 10.9% (54/496), respectively. According to WHO, to proceed to a full stop MDA survey, the prevalence threshold for IUs to "pass" pre-stop is <2%. We realized only two counties have crossed this benchmark, onchocerciasis transmission is still ongoing in Rivercess county and there is a need for support to conduct similar testing in the remaining 10 counties.

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DEVELOPMENT OF A SIMPLE AND SENSITIVE SPLINTR LIGASE MEDIATED MICRORNA DETECTION METHOD FOR FILARIAL MIR71 AND BANTAM

Zhiru Li, Katell Kunin, Amit Sinha, Larry A. McReynolds, Clotilde K.S. Carlow

New England Biolabs, Ipswich, MA, United States

MicroRNAs (miRNA) are short (19-25 nt) non-coding RNAs that are found in an evolutionarily diverse assortment of organisms ranging from sponges to vertebrates, including filarial worms. Some miRNAs appear to be filarial-specific and differentially expressed in different stages of worm development. miR-71 is one of the most ubiquitous, conserved and highly expressed miRNAs in helminths, including *Brugia malayi*. It regulates multiple cellular processes and plays an important role in host-nematode interactions. It is found in extracellular vesicles secreted by filarial nematodes that could be internalized by host immune cells and regulate the host immune response. Even for the parasite such as *Onchocerca volvulus* that does not live in the bloodstream, circulating parasite-derived miR-71 has been found in human serum samples from infected human subjects, but not in uninfected ones, indicating that miRNA could serve as potential biomarkers. However, to detect the low levels of the filarial miRNA in human serum, a sensitive detection assay is essential for field application. Here we describe the development of an optimized SplintR ligase mediated microRNA detection method that uses a combined hybridization and ligation step of two DNA probes followed by sensitive qPCR detection for two filarial miRNAs: miR-71 and bantam. The assays showed higher sensitivity than other commercial miRNA detection methods and can specifically detect less than 100 copies of microRNA within 2 hours. Both microRNA can be detected in RNA extracted *Dirofilaria immitis* and *B. malayi*. Potential application was also demonstrated by detection of miRNA

in serum from infected host. This technique holds the promise of broad utilization as a miRNA detection tool in both scientific research and clinical settings.

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PERFORMANCE OF ELISAS BASED ON CHIMERIC PROTEINS TO DETECT ANTIBODY TO *ONCHOCERCA VOLVULUS* INFECTION

Sylvia Ossai[1], Yong Wang[1], Kimberly Y. Won[1], Kathy Kamath[2], Jack Reifert[2], William E. Secor[1], Sukwan Handali[1]

[1]Centers for disease control and Prevention, Atlanta, GA, United States, [2]Seraimmune, Goleta, CA, United States

WHO's target product profiles (TPP) for onchocerciasis outline stringent criteria, requiring tests intended for mass drug administration stopping decisions to have a sensitivity of ≥89% and a specificity of ≥99.8%. Achieving this specificity will require the use of multiple biomarkers. To identify *Onchocerca volvulus*-specific antigens to use in combination with Ov16, we utilized a serum epitope repertoire analysis (SERA) platform that employs a 12-amino acid peptide library display followed by next generation sequencing with proprietary informatics to screen unique reactivity to sera. 60 *O. volvulus* confirmed positive sera, 60 *O. volvulus* negative sera, and 60 *Wuchereria bancrofti* positive sera to eliminate cross-reactive epitopes were screened using SERA. Ninety-nine peptides were identified that showed reactivity for total IgG, IgG1, or IgG4 in positive *O. volvulus* specimens and no reactivity in negative or *W. bancrofti* specimen. These peptides underwent further screening using peptide arrays, with 24 epitopes exhibiting signal-to-noise (S/N) ratios ≥10. Candidate epitopes were mapped to specific proteins, synthesized as 24 amino acid biotinylated peptides, and screened in peptide ELISA against cross-reactors such as *W. bancrofti, Mansonella perstans,* and *Loa loa* pooled positive sera. We identified 19 peptides with S/N>10 and no reactivity against the cross-reactors. We created seven multi-epitope, chimeric (c) proteins using various peptide combinations, evaluated their antigenicity using the VaxiJen prediction program, and expressed them in an *E. coli* bacterial expression system. The most effective antigen combination (rOv16-rOv18c-rOv53c) demonstrated an improved sensitivity of 98% compared to the 89.5% sensitivity of rOv16 ELISA alone. None of these antigens alone or when used as combination was able to meet the WHO specificity requirements, and as such efforts are ongoing to identify additional biomarkers to meet the goal. Nevertheless, combining these antigens to detect IgG4 antibodies effectively met the minimum TPP sensitivity criteria for onchocerciasis mapping and stopping decisions.

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DEVELOPMENT OF A NEW RAPID DIAGNOSTIC TEST TO SUPPORT ONCHOCERCIASIS ELIMINATION

Marion Darnaud[1], Karen Louis[1], Marie Koenig[1], Viet-Dung Tran[1], Charlotte Mignon[1], Stéphanie Donnat[1], Romain Clément[1], Sasisekhar Bennuru[2], Thomas Nutman[2], Jacob Souopgui[3], Robert Colebunders[4], Linda Djune-Yemeli[5], Hugues C. Nana-Djeunga[5], Joseph Kamgno[5], Dziedzom K. de Souza[6], Bruno P. Mmbando[7], Michelle Chavez[8], Bret Sheffield[8]

[1]BIOASTER, Lyon, France, [2]Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD, United States, [3]Department of Molecular Biology, IBMM, ULB, Brussels, Belgium, [4]Global Health Institute, University of Antwerp, Antwerp, Belgium, [5]ISM, Yaounde, Cameroon, [6]Parasitology Department, NMIMR, Accra, Ghana, [7]NIMR, Tanga, Tanzania, United Republic of, [8]DCN Dx, Carlsbad, CA, United States

Around 21 million people are estimated to have onchocerciasis (river blindness), a parasitic disease caused by the filarial nematode *Onchocerca volvulus* (Ov). Currently, the primary strategy for combating onchocerciasis is community-directed treatment with ivermectin (CDTI), requiring a minimum of 80% annual therapeutic coverage for 12-15 years. For onchocerciasis mapping and to know when and where CDTI could be stopped, highly sensitive and specific onchocerciasis diagnostic tests are needed. Rapid tests detecting Ov16 IgG4 antibodies in blood have been developed but showed diagnostic performances slightly lower than the 99.8% specificity as defined in the target product profiles generated by the WHO. To improve the existing Ov16 lateral flow immunoassay (LFA), the goal of this project is to achieve the targeted specificity performance by multiplexing immunogenic Ov antigens. First, we completed an *in silico* evaluation of 45 published Ov antigens using pairwise alignment on proteomes of helminths co-endemic with onchocerciasis. We selected 4 Ov candidate antigens (OVOC3261, OVOC10469, OvMCBL02 and LBE8) with ≤70% amino acid sequence identity over >70% of the total protein length with orthologs from related filarial and other helminth species. To further assess these candidate antigens, each antigen was separately immobilized on ELISA microplates, as well as on LFA membranes, and tested using plasma samples from patients with onchocerciasis, loiasis, mansonellosis and lymphatic filariasis along with healthy controls to confirm sensitivity, specificity, and absence of cross-reactivity with other helminths. For this purpose, we worked with partners in Africa to source a panel of clinical specimens to enable development and performance evaluation of the new onchocerciasis LFA. Then, prototyping of singleplex LFAs was performed in collaboration with DCN Dx to identify best mutual test conditions prior multiplexing. The next milestone of the project will focus on the feasibility, optimization, and clinical diagnostic performance evaluation of the prototype multiplex LFA to support WHO's goal of eliminating onchocerciasis.

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MAMMALIAN EXPRESSED OV16 ELISA PERFORMANCE ON GHANA PROGRAM SAMPLES IN COMPARISON TO ELUTED DRIED BLOOD SPOT ON OV16 RAPID DIAGNOSTIC TEST

Eric Scott Elder[1], Gifty Boateng[2], Sylvia Ossai[1], Andrew Abbott[1], Lorreta Antwi[2], Kofi Asemanyi-Mensah[3], Ben Masiira[4], Lakwo Thomson[4], Ernest Kenu[4], Odame Asiedu[3], Jessica Prince-Guerra[1], Kimberly Won[1], Karana Wickens[1], Maria Ulke[1], Sukwan Handali[1], William Evan Secor[1], Joseph Opare[3], Paul Cantey[1]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]National Public Health and Reference Laboratory, Accra, Ghana, [3]Neglected Tropical Diseases Program, Ghana Health Services, Accra, Ghana, [4]African Field Epidemiology Network, Kampala, Uganda

Onchocerciasis elimination programs are challenged by the lack of diagnostic tests that meet the WHO target product profile criteria for stopping mass drug administration (MDA). We developed a new Ov16 ELISA using a mammalian expressed Ov16 antigen (Ov16m ELISA) with improved assay performance, shorter time to result, and using standardized pre-coated and dried plates. Validation of the Ov16m ELISA showed excellent performance for precision (<15% CV), limit of detection, and stability. Using a validation panel of 314 samples, the Ov16m ELISA had sensitivity and specificity of 92.9% and 98.5%, respectively. Here we show data from an evaluation of the Ov16m ELISA using Ghana onchocerciasis program samples and compared with a current test used by programs, the eluted dried blood spot (DBS) on the SD Bioline Ov16 rapid diagnostic test (RDT). To validate the new ELISA 2,723 DBS samples were collected from participants aged 0-85 years in 4 districts in Northern Ghana where MDA has been ongoing for >15 years as part of a project to evaluate a 2% seroprevalence threshold for stopping MDA. All samples were tested by Ov16m ELISA at CDC and DBS RDT in Ghana. There were 57 positives by DBS RDT (2.1%) and 27 positives by Ov16m ELISA (1.0%). Of the 27 Ov16m ELISA positives, 21 were also positive by DBS RDT. The Ov16m ELISA showed 36.8% percent positive agreement and 99.8% percent negative agreement with the DBS RDT. In children aged 5-9 years (n = 2126) there were 30 positives by DBS RDT (1.4%) compared to 5 positives on the Ov16m ELISA (0.2%). Comparatively, in adults ≥20 years (n = 198) there were 20 positive by RDT (10.1%) compared to 19 positives (9.6%) on the Ov16m ELISA. The difference in positivity by the two tests could be due to Ov16m ELISA being either less sensitive or more specific than the DBS RDT. Because the DBS RDT has not undergone a rigorous validation, while the Ov16m ELISA's performance characteristics have been documented as part of a rigorous validation, the differences here may be due to the

Ov16m ELISA possessing a higher specificity. Comparing these and other upcoming assays using a defined panel of well-characterized specimens will be crucial.

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WHO LABORATORY CAPACITY REVIEW TOOL FOR ONCHOCERCIASIS

Stephen Lindstrom[1], Vanessa Scholtens[2], William E. Secor[1], Jessica E. Prince-Guerra[1], Patrick Lammie[2], Sammy M. Njenga[3], Camilla L. Ducker[3], Maria Rebollo Polo[3]

[1]Centers for Disease Control and Prevention, Atlanta, GA, United States, [2]The Task Force for Global Health, Atlanta, GA, United States, [3]World Health Organization, Geneva, Switzerland

The World Health Organization (WHO) NTD 2021-2030 road map has identified onchocerciasis (river blindness) as one of the diseases targeted for elimination. The road map also highlights critical areas necessary to achieve the onchocerciasis elimination targets, one of which is quality laboratory capacity to conduct testing for monitoring and evaluation (M&E) of programs and perform post-elimination surveillance. The WHO Onchocerciasis Laboratory Capacity Survey is an online data gathering tool developed to assess laboratory capabilities and capacities, with an emphasis on onchocerciasis elimination programs. The information collected from the survey will be used to identify a laboratory's strengths and needs. The survey tool was used to conduct an assessment of various general laboratory aspects, specifically their capacity to perform PCR testing of blackflies, one of the key elements needed to verify onchocerciasis elimination. The tool consists of 40 questions addressing areas including general laboratory facilities, testing capabilities, quality assurance, data management and test reporting, specimen shipping and receiving, training activities, and laboratory safety. Twenty-two institutions from 17 French and English-speaking onchocerciasis-endemic African countries were invited to participate in the survey. At the time of abstract submission, 17 institutions (77.3%) had completed the survey. Among respondents, 15 labs (88.2%) responded that they perform PCR and 15 (82.3%) perform PCR for onchocerciasis. Seven labs (52.9%) responded they currently have capacity for qPCR testing while seven labs (41.1%) perform qPCR testing for onchocerciasis. Fourteen labs (82.4%) indicated they performed human serology testing for onchocerciasis on over 1000 samples per year. The WHO Onchocerciasis Laboratory Capacity Survey compiles information electronically as quantifiable metrics that can be analyzed between/among countries to identify current status and gaps as well as to evaluate metrics over time to understand successful improvement in capacity/capability and identify needs for further investment and support.

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SAFETY OF A SINGLE DOSE OF MOXIDECTIN AND OF IVERMECTIN: FIRST RESULTS OF A LARGE STUDY IN INDIVIDUALS LIVING IN AN ONCHOCERCIASIS ENDEMIC AREA OF THE DEMOCRATIC REPUBLIC OF CONGO AND IN AN ONCHOCERCIASIS-LYMPHATIC FILARIASIS CO-ENDEMIC AREA IN CÔTE D'IVOIRE

Tony O. Ukety[1], Michel Mandro-Ndahura[2], Benjamin Koudou[3], Pascal Adroba[1], Deogratias Ucima[1], Françoise Ngave[1], Kaki Kambale-Tsongo[1], Amos Nyathirombo[1], Innocent Mananu[1], Jack Zawadi[1], Gisèle Abeditho[1], Patrick Ubimo[1], Jules Upenjirwoth[1], Moise Alidra[1], Joël Mande[1], Germain Abafule[1], Claude Uvon[1], Anuarite Raciu[1], Salomon Maki[1], Séverin Cwinyày[1], Lyna Biwaga[1], Mathieu Njabu[1], Olivier Kouadio[4], Toki Pascal Gabo[5], Allassane Ouattara[4], Serge Marcel Adouan[6], Georgina Angoa[4], Aupnin Djeneba Coulibaly[6], Dja Jean Marius Digue[6], Komenan Issa Djanikro[6], Sinaly Kamagate[6], Koffi Kouame[6], Yegnigui Marie-Michelle Silue[6], Romeo Elvis Koudou[5], Jean Landry Aka[6], Kouadio Jean Brou[6], Ehonlan Arthur Anzara[6], Arsene Ekissi[6], Kouassi Okouchi[6], Djedje Liliane Zahui[6], Christian Sadia[6], Brou Hyacinthe Anzian[6], Philip Budge[7], Catherine Bjerum[8], Annette C. Kuesel[9], Beatriz Mosqueira[10], Mupenzi Mumbere[10], Peya Gaye[10], Melinda Lowe[10], Sally Kinrade[10]

[1]Centre de Recherche en Maladies Tropicales Ituri, Rethy, Congo, Democratic Republic of the, [2]Ituri Provincial Health Division, Bunia, Congo, Democratic Republic of the, [3]Centre Suisse de Recherches Scientifiques,, Abidjan, Côte D'Ivoire, [4]Centre Suisse de Recherches Scientifiques, Abidjan, Côte D'Ivoire, [5]Centre Hospitalier Regional d'Agboville, Agboville, Côte D'Ivoire, [6]District Sanitaire d'Akoupe, Akoupe, Côte D'Ivoire, [7]Washington University School of Medicine, St Louis, MO, United States, [8]Case Western Reserve University, Cleveland, OH, United States, [9]World Health Organization Special Programme for Research and Training in Tropical Diseases (TDR), Geneva, Switzerland, [10]Medicines Development for Global Health, Southbank, Australia

Community-directed treatment with ivermectin (IVM) over decades has controlled onchocerciasis as a public health problem in Africa and may have eliminated onchocerciasis in some areas, but alternative strategies are required for elimination across Africa. Moxidectin (MOX) reduces skin microfilariae levels (SmfL) more and for longer than IVM. MOX 8 mg is approved by the US Food and Drug Administration for treatment of onchocerciasis in patients ≥12 years old. MDGH is seeking regulatory approval for children 4 to 11 years old. A double-blind study is comparing the safety of a MOX and a 150 µg/kg IVM dose (MOX:IVM randomization ratio 4:1) in two locations: in onchocerciasis endemic areas in Ituri province of the Democratic Republic of Congo (DRC) and the onchocerciasis–lymphatic filariasis co-endemic Akoupé district of Côte D'Ivoire (CDI) where 400 mg albendazole is co-administered. Participants ≥8 years old received 8 mg MOX and those 4-7 years old 4 mg MOX. Individuals ≥12 years old with or without detectable SmfL (across 2 iliac crest snips), circulating filarial antigen (filarial test strip) or night microfilaremia were eligible. SmfL were not measured in children. All participants were assessed daily for adverse events (AEs) to 5 days after treatment and at Month 3. In DRC, 8026/8925 people screened were randomized and treated in this study, and 323 in a concurrent repeat-dose efficacy and safety study requiring ≥10 mf/mg skin for eligibility. Of the 7839 participants ≥12 years, 96% had undetectable SmfL; the remainder had between 0.1 and 34.8 mf/mg skin. In CDI, enrolment of children is ongoing. Of 4316 people ≥12 years screened, 4130 were randomized and treated: 93% had undetectable SmfL (the remainder had between 0.3 and 51.9 mf/mg skin) and 99% had undetectable night microfilaremia. To date, 5% of participants in DRC and 26% in CDI reported at least one AE. The types of AEs were similar to those in the Phase 2 and 3 studies, occurring primarily in the 5 days after treatment. In DRC and CDI, respectively, 96% and >99% of AEs were mild or moderate in severity. Details of the study design, participant population and safety results will be presented.

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FEASIBILITY OF A NOVEL ONCHOCERCIASIS RAPID DIAGNOSTIC TEST IN MARIDI, SOUTH SUDAN

Amber Hadermann[1], Stephen R. Jada[2], Chiara Trevisan[3], Joseph N. Siewe Fodjo[1], Katja Polman[3], Marco Biamonte[4], Yak Yak Bol[5], Robert Colebunders[1]

[1]UAntwerpen, Wilrijk, Belgium, [2]AMREF Africa, Juba, South Sudan, [3]Institute of Tropical Medicine, Antwerpen, Belgium, [4]Drugs & Diagnostics for Tropical Diseases, San Diego, CA, United States, [5]Ministry of Health, Juba, South Sudan

Point-of-care diagnostic tests are most indicated for confirming *Onchocerca volvulus* transmission in remote, resource-limited communities. In this regard, we conducted a serosurvey in Maridi (South Sudan) to determine the field feasibility and performance of a novel "Biplex A" rapid diagnostic test (RDT) developed by the company DDTD. In February 2023, children aged 3-9 years were recruited from five study sites situated at different distances from the Maridi Dam (blackfly breeding site). *O. volvulus* antibodies were detected with the prototype Biplex A RDT (detects antibodies to Ov16 and OvOC3261 at test line 1, and to Ov33.3 and OvOC10469 at test line 2), and the well-established Ov16 SD Bioline RDT using whole blood obtained by finger-pricking the participants. The feasibility and acceptability of the prototype Biplex A RDT were assessed, and the results of both tests were recorded. The Ov16 seroprevalence with the Ov16 RDT was 76/248 (30.6%), with the highest prevalence in children living closest to the Maridi Dam. Testing the children with the Biplex A RDT was found to be feasible and acceptable; additionally, testers reported its ease of use. Biplex A, test line 1, indicating a combined seroprevalence to Ov16 and OvOC3261, was positive in 84/239 (35.1%) of the children. Test line 2, reflecting seropositivity towards Ov33.3 and OvOC10469, was positive in 44/239 (18.4%) of the children. Both lines of the Biplex A RDT were simultaneously visible in 37/239 (15.5%) of the cases. In conclusion, the prototype Biplex A RDT was easy to use in the field, and its performance relative to the SD Bioline RDT was acceptable. Additional studies with skin snip test results, evaluating other types of this Biplex are currently being analysed. The high Ov16 seroprevalence suggests high ongoing *O. volvulus* transmission around the Maridi Dam. Therefore, strengthening the onchocerciasis elimination programme in Maridi is required.

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A ROBOTIC AI MICROSCOPE FOR AUTONOMOUS FILARIASIS QUANTIFICATION BASED ON SMARTPHONES AND OPTICAL MICROSCOPY

Jaime García-Villena[1], Ethan Recalde-Jaramillo[1], David Brau-Queralt[1], Ramón Vallés-López[1], Lucia Pastor[1], Oscar Darias-Plasencia[1], Daniel Cuadrado[1], Roberto Mancebo-Martín[1], David Bermejo-Peláez[1], Lin Lin[2], Andrés Santos[3], María Jesús Ledesma-Carbayo[3], José M. Rubio[4], Elena Dacal[1], **Miguel Luengo-Oroz**[1]

[1]Spotlab, Madrid, Spain, [2]Spotlab; Biomedical Image Technologies, ETSI Telecomunicación, Universidad Politécnica de Madrid; CIBER de Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, Madrid, Spain, [3]Biomedical Image Technologies, ETSI Telecomunicación, Universidad Politécnica de Madrid; CIBER de Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, Madrid, Spain, [4]Malaria and Emerging Parasitic Diseases Laboratory, National Microbiology Centre, Instituto de Salud Carlos III; Centro de Investigación Biomédica en Red de Enfermedades Infecciosas Instituto de Salud Carlos III, Madrid, Spain

Filariasis, a neglected tropical disease caused by roundworm infections, presents substantial health burdens in endemic regions worldwide. The accurate detection and quantification of filarial parasites is essential for providing timely access to treatment and effective disease management. Optical microscopy remains the gold standard method for filariasis diagnosis in blood samples, however, it suffers from low sensitivity, time-consuming procedures, and the need for skilled analysts at the point-of-care. In line with the WHO target product profile, we developed a prototype of a robotic AI system that automatically detects microfilariae in real time in blood smears, upgrading a conventional optical microscope and without need for internet connection. The components of the system, in addition to an optical microscope, are a mobile phone, securely attached to an eyepiece through a 3D printed adapter, and a mechanical system controlled by the smartphone app, which moves the sample in along the X and Y axis as well as adjusts the focus automatically along the Z axis. The smartphone app manages and controls the mechanical system, acquires images with the mobile camera, and analyzes images to detect microfilariae using an AI algorithm on the edge in real-time. The system is able to scan a blood smear with a 10x objective, digitize images, and run real time AI analysis at the same time in under 6 minutes. The AI model, which was previously validated on a clinical workflow, detects microfilariae with a precision and recall of 94% and 91%.
Additional field validations could contribute to optimizing the system. We envision a simple, scalable and easy to use device which works in low resource settings and is able to upgrade existing optical microscopes and transform them into AI driven microscopy diagnostic systems, contributing to reducing the diagnosis burden of disease.

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PREGNANCY, *ONCHOCERCA VOLVULUS* INFECTION AND IVERMECTIN USE: A CROSS-SECTIONAL STUDY

Chiara Trevisan[1], Stephen Jada[2], Amber Hadermann[3], Joseph Siewe[3], Jak Jak Bol[4], Katja Polman[1], Robert Colebunders[3]

[1]Institute of Tropical Medicine, Antwerp, Belgium, [2]AMREF Africa, Juba, South Sudan, [3]University of Antwerp, Antwerp, Belgium, [4]Ministry of Health, Juba, South Sudan

Treatment with ivermectin (IVM) should not be given to pregnant women in onchocerciasis endemic areas according to World Health Organization guidelines as drug safety has yet to be assessed. Onchocerciasis infection during pregnancy might lead to parasite tolerance in the newborn and affect pregnancy outcomes. In our study we determined the proportion of pregnant women who were exposed to *Onchocerca volvulus*, who inadvertently took IVM and assessed the knowledge on IVM in relation to pregnancy. A hospital-based cross-sectional study was conducted in 2023 at Maridi hospital in Maridi County, an onchocerciasis endemic area in South Sudan. All pregnant or one-week *post-partum* women willing to participate were interviewed and tested with the Ov16 Bioline rapid diagnostic test (RDT). A total of 317 women aged between 14 and 44 years participated in the study [median age: 23, interquartile range (19-29 years]. Of 290 women who were tested, almost two out of three (62%) were Ov16 RDT positive and reported experiencing high levels of skin itching (40%). Seventeen percent of the women had never taken IVM, and 6% inadvertently took IVM during the last round of community-directed treatment in May 2023. Of the 16 women who took IVM during pregnancy, half of them knew that they were pregnant. Overall, knowledge on IVM and pregnancy was high, as 87% of the women knew that it was not advised to take IVM during pregnancy. Out of 248 women with children, 9 (3.6%) had children suffering from epilepsy; two of them had two children with epilepsy. No abnormalities were reported in the children of the women who inadvertently took IVM. Our results show that a high proportion of exposed pregnant women are missing out on IVM treatment, potentially affecting the pregnancy outcome and the life of the future offspring. We recommend that women should have access to IVM treatment *post-partum* in vaccination centers and that all women who inadvertently take IVM should be registered to further explore safety of IVM. In addition, a clinical trial evaluating the potential beneficial effect of treating *O. volvulus* infected pregnant women with IVM should be considered.

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PRE-CLINICAL DEVELOPMENT OF THE ANTI-WOLBACHIAL DRUG CORALLOPYRONIN A TO TREAT FILARIASES: END RUN TO PHASE 1 TRIAL

Kenneth Pfarr[1], Andrea Schiefer[1], Katharina Rox[2], Frederic Risch[1], William Shafer[3], Jennifer Edwards[4], Magnus Unemo[5], Gabriele Bierbaum[1], Stefan Kehraus[6], Miriam Grosse[2], Rolf Müller[7], Tanja Schneider[6], Thomas Hesterkamp[8], Marc Stadler[2], Marc P. Hübner[1], Karl G. Wagner[6], Achim Hoerauf[1]

[1]University Hospital Bonn, Bonn, Germany, [2]Helmholtz Centre for Infection Research, Braunschweig, Germany, [3]Emory University School of Medicine, Atlanta, GA, United States, [4]Ohio State University, Columbus, OH, United States, [5]Örebro University, Örebro, Sweden, [6]University of Bonn, Bonn, Germany, [7]Helmholtz Institute for Pharmaceutical Research Saarland, Saarbrücken, Germany, [8]German Center for Infection Research (DZIF), Braunschweig, Germany

The bacterial RNA polymerase inhibitor Corallopyronin A (CorA) is in late pre-clinical development to treat filariases. As an anti-wolbachial compound, it depletes the essential obligate intracellular *Wolbachia* symbionts of filarial nematodes, resulting in sterility and death of the worms. Our consortium has achieved the following significant milestones: 1) produced drug substance with >95% purity by heterologous production in *Myxococcus xanthus*, 2) received formal Scientific Advice from the German regulatory agency BfArM approving our proposed drug substance purity for toxicology studies, 3) upscaled upstream and downstream processes to industrial-scale, 4) developed oral formulations with increased CorA solubility and stability that are suitable for GLP pre-clinical studies and the phase 1 trial, 5) successfully completed non-GLP safety and toxicology studies with no relevant results that would halt development, 6) contracted a cGMP CMO to conduct a feasibility study and perform technical/engineering production runs of GMP material, and 7) expanded development to including difficult-to-treat *Staphylococcus aureus* and *Neisseria gonorrhoeae* infections. We have received support from the Global Health Innovative Technology Fund (GHIT) to complete the pre-clinical development: conduct PK/PD in *Dirofilaria immitis* infection, support a GLP toxicology study in dogs, produce GMP CorA and CorA standards, conduct a quantitative whole-body autoradiography study, perform CMC to further improve the oral formulations, and prepare the phase 1 trial planned for 2026. Successful completion of the phase 1 trial will derisk the project to continue development of CorA for registration.

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PERFORMANCE OF QUANTITATIVE PCR FOR THE DETECTION OF SOIL-TRANSMITTED HELMINTHS IN COMPARISON TO KATO-KATZ PRECEDING AND FOLLOWING COMMUNITY-WIDE MASS DRUG ADMINISTRATION IN TAMIL NADU, INDIA

Sean R. Galagan[1], Malathi Manuel[2], Zayina Z. Manoharan[2], Ajith K. Muthukumar[2], Manigandan Sekar[2], Gideon J. Israel[2], Rohan M. Ramesh[2], Kristjana Ásbjörnsdóttir[3], Jeanne L. Goodman[1], Nils Pilotte[4], Mariyam K. Shaikh[1], Katherine C. Sharrock[1], Steven A. Williams[5], Judd L. Walson[6], Sitara S.R. Ajjampur[1]

[1]University of Washington, Seattle, WA, United States, [2]Christian Medical College, Vellore, Vellore, India, [3]University of Iceland, Reykjavík, Iceland, [4]Quinnipiac University, Camden, CT, United States, [5]Smith College, Northampton, MA, United States, [6]Johns Hopkins University, Baltimore, MD, United States

Accurate diagnostic tools to assess soil-transmitted helminth (STH) prevalence are critical for monitoring school-based and community deworming programs. Several studies have demonstrated that Kato-Katz is less sensitive in detecting STH than quantitative PCR (qPCR), especially at low intensity of infection. This secondary analysis, using data from the DeWorm3 India trial site in Tamil Nadu, seeks to assess the concordance of Kato-Katz and qPCR and compare intensity by both methods (eggs per gram of stool and cycle threshold [Ct]) using a large dataset of paired test results prior to and following multiple rounds of deworming. Stool samples were collected from randomly sampled participants at baseline (prior to mass drug administration [MDA]) and endline (following six rounds of MDA and two years without deworming) and tested for STH using Kato-Katz microscopy and qPCR. In total, 6,014 and 2,013 paired test results were available at baseline and endline, respectively, and nearly all infections observed were due to *N. americanus*. At baseline, the prevalence of *N. americanus* was 16.6% by Kato-Katz and 24.2% for qPCR (concordance was 90.8%) with most discordance due to samples that were only positive by qPCR (8.4%). The ratio of positivity, comparing qPCR to Kato-Katz, increased from 1.46 at baseline to 1.99 at endline, and concordance was 91.2% at endline. Among participants whose stool sample tested positive for *N. americanus* by qPCR, participants with moderate- (N=50) or heavy-intensity (N=26) hookworm infection by Kato-Katz had lower Ct distributions (median: 19.48, interquartile range [IQR]: 18.31-20.40 and median: 18.63, IQR: 17.47-18.97, respectively) compared to participants with light-intensity infection (N=1,028, median: 22.91, IQR: 21.05-24.96) and participants who did not test positive by Kato-Katz (N=668, median: 26.78, IQR: 25.50-28.38). These results demonstrate improved sensitivity of qPCR compared to Kato-Katz and suggest this difference is even more pronounced following deworming as prevalence and intensity decrease.

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STATUS OF SOIL TRANSMITTED HELMINTHIASIS AND THEIR RISK-FACTORS AMONG SCHOOL PUPILS AND NOMADIC -FULANIS IN SELECTED COMMUNITIES IN OSUN-STATE, SOUTHWEST, NIGERIA

Akinlabi Mohammed Rufai

Osun State University, Osogbo, Nigeria

Soil transmitted helminthiasis (STHs) occur endemically in many rural communities of Nigeria with school aged children mostly affected. Though, there has been significant progress in STHs' control over the past decade through increased collaboration, country commitment, and donors support. However, these interventions did not cover the Nomadic Fulanis who continuously moves from one place to another with possible release of STHs eggs into the environment through their indiscriminate defecation. There is paucity of published data on prevalence, burdens and risk factors associated with STH infections among primary school pupils in Osun State. The study was carried out to assess the status of STHs among 200 primary school pupils and 100 children of the Nomadic Fulanis in three selected communities of Osun State, Southwest, Nigeria. Stool samples were collected and processed using filtration technique and examined microscopically. Intensity of infection was determined on positive samples using Kato Katz techniques. Questionnaire survey was administered to the participants to test their knowledge of STHs. 18.0% of the pupils compared to 87.6% of children of the Nomadic Fulanis were found to be infected with intensity of infection from 1 to 68520 (mean = 342.6) eggs/ 5g of faeces among the primary school pupils and from 30 to 96380 (mean = 963.8) eggs/ 5g of faeces among the children of the Nomadic Fulanis. 26 (13.0%) of 147 (73.5%) of the primary school pupils who rarely wash their hands after having contact with contaminated sites were found to be infected compared to 100 (100.0%) of Nomadic Fulani children. The STHs recovered in both groups include: *Ascaris lumbricoides*, *Ancylostoma duodenale Trichuris trichiura with T. trichiura* found only in children of the Nomadic Fulani. This research reveals that the children of the Nomadic Fulanis harbored high intensities of STHs and can be an absolute agent of the spread STHs. Including the children of the Nomadic Fulanis in the existing control measures could enhance eradication.

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EVALUATION OF *STRONGYLOIDES STERCORALIS* SS-IR RECOMBINANT ANTIGEN FOR DIAGNOSTIC AND SURVEILLANCE USING A BEAD-BASED IMMUNOASSAY

Mauhaun Taheri

Center for Disease Control, Atlanta, GA, United States

Infection with the soil-transmitted helminth *Strongyloides stercoralis* is normally asymptomatic but can lead to a life-threatening hyperinfection syndrome in immunocompromised individuals. Serological testing for antibodies to *S. stercoralis* is the method of choice for diagnosis, but ELISAs for *S. stercoralis* lack reproducibility and specificity. There is an effort to modernize diagnostic testing at CDC by moving serological testing to a multiplex bead assay (MBA) platform. However, Ss-NIE, the best characterized recombinant antigen from *S. stercoralis*, suffers from variable results in the MBA. The antigen Ss-IR was therefore evaluated for use in the MBA. Ss-IR was coupled to microspheres at 5 concentrations in two different coupling buffers, then tested using 5 positive and 5 negative samples. The optimal coupling condition (i.e. the best signal-to-noise ratio between positives and negatives) was 1.5 µg antigen in 1X PBS (pH 7.2). To determine sensitivity and specificity of the assay, sera from individuals testing stool-PCR positive for *S. stercoralis* (n = 50) and from US based presumed negative individuals with no prior travel history (n = 185) were tested. The median fluorescence intensity (MFI) with background subtracted (MFI-bg) was determined for each specimen. A receiver operating characteristic (ROC) analysis set to maximize sensitivity and specificity calculated the cutoff to be an MFI-bg of 192, with a sensitivity of 90% (95% CI 78.64% to 95.65%) and a specificity of 99% (95% CI 96.14% to 99.81%), compared with a sensitivity of 84% (95% CI 71.49% to 91.66%) and specificity of 100% (95% CI 97.97% to 100.0) for the same specimens tested at the same time in the MBA for antibodies to Ss-NIE. To assess reproducibility, 10 positive and 10 negative samples were tested by two operators over a span of 10 days, using different critical reagents in the MBA process. The correlation coefficient (R-squared) was 0.976, indicating a robust assay with minimal variation between users and reagent lots. Overall, the Ss-IR antigen has a high sensitivity, specificity, and reproducibility, warranting more extensive validation for surveillance use.

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EUKARYOTIC ENTERIC PATHOGENS RELATIONSHIP WITH THE GUT FUNGAL COMMUNITY IN MALIAN CHILDREN

Aly Kodio[1], Estelle Menu[2], Safiatou Doumbo[1], Drissa Coulibaly[1], Abdoulaye Kassoum Koné[1], Salimata Konaté[3], Lamine Tall[4], Didier Raoult[4], Mahamadou Aly Thera[1], Stéphane Ranque[5]

[1]Malaria Research and Training Centre-International Center for Excellence in Research (MRTC-ICER), Faculty of Pharmacy, University of Sciences, Technique and Technology of Bamako, Point G, BP 1805 Bamako, Mali, Bamako, Mali, [2]Aix Marseille Université, Institut de Recherche pour le Développement, Assistance Publique-Hôpitaux de Marseille, Service de Santé des Armées, VITROME : Vecteurs – Infections Tropicales et Méditerranéennes, 19-21 Boulevard Jean Moulin, 13005 Marseille,, Marseille, France, [3]Malaria Research and Training Centre-International Center for Excellence in Research (MRTC-ICER), Faculty of Pharmacy, University of Sciences, Technique and Technology of Bamako, Point G, BP 1805 Bamako, Mali., Bamako, Mali, [4]Aix Marseille Université, Institut de Recherche pour le Développement, Assistance Publique-Hôpitaux de Marseille, Service de Santé des Armées, MEPHI : Microbes, Evolution, Phylogénie et Infection, 19-21 Boulevard Jean Moulin, 13005 Marseille, France, Marseille, France, [5]Aix Marseille Université, Institut de Recherche pour le Développement, Assistance Publique-Hôpitaux de Marseille, Service de Santé des Armées, VITROME : Vecteurs – Infections Tropicales et Méditerranéennes, 19-21 Boulevard Jean Moulin, 13005 Marseille, Marseille, France

The fungal gut microbiome (gut mycobiome) plays a role in protecting against certain dangerous microbes and regulating the immune system, but it could also be the cause of certain chronic diseases. However, the interaction between gut mycobiome and eukaryotic enteric pathogens (EEPs) is a less explored. To assess the relationship between EEPs and gut mycobiont, we conducted a case-control study among children in Bandiagara. Stool samples were collected from 296 Malian children. The presence of EEP was assessed by qPCR and the gut mycobiome was characterized by Illumina MiSeq™ rRNA ITS1 and ITS2 regions metabarcoding. The 100 (33.8%) children in whom no EEP was detected were considered as EEP negative; they were compared to: a) 196 (66.2%) children who had at least one EEP; b) 91 (30.7%) children who had only *Blastocystis*; c) 35 (11.8%) children who had only *Giardia intestinalis* in terms of stool consistency and mycobiome status. The results showed a significative difference in Shannon indice of negative EEP compared to positive EEP and to Shannon indice of *Giardia intestinalis* group. The Chao-1 indice of negative EEP was significatively decrease than that of positive EEP and *Giardia intestinalis*. Linear size effect discriminant analysis highlighted five species, including *Fusarium longipes* and *Penicillium caseilulvum*, which were relatively more abundant in children with at least one EEP whereas 28, including *Aspergillus sydowii* and *Microdochium colombiense* were more abundant in EEP negative. Regarding *Blastocystis* infected children, the abundance of *Fusarium*, *Pyxidiophora*, and *Stereum* genera was higher in infected children, whereas *Ogataea* and *Allocryptovalsa* were more abundant in EEP negative. Regarding *Giardia intestinalis*, *Sordariales* and *Mortierellales* abundance was higher in infected children, whereas *Agaricales* and *Capnodiales* abundance was higher in EEP negative. Overall, EEP significantly impact the global gut fungal community structure, but further studies are warranted to confirm our finding that taxa of the gut mycobiota are associated with susceptibility or resistance to specific EEP.

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PHARMACOPHORE APPROACH TO THE PREDICTION OF ACTIVATORS OF DAF-12 RECEPTOR TO DEACTIVATE AUTO-INFECTION LIFE CYCLE STAGE OF *STRONGYLOIDES STERCORALIS*

Erica A. Akanko[1], Desmond O. Amoah[1], Michael Cappello[2], Samuel K. Kwofie[3], Michael D. Wilson[1]

[1]Noguchi Memorial Institute for Medical Research, Accra, Ghana, [2]School of Medicine, Yale University, New Haven, CT, United States, [3]Department of Biomedical Engineering, University of Ghana, Accra, Ghana

Strongyloidiasis caused by infections with *Strongyloides stercoralis* affects over 600 million people globally, predominantly in the tropics. It is among the most neglected of all the NTDs. Infections are mainly asymptomatic and clinically silent and its symptoms include fever, gastrointestinal pain, anorexia, diarrhea and fatigue. Ivermectin is the current treatment drug with a cure rate of 88-96% against adult parasites but possible drug resistance has been reported. The life cycle alternates between free-living and parasitic stages involving autoinfection that leads to hyper infection and 90% mortality if left untreated. The overall goal of the study was to understand the mechanism of autoinfection and to devise strategies to prevent it in human infections using computational methods. To achieve this goal, activators of the abnormal Dauer Formation Protein 12 (DAF-12) receptor known to influence the transition between developmental arrest and growth to reproductive adults were predicted. Two *Caenorhabditis elegans* activators of DAF-12 and Dafachronic acid were used to generate a 3D chemical feature pharmacophore model using *LigandScout*. The validated model was screened against pre-filtered libraries containing 1871 and 4924 compounds in the EANPDB and NANPDB databases respectively. 179 and 69 compounds respectively, with fit scores above 66.59 were docked against the structure of the DAF-12 receptor to generate hits using Autodock Vina. Three compounds hispidol B, 3-O-(3'-acetoxy-2'-hydroxy-2' methylbutyryl) cuauthemone, and toonapubesin F with binding affinities of –10.8,-10.7, and –10.4 kcal/mol against DAF-12 receptor respectively were identified as potential candidates. Structural insights into the binding mechanisms were elucidated using LigPlot+ and Molecular Dynamics simulations. All three ligands passed the adsorption, distribution, metabolism, elimination, and toxicity (ADMET) tests. Our next step is to evaluate their efficacies in animal models e.g. in the Mongolian gerbil. Our findings open the avenues for combination therapy that also arrest auto infections against *S. stercoralis* infections

6598

EFFECT OF KNOWLEDGE, AWARENESS AND PARTICIPATION ON SUSTAINED REDUCTION OF SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG SCHOOL-AGE CHILDREN IN RIVERS STATE NIGERIA

Temitope Michael Ogunbi[1], Ifeanyiwa Chime[1], Jerry Mbaka[1], Kate McCracken[2], Mark Minnery[2], Ayoola Adegbile[1], Anam Abdulla[2], Rodgers Curtis[2], Ima Umah[3], Fatai Oyediran[3], Toochi Ohaji[1], Ima Chima[1]

[1]Evidence Action, Abuja, Nigeria, [2]Evidence Action, Washington DC, WA, United States, [3]Nigeria Federal Ministry of Health, Abuja, Nigeria

Preventive chemotherapy (PC) is an effective intervention strategy for the control and elimination of soil-transmitted helminthiasis (STH). Achieving high PC coverage in every treatment round is critical for attaining control and elimination goals. Sustained high levels of participation in every round of PC is crucial to achieving effective coverage, and individuals who do not accept PC are unlikely to participate in the intervention. To improve PC compliance, community sensitization and mobilization are conducted prior to each round, combining mutually reinforcing social and behavior change approaches like announcements by village announcers, radio jingles, word of mouth, posters, live radio and TV phone-in programs. During 7 years of PC in Rivers State, 1,493 parents of school-age children (5-14 years) were surveyed in sampled communities where PC was planned, to check awareness, knowledge and willingness to participate. Survey results showed 74% of respondents were aware of the deworming exercise, and 58% of respondents correctly mentioned intestinal worms/STH as the infection target. 87% of the parents were willing to have their children participate in the deworming exercise. The major reasons provided for not participating were lack of awareness (37%), already having dewormed their children at home (15%), or had not enrolled their children in school yet (9%). Only 6% of respondents expressed fear of/ lack of trust in the medicines. Following the 7 years of PC with consistently improving reported coverage, validated by 50% of the surveyed coverage, a 2023 prevalence survey showed a 71% relative reduction in STH prevalence in the state from baseline. A multivariable analysis showed statistically significantly increased odds of parent's willingness to send child(ren) for deworming associated with knowledge of the deworming treatment (OR: 4.164(P=0.006), 95%CI: 2.494 - 6.955) and awareness of the deworming exercise (OR: 1.002(P=0.006), 95%CI:1.000 - 1.003). Sound public awareness and sensitization around MDAs are valuable to achieving and sustaining high levels of treatment coverage to reduce the burden of disease.

6599

A TWO-PRONGED BIG DATA APPROACH TO CRITICALLY ANALYZE *STRONGYLOIDES STERCORALIS* INFECTIONS AMONG RURAL, IMPOVERISHED SOUTH CAROLINA RESIDENTS

Matthew S. Haldeman[1], Henry Heidt[2], Christina Bhola[2], Salome J. Gass[2], Melissa Nolan[2]

[1]University of South Carolina Family Medicine, Columbia, SC, United States, [2]University of South Carolina School of Public Health, Columbia, SC, United States

Strongyloides stercoralis, a soil-transmitted helminth, is known to persist throughout rural areas in the southeastern United States, but high-quality prevalence data is lacking.[1–3] This project aimed to (1) estimate the current prevalence of human *Strongyloides* infections, and (2) assess risk factors associated with *Strongyloides* infections among residents of South Carolina. To achieve this, two approaches were employed. First, to estimate prevalence, active surveillance was performed using *Strongyloides* serology testing via sampling of a subset of banked serum samples. Demographic, socioeconomic, and exposure data were collated from serum sample questionnaires. Positives were contacted and visited, during which an exposure survey, confirmatory testing, and offer of treatment were administered. Second, passive surveillance was conducted via electronic health records query for *Strongyloides* cases over a 5-year time period. Demographic, socioeconomic, risk factor, and health outcomes data were collected for all positive cases and two matched controls. Participant characteristics were compared between seropositive and seronegative groups, using ANOVA and Fisher's exact statistics. We tested a total of 1,572 serum samples, of which 77 (4.9%) were positive. Significant differences in race/ethnicity and level of education were noted between cases and controls. Geospatial analysis revealed the greatest hotspot to be in the northwest region of the state. Home visits are ongoing but so far 1/3 (10/30) of positives report no international travel in the past decade, while 1/2 (15/30) report regular time spent outdoors barefoot. Review of electronic health records revealed 26 patients diagnosed with *Strongyloides*, of which 6 (23.1%) had no travel history documented. Significant differences in race/ethnicity and place of birth were noted. In this study, we found a small but non-negligible prevalence of *Strongyloides* among residents of South Carolina. Further study will be needed to better characterize the burden and distribution of *Strongyloides* in South Carolina, which may inform future targeted public health interventions.

6600

APPLICATION OF QPCR TO DETERMINE COMMUNITY PREVALENCE OF *STRONGYLOIDES STERCORALIS* IN Y INDIA

Malathi Manuel[1], Gideon J. Israel[1], Sean R. Galagan[2], Manigandan Sekar[1], Rohan Michael Ramesh[1], Nils Pilotte[3], Steven A. Williams[4], Judd L. Walson[5], Sitara S.R. Ajjampur[1]

[1]The Wellcome Trust Research Laboratory, Christian Medical College, Vellore, India, [2]University Washington, Seattle, WA, United States, [3]Department of Biological Sciences, Quinnipiac University, Hamden, CT, United States, [4]Department of Biological Sciences and Biochemistry, Smith College, Northampton, MA, United States, [5]Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States

Strongyloides stercoralis, an intestinal nematode prevalent in the tropics and subtropics, infects ~370 million individuals globally. While most infections are asymptomatic, they can lead to severe disseminated infections in immunocompromised individuals. While most national programs focusing on soil-transmitted helminth infections do not include drugs active against *Strongyloides*, the WHO NTD roadmap 2030 recommends targeted deworming of school-aged children with ivermectin if prevalence >10% and emphasizes the need for precise estimates of burden and sensitive diagnostics. In this study, we leveraged stool samples collected at baseline of a cluster randomized trial on community-wide deworming (DeWorm3) to determine prevalence of S. stercoralis by qPCR in India. The study site included rural (Timiri) and tribal (Jawadhu hills) blocks in Tamil Nadu, and samples tested (n=6091) from an age-stratified cohort of pre-school-aged and school-aged children (PSAC, SAC) and adults (15+ years). Age and cluster-weighted prevalence of *S. stercoralis* was 4.4% (95% CI: 3.9-5.0%), with a higher prevalence in the rural block (4.9%, 4.2-5.6%) than the tribal block (2.96%, 2.0-4.3%). Adults had more infections (5.5%, 4.8-6.3%) than PSAC (0.6%, 0.3-1.4%) and SAC (0.4%, 0.2-0.9%). Older age (mOR=10.1, 95% CI: 4.2-24.3), belonging to farming households (mOR=1.4, 1.02-2.04), and middle socio-economic strata (mOR=1.9, 1.1-3.6) were associated with increased odds of *S. stercoralis* infection. Female gender (mOR=0.6, 0.4-0.8), belonging to households with females possessing higher secondary education (mOR=0.6, 0.3-0.9), and access to handwashing facilities (mOR=0.5, 0.3-0.9) were protective. The weighted prevalence of *N. americanus* in the same community was 29.6% by qPCR. While ecological niche models suggest that hookworm prevalence would be predictive of *Strongyloides*, our findings indicate a lower prevalence of *Strongyloides* by qPCR. A combination of molecular and serological diagnostic approaches may be needed to accurately estimate the burden of *Strongyloides* to help plan and prioritize appropriate interventions for control.

6601

IMPACT OF PREVENTIVE CHEMOTHERAPY ON THE STATUS OF SOIL-TRANSMITTED HELMINTHIASIS ACROSS THREE IMPLEMENTATION UNITS IN ONDO STATE, NIGERIA

Francisca Olamiju[1], **Hammed Mogaji**[2], Oyinlola Fajana[1], Olanike Oladipupo[3], Imaobong Umah[4], Fatai Oyediran[4], Moses Aderogba[5], Louise Makau-Barasa[5], Uwem Ekpo[6]

[1]Mission To Safe The Helpless, Lagos, Nigeria, [2]Federal University Oye-Ekiti, Ekiti State, Nigeria, [3]Neglected Tropical Diseases Program, Ondo State Ministry of Health, Ondo State, Nigeria, [4]Neglected Tropical Diseases Program, Federal Ministry of Health, Abuja, Nigeria, [5]EndFUND, New York, NY, United States, [6]Federal University of Agriculture Abeokuta, Ogun State, Nigeria

Routine epidemiological data are invaluable for tracking the progression of preventive chemotherapy (PC), optimising resource allocation, and addressing emerging needs for the elimination of soil-transmitted helminthiasis. This study was conducted to assess the prevalence, intensity, and WASH conditions in the three local government areas (LGAs) of Ese-Odo, Irele, and Ile-Oluji in Ondo State, Nigeria. Stool samples were collected from 2,093 children aged 5-14 years across 45 schools and analysed using Kato-Katz techniques. Standardised questionnaires were also used to collect information on access to WASH resources. Parasitological findings reveal significant decline in aggregated prevalence estimates across the three LGAs. In Ese-Odo, prevalence was 25.8% (95% CI: 23.0, 29.0) versus 39% at baseline (d = -34%, p=0.00). Also, in Irele, the aggregated prevalence estimate was 9.7% (95% CI: 7.6, 12.0) versus 51.3% at baseline (d= -81%, p =0.00). In Ile-Oluji, the aggregated prevalence was 6.4% (95% CI: 4.6, 8.7) versus 23% at baseline (d=-72.2%, p =0.00). *Ascaris lumbricoides* was the most prevalent STH across all three IUs, with rates of 25.5%, 9.4%, and 6.4% in Ese-Odo, Irele, and Ile-Oluiji, respectively, followed by *Trichuris trichiura* in Ese-Odo (2.7%) and Irele (0.4%), whereas hookworm infection was only observed in Irele (0.7%). Most infected individuals exhibited low infection intensity in Ese-Odo (91.0%), Irele (96.8%) and Ile-Oluiji (100%). Prevalence rates did not vary significantly by sex or age category across the three IUs ($p < 0.05$). However, WASH data revealed deplorable access to improved sanitation (17.7%, 54.9%, and 58.2%, $p<0.05$), improved water sources (24.5%, 66.1%, and 69.8%, $p<0.05$), and handwashing facilities (9.0%, 39.6%, and 25.4%) across Ese-Odo, Irele, and Ile-Oluiji, respectively. Open defaecation was practiced by 54.2%, 36.3%, and 34.3% of participants recruited in Ese-Odo, Irele, and Ile-Oluji, respectively. These findings show significant progress in STH elimination in the three IUs with PC but call for more efforts in the provision and usage of WASH facilities.

6602

RESISTANCE OF SOIL TRANSMITTED HELMINTHS TO SINGLE DOSE ALBENDAZOLE AND RESULTS OF COMBINED THERAPY WITH ALBENDAZOLE AND IVERMECTIN IN CHILDREN AGED 2 TO 11 YEARS IN THE PERUVIAN AMAZON

Paul Francis Garcia Bardales[1], Greisi Curico Huanci[2], Tackeshy N. Pinedo Vazquez[1], Wagner V. Shapiama Lopez[1], Maribel Paredes Olortegui[1], Francesa Schiaffino[3], Pablo Penataro Yori[4], Josh M. Colston[4], Thomas G. Flynn[4], Graciela R. Meza Sánchez[2], Hermann F. Silva Delgado[5], Richard A. Oberhelman[6], Margaret N. Kosek[7]

[1]Asosciacion Benefica Prisma, Iquitos, Peru, [2]Universidad Nacional de la Amazonia Peruana, Iquitos, Peru, [3]Universidad Peruana Cayetano Heredia, Lima, Peru, [4]University of Virginia, Charlottesville, VA, United States, [5]Universidad Nacional de la Amazonia Peruana UNAP, Iquitos, Peru, [6]Tulane University, New Orleans, LA, United States, [7]Universidad Nacional de la Amazonia Peruana, Charlottesville, VA, United States

In countries where soil- transmitted helminth (STH) infections are endemic deworming programs are crucial for reducing morbidity. However, the growing concern over increasing resistance to benzimidazoles requires continuous monitoring of treatment efficacy. In this observational study conducted in Peru, we evaluated the clinical efficacy of a single dose of 400 mg albendazole in children aged 2 to 11 years. Our aims were to assess clinical resistance to albendazole at 20 days post-treatment and to investigate reinfection with STH four months after treatment. We enrolled 426 participants, among whom 52.3% were infected with at least one STH, specifically, 33.8% were positive for Ascaris (41.8% light, 50.8% moderate, and 7.4% heavy), 34.5% were positive for Trichuris (75.2% light, 22.5% moderate, and 2.3% heavy), and 1.1% were positive for hookworm species (100% light). Additional stool samples were collected and examined at 20 days, 90 days, and 130 days after the initial treatment. At 20 days post-administration of albendazole, the cure rate (CR) for Ascaris was 80.1% (95% CI: 73.5-86.7), with an egg reduction rate (ERR) of 70.8% (95% CI: 57.8-88.7). For Trichuris, the CR was 27.1% (95% CI: 20.0-34.3), with an ERR of 29.8% (95% CI: -1.40-57.5). Among participants with a positive stool sample indicating persistent or recurrent Trichuris infections, treatment with combined therapy of albendazole (400 mg) and ivermectin at 600 µg/dose increased the overall CR for Trichuris to 75.2% (95% CI: 67.3-83.2%) with an ERR of 84.2% (95% CI: 61.3-93.8%). Albendazole administration alone for the control of STH showed high rates of treatment failure, particularly for Trichuris. However, combined single doses of albendazole and ivermectin appeared to improve efficacy.

6603

IDENTIFICATION OF NOVEL BIOMARKERS FOR SEROSURVEILLANCE OF HUMAN HOOKWORM INFECTIONS

Santosh George[1], Hetali Shah[1], Vashti Irani[1], Lisa Marie Harrison[2], Michael D. Wilson[3], Michael Cappello[4], Andrew Levin[1]

[1]Kephera Diagnostics, Framingham, MA, United States, [2]Department of Pediatrics, Yale School of Medicine, New Haven, CT, United States, [3]Department of Parasitology, Noguchi Memorial Institute for Medical Research, Legon, Accra, Ghana, [4]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, United States

Hookworm, a blood-feeding, soil-transmitted helminth parasite, infects about 500 million people globally, including pregnant women and children. This Neglected Tropical Disease (NTD) is prevalent in sub-Saharan Africa, Asia, and parts of South America. The World Health Organization (WHO) recommends Mass Drug Administration (MDA) of benzimidazole anthelmintics to combat morbidity, while for diagnosis, it suggests Kato-Katz thick smear, a labor-intensive method, lacking sensitivity. PCR-based tests are more accurate but require well-equipped labs and are rarely used in endemic regions due to resource limitations. Addressing these challenges, the WHO Target Product Profile emphasizes the need for improved surveillance tools with higher sensitivity. As for other NTDs, integrating serosurveillance into monitoring efforts can facilitate decision-making for MDA programs. To this end, we sought to identify sensitive and specific hookworm biomarkers for use in an ELISA for serosurveillance. We screened ~11,000 peptides for IgG reactivity on a high-density microarray, generated from 34 hookworm proteins identified through LC-MS/MS analysis of hookworm Excretory/Secretory and L3 soluble extracts, along with a bioinformatics analysis and literature search. Further down-selection of peptides from the microarray was based on fluorescence intensity and signal to noise ratio. Six peptides, combined in a single mixture, were ultimately selected for final screening by ELISA on hookworm positive (Kato-Katz thick smear, n=109) and negative (non-endemic U.S., n=224) sera, yielding a sensitivity of 86% and specificity of 92%, with an AUC of 0.95 and p-value <0.0001. Serum samples from other STH infections including *Ascaris* sp. (n=3), *Trichuris* sp. (n=1) and *Strongyloides* sp. (n=5) were negative on the ELISA. In conclusion, we have identified, for the first time, highly sensitive and specific hookworm biomarkers, demonstrating promising potential for serosurveillance as a new tool to improve monitoring of MDA programs in endemic regions

6604

SOIL-TRANSMITTED HELMINTHS (STHS) IDENTIFIED IN ENVIRONMENTAL SAMPLES (SOIL AND FECAL MATTER) COLLECTED FROM SOME PRIMARY SCHOOLS IN GHANA

Lordina Nkansah-Gyan, Papa Kofi Amissah-Reynolds, Victor Agyei, Opoku Gyamfi, Philip Ofori Asante, Edward Ankapong, Frank Essem, Kofi Agyapong Addo

Akenten Appiah-Menka University of Skills Training and Entrepreneurial Development, Kumasi, Ghana

Soil-transmitted helminths (STHs) are common parasitic infections that present a notable risk to the health and development of school-aged children, especially in the tropics. This study aimed to investigate the diversity of STHs in soil and faecal samples were collected from selected primary schools. A survey was conducted across 24 primary schools; each school was divided into 5 locations (playgrounds, school fields, canteens, cafeterias, and walkways). 100g of soil samples (50g each) were collected from 2 points (20 meters away) in each location. Fecal matter of stray animals was collected for analysis, where found. Thus, a total of 240 soil and 20 fecal samples were collected from different school locations; and analyzed using the flotation technique. Microscopic examination of soil samples revealed the following organisms: Ascaris lumbricoides (55; 22.9%), Strongyloides spp (13; 5.4%), Schistosoma spp. (8; 3.3%), Fasciola spp. (8; 3.3%), Hookworm (7; 2.9%) Hymenolepis spp. (6; 2.5%), Trichuris trichiura (4; 1.7%), Diphyllobothrium spp (2; 0.8%) and Taenia (1; 0.4%). The playgrounds recorded the highest positivity rate (22; 9.2%), while school fields and canteens recorded the lowest positivity rate of 5.8% (14) each. Ten (50%) out of the 20 faecal samples were found to contain STHs with Ascaris lumbricoides (25%) mostly observed. The results suggest a significant presence of STHs in the schools' environment, emphasizing the immediate need for specific public health actions. Initiatives such as deworming programs, advocating for better hygiene and sanitation practices within schools, and increasing awareness are crucial measures in mitigating health impacts associated with STHs.

6605

SEROPREVALENCE AND ASSOCIATED FACTORS OF *STRONGYLOIDES STERCORALIS* INFECTION AMONG AT-RISK POPULATION IN NORTHERN TAIWAN

Sung-Hsi Huang[1], Hong-Ming Hsu[2], Chien-Ching Huang[3]

[1]National Taiwan University Hospital, Hsin-Chu Branch, Hsinchu City, Taiwan, [2]National Taiwan University College of Medicine, Taipei City, Taiwan, [3]National Taiwan University Hospital, Taipei City, Taiwan

Many case reports of strongyloidiasis from Taiwan have been published in the literature over the years, with a high rate of mortality. Despite its health impact, the prevalence of *Strongyloides stercoralis* infection (SSI) have not been systematically investigated in Taiwan. We conducted a prospective serological survey at National Taiwan University Hospital (NTUH), NTUH Hsin-Chu Branch, and NTUH Biomedical Park Branch. Two different ELISAs were used to detect *Strongyloides* IgG. Individuals were eligible for enrollment if they had a history of eosinophilia, soil-contact activities, immunocompromising medical conditions, or clinical manifestations that could be attributable to strongyloidiasis. We defined seropositive, indeterminate, and seronegative as having both ELISAs positive, either ELISA positive, or both ELISAs negative, respectively. Factors associated with seropositivity were assessed in a multivariable model. between 2021 and 2023, 453 participants were enrolled. The mean age was 62.8 years (range 22 to 99) and 33.3% were female. Comorbid conditions were common, including 37.7% with chronic kidney diseases (stage 3 or higher), 33.6% with diabetes mellitus, 27.4% with chronic airway diseases, 16.3% with malignancy, 14.8% with autoimmune diseases, 59.2% with steroid exposure, and 15.2% were transplant candidates. Among all participants, seropositivity of SSI was 4.2%, while indeterminate serostatus was observed in 12.8%. In multivariable models, participants born after 1960 were less likely to be seropositive compared to those born before 1945 (adjusted odds ratio [aOR] 0.184, 95% CI 0.047 - 0.592), while mainlanders and indigenous populations were more likely to be seropositive (aOR 4.333, 95% CI 1.405 - 12.838). Six-month mortality was higher among seropositive participants (36.8% versus 11.2% among those who were seronegative, p-value = 0.004). Our seroepidemiological survey shows that SSI is still prevalent in Taiwan, at least among at-risk populations. Ongoing efforts are needed to expand SSI screening to different regions of Taiwan and identify proper confirmation tests.

6606

HIGH PREVALENCE OF INTESTINAL PARASITES AMONG ADULTS LIVING IN 36 VILLAGES IN NORTHERN GABON AND RELATIONSHIP WITH BODY MASS INDEX : CROSS-SECTIONAL STUDY

Noé Patrick M'Bondoukwé[1], Luccheri Ndong Akomezoghe[1], Jacques Mari Ndong Ngomo[2], Roger Haldry Sibi Matotou[1], Mérédith Flore Ada Mengome[1], Valentin Migueba[1], Bridy Chelsy Moutombi Ditombi[1], Coella Joyce Mihindou[1], PHYLECOG PARCAM team[1], Denise Patricia Mawili Mboumba[1], Marielle Karine Bouyou Akotet[1]

[1]Université des Sciences de la Santé du Gabon, Owendo, Gabon, [2]Université des Sciences de la Santé du Gabon, UNITE MOBILE LPGD, Gabon

Intestinal parasitic infections (IPIs) are widespread worldwide and can constitute a public health problem. These parasitoses are mainly studied in school-aged children due to their impact on growth retardation, cognitive development, anemia, etc. However, since 2015, certain studies carried out in Gabon have shown that the population at risk of IPIs consists of adults. No studies have focused solely on this neglected population and the impact of intestinal parasites on nutritional status. To fill this gap, a prospective cross-sectional study was carried out in rural areas of northern Gabon. This study was part of the clinical trial on the treatment of hypermicrofilaremic loiasis: PHYLECOG. Adults aged at least 18 years were included after signing informed consent and sociodemographic, clinical and lifestyle data were recorded on a paper case report form. Weight and height were measured and used to determine body mass index (BMI). For the diagnosis of IPIs, a stool sample was collected to perform merthiolate-iodine-formaldehyde staining and concentration, Kato-Katz and parasite culture. A total of 1,363 subjects were included. The proportion of IPIs in adults was 53.8% with 23.4% helminths, 52.6% protozoa and 24.0% protozoa+helminths. An unbalanced nutritional state based on BMI calculation was found in 47.1% of the study population: 25.7% overweight, 17.4% obese and 4.0 underweight. Age- and sex-adjusted odds ratios showed that populations with IPIs had twice the risk of being thin compared to populations with normal BMI (aOR = 2.2, [95% CI : 1.1-4.2], p = 0.02). These results showed the importance of including adult populations aged over 15 years in the national campaign to combat IPI and constitute an important parasitic reservoir in both urban and rural areas.

6607

THE OCCURRENCE OF CROSS-HOST SOIL TRANSMITTED HELMINTH (*ASCARIS*, *TRICHURIS* AND *ANCYLOSTOMA SPP.*) INFECTIONS IN HUMANS AND DOMESTIC/ LIVESTOCK ANIMALS: A SYSTEMATIC REVIEW

Uniqueky Gratis Mawrie[1], Riviarynthia Kharkongor[2], Rajiv Sarkar[2], Rachel Pullan[1]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Indian Institute of Public Health, Shillong, Meghalaya, India

The role of zoonotic soil transmitted helminth (STH) species such as *Ancylostoma ceylanicum*, *Ancylostoma caninum*, *Ancylostoma baziliense*, *Ascaris suum*, *Trichuris suis* and *Trichuris vulpis*, are increasingly acknowledged as potential sources of human infection. However, the extent of transmission in humans remains poorly understood due to reliance on morphological diagnostics, which hinders accurate species identification. This systematic review compiled data on the occurrence of cross-host STH infections (i.e., the occurrence of zoonotic STH in humans and/or

human STH in domestic/livestock animals). Following PRISMA guidelines, studies published in PubMed, Medline, and Web of Science were searched from inception to October 2023. Inclusion criteria encompassed studies identifying evidence of cross-host infections confirmed through molecular methods, and published in English. Exclusion criteria included experimental and wildlife studies, studies that did not find cross-host infections and those without the availability of full-texts. AXIS and Joanna Briggs Institute critical appraisal tools were used for bias assessment of studies. The protocol is registered with PROSPERO (CRD42024519067). A total of 3873 titles and abstracts were screened; 45 studies were included. *Ancylostoma ceylanicum* was the commonest zoonotic STH species, reported mostly from studies in Southeast Asia. Other zoonotic STH such as *Ancylostoma caninum*, *Ancylostoma braziliense*, *Trichuris vulpis* and *Ascaris suum* were also reported. The presence of *Trichuris trichiura*, *Necator americanus*, *Ancylostoma duodenale*, and *Ascaris lumbricoides* in dogs, cats, and pigs were also reported. The findings underscore the need for epidemiological investigations of humans and animals in sympatric environment, using molecular tools, to better understand transmission dynamics and estimate the risk of zoonotic STH infections.

6608

ENVIRONMENTAL SURVEILLANCE TOOLS FOR MONITORING COMMUNITY-LEVEL SOIL-TRANSMITTED HELMINTH PREVALENCE

Kendra J. Dahmer[1], Edoux J E Siko[2], Zayina Zondervenni[3], Heather K. Amato[1], Christopher LeBoa[1], Michael Harris[1], Venkatesh Prabhu Janagaraj[3], Parfait Houngbegnon[2], Souad Saïdou[2], Bernadin Bouko[4], Nils Pilotte[5], Adrian J F Luty[6], Rohan M. Ramesh[3], Moudachirou Ibikounlé[2], Sitara S R Ajjampur[3], Amy J. Pickering[1]

[1]University of California Berkeley, Berkeley, CA, United States, [2]Institut de Recherche Clinique du Bénin, Abomey-Calavi, Benin, [3]Christian Medical College, Vellore, India, [4]Institut de Recherche Clinique du Bénin, Abomey-Calavi, Bénin, Benin, [5]Quinnipiac University, Hamden, CT, United States, [6]Institut de Recherche pour le Développement, Paris, France

Soil-transmitted helminths (STH) are one of the most prevalent infections world-wide and current recommendations from the WHO include targeted deworming and improvements in water, sanitation and hygiene. Elimination of STH typically requires improved infrastructure due to environmental reservoirs. Current surveillance strategies for STH focus on identifying eggs in stool samples via microscopy, which is expensive and exhibits poor sensitivity and specificity especially in settings with low intensity infections. Wastewater epidemiology is a prominent surveillance tool used to detect pathogen circulation and potential reservoirs of disease, but sampling strategies for settings lacking networked sanitation are not well developed. Here, we deploy environmental surveillance strategies in India and Benin where STH are endemic (around 20% human infection prevalence of any STH in both countries). Our group has optimized DNA extractions from large quantities of soil and non-networked wastewater. We use multi-parallel qPCR assays to detect STH DNA in soil collected from high foot traffic locations and three types of wastewater samples in Comè, Benin and Timiri in Tamil Nadu, India. We report detection of STH in soil (India n=95, Benin n=125) and wastewater (India n=61, Benin n=68) with a detection frequency across all sample types of 37% in India and 24% in Benin. We evaluate which sample locations and types allow for more sensitive detection of STH DNA. We determine that wastewater sediment (India 63%, Benin 18%) samples outperform wastewater Moore swabs (India 37%, Benin 6%) and, in India, wastewater grab samples (India 27%, Benin 18%). Wastewater sediment (63%) and soil from markets (50%) had the highest detection frequency in India while soil from open defecation fields (37%) and community water taps (40%) had the highest detection frequency in Benin. We expand our methods to include other enteric pathogens using multiplexed qPCR for wastewater samples. Our results are useful for designing sampling strategies for environmental and wastewater surveillance in settings without networked sanitation across a wide range of enteric pathogens.

6609

TARGET MOLECULES OF *BACILLUS THURINGIENSIS* CRYSTAL PROTEINS AND ANTHELMINTHIC COMPOUNDS IN *CAENORHABDITIS ELEGANS*

Youmie Kim, Mostafa Elfalwal, Emily Goetz, Raffi Aroian

UMASS CHAN MED, Worcester, MA, United States

Bacillus thuringiensis (Bt) produces a variety of crystal (Cry) proteins during sporulation. Cry proteins have been used as agricultural pesticides against insects for decades. Our lab has pioneered work on Cry proteins, e.g., Cry5Ba, active against nematodes, and these are being developed for use against gastrointestinal nematode (GIN) parasites. The related Cry proteins, CryH16 and CryH18, have been under the development as anthelminthics against GINs as well. To understand how these Cry proteins worked we screened for mutants resistant to these proteins and have found 2 rare alleles. Both are conditional mutants. Whole genomic sequencing was used to identify the bre-6 gene, which mutants to CryH16/18 resistance, and it was found to encode a gene involved in transcriptional regulation of a key intracellular pathway. RNAi, extrachromosomal complementation, RNAi knockdown and the Crispr gene editing experiments confirmed that the gene is required for the resistance to CryH16 and CryH18. *bre-6(ye123)* animals have significant fitness costs, suggesting resistance via this mechanism is difficult. In addition to Cry proteins, we have discovered new compounds that have anthelmintic activity against *A ceylanicum* and *Trichuris muris* as part of a 30,000+ compounds high-throughput screen against parasitic nematodes. We have found several new families of compounds highly effective *in vivo* against hookworms but the mechanism of action is unknown. To address this, we obtained two mutant *Caenorhabditis elegans* strains resistant to one class of compounds using forward genetic screens. Mapping and cloning is underway. Uncovering the mechanism of action of these compounds is important for medicinal chemistry and improving activity of this class of compound for eventual clinical deployment.

6610

CHARACTERIZING GENETIC DIVERSITY AND POPULATION STRUCTURE OF HUMAN HOOKWORMS USING WHOLE GENOME DATA FROM ACCESSIBLE SAMPLE TYPES

Kaylee S. Herzog[1], Lisa M. Harrison[2], Michael D. Wilson[3], Michael Cappello[2], Joseph R. Fauver[1]

[1]University of Nebraska Medical Center, Omaha, NE, United States, [2]Yale School of Medicine, New Haven, CT, United States, [3]University of Ghana, Legon, Ghana

Human hookworms infect >500 million individuals worldwide and targeted treatment through Mass Drug Administration (MDA) of anthelmintic drugs reaches hundreds of millions of people every year. Using genomic data to understand how parasite populations are structured, and how that structure changes through time and in response to treatment campaigns, is a novel approach to measure the impact of global health programs. Larvae are the ideal sample type for hookworm genomic studies as they are both more accessible from natural populations than adults and easier to manipulate than eggs; however, the amount of genomic DNA (gDNA) extracted from individual larvae is insufficient for whole genome sequencing. We explore the use of whole genome amplification (WGA) of third-stage hookworm larvae to generate complete genomic data from individual specimens. To first ensure that WGA does not systematically bias next-generation sequencing (NGS) datasets, we validated our approach using adult worms. Genomic DNA extracted from individual adults was serially diluted tenfold (10^{-1} to 10^{-4}) and dilutions were amplified prior to library preparation. Following sequencing, genome breadth at 10x depth of coverage (DOC) varied from 93.8% in undiluted samples to 15.15% in the lowest dilution. Quality-controlled NGS data were aligned to a reference genome and single nucleotide polymorphisms (SNPs) were called to measure false discovery rate and genotype concordance between amplified dilutions and unamplified gDNA sequenced from the same individual. Following validation, gDNA was extracted from individual larvae. Successful

extractions were confirmed with qPCR and used for WGA and NGS. Breadth of coverage ranged from 67.96-92.92%, indicating that the majority of the genome of individual larvae can be sequenced to >10x DOC using this approach. To assess genetic differences between individuals, SNP datasets were analyzed using discriminant analysis of principal components (DAPC), STRUCTURE, and RAxML. Moving forward, this approach can be used to characterize hookworm population structure and diversity in natural populations.

6611

PREVALENCE AND RISK FACTORS OF SOIL-TRANSMITTED HELMINTH INFECTIONS AMONG SCHOOL CHILDREN IN BIOKO NORTE PROVINCE, EQUATORIAL GUINEA

Alejandro Lopelo Bolopa[1], Elizabeth Nyakarungu[1], Cristina Nka Eskolete[1], Vicente Urbano Nsue[2], Micaela Mbomio[1], Wonder P. Phiri[3], Carlos A. Guerra[4], Guillermo A. García[4], Claudia A. Daubenberger[5], Florentino Abaga Ondo[2]

[1]Baney Reference Laboratory, Ministry of Health and Social Welfare of Equatorial Guinea, Baney, Equatorial Guinea, [2]Ministry of Health and Social Welfare of Equatorial Guinea, Malabo, Equatorial Guinea, [3]MCD Global Health, Malabo, Equatorial Guinea, [4]MCD Global Health, Silver Spring, MD, United States, [5]Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, University of Basel, Basel, Switzerland

Soil-transmitted helminths (STHs) are intestinal worms that affect more than a quarter of the world's population, causing significant health problems. In Equatorial Guinea, STHs remain a major public health issue, with *Ascaris lumbricoides, Trichuris trichiura, and Ancylostoma duodenale* being the most common species. The health impact of STH infections is directly related to the worm burden, with severe infections contributing to anemia, malnutrition, stunting, and low birth weight. This study aims to investigate the prevalence of STHs and associated risk factors among school children in Bioko Norte Province, Equatorial Guinea. The research will also evaluate the effectiveness of current prevention and control measures. A community-based cross-sectional study will be conducted in Bioko Norte Province from May to September 2024. A total of 250 school children aged 1-15 years will be recruited using a multistage sampling technique. The study will analyze data on clinical and laboratory findings of study participants to assess the prevalence of STHs in different schools, identify risk factors associated with their transmission, and evaluate the effectiveness of implemented control strategies. The study will provide up-to-date data on the prevalence of STH infections among school children in Bioko Norte Province. Risk factors associated with STH transmission, such as socioeconomic status, hygiene practices, and environmental conditions, will be identified. The effectiveness of current prevention and control measures will be evaluated, and recommendations for improvement will be proposed. The findings of this study will contribute to a better understanding of the epidemiology of soil-transmitted helminthiases in Equatorial Guinea. The results will inform public health authorities and guide the development of targeted interventions to reduce the incidence of STH infections and improve the quality of life of affected populations.

6612

INOCULUM DEPENDENT ANEMIA AND HUMORAL IMMUNE RESPONSES IN HAMSTERS INFECTED WITH A FIELD-ADAPTED STRAIN OF *NECATOR AMERICANUS*

Richard D. Bungiro[1], Christina Paraggio[2], Lisa M. Harrison[3], Michael Cappello[4]

[1]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, United States, [2]Graduate Program in Microbiology, Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT, United States, [3]Department of Pediatrics, Yale School of Medicine, New Haven, CT, United States, [4]Department of Pediatrics, Yale School of Medicine and Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, United States

Laboratory passage of an African strain of *Necator americanus* hookworms has been sustained through 15 passages in outbred golden Syrian hamsters using infectious third-stage larvae (L3) cultivated from human study subjects in Beposo, Ghana. Patent infections have been sustained by subcutaneous infection of weanling hamsters provided *ad libitum* drinking water containing dexamethasone. Here we present the results of a study in which animals were infected with 200 or 400 *N. americanus* L3 and followed for 91 days to characterize pathology and parasite-specific humoral immune responses. When compared to uninfected controls, infected hamsters developed anemia in a dose-dependent manner, with mean blood hemoglobin levels reduced by approximately 21% in the 200 L3 group ($P = 0.08$) and by 55% in the 400 L3 group ($P = 0.004$) at day 42 postinfection. Mean blood hemoglobin levels remained depressed in infected animals for the remainder of the observation period; in the 400 L3 group the reduction was profound and significant, ranging from 45.3% to 58.1% ($P < 0.05$ at all time points). At the time of sacrifice mean +/- SEM intestinal worm burdens were found to be 5.4 +/- 1.8 in the 200 L3 group and 14.2 +/- 2.5 in the 400 L3 group. Intestinal worm burdens were found to be highly correlated with final blood hemoglobin levels ($r^2 = 0.8995$, $P < 0.0001$). Analysis of hookworm-specific humoral immune responses exhibited robust serum IgG responses to soluble L3 extract and adult excretory-secretory (ES) antigens. ES-specific secretory IgA responses were also detected in soluble intestinal flush and soluble fecal extracts prepared from infected animals at the time of sacrifice. These results provide further support for the utility of the hamster *N. americanus* model for the evaluation of hookworm pathogenesis, immune responses, diagnostics and vaccination.

6613

GUT DYSBIOSIS IN MATERNAL HELMINTH INFECTION

Meagan A. Barry[1], Jordan Lawson[1], Joselynn R. Wallace[1], Veronica Tallo[2], Marianne J. Sagliba[2], Amabelle J. Amoylen[2], Jennifer F. Friedman[1], Jeffrey A. Bailey[1], Ashok Ragavendran[1], Emily A. McDonald[1]

[1]Brown University, Providence, RI, United States, [2]Research Institute for Tropical Medicine, Manila, Philippines

Intestinal helminth infections may alter the bacterial composition of the host gut microbiome. The infant gut microbiome is thought to be established through vertical transfer during birth or with breastfeeding. The effect of maternal helminth infection on gut microbiome composition, with implications for establishment of the infant gut microbiome, has yet to be investigated. To address this, a cohort of 400 pregnant women in Leyte, Philippines were enrolled during the second trimester and evaluated by Kato-Katz for helminth infections. Women with hookworm, *Schistosoma japonicum*, *Trichiura trichuris*, *Ascaris lumbricoides*, or coinfection were matched to uninfected controls. Of these 154 women, 16S rRNA was sequenced using Oxford Nanopore and long reads were mapped using Emu and the Ribosomal Database Project. Differentially abundant taxa were determined using ZicoSeq followed by linear model hypothesis testing. At 32 weeks gestation, women infected with hookworm, *S. japonicum*, *T. trichuris*, and *A. lumbricoides*, were found to have significantly increased abundance of *Enterococcus hirae* when compared to uninfected controls. Overgrowth of *Enterococcus spp.* have been associated with colon cancer and can lead to bacteremia. Women with hookworm, *S. japonicum*, and *T. trichuris* were also found to have significantly decreased abundance of *Bacteroides galacturonicus*. *Bacteroides spp.* are a commensal species of the gut, providing protection from pathogens and supplying nutrients to other commensals. These findings suggest that helminth infection leads to dysbiosis of the gastrointestinal tract. This is the first study to investigate the gut microbiome of pregnant women harboring helminth infections, which has potential implications for the early infant gut microbiome. Future work will investigate the gut microbiomes in children born to women with helminth infection.

6614

DISENTANGLING THE COVARYING EFFECTS OF MOTOR DEVELOPMENT AND WEANING FROM BREAST MILK ON INTESTINAL PARASITE INFECTIONS AMONG CHILDREN AGED 0-2 YEARS IN NORTHERN COASTAL ECUADOR

Jesse D. Contreras[1], Manuel Calvopiña[2], Caitlin Hemlock[3], William Cevallos[2], Gwenyth O. Lee[4], Karen Levy[3], Joseph N.S. Eisenberg[1]

[1]University of Michigan, Ann Arbor, MI, United States, [2]Universidad San Francisco de Quito, Quito, Ecuador, [3]University of Washington, Seattle, WA, United States, [4]Rutgers University, New Brunswick, NJ, United States

Intestinal parasite infections (IPI) contribute significantly to child morbidity, particularly in settings with poor sanitation, and have harmful effects on growth and development. Incidence of IPI is low during the first year of life, even in high-burden settings, before rising rapidly. Breastfeeding protects against IPIs by enhancing development of the immune system and microbiome, and weaning is hypothesized to cause the rise in IPIs after 1 year. But children experience many concurrent changes during this period, such as learning to walk independently, which increase contact with the environment and may lead to increased ingestion of parasites. We aimed to disentangle the influence of weaning and increased motor development on IPIs among children in the ECoMiD birth cohort conducted in coastal Ecuador. A total of 1,503 stool samples were collected from 465 children during quarterly visits between ages 3-24 months. IPIs were determined by microscopy. In an age-adjusted regression model, breastfeeding was not associated with IPI, while children who could walk independently had a 2.75-fold higher prevalence of any IPI compared to children who could not yet crawl. However, all children over 12 months were able to crawl and few children under 12 months could walk independently; thus, residual confounding by age might still explain the association. To reduce confounding, we fit stratified models restricted to ages at which breastfeeding or motor development had substantial variation. Among 12-month-olds, breastfeeding was not associated with IPI, while children who could walk independently had 42% fewer infections compared to those who could crawl only (PR = 0.58, 95% CI 0.31, 1.08). Among 15-24-month-olds, children who partially breastfed had 63% more helminth infections but 34% fewer protozoa infections compared to fully weaned children. For highly correlated variables, combined models can mask or invert associations present within finer strata. Breastfeeding's converse associations with helminth and protozoa infections among older children suggest diverse transmission pathways that should be distinguished in studies of IPIs.

6615

HIV MORTALITY TRENDS AMONG THE UNITED STATES POPULATION, FROM 1999-2023: A CDC WONDER DATABASE STUDY

Muhammad Sohaib Asghar[1], Abuoma Cherry Ekpendu[1], Nisar Ahmed[2], Zain Khalid[3], Luis Angel Duharte-Vidaurre[1], Chad Kelly Brands[1]

[1]AdventHealth Sebring, Sebring, FL, United States, [2]Rapido Clinica Familiar, Chicago, IL, United States, [3]University of Kentucky, Lexington, KY, United States

Despite the progress made in managing HIV, the mortality trends among the general population in the United States remain understudied. This lack of information hampers the ability to implement evidence-based interventions at community levels. Our aim was to analyze the trends in HIV-related mortality among US residents by demographic characteristics such as age, gender, race/ethnicity, urbanization, and US Census Regions. State-wide Age-Adjusted Mortality Rates (AAMR) and county-wide data were subsequently analyzed. We abstracted national mortality data from the multiple cause of death files in the CDC-WONDER Database. The ICD-10 codes (B20-B24) were used to identify HIV deaths from 1999-2023. Trends in age-adjusted mortality rate (AAMR) were assessed using Joinpoint regression analysis. Results were expressed as annual percentage changes (APC), average annual percentage changes (AAPC), and 95% confidence intervals (CI). Between 1999 and 2023, a total of 271,568 HIV-infected patients died within the US (AAMR=3.4 per 100,000; 95% CI: 3.3-3.5). Overall mortality trends decreased at an annual rate of -4.66% (95% CI: -4.96, -4.43) from 1999-2023 across the entire population. Specifically, the mortality trends increased among males (from the year 2018-2021), age groups 65-74 and 75-84 (overall), Non-Hispanic American Indian or Alaskan natives (from 2017-2023), across all regions (during 2018-2021), and increased slightly from 2017-2019 onwards across the urbanization divide. States in the top 90th percentile included: the District of Columbia, Florida, Maryland, Louisiana, New York, and Georgia. Union County and Miami-Dade County are highly affected within the state of Florida. Maryland showed a slight increase in trend in recent years, while Mississippi showed the slowest decline overall. HIV mortality among the US population has decreased overall from 1999 to 2023, but with varying demographic and geographic trends. These trends highlight the need for enhanced public health surveillance to better understand the scope of HIV mortality and to identify high-risk demographic and regional subgroups for targeted interventions.

6616

T CELL RECEPTOR REPERTOIRE ANALYSIS REVEALS A DISTINCT PHENOTYPE OF *MYCOBACTERIUM TUBERCULOSIS* (MTB) SPECIFIC T CELL FUNCTION IN PEOPLE LIVING WITH HIV (PLHIV)

Elizabeth Tchaiwe Chimbayo[1], Jimmy Banda[1], Steven Mitini Nkhoma[1], David Mhango[1], Anstead Kamkwatira[1], Paul Garside[2], James Brewer[2], Henry Mwandumba[1]

[1]Malawi Liverpool Wellcome Programme, Blantyre, Malawi, [2]University of Glasgow, Glasgow, United Kingdom

People living with HIV (HIV) have an increased risk of developing lower respiratory tract infections, such as tuberculosis (TB), due to compromised Mtb-specific T cell function. However, the impact of HIV on Mtb-specific T cell receptor (TCR) in the alveolar T cells is incompletely described. Our study aimed to assess the effect of HIV and antiretroviral therapy (ART) on Mtb antigen-specific T-cell receptor (TCR) diversity and clonality. Peripheral blood and bronchoalveolar lavage (BAL) samples were collected from PLHIV on long-term ART and HIV-uninfected adults recruited at Queen Elizabeth Central Hospital, Blantyre Malawi and analysed using flow cytometry and bulk sequencing. Notably, Mtb-specific TCR repertoires in HIV-uninfected individuals showed increased clonality and diversity compared to PLHIV in both the airway and blood. ART was associated with the restoration of the repertoire clonality in PLHIV. Additionally, lower frequencies of Mtb-specific CD4 IFN-γ-producing cells were observed in both blood and airway in PLWH compared to HIV-uninfected individuals (P=0.003 and P= 0.013 respectively). Significant alterations in TCR Vβ expressions were noted in CD4+ T-cells in PLHIV compared to healthy controls. Vβ1, Vβ7.2, and Vβ23 were higher ($p < 0.05$), while Vβ9 and Vβ18 were lower in blood and airway in PLHIV than in HIV uninfected individuals. In CD8 T cells, no significant differences were found in TCR Vβ specificities in the blood. However, in the lung, Vβ5.1, Vβ16, and Vβ17 were increased, while Vβ14 was decreased in PLHIV. The elevated TCR Vβ in the lung & blood in PLHIV suggests their potential involvement in HIV immune response whilst depletion of certain TCR Vβ clones may indicate HIV-induced alteration in the repertoire. Together, these findings suggest a more restricted TCR repertoire in PLHIV with alterations in certain TCR families, potentially impacting antigen recognition and decreasing protection against infections, including TB. Identifying key TCR chains associated with cytokine production may offer targets for vaccine development, improving outcomes for PLHIV and reducing the risk of TB and other infections.

6617

THE PREVALENCE OF CRYPTOCOCCAL ANTIGENEMIA AMONG PATIENTS WITH ADVANCED HIV DISEASES IN SOUTHWEST AND NORTHCENTRAL NIGERIA

Justin Onyebuchi Nwofe, Mary Onyenike, Adeola Awolola, Olabamiji Osho, Patrick Okonkwo, Daniel Offie, Emmanuel Ojo, Femi Emmanuel Owolagba, Eke Ofuche, Jay Samuels
APIN Public Health Initiatives, Abuja, Nigeria

Cryptococcal meningitis (CM) is a serious opportunistic infection that is a major cause of morbidity and mortality in people living with HIV (PLHIV) with advanced disease. Nigeria ranks first in the global burden of cryptococcal meningitis with an estimated annual incidence of 27,100 accounting for 18% of the global incidence of CM. In this study, we determined the prevalence and risk factors for cryptococcal antigenemia in adult people living with HIV (PLHIV) to advocate for the implementation of routine CM screening before ART commencement with support from US-CDC through PEPFAR funding. A multicenter retrospective study of AHD package of care implementation in 334 treatment sites across APIN-supported states in Nigeria. People who present with advanced HIV who were screened for cryptococcal infection between October 2022 and September 2023 were assessed. Data was exported from the facility register into Excel and was analysed using SPSS version 23 Chicago, IL. Logistic regression was conducted to identify risk factors for cryptococcal antigenemia. 7618 was identified as AHD either by CD4<200 cells/μL or clinical stage 3-4. 6933 (91%) had access to CM screening using the Immy Cryptococcal antigen (CrAg) kit. 180(2.6%) were positive for Immy serum cryptococcal antigen. 74(41%) had lumbar puncture and CSF Cryptococcal antigen screening. 27(36%) was positive for CSF CrAg. Cryptococcal antigenemia is higher in treatment-experienced individuals who are failing treatment and those returning to care than those who are treatment-naive. Other risks of cryptococcal antigenemia include lower CD4 cell count <100 cells/mm^3, prolonged immunosuppression, poverty and occupation. Cryptococcal meningitis still poses a great challenge in the global battle to end HIV as an epidemic in 2030. Unsuppressed clients and those with CD4 <100 cells/mm3 possess a higher risk of cryptococcal antigenemia. There is a need to consistently screen all newly diagnosed HIV clients, Clients returning to care and patients with unsuppressed viral load for >1 year of treatment for cryptococcal infection to reduce cryptococcal-related AIDS death.

6618

THREE NOVEL EPIGENETIC-MODIFYING COMPOUNDS IDENTIFIED AS HIV LATENCY-REVERSING AGENTS IN GHANA

Christopher Zaab-Yen Abana[1], Anthony Twumasi Boateng[1], Araba Abaidoo-Myles[1], James Odame Aboagye[1], Kolin M. Clark[2], Liang Shan[2], Helena Lamptey[3], Osbourne Quaye[4], Evelyn Yayra Bonney[1], George Boateng Kyei[1]
[1]Virology Department, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Accra, Ghana, [2]Division of Infectious Diseases, Department of Medicine, Washington University in St. Louis, USA, St. Louis, MO, United States, [3]Immunology Department, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Accra, Ghana, [4]Biochemistry, Cell and Molecular Biology, University of Ghana, Legon, Accra, Ghana

The persistence of latent reservoirs has hindered HIV cure. These reservoirs serve as the source of viral rebound when ART is interrupted. One potential strategy for an HIV cure involves reversing viral latency using small molecules known as latency-reversing agents (LRAs). A critical mechanism by which HIV remains latent during ART involves modifications to the chromatin surrounding the virus. We hypothesized that epigenetic-modifying compounds might effectively serve as LRAsWe utilized the JLAT 10.6 cell line to screen 150 epigenetic compounds. Positive hits were further screened in various J.LAT clones (6.3, 8.4, 15.4). A primary cell latency model was used to identify lead compounds, which were then screened in a macrophage cell line (THP-1 55.2). Lead compounds were validated using RT-qPCR and intracellular HIV p24 staining. The lead compounds were further screened in CD4+ T cells of four individuals living with HIV on suppressive ART.We identified five positive hits (MC1568, Abexinostat, Pracinostat, EPZ2015666, CXC6258-HCL) from the J.LAT 10.6 cell culture system with GFP-positive cells (20-91%). Among the various J.LAT clones (6.3, 8.4, and 15.4). The primary latency model screening revealed three lead compounds (MC1568, Abexinostat, and Pracinostat) that significantly induced GFP positive cells (30-80%) in the macrophage cell model screening. The lead compounds significantly increased HIV gag expression (10-19-fold) and induced intracellular HIV p24 production (43-94%). Importantly, in four individuals on suppressive ART (the lead compounds caused a significant increase (6 to 19-fold) in intracellular HIV-1 transcript levels.We have successfully established for the first time in Ghana, a medium- to high-throughput drug screening system for HIV latency reversal. We have pinpointed three novel LRAs (MC1568, Abexinostat, and Pracinostat). These compounds effectively reactivated latent HIV-1 in vitro and induced HIV expression ex vivo. Our findings suggest that these LRAs hold promise for reactivating latent HIV in individuals living with the virus.

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HIV SCREENING ON NEUROSURGICAL PATIENTS IN SRI LANKA; INSIGHT TOWARDS WHEN TO DO IT

Dewa Lal
National Hospital Kandy, Kandy, Sri Lanka

HIV/AIDS is gaining an increasing interest in Sri Lanka as the incidence is growing up. Cerebral Infections and lymphomas are well recognized neurosurgical complications of HIV/AIDS. Currently screening for HIV infection is not routinely carried out on these patients unless the clinical picture suggests the possibility of HIV infection. The objective of this study is to evaluate the extent of HIV/AIDS related neurosurgical disease spectrum in Sri Lanka. HIV status of the sexually active patients who underwent neurosurgical interventions for HIV/AIDS related cerebral pathology over 3 years were evaluated using standards laboratory diagnostics. This was done as a part of the clinical management of the patients and data related to patient's identity was not included in the study. 59 patients (26 females and 33 males, age between 24 to 58 years) have undergone neurosurgical interventions (aspiration, biopsy, excision, debulking) for HIV/AIDS related cerebral pathology. Bacterial abscess, fungal abscess, tuberculous lesions, Toxoplasmosis and lymphoma were the pathology among 26, 04, 08, 09 and 12 patients respectively. HIV infection was diagnosed in one patient with bacterial abscess (3.8%), one patient with fungal abscess (25%) and three patients with toxoplasmosis (33%). No HIV was detected in patients with tuberculosis and lymphomas. HIV/AIDS is unlikely to be a significant predisposing factor for cerebral tuberculosis and lymphomas, but it is a definite predisposing factor for fungal infections and toxoplasmosis of the brain. Therefore, routine screening for HIV status among patients with cerebral fungal infections and toxoplasmosis is recommended for Sri Lankan population.

6620

IMPACT OF MHV-68'S HEPATOTROPISM ON A SUBSEQUENT LIVER INFECTION BY MALARIA PARASITES

Andreia F. Mósca[1], Beatriz Cancio[1], Viriato M'Bana[2], Ana Fraga[1], Helena Nunes-Cabaco[1], Pedro Simas[3], **Miguel Prudencio**[1]
[1]Instituto de Medicina Molecular, Lisboa, Portugal, [2]UMass Chan Medical School, Worcester, MA, United States, [3]Católica Medical School, Lisboa, Portugal

Concurrent infections by gammaherpesviruses, such as Epstein-Barr virus (EBV), and *Plasmodium* parasites, the causative agents of malaria, are highly prevalent in the sub-Saharan region and are etiologically linked to several malignancies. Host-mediated interactions between these pathogens thus appear inevitable, and may impact either infection and/or disease progression.During the clinically silent but obligatory liver stage of *Plasmodium* infection of its mammalian host, parasites multiply within hepatocytes before egressing into the bloodstream, ultimately leading to

the onset of malaria symptoms. Although hepatomegaly and mild hepatitis are common EBV-related hepatic manifestations, the consequences of the viral hepatotropism on a subsequent liver-stage infection by *Plasmodium* remain underinvestigated. We established a mouse co-infection model employing murine gammaherpesvirus-68 (MHV68) and rodent *P. berghei* parasites as surrogates for their human-infective counterparts, to investigate their crosstalk in the livers of C57BL/6 mice. We showed that an early latent infection by MHV68 markedly inhibits a subsequent liver infection by *P. berghei*, suggesting that MHV68 alters the liver environment and influences *Plasmodium*'s ability to establish a hepatic infection. Our results also show that infection by MHV68 prior to *P. berghei* inoculation significantly decreases malaria severity and associated mortality. Our characterization of the liver's pathological and immunological responses to MHV68 infection revealed noticeable virus-associated alterations in hepatic morphology and immunological microenvironment, with a pronounced increase of specific cytotoxic T cell populations. Our findings unveil a previously unknown effect of gammaherpesvirus infections on the liver microenvironment, which may shape the host's response to subsequent infections by malaria parasites. These findings may not only influence the clinical management of these diseases in malaria-endemic regions, but also impact the efficacy of whole-sporozoite and pre-erythrocytic vaccination against malaria in EBV-infected patients.

6621

RESPIRATORY VIRUSES AND BACTERIA CARRIAGE AMONG PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS IN ACCRA, GHANA

Lawrencia Ami Emefa Ativi[1], Mildred Adusei-Poku[1], Beverly Egyir[2]

[1]University of Ghana, ACCRA, Ghana, [2]Noguchi Memorial Institute for Medical Research, ACCRA, Ghana

Respiratory infections are particularly prominent among individuals with compromised immune systems, representing the most common opportunistic infections. While these infections are typically self-limiting, they pose significant risks to immunocompromised individuals, especially those living with human immunodeficiency virus (PLHIV). Despite the substantial burden of respiratory infections in the sub-Saharan region, there is a scarcity of data on this specific issue among PLHIV.To address this gap, a cross-sectional study was carried out among 240 PLHIV on antiretroviral therapy in three hospitals; Korle Bu Teaching Hospital, Lekma Hospital and University of Ghana Hospital in the Greater Accra region of Ghana from January to May 2023. Participants underwent confirmation of their HIV status, determination of HIV serotype, and measurement of plasma viral load. Nasopharyngeal and oropharyngeal swab samples were collected for respiratory virus and bacteria screening using Real Time Polymerase Chain Reaction (RT-PCR) and Culture and Sensitivity testing, respectively.Among the enrolled participants, 32% tested positive for at least one viral respiratory pathogen, while 28% harboured at least one respiratory bacterium. The predominant virus was NL63, detected in 52 participants, while Staphylococcus aureus was the prevalent bacterium in 38 participants. Notably, the highest occurrence was observed between NL63 and Staphylococcus aureus. The study also highlighted substantial resistance patterns, particularly against Trimethoprim/Sulfamethoxazole, tetracycline, cephalosporins, ampicillin, chloramphenicol, and ampillicin-clavulanate for various bacterial species.The findings indicated a higher detection rate of respiratory viruses compared to bacteria in the respiratory tracts of PLHIV. However, the prevalence of respiratory virus/bacteria-associated occurrences did not demonstrate significant associations with HIV viral load or symptoms. Additionally, the assessment of antimicrobial resistance among nasal bacterial isolates indicated an overall high resistance pattern.

6622

PLACENTAL AND CONGENITAL MALARIA IN HIV POSITIVE PREGNANT WOMEN AND HIV EXPOSED NEONATES IN ABUJA NIGERIA

Chinyere Nneka Ukaga[1], Treasure Njideka Njokuobi[2], Ann Ijeoma Ogomaka[2], Chika Maureen Ezenwa[2]

[1]Wigwe University Isiokpo, Lagos, Nigeria, [2]Imo State University, Owerri, Nigeria

HIV and Malaria are two of the greatest medical challenges facing Sub-Saharan Africa today, and despite this, there is minimal data on the interaction between these two infections in the highest risk group for both infections in Nigeria, sub-Saharan Africa. Placental and congenital malaria was assessed in HIV^+ pregnant women on antiretrovirals visiting 4 hospitals in Abuja Nigeria, between 2017 - 2020 to bring out the possible interaction of these infections and the birth outcomes. Informed and duly signed consents were obtained from the relevant agencies as well as from the participants. Venous blood samples (2mls) were collected from the peripheral blood of consenting near-term pregnant women and used to confirm the HIV status, CD4 cells, PCV and malaria parasitemia pre-delivery. Post delivery, 1ml blood sample respectively was collected from the incision made between the maternal and fetal surface of the placenta, and from Cord blood immediately after separation of placenta from the neonate. Parasitological examination was through microscopy and RDT. The neonatal anthropometric parameters were measured and noted. A total of 237 pregnant women participated in this study; 116(48.94%) HIV^+ while 121(51.05%) were HIV^-. The PCV levels of the HIV^+ participants pre-delivery were ≤32 in 60(51.72%) and ≥33% in 56 (48.27%) respectively. The CD4 cell counts of the HIV^+ participants pre-delivery had 700-799 cells range in 85 (73.27%) and 31 (26.72%) had ≥800 cells. Peripheral malaria was seen in 84 (72.41%) of the HIV+ participants and post-delivery placental malaria in 76 (65.52%) out of whom (45 (59.21%) were primigravids, 27 (35.53%) were secundigravids while 4(5.26%) were multigravids). Congenital malaria was observed in 60(51.72%) of the neonates exposed to HIV with 28 (24.14%) weighing between 2.5 - 3.0kg and, 46(39.66%) weighed between 3.1 - 3.5kg. Congenital malaria in HIV exposed neonates should be given urgent attention especially as malaria prevention is much less effective pregnant women living with HIV.

6623

THE IMPACT OF HEPATITIS B CO-INFECTION ON T-CELL RESPONSES IN VIROLOGICALLY SUPPRESSED HUMAN IMMUNODEFICIENCY VIRUS PATIENTS ON ANTIRETROVIRAL THERAPY IN GHANA

Helena Lamptey[1], **Abigail N A Pobee**[1], James O. Aboagye[1], Anthony T. Boateng[1], Christopher Z-Y Abana[1], Kwadwo Asamoah Kusi[1], Evelyn Y. Bonney[1], George B. Kyei[2]

[1]Noguchi Memorial Institute for Medical Research, Legon, Accra, Ghana, [2]Department of Medicine, Washington University School of Medicine in St Louis, St. Louis, MO, United States

Antiretroviral therapy can suppress HIV in many patients however, people living with HIV (PLWH) are still prone to other infections, even when virologically suppressed. Among PLWH in Africa, 15% are co-infected with Hepatitis B virus. Co-infections complicate disease progression and lead to higher mortality rates in HIV but their impact on T-cell responses is not well understood. Since HIV/HBV co-infection results in over-activation of the immune system, due to residual viral production, we assessed the differences in T cell responses in HIV/HBV co-infected patients and mono-infected controls. We screened 390 archived samples from PLWH for HBV and selected HIV/HBV co-infected samples for this study. Archived peripheral blood mononuclear cells from thirty-one (31) HIV/HBV-coinfected individuals, were stimulated with PMA and ionomycin, stained for activation and exhaustion markers (CD25, CD38, CD69, HLA-DR, CTLA4, PD-1) cytokines (IL-2, IFN-γ, TNF-α) and measured by flow cytometry. Levels of these markers from HIV/HBV co-infected patients were compared with thirty one (31) paired HIV mono-infected, twenty five (25) HBV mono-

infected, and six (6) healthy non-HIV controls. The prevalence of HBV/HIV was 7.9%. We found higher levels of CD69, CTLA4, and HLA-DR in HIV mono-infected and HBV mono-infected individuals compared to the other groups. We also found higher levels of CD25, CD69, and CTLA4 in HIV/HBV co-infected and HBV mono-infected individuals compared to the other groups. The healthy non-HIV controls had higher CD69 levels. No significant differences were observed in the expression levels of immune activation and exhaustion markers or cytokines between HIV/HBV co-infected and HIV mono-infected individuals. However, lower expression levels of IL2 and TNFα were observed in the HIV/HBV co-infected compared to the mono-infected individuals. Immune activation and exhaustion markers were highly expressed even in virologically suppressed HIV-1 pateints, an indication of ongoing residual viral production.

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EXPLORING HISTOPLASMOSIS IN NON-ENDEMIC AREAS: COMPARATIVE ANALYSIS OF CLINICAL FEATURES, RISK FACTORS, AND OUTCOME OF HISTOPLASMOSIS IN HIV-POSITIVE AND HIV-NEGATIVE COHORTS IN WESTERN INDIA

Akshatha Ravindra[1], Deepak Kumar[1], Santhanam Naguthevar[1], Abhishek G P[2], Gopal Krishana Bohra[1]

[1]AIIMS Jodhpur, Jodhpur, India, [2]KGMU, Lucknow, India

Histoplasmosis, caused by the *Histoplasma capsulatum*, is a significant public health concern predominantly in regions where it is endemic. While it is endemic in certain regions of the world, it is considered rare in India. It is more common along the Gangetic belt, however, sporadic cases have increasingly been reported in western India, suggesting a wider than recognized distribution. Disseminated histoplasmosis is of particular concern it often mimicks tuberculosis. This prospective study evaluated the clinical features, treatment, and outcomes of disseminated histoplasmosis in Western India, comparing HIV and Non- HIV cohorts. The study was conducted between January 2022 - December 2023 in Infectious diseases division, AIIMS Jodhpur. Patients aged >18 years with clinically suspected disseminated histoplasmosis were screened using a urinary lateral flow test. Other samples such as Blood, biopsy etc, were collected for confirmatory tests from patients. Demographic data, comorbidities, symptoms, antifungals & outcomes were recorded. A total of 112 patients were recruited, of which 38 confirmed cases were included. The mean age for the HIV group was significantly younger than HIV-negative group (p=0.0042) & was predominantly male patients. Fever & cough was significantly more prevalent in the HIV group compared to the Non-HIV group.Detection of urinary Histoplasma antigen was notably higher in the HIV group compared to the Non-HIV group (p=0.0554). Biopsy confirmation rates were significantly higher in the Non-HIV group (47.37% vs 22.22%) compared to the HIV group. The detection of histoplasmosis from bone marrow samples in HIV vs Non-HIV patients (22.22% vs 5.26%). The mortality rate was relatively low (11.11% vs 10.53%).The findings demonstrate a notably higher prevalence of histoplasmosis among the HIV cohort, & a lower mean age compared to the non-HIV group. HIV patients had a higher rate of positive bone marrow biopsies, possibly due to more frequent disseminated infections. Despite similar mortality rates across groups, we advocate for targeted interventions to enhance outcomes.

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UNVEILING THE NEXUS: PREVALENCE AND ATTRIBUTES OF TUBERCULOSIS POSITIVITY AMONG PEOPLE LIVING WITH HIV IN BANGLADESH

Farzana Zaman

Directorate General of Health Services (DGHS), Dhaka, Bangladesh

Tuberculosis (TB) poses a significant threat to individuals living with HIV/AIDS (PLHIVs) globally. Unfortunately, it is also a pressing concern for TB control efforts in Bangladesh. Due to low prevalence rate of HIV/AIDS in Bangladesh, its impact on national TB control program has not been studied adequately. Therefore, it is utmost necessity to understand the prevalence and potential factors contributing to TB positivity among PLHIVs in the country. In this context, we conducted a cross-sectional study to obtain necessary data from the Infectious Disease Hospital, the largest Anti-retroviral therapy (ART) center in Bangladesh. The data of the PLHIVs on ART recorded between January to December 2023 had been included. The prevalence of TB among PLHIVs in Bangladesh was found 8.7%. Among the 813 PLHIVs included, males constituted 67.4%, females 31.1%, and transgenders 1.2%, with the majority falling within the 30-39 age group (38.3%). Notably, the risk of TB development was higher among male PLHIVs, those whose HIV has progressed to advanced stage (WHO stages 3 and 4 with CD4 cell count<200 cells/mm3), and individuals with a family history of TB. In addition, TB testing using Gene-Xpert was conducted on 38.2% of PLHIVs, which yielded 9.3% TB positivity rate, considered to be very high. TB-positive PLHIVs were significantly older (p=0.002*) than younger counterparts (≤40 years) (55.2% vs. 44.8%, p=0.008*). Moreover, clients of sex workers and Men who have Sex with Men (MSMs) demonstrated higher TB positivity rates (44.8% and 17.2% respectively, p=0.0001*) compared to other groups. Our study findings provide valuable insights for policymakers and health managers grappling with the dual burdens of HIV and TB in Bangladesh. The identification of specific risk groups and demographic trends underscores the urgency of targeted interventions to effective mitigation of the national HIV and TB burdens.

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AGEING AND FRIALTY: THE CASE OF HIV-POSITIVE AND HIV-NEGATIVE INDIVIDUALS IN ASUTIFI-SOUTH DISTRICT AND TECHIAMAN MUNICIPALITY IN AHAFO AND BONO REGIONS OF GHANA

Paul Ntiamoah[1], Max E. Ananni-Akollor[1], Dennis Adu-Gyasi[2], Magaret T. Frempong[1], Mohamed Mutocheluh[3], PatricK W. Narkwa[3], Samuel K. Aordzo[1]

[1]Department of Molecular Medicine, School of Medicine and Dentistry,Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, [2]Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo North Municipality, Bono East Region, Ghana, Kintampo, Ghana, [3]Department of Clinical Microbiology, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, Kumasi, Ghana

Frailty remains a critical problem associated with age, which can be further aggravated with infections such as HIV infection. The dearth of indepth knowledge on frailty among Ghanaians especially in persons living with HIV, informed our decision to investigate the prevalence and factors associated with frailty among older adults with or without HIV infection in Ghana. This was a case control study conducted from January 2020 to December 2020. A total of 181 elderly persons were recruited into this study. Sociodemographic and lifestyle data were obtained with a well-structured questionnaire. Blood samples were obtained to determin the HIV-status of individuals whose HIV-status was unknown. Frailty was assessed by the Frailty Phenotype Tool. Statistical values with $p < 0.05$ was considered statistically significant. Of the 181 participants, 42.5% (n=77) were known HIV positive individuals on antiretroviral therapy whereas 57.5% of participants of this study were HIV-negative. Whilst the overall prevalence of frailty was 15.5% (n=28), the prevalence of frailty among HIV-negative adults was 12.5% (n=13) and 19.5% (n=15) for the HIV-positive adults. Occupation ($p = 0.020$), age ($p = 0.049$), smoking status ($p = 0.029$**)**, and not having multiple sex partners ($p = 0.031$) were associated with frailty among older HIV-negative adults. Frailty is more common among elderly persons with HIV-infection than those without HIV-infection, with nearly 2 out of 10 elderly persons with HIV being frail. No significant association was observed between frailty status and the socio-demographics and lifestyle characteristics among the HIV-positive participants. We conclude that, frailty is common among Ghanaian older adults and it is a bigger problem in the elderly living with HIV-infection.

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TATTOOING, CHRONIC DIARRHEA AND ANEMIA - A CLINICAL TRIAD OF HIV INFECTION

FNU Harshita, Jaideep Pilania, Prasan K. Panda
All India Institute of Medical Sciences, Rishikesh, Rishikesh, India

Tattooing has rarely been documented as a mode of transmission in HIV infection. HIV wasting is the involuntary weight loss of more than 10% of an individual's body weight while having diarrhea or weakness, and fever for more than 30 days. Anemia is a predictor of poor prognosis in individuals with HIV independent of the CD4 count. This triad is rarely seen in HIV.A male in his 30s, bank manager by profession, who recently tested positive for antibodies to HIV 1, presented with watery diarrhea, fever and significant weight loss for 6 months. Deranged kidney function also indicated acute kidney injury. Further workup showed low CD4 counts (71/µL) and high HIV viral load, making the patient immunocompromised. The presence of anemia (Hemoglobin-5.5g/dL) increased the complexity of this case. It was confirmed to be autoimmune hemolytic anemia (AIHA) based on findings of hemolysis (LDH-510.0U/L), reticulocytosis (4.12%), and a positive direct antiglobulin test (DAT). Initially, the patient was stabilized with intravenous fluids, and metabolic acidosis and hypokalemia were corrected. Adding co-trimoxazole and nitazoxanide led to clinical improvement of the patient's diarrhea. HAART was initiated for the HIV infection/AIDS CDC Stage 3 on Day 12 of admission. Prednisolone was prescribed for AIHA, and blood transfusion was required because of a decline in hemoglobin levels in the blood.Transmission of HIV through tattooing calls for stricter regulations on tattooing while ensuring proper hygiene, use of sterile equipment, and proper disposal after the procedure, especially in developing countries. It should also be ensured that only those individuals with a valid license perform tattooing. Chronic diarrhea, attributed to HIV enteropathy or opportunistic infections leading to malabsorption, could have contributed significantly to the waste in this patient. Prevention or reversal of weight loss can be done by intensive nutritional rehabilitation. Anemia in HIV is mostly anemia of chronic disease, while AIHA is rarely seen as in this patient. When this triad of tattooing, wasting and AIHA is present, one should suspect HIV infection.

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OPTIMIZING SEROLOGICAL DIAGNOSIS OF TOXOPLASMOSIS: HETEROLOGOUS EXPRESSION OF GRA1 PROTEIN OF TOXOPLASMA GONDII IN E. COLI AS A KEY ANTIGEN IN CHRONIC INFECTION

Briguitte Fiorella Rivera[1], Stefany Quiñones[1], Luis Canales[1], Alonso Flores[1], Kevin Obando[1], Jimena Raez[1], Seichi Mochizuki[1], Fabrizio Vasquez[1], Robert Gilman[2], Mirko Zimic[1], Maritza Calderon[1], Patricia Sheen[1]
[1]Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Johns Hopkins University, Lima, Peru

Toxoplasma gondii (TG), a protozoan parasite, typically induces mild infections in immunocompetent hosts but may cause severe complications in immunosuppressed individuals, such as those with HIV, by reactivating latent infections, leading to potentially acute and fatal neurotoxoplasmosis. Differentiating between the IgM antibodies, acute infection (tachyzoites), and IgG antibodies, as well as chronic infection (bradyzoites), is crucial in these patients. However, the sensitivity and specificity of many commercial serological assays are compromised by their reliance on total lysate antigens, which include a broad spectrum of parasite proteins. Diagnostics using recombinant antigens from the MICs, ROPs, and GRAs protein families have shown variable results, highlighting the need for enhanced precision in toxoplasmosis diagnostics. In response to this problem, we focus on the GRA1 protein, which is predominantly expressed in tachyzoites and known for its high immunogenicity as a principal antigen. We produced the recombinant GRA1 protein (rGRA1) using an *E. coli* expression system. Our first results showed the specificity of rGRA1 with sera pools from HIV patients; the first had six IgG-positive serums, and the other had ten IgG-negative. The Western Blot analysis showed a distinct and intense 25 kDa band corresponding to the GRA1 protein in IgG-positive samples, absent in IgG-negative samples. These results validate the use of our rGRA1 protein for diagnostic purposes and suggest its potential to significantly improve the diagnosis of chronic toxoplasmosis among immunocompromised patients.

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DETERMINANTS OF HEALTH AFFECTING THE CARE CASCADE OF VULNERABLE PEOPLE LIVING WITH HIV IN SENEGAL

Yasmine M. Elmi[1], Mohamed N'dongo Sangaré[2], Louise Fortes[3], Diadie Saer[3], Fatimata Wone[3], Mabel Carabali[1]
[1]McGill University Department of Epidemiology, Biostatistics, & Occupational Health, Montreal, QC, Canada, [2]Université du Québec en Abitibi-Témiscamingue (UQAT), Rouyn-Noranda, QC, Canada, [3]Université Cheikh Anta Diop, Dakar, Senegal

HIV infection poses a global health challenge, with significant implications for countries worldwide, including Senegal where it remains a pressing social issue. Today, the global goal in the fight against HIV/AIDS infection is to achieve UNAIDS' 95-95-95: 95% of people aware of their status, 95% of diagnosed individuals treated, and 95% on treatment achieving viral suppression. High lost-to-follow-up rates, especially among women, hinder progress. In Senegal, women's vulnerability to HIV care is exacerbated by factors like gender inequality that restrict their control over their sexual and reproductive health, hindering safer sexual practices. Addressing these issues is crucial to reducing HIV incidence and improving women's well-being. This study focuses on understanding social determinants (SDHs) of health affecting the HIV care cascade in Senegal's vulnerable populations, namely women. This cross-sectional descriptive pilot led by prominent researchers from Senegal and Canada, aims to address the gap in HIV care and management for vulnerable groups. The project is carried out at Dakar's Dalal Jam Hospital with data on women diagnosed seropositive and followed up since 2007. The analysis strategy employs descriptive methods to investigate SDHs of HIV care cascade in Senegal's vulnerable populations. It encompasses trend analysis and potential associations with SDH factors. Data will be described using means (standard deviations), or medians (1st quartile-4th quartile) for quantitative variables, and frequencies with confidence intervals for categorical variables. The findings, set to be shared with key stakeholders in May 2024, will reveal insights into the relationship between SDHs and HIV care continuums. The anticipated outcomes will be crucial in designing tailored care programs, enhancing HIV care, well-being, and social equality, thereby improving patient follow-up. In sum, this research not only aims to contribute to achieving the UNAIDS targets in Senegal but also offers a model that may applied in similar contexts globally, thus advancing the fight against the HIV epidemic and empowering vulnerable women.

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UNVEILING A BROADER STI SPECTRUM: THE ADVANTAGES OF MULTIPLEX PCR FOR TRANSGENDER WOMEN'S HEALTH

Alvaro Jose Martinez Valencia[1], Jose David Ramírez Ayala[1], Jonny Garcia-Luna[1], Sebastian Silva-Pena[1], Juan Hurtado[1], Laura Aguirre-Martinez[1], Adrian Smith[2], Justin Radolf[3], Juan Salazar[3]
[1]CIDEIM, Cali, Colombia, [2]Oxford University, Oxford, United Kingdom, [3]Connecticut Children's, Hartford, CT, United States

Background Transgender women (TGW) are highly vulnerable to sexually transmitted infections (STI). In Colombia exist a lack of research on STI prevalence and are few data on the utility of multiple pathogen testing in samples from the sites of sexual exposure. We conducted a transversal study in Cali, Colombia to assess STI frequency and etiology in TGW comparing dual and multiplex PCR-diagnostic methods across various sample types.Methods TGW were enrolled from the community. Oropharyngeal and anorectal swabs were obtained and pooled for each patient, and urine was collected. All the samples were tested using a dual assay for Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG), and

a multiplex assay for CT, NG, Mycoplasma genitalium (MG), Mycoplasma hominis (MH), Ureaplasma urealyticum (UU), Trichomonas vaginalis (TV), Haemophilus ducreyi (HD), Treponema pallidum (TP), Herpes simplex 1 (HS1) and Herpes simplex 2 (HS2). Data were collected in Redcap for descriptive analysis.Results Between May and October 2023, samples from 50 TGW were collected. From the pooled samples 10/50 (20%) were positive for CT only, 8/50 (16%) for NG only and 5/50 (10%) for the two bacteria, by both methods. Among samples with CT/NG detection, 17/23 (74%) were positive for one to four additional pathogens by the multiplex assay: 11/23 (48%) UU, 24/23 (17%) TV and MG, 9/23 (39%) MH, 2/23 (9%) TP and 1/23 (4%) HS2. None of the urine samples were positive for CT/NG. Among samples negative for CT/NG, 15/27 (53%) were positive for one to three different pathogens: 5/27 (18%) MH and UU, 4/27 (15%) TV, 3/27 (11%) TP and 1/27 (4%) HS1 and HS2. Only 25/38 (66%) of the participants with STI diagnosis were symptomatic.Conclusions There is an extreme burden of STI in TGW in Cali, Colombia. Molecular methods for STI diagnosis are not available in the routine of care. The multiplex assay facilitated the diagnosis of additional pathogens in the same samples used for the dual assay, detecting asymptomatic infections, and having the potential to impact treatment decisions. These findings emphasize the need for expanded STI screening and advanced diagnostics in TGW populations.

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NEURODEVELOPMENTAL OUTCOMES IN UGANDAN PERINATALLY-INFECTED CHILDREN WITH HIV AT PRESCHOOL AGE WHO ARE NOT IMMUNE-COMPROMISED

Jenus Shrestha[1], Michael J. Boivin[1], Itziar M. Familiar-Lopez[1], Joseph Wong[2]

[1]Michigan State University, East Lansing, MI, United States, [2]University of California - San Francisco, San Francisco, CA, United States

Neurodevelopmental delays have been well documented in children living with HIV, especially in impoverished settings host to many risk factors. The present exploratory study compares a cohort of immunologically stable Ugandan preschool-age children living with HIV (prior to antiretroviral treatment initiation), to a comparable cohort of non-exposed or infected children matched for age and living situation. We hypothesize that immunologically stable perinatally infected Ugandan children living with HIV (CLWHIV) in early childhood will be neurodevelopmentally comparable to non-infected children, even in the absence of early ART intervention. To test this hypothesis a cohort of CLWHIV (12 boys, 12 girls; mean age 4.6 yrs, SD 0.77) were compared to demographically similar non-exposed/non-infected children (14 boys, 17 girls; mean age 4.8 yrs, SD 0.78) using the Mullen Scales of Early Learning (MSEL) and the Color Object Association Test (COAT), an experimental measure for object placement immediate recall and learning. CLHIV children were immunologically stable in that all but one child was at WHO stage 0 or 1 and children included in this study had CD4% levels above 20 (mean 29.0 (SD 7.4). After adjusting for socio-economic status (SES), gender, age, and quality of caregiving (HOME scale), the HIV cohort was significantly lower than their non-infected counterparts on overall MSEL cognitive performance ($p<0.05$). MSEL differences were especially apparent on receptive language and expressive language. These groups differed on overall learning outcomes with the COAT assessment ($p<0.05$). MSEL and COAT performance was not related to immunology status (CD4, CD4%, viral load), although they were strongly correlated with SES and HOME environment. We conclude that immunologically stable CLWHIV may be at risk neurodevelopmentally for delays or deficits when compared to the non-infected counterparts. These deficits may be the direct result of the disease itself, as well as from the effects of environmental risk factors precipitating both risk for HIV in an impoverished urban Ugandan family and compromising caregiving in affected households.

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INTEGRATING SMOKING CESSATION INTO HIV CARE SETTINGS: A SYSTEMATIC REVIEW OF THE EVIDENCE BASE ON INTERVENTION EFFECTIVENESS AND COST-EFFECTIVENESS

Van M. Nguyen[1], Thanh Hoang[1], Yesim Tozan[2], Mikael Svensson[1], Minh V. Hoang[3], Nawi Ng[1]

[1]School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [2]New York University School of Global Public Health, Department of Global and Environmental Health, New York, NY, United States, [3]Hanoi University of Public Health, Hanoi, Vietnam

Tobacco smoking is a leading risk factor for non-communicable diseases. The prevalence of smoking among patients with HIV is significantly higher than in the general population, and smokers with HIV are more vulnerable to smoking- and HIV-related co-morbidities. The majority of patients and smokers with HIV live in low- and middle-income countries (LMICs), stressing the need for effective and cost-effective smoking cessation services for this vulnerable population in resource-constrained settings. This study systematically reviewed the published literature on the effectiveness and cost-effectiveness of smoking cessation interventions for smokers with HIV. Searches were conducted on four different databases (PubMed, Cochrane, Scopus, Web of Science) in December 2023. Only interventional and quasi-experimental studies assessing the effectiveness and cost-effectiveness of smoking cessation interventions for HIV-infected smokers were included. Of the 4,408 citation hits**,** only 24 studies met the eligibility criteria. All of the included studies were conducted in high-income countries, and the review identified no cost or cost-effectiveness studies. Smoking cessation interventions varied by type of treatment (behavioral, pharmacotherapy), treatment duration and intensity, and type of provider across studies. The included studies had low to moderate risk of bias. The findings of this review further showed that there was a considerable variability across studies in terms of their design and measurement of outcomes, which limited our ability to compare and generalize the findings of the studies. This systematic review provides the most up-to-date evidence on the effectiveness of smoking cessation interventions among smokers with HIV and reveals two critical gaps in the published literature. First, there is a lack of cost and cost-effective evidence on smoking cessation interventions for smokers with HIV, and second, none of the included intervention studies were conducted in LMIC settings.

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COST ANALYSIS OF SMOKING CESSATION INTERVENTIONS FOR SMOKERS WITH HIV IN HIV OUTPATIENT CLINIC SETTINGS IN VIETNAM

Van M. Nguyen[1], Donna Shelley[2], Nam Nguyen[3], Nawi Ng[1], Mikael Svensson[1], Minh V. Hoang[4], Yesim Tozan[5]

[1]School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [2]New York University School of Global Public Health, Department of Public Health Policy and Management, New York, NY, United States, [3]Institute of Social and Medical Studies, Hanoi, Vietnam, [4]Hanoi University of Public Health, Hanoi, Vietnam, [5]New York University School of Global Public Health, Department of Global and Environmental Health, New York, NY, United States

Smoking prevalence is greater in smokers with HIV compared to the general population and smokers with HIV have a higher risk of developing HIV- and non-HIV-related illnesses than non-smokers with HIV. There is, however, a lack of studies on the effectiveness and cost-effectiveness of smoking cessation interventions for this vulnerable population, particularly in low- and middle-income country (LMIC) settings. We conducted a prospective costing study of three different smoking cessation interventions targeted at smokers with HIV and utilized an activity-based, micro-costing approach in our analysis. The costing study was nested within a randomized controlled trial in Vietnam (VQuit), which aimed to assess the effectiveness and cost-effectiveness of the three interventions in HIV outpatient clinic settings: (1)

Ask, Advise, and Assist and Refer to Vietnam National Smoker's Quitline (3As+R); (2) 3As and six in-person intensive Counselling sessions and text messages (3As+C); and (3) 3As+C and Nicotine replacement therapy (3As+C+N). Costs from the provider's perspective included the recurrent costs of the interventions, including personnel, overheads, materials and supplies, as well the capital costs of equipment. From the patient's perspective, we included direct non-medical and indirect costs incurred by patients due to their participation in the interventions. Our preliminary analysis showed that the total cost per smoker was US$38 for 3As+R, $179 for 3As+C, and $284.2 for 3As+C+N. These costs are likely to be overestimates due to the intensive technical and financial support provided for the implementation of these interventions in research setting and hence are conservative estimates. To our knowledge, this is the first cost analysis of smoking cessation interventions for smokers with HIV in an LMIC setting.

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LEPROSY, PARASITIC CO-INFECTION, AND FOOD INSECURITY: A CROSS-SECTIONAL STUDY IN MINAS GERAIS, BRAZIL

Alia R. Bly[1], Heloine M. Leite[2], Pedro H.F. Marçal[3], Dirce R. de Oliveira[2], Maisa Pereira Vieira[2], Audra Bass[4], Marcos D.S. Pinheiro[2], Erica B.M. Silva[2], Julie A. Clennon[5], Thomas R. Ziegler[6], Jeffrey M. Collins[4], Lance A. Waller[7], José A. Ferreira[8], Lucia A.O. Fraga[2], Jessica K. Fairley[4]

[1]Department of Epidemiology, Rollins School of Public Health, Atlanta, GA, United States, [2]Universidade Federal de Juiz de Fora-Campus GV, Governador Valadares, Brazil, [3]Universidade Vale do Rio Doce, Governador Valadares, Brazil, [4]Division of Infectious Diseases, Emory University School of Medicine, Atlanta, GA, United States, [5]Department of Environmental Sciences, Emory University, Atlanta, GA, United States, [6]Division of Endocrinology, Metabolism and Lipids, Department of Medicine, Emory University School of Medicine, Atlanta, GA, United States, [7]Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Atlanta, GA, United States, [8]Faculdade da Saúde e Ecologia Humana, Vespasiano, Brazil

According to epidemiologic and immunologic evidence, undernutrition and co-infection with helminths may be risk factors for Hansen's disease (HD) due to suppression of cell-mediated immunity. We examined associations of food insecurity, HD, and parasitic infection through antibody reactivity and self-reported infection history. Persons aged ≥3 years in 4 municipalities of eastern Minas Gerais, Brazil (n = 1,313) were tested for antibodies against *M. leprae* (LID-1, a marker of infection), *S. mansoni* (SEA), and *S. stercoralis* (NIE) via a multiplexed bead assay. Descriptive analyses and multivariable logistic regression were performed to assess associations of food insecurity with infection. Of the participants, 94(7.2%) were anti-LID-1+, 153(11.6%) were anti-SEA+, and 69(5.3%) were anti-NIE+. Seventy-two (5.5%) reported a history of HD, fifty-four of whom reported past parasitic infection. Compared to participants without history of infection, participants who reported both HD and a parasite were more likely to report running out of food without money to purchase more (aOR = 2.24, 95% CI 1.20, 4.20); running out of money for a healthy, varied diet (aOR = 2.54, 95% CI 1.38, 4.68); and reducing meal size due to lack of money (aOR = 2.67, 95% CI 1.43, 4.98), adjusting for sex. Participants with a history of HD and roundworms were more likely to experience the same metrics of food insecurity, respectively (aOR = 2.94, 95% CI 1.43, 6.07; aOR = 2.97, 95% CI 1.40, 6.28; aOR = 3.12, 95% CI 1.53, 6.36), than participants without a history of either infection. Though not statistically significant, anti-LID-1+/anti-SEA+ (n = 9) and anti-LID-1+/anti-NIE+ (n = 7) participants were observed to be more likely to reduce the size of meals due to lack of money (OR = 1.79, 95% CI 0.44, 7.24; OR = 1.64, 95% CI 0.34, 7.88) compared to LID-1 mono-infected persons. HD mono-infection history was not significantly associated with the food insecurity metrics. In conclusion, food insecurity was observed as more common among participants with multiple infections. Further investigation is needed to discern if food insecurity is a consequence of infection or a predisposing factor.

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CO-INFECTION DYNAMICS: PREVALENCE AND DEMOGRAPHIC INSIGHTS OF HEPATITIS B AND C AMONG HIV PATIENTS

Charity Ndidi Obum-Nnadi, Chika Maureen Ezenwa, Saheed Ayodeji Adekola, Khadijat Toyin Musah

University of Abuja, -- Abuja --, Nigeria

The prevalence and demographic characteristics associated with co-infection of hepatitis B (HBV) and hepatitis C (HCV) among individuals living with HIV were investigated. Despite significant advancements in antiretroviral therapy (ART), co-infections with viral hepatitis remain a major concern due to overlapping routes of transmission and shared risk factors. Co-infection hastens viral replication, fosters the advancement of chronic liver conditions, and presents hurdles for antiviral treatment. Understanding the prevalence rates and demographic profiles of co-infection is crucial for informing targeted prevention strategies and optimizing clinical management protocols. The Co-Infection Dynamics was studied using the Rapid Test Detection (RTD) strips, Enzyme-Linked Immunosorbent Assay (ELISA) and Polymerase Chain Reaction (PCR) method. Non-HIV volunteers in the same area served as control. A total of four hundred (400) subjects were involved in the study using the Stratified Random Sampling method; two hundred (200) from the district hospital for HIV patients and two hundred (200) from the non-HIV volunteers within the study area. The overall prevalence of hepatitis in the district hospital using RTD was 4% and 6% respectively for HBV and HCV as against 20% for both when the PCR method was used. Young adults within the age group 25-35 had the highest prevalence of HIV/HBV while the age ranging 45-55 had the highest prevalence of HIV/HCV. Co-infection of either HIV/HBV or HIV/HCV was higher among the participants who ignorant, civil servants, public servants, petty traders and international business men. Health literacy should be advocated to control these infections.

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DEVELOPMENT OF A CHAGAS DISEASE SEROLOGIC SCREENING PROGRAM WITHIN AN ACADEMIC PUBLIC SAFETYNET HOSPITAL IN CALIFORNIA

Emily A. Kelly, Carina Marquez, Jonathan D. Davis, Rachel Alfaro Leone, Caryn Bern, Jeffrey D. Whitman

University of California, San Francisco, San Francisco, CA, United States

Undertesting and inappropriate testing for Chagas disease (CD) is widespread among clinical populations with risk factors in California, predominantly Latin American immigrants. Towards the goal of increasing recommended risk-based screening and developing research cohorts, we identified two clinics at San Francisco General Hospital (SFGH) with expected increased morbidity from CD: Heart Failure Clinic and HIV Clinic. Employing an interdisciplinary team of laboratory medicine, cardiology, and infectious disease specialists, we performed process mapping for CD clinical screening. We additionally evaluated clinic staff understanding of CD using a brief knowledge and attitudes survey. These assessment tools identified variable provider knowledge of risk factors for CD and indications for clinical screening and confirmatory testing. To address provider knowledge gaps, we facilitated expert presentations to SFGH internal medicine, cardiology, and infectious disease clinicians and provided a targeted educational intervention to clinic staff. To address limited understanding of the CD diagnostic algorithm—which required provider familiarity with confirmatory testing requirements and patient presentation for two blood draws—we developed an in-house tandem serology testing algorithm. Using an automated ELISA platform, two distinct commercial serologic assays are run in parallel on a single serum sample for integrated diagnosis and confirmation of chronic Chagas disease, with a streamlined process for send out to CDC in case of discordance. To address results misinterpretation, we developed interpretive result comments for the battery of CD serology tests with accompanying recommendations for next steps and references to clinical recommendations. Towards development of high-quality CD research cohorts, we designed a secure database and workflow

for prospective collection of remnant clinical specimens and review of patient data under IRB-approved protocols. These interventions represent targeted responses to a CD diagnostic needs assessment through development of a novel clinical testing and research program.

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PRELIMINARY VALIDATION OF *ACANTHAMOEBA* PCR IN A UK PARASITOLOGY REFERENCE LABORATORY

Owain Donnelly[1], Melanie Turner[2], Laura Nabarro[1], Spencer Polley[2]

[1]Hospital for Tropical Diseases, University College London Hospitals (UCLH) NHS Foundation Trust, London, United Kingdom, [2]Department of Clinical Parasitology, Health Services Laboratories, London, United Kingdom

Free-living amoebae (FLA) of the genus *Acanthamoeba* may cause keratitis (AK) and, more rarely, granulomatous amoebic encephalitis (GAE). The parasitology reference laboratory at the Hospital for Tropical Diseases, London, uses the published multiplex qPCR assay from Qvarnstrom *et al.* (2006) for central nervous system (CNS) FLA diagnostics. In order to evaluate the sensitivity of this assay and establish its utility for AK (currently diagnosed within HSL by *in vitro* culture), a series of positive *Acanthamoeba* cultures from clinical isolates were evaluated. Here, we describe the preliminary testing and validation of several *Acanthamoeba* PCR tests in our laboratory. Two previously published PCR primer sets were assessed, along with three primer sets designed in-house (AcCOX 1, 2 and 6). Primer annealing temperatures were tested, followed by serial dilutions of control *Acanthamoeba* DNA. Quantitative PCR (qPCR) was then performed on these serial dilutions, as well as six clinical isolates of *Acanthamoeba* extracted in duplicate directly from cells resuspended in PBS and cells immobilised on a dry cotton swab. These extracts were tested using (1) the Riviere and Qvarnstrom primers with SYBR Green and (2) the standard triplex Qvarnstrom assay using a fluorescent probe. The Riviere and Qvarnstrom primers had the highest analytical limit of detection (dilution of $2.5x10^{-4}$) in standard and qPCR assays. The Qvarnstrom assay detected 6/6 clinical isolates, whereas the Riviere assay detected 5/6 and yielded less DNA per reaction. Results suggest that use of the Qvarnstrom qPCR in our laboratory is valid, and that it performs better than the Riviere qPCR. SYBR Green qPCR gave comparable results to the published multiplex assay, may be more cost-effective than fluorophore-labelled probes. The literature suggests that the Riviere assay only detects genotype T4 isolates, and the negative sample had an atypical melt temperature with Qvarnstrom primer SYBR Green PCR. Next steps will be sequencing the discordant clinical isolate to confirm its genotype, and comparing qPCR with culture on AK clinical samples.

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EVALUATION OF ANTIGENIC REGIONS OF GRA7 FOR THE DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC PHASES OF TOXOPLASMOSIS

Valeria Velasquez H[1], Sebastian Rodriguez G[1], Luis Canales G[1], Fabrizio Vazquez[2], Robert H. Gilman[3], Mirko Zimic[1], Maritza Calderón[2], Patricia Sheen[1]

[1]Laboratorio de Bioinformática, Biología Molecular y Desarrollos Tecnológicos. Facultad de Ciencias e Ingeniería. Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Laboratorio de Enfermedades Infecciosas - LID. Facultad de Ciencias e Igeniería. Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Department of International Health. Bloomberg School of Hygiene and Public Health. Johns Hopkins University, Baltimore, MD, United States

Toxoplasma gondii, an opportunistic intracellular parasite, infects approximately one-third of the global population and can cause severe or even fatal conditions, particularly in immunocompromised individuals. Accurate and early diagnosis is essential to facilitate prompt treatment and prevent disease progression. Conventional diagnostic methods, relying on natural antigens, often lack the specificity required to differentiate between the acute and chronic phases of toxoplasmosis. This challenge is critical in HIV/AIDS patients, where the infection stage dictates the therapeutic approach. In pursuit of precise differential diagnosis, we investigated the potential of recombinant proteins, specifically dense granule proteins (GRA), with an emphasis on GRA7, known for its high immunogenicity in both tachyzoites and bradyzoites. Serological evaluations of GRA7 have demonstrated its capacity to detect anti-*T. gondii* antibodies, exhibiting enhanced sensitivity in detecting acute infections. Further comparative studies on *T. gondii* proteins, SAG2, MIC 1 and GRA8, revealed variable antigenic reactivities, highlighting the necessity of extensive assays. To address these challenges, we employed bioinformatics tools to predict antigenic epitopes of GRA7, enhancing our understanding of its interaction with the host immune system. Our detailed bioinformatic analysis utilizing the IEDB Analysis Resource, Ellipro and ABCpred, identified three linear epitopes of GRA7. Notably, two of these epitopes are part of a larger discontinuous or conformational epitope. Antigenicity levels of these epitopes were quantified using VaxiJen 2.0, with threshold scores exceeding 0.5, indicating significant antigenic potential. This study underscores the complexity of GRA7 and its diagnostic capabilities, revealing distinct reactivities of identified epitopes against sera from acute and chronic toxoplasmosis cases in HIV/AIDS patients. These findings suggest a promising avenue for the development of more targeted diagnostic tests, currently under further evaluation.

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FIRST DOCUMENTED DETECTION OF *TRYPANOSOMA CRUZI* IN *PARATRIATOMA HIRSUTA*

Bernardo Delgado[1], Paula E. Stigler Granados[2], Ian E. Copeland[1], Francisco X. Sanchez[1], Walter D. Roachell[3], Mauricio E. Solis[3], Paul A. Lenhart[3], MaeJean B. Ramnarace[1], **Robert L. Fathke**[1]

[1]Department of Defense Food Analysis and Diagnostic Laboratory, Public Health Command, West, San Antonio, TX, United States, [2]San Diego State University School of Public Health, San Diego, CA, United States, [3]Entomological Sciences Division, Public Health Command, West, San Antonio, TX, United States

We present the first documented detection of *Trypanosoma cruzi* in *Paratriatoma hirsuta*. Entomologists within the Entomological Science Division, US Army Public Health Command, West, collected kissing bug samples and submitted them to their collaborators at the Department of Defense Food Analysis and Diagnostic Laboratory at Fort Sam Houston, Texas. Each sample was speciated by the entomology laboratory, accessioned, and submitted for molecular analysis. Sample processing was performed using the automated QIACube HT instrument with the QIAamp 96 QIACube HT Kit. Initial *T. cruzi* PCR screen analysis was performed using two assays: CRUZI 1-3 and 32F, 148R, 71P LNA probe. Six presumptive positive *T. cruzi* samples were identified. These samples were re-analyzed using a novel kinetoplast PCR/Sanger sequencing assay based on published validated targets. Traditional PCR amplicon was submitted to an external laboratory for sequencing. Analysis of the Sanger sequence data for a unique 20 base pair region confirmed *T. cruzi* identification in each of the *P. hirsuta* samples. To the best of our knowledge, this is the first documented detection of *T. cruzi* in *P. hirsuta*. This finding may help inform Chagas disease preventive measures in geographic areas populated by *P. hirsuta* vectors.

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EXPLOITING THE HUMAN AND ANIMAL HOST INTERACTION WITH *TRYPANOSOMA BRUCEI GAMBIENSE* FOR RAPID DIAGNOSTIC TEST DEVELOPMENT

Jones A. Amponsah[1], Gloria Ivy Mensah[2], Benjamin Amoani[1], Irene Ayi[2], Kennedy Kwasi Addo[2], Kwadwo Asamoah Kusi[2], Daniel Haydon[3], Patient Pati Pyana[4]

[1]University of Cape Coast, Cape Coast, Ghana, [2]University of Ghana, Accra, Ghana, [3]University of Glasgow, Glasgow, United Kingdom, [4]Institut National de Researche Biomedical Kinshasa, Kinshasa, Congo, Democratic Republic of the

Trypanosoma brucei gambiense is an extracellular, single-celled parasite causing fatal human African trypanosomiasis (HAT) due to neurological

involvement. Ghana and Democratic Republic of Congo (DRC) are among the 38 countries affected by Tsetse fly invasion (or infestation) and Trypanosomiasis on the African continent. More than 90% of the total land area of Ghana and DRC are infested with tsetse fly hindering productivity. Tools for early diagnosis of latent *T. b. gambiense* Human African Trypanosomiasis (gHAT) are not available and existing methods have low sensitivity, are not rapid, are costly and require sophisticated equipment and skilled personnel to perform. Early detection and insecticide treatment of domestic animals hold promise for current control strategies. Plasma cytokines have been reported as potential biomarkers of *T. b. rhodesiense* HAT infection and treatment. The study will identify host plasma biomarkers as potential agents for early diagnosis of latent gHAT in Ghana and DRC. Venous blood samples from people living in gHAT endemic area in DRC and non-endemic areas in Ghana will be analysed for the prevalence of gHAT using SD BIOLINE HAT RDT kits and confirm using nested PCR. T-cell functionality in gHAT will be assessed by relevant cytokine biomarkers in plasma and cell culture supernatant of *T. b. gambiense*-infected individuals using Magpix or Luminex 200 analyzer in a multiplex immunoassay. Appropriate controls will be included in all assays. Demographic and other relevant data will be collected. Prevalence of gHAT and other infecting parasite species in humans will be reported. Correlations between participants' gHAT status and demographic data will be reported. Potential host biomarker in culture supernatants, plasma and cell surface activation marker will be known. The predictive biomarkers for early detection of latent *T. b. gambiense* will be reported.

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EVALUATION OF THE ELISA TECHNIQUE USING SAG1 AND TOTAL ANTIGEN TO DETECT IGG ANTIBODIES AGAINST *TOXOPLASMA GONDII* IN HEALTHY AND HIGH-RISK HUMAN SERUMS

Camila A. Gutierrez Cobos[1], Edith S. Málaga Machaca[2], Gabriel A. Soto Soto[1], Carol A. Sánchez Chicana[1], Maritza M. Calderón Sánchez[2], Juan A. Jiménez Chunga[1]

[1]Universidad Mayor de San Marcos, Lima, Peru, [2]Universidad Peruana Cayetano Heredia, Lima, Peru

Toxoplasma gondii is an obligate intracellular protozoan parasite that infects humans, domestic and wild warm-blooded animals. This parasite produces a generally asymptomatic primary infection; however, it can be hazardous in immunosuppressed hosts and cases of vertical transmission(mother-fetus) during gestation. The ELISA test is commonly used to diagnose toxoplasmosis, which can identify immunoglobulins. This test is relatively simple and is available in commercial kits with its execution protocol, usually using total lysed antigens. However, the recombinant antigens could be highly beneficial in this application. The present study aimed to evaluate the ELISA technique using recombinant SAG 1 and total antigen (TLA) of *T. gondii* in 33 serums from the human population at risk and in 42 serums from a healthy population. The results concerning tail frequency found with recombinant SAG 1 antigen in the high-risk population was 96.96% (32/33), while in the healthy population, it was 19.04% (8/42). With the total antigen (TLA), the frequency of IgG anti-*T.gondii* antibodies were 96.96% (32/33) in the population at risk as opposed to 7.14% (3/42) in the healthy population. The frequency found in the healthy population using SAG 1 and TLA was lower than the average reported worldwide; however, TLA was detected more than twice as often as SAG 1 in the healthy population. The frequency of anti-*Toxoplasma gondii* IgG antibodies found in both populations with TLA and SAG 1 was equal, with no significant difference between the antigens. The use of recombinant proteins for the immunodiagnosis of *T. gondii* is a crucial contribution because no studies have been carried out on the population at risk in Peru.

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PROLIFERATING PARASITES- INCREASES IN THE IDENTIFICATION OF CUTANEOUS LEISHMANIASIS CASES IN NEW YORK STATE

Brooke Clemons[1], Kimberly Mergen[1], Alissa Collins[1], Allen Teal[1], Greicy Zayas[2], Susan Madison-Antenucci[1]

[1]New York State Department of Health Wadsworth Center, Albany, NY, United States, [2]SUNY Downstate Medical Center, Brooklyn, NY, United States

Classically described as a tropical disease, leishmaniasis cases are increasingly being diagnosed in non-endemic areas. This is especially true within New York State, USA where travel of residents and surges in human migration have brought substantial increases in the number of parasitic diseases identified. When cutaneous leishmaniasis is suspected, traditional methods of *Leishmania* detection have relied on microscopy and specialized culture techniques. These tests require highly trained staff and are typically available only at reference laboratories. To provide a less labor intensive and more sensitive assay for *Leishmania* detection and identification, the Wadsworth Center Parasitology Laboratory developed molecular-based assays. We first perform a real-time PCR assay (Clemons et al., 2021) to detect the amino acid permease 3 gene (AAP3) and the 70-kDa heat shock protein (HSP70). *Leishmania* spp. are further identified to the species or complex level by sequencing of the internal transcribed spacer 2 (ITS2) region of the ribosomal RNA gene. In just the first quarter of 2024 the laboratory reported 11 positive specimens compared with only 7 in all of 2023. Cases are largely linked to recent migration through South and Central American countries, which is consistent with a majority of the specimens containing *L. (V.) panamensis* or *L. (V.) braziliensis.* Overall *Leishmania* species identified by the laboratory to date using molecular detection and sequencing include *L. donovani* complex, *L. (V.) braziliensis, L. (V.) panamensis, L. tropica and L. major.* Leishmaniasis cases are not currently tracked in the United States. However, given changes in migration patterns and climate it is important to raise awareness for healthcare providers in non-endemic areas and provide species identification to inform treatment decisions.

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EVALUATING THE KNOWLEDGE, ATTITUDES, AND PRACTICES OF CHAGAS DISEASE AMONG HEALTH PROFESSIONALS IN SOUTH FLORIDA, USA

Chanakya R. Bhosale[1], Ambika Kapil[1], Thomas Matthews[1], Angeline Triyono[1], Santiago Ortiz[1], Anna K. Potter[2]

[1]Nova Southeastern University, Dr. Kiran C. Patel College of Osteopathic Medicine, Fort Lauderdale, FL, United States, [2]Nova Southeastern University, Dr. Kiran C. Patel College of Osteopathic Medicine, Foundational Sciences, Tampa Bay, FL, United States

Chagas Disease (CD) is a vector-borne illness caused by the parasite Trypanosoma cruzi. The confluence of immigration/travel from endemic areas, limited blood bank data, and the presence of the disease vector or epidemiological factors has created a potential for CD cases in the Southern United States, including the State of Florida, with an estimated >18,000 people living with CD. Given this potential risk, we identified South Florida as an important region in the state to track CD. Prior research has highlighted a notable deficiency in awareness of CD in the US, with no studies conducted in Florida, or South Florida across medical specialties of interest or in practices where patients may present with classic acute or chronic clinical findings of CD. Thus, this IRB exempt cross-sectional study utilizes an online 25 question survey measuring demographic information (e.g. specialty of medicine), knowledge, attitudes, and practices (KAP) among health care professionals (physicians, medical residents, nurse practitioners & physician assistants) in South Florida. Responses are evaluated using statistical evaluations. Our current survey responses showcase significant differences in KAP from N=51 health professionals (a majority of physicians) across N=19 sub-specialties (a majority from family medicine, pediatrics, & internal medicine) with varying years of experience,

ethnicity, region of medical training, and types of medical setting. Many respondents do not feel very confident in their CD practices (92.16% Wilson 95% CI 81.5%-96.9%), are unable to completely identify the modes of transmission/epidemiology for CD (100% 93.0%-100.0%), believe CD is misdiagnosed (92.16% 81.5%-96.9%), underdiagnosed (62.75% 49.0%-74.7%), or that more training is needed in the state (88.24% 76.6%-94.5%). Specialists (17.65% 9.6%-30.3%) within family medicine, pediatrics, cardiology, and infectious disease have even confirmed a diagnosis of CD. Our pilot study aids awareness and management of CD and informs future steps for research, education, community outreach, and training across health professions on this neglected tropical disease.

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APPLICATION OF RKMP11 BASED ELISA FOR DIAGNOSIS OF CUTANEOUS LEISHMANIASIS CAUSED BY *LEISHMANIA DONOVANI*

Sachee Bhanu Piyasiri, Nilakshi Samaranayake, Rajika Dewasurendra, Charani Karunathilake, Ganga Rajapakse, Sanath Senanayake, Nadira D. Karunaweera

Faculty of Medicine, University of Colombo, Colombo, Sri Lanka

Serology-based diagnostic tools for leishmaniasis can vary in terms of sensitivity, specificity & reliability. The KMP-11 antigen has been studied primarily as a potential vaccine candidate antigen against leishmaniasis. Sri Lanka predominantly reports cutaneous leishmaniasis (CL) caused by *Leishmania donovani*. This study aimed to compare the efficacy of recombinant KMP-11 antigens prepared from *L. donovani* and *L. infantum*, along with crude *L. donovani* antigen, in detecting CL infections in Sri Lanka using enzyme-linked immunosorbent assays (ELISA). An optimized indirect ELISA was employed to determine the cut-off values, sensitivities & specificities for the three selected antigens. The cut-off value for each test was determined using a receiver operating characteristic (ROC) curve based on the absorbance values of sera from 21 CL patients confirmed by microscopy & 21 healthy individuals from non-endemic areas. The cut-off values for KMP-11 antigens were 0.169 for *L. donovani* and 0.162 for *L. infantum*, with sensitivities of 95.2% and 79.2% and specificities of 100% and 71.4%, respectively. The cut-off for crude *L. donovani* antigen was 0.150, with a sensitivity of 98.0% and specificity of 90.3%. A positivity of 95.2% (95% CI: 87.1-100) was observed for ELISA based on KMP-11 for *L. donovani* in comparison with 81.0% (95% CI: 71.6- 90.4) for KMP-11 of *L. infantum* and 100% for crude antigen. All antigens yielded negative results for non-endemic healthy controls. Crude antigen showed the highest sensitivity, while the recombinant KMP-11 antigen for *L. donovani* displayed comparable performance in the detection of CL infections. Further validation, including a larger cohort from different settings reporting CL due to *L. donovani*, is needed to assess its potential for use as a candidate diagnostic biomarker.

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IDENTIFICATION OF ANTIBODY BIOMARKERS TO DIFFERENTIATE POST KALA AZAR DERMAL LEISHMANIASIS FROM LEPROSY

Maurice T. Royal, Kimberly Y. Won, William E. Secor, Sukwan E. Handali

Center for Disease Control, Atlanta, GA, United States

Post Kala Azar Dermal Leishmaniasis (PKDL) is a complication of visceral leishmaniasis with skin lesions that can be difficult to differentiate from leprosy. Because treatment decisions differ between these diseases and an accurate diagnosis is imperative for proper patient care, we are seeking to develop improved test that can rapidly identify the infectious agent. We used the serum epitope repertoire analysis (SERA) platform that combines a bacterial display library technology, next-generation sequencing, and bioinformatics to identify antibody binding epitopes specific to a disease state. For epitope discovery, we used sera from patients with confirmed visceral leishmaniasis (n=40), cutaneous leishmaniasis (n=25), or leprosy (n=30); and patients negative for leishmaniasis (29) or leprosy (n=30). For validation, we used a panel that included sera from the same patient categories (66 visceral leishmaniasis positive sera, 24 cutaneous leishmaniasis sera, 30 leishmaniasis negative sera, 16 defined positive leprosy sera, 28 defined negative leprosy sera), as well as sera from 31 leprosy contacts. SERA screening identified 15 epitope motifs that uniquely reacted with sera from leishmania patients. These epitopes mapped to Histone H2A, an uncharacterized protein with 33 repeats, Histone H2A.1/2, and a J domain-containing domain. SERA screening also identified 14 epitope motifs that uniquely reacted with sera from leprosy patients. These epitopes mapped to putative secreted p60-family protein, Ag85A, Ag85B, UvrABC system protein A, and MTB12. We followed up with peptide array by testing 1,127 peptides (from SERA targets and *in-silico* analysis) and expressed 31 candidate proteins. Four proteins of *L. donovani* and 4 proteins of *M. leprae* differentiated significantly. We conducted large expression of these proteins and developed ELISAs. The next step is validation of these antigens.

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COMPARATIVE EVALUATION OF FOUR MOLECULAR DIAGNOSTIC TESTS FOR THE DETECTION AND IDENTIFICATION OF CUTANEOUS *LEISHMANIA* PARASITES

Yusr Saadi[1], Hamed Chouaieb[2], Hejer Souguir[1], Ahmed Chakroun[3], Insaf Bel Haj Ali[1], Akila Fathallah-Mili[2], Ikram Guizani[1]

[1]Laboratory of Molecular Epidemiology and Experimental Pathology (LR16IPT04), Clinical Investigation Center, Institut Pasteur de Tunis, Université Tunis El Manar, Tunis, Tunisia, [2]Parasitology Department, Farhat Hached University Hospital, Sousse, Tunisia, [3]Laboratory of Molecular Epidemiology and Experimental Pathology (LR16IPT04), Institut Pasteur de Tunis, Université Tunis El Manar, Tunis, Tunisia

Cutaneous Leishmaniases (CL) are a group of diseases considered as the most NTDs. In Tunisia and many countries in MENA region CL present a complex epidemiological situation with the proven implication of at least 3 *Leishmania (L.)* species (*L. infantum, L. major, L. tropica*) with diverse clinical presentations. *L.* species identification is essential for etiological diagnosis, patient's management and surveillance. PCR based assays are the most accurate diagnostic tests for CL because of their higher sensitivity and specificity. The aim of this study is to compare the performances of different PCR based assays we developed for simultaneous *L.* species detection & identification to improve the diagnostic accuracy of generic tests. A total of 91 cutaneous samples collected during routine diagnosis at the Parasitology department of the Farhat Hached UH were used to assess and compare the performances of 4 molecular tests: 2 conventional tests (a genus-specific PCR Lei-70, PCR RFLP ITS1 which profiles are used to identify species) and 2 tests we recently developed (PCR HRM assay, Multiplex PCR assay coupled to Lateral Flow DNA chromatography (Mx PCR LF)) which concomitantly detect & identify the *L.* species. Among the 91 samples, 54 were revealed (+) by at least 1 of the molecular tests. Considering the Direct Examination as the gold standard method, the sensitivities of detection of the PCR Lei-70, PCR ITS1, PCR HRM and Mx PCR assay were 92%, 80%, 88% and 82%, respectively. PCR Lei-70, PCR HRM & Mx PCR LF assays showed similar specificities (95%) while PCR ITS1 showed a specificity of 92%. *L.* species identification was possible with RFLP ITS1, Mx PCR LF and PCR HRM methods. Of 43 PCR^+, RFLP ITS1 identified 39 and PCR HRM 35; Mx PCR LF identified 45 out of 46 PCR^+. This latter was the most performant in terms of species identification. Identity was congruent with the 3 molecular tests, but ambiguities mainly seen with PCR RFLP ITS1 and PCR HRM were resolved with the Mx PCR LF. According to these results, the Mx PCR LF holds promise for accurate simultaneous detection & identification of *L.* parasites in clinical samples that could be used to improve CL diagnosis in health centres

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PHAGE DISPLAY IMMUNOPRECIPITATION SEQUENCING (PHIP-SEQ) FOR THE IDENTIFICATION OF *TRYPANOSOMA CRUZI* ANTIGENS WITH DIAGNOSTIC POTENTIAL

Ryan J. Marczak, Hannah Kortbawi, Stathis D. Gennetas, Caryn Bern, Joseph L. DeRisi, Jeffrey D. Whitman

University of California, San Francisco, San Francisco, CA, United States

Trypanasoma cruzi infection, also known as Chagas disease, is predominantly diagnosed in the chronic phase, requiring confirmation by two distinct IgG serology assays. In the United States, few serological diagnostics are cleared for detecting anti-*T. cruzi* antibodies. Performance evaluations of these tests have shown variable test performance between assays and infected populations throughout endemic regions of the Americas. We hypothesized that using the next-generation technology of phage display immunoprecipitation sequencing (PhIP-Seq), which presents linear peptide fragments across an entire genome within a library of bacteriophages for immunoprecipitation with plasma, will elucidate better antigen targets for laboratory diagnostics. The advantage of PhIP-Seq is that it allows for the antibody profile assessment of each individual without pooling specimens. Our phage library spans the entire *T. cruzi* genome (CL Brener) composed of 228,127 peptide fragments, each being a 47-mer with 19-residue overlap. This *T. cruzi* phage library was immunoprecipitated using plasma samples with confirmed blood donor testing (n=90; 64 seropositive, 26 seronegative), including donors from Mexico, Central and South America. The phage library underwent two rounds of selection before sequencing to identify antigenic peptides. Sequencing reads were normalized, and a z-score was calculated for each peptide within a sample, compared to seronegative controls. To orthogonally validate our findings, we used a mass-univariate generalized linear model. We identified 15 peptide fragments with a z-score ≥4 in 57/64 seropositive samples (≥90% PPA), and in 0 seronegative samples; including microtubule-association proteins (MAPs), surface-antigen (CA-2), 60S ribosomal proteins L23a, and trans-sialidase proteins. One trans-sialidase peptide fragment had a z-score ≥4 in all seropositive samples. These analyses show insight into antigenic peptides that could be easily translated into an immunoassay format. Future steps will validate in larger, real-world infected populations to evaluate test performance to commercial diagnostics.

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PRODUCTION AND EVALUATION OF LB6H RECOMBINANT ANTIGEN PRODUCED IN BRAZIL TO DIAGNOSE AMERICAN TEGUMENTARY LEISHMANIASIS

Ruth T. Valencia-Portillo[1], Ana P. Fernandes[2], Santuza R. Teixeira[2], Nailma Aprigio[2], Ludmila B. Da Silva[2], Natalia Salazar[2], Jose L. Lindoso[3], Beatriz J. Celeste[1], Hiro Goto[1], **Maria Carmen A. Sanchez**[1]

[1]Instituto de Medicina Tropical da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, [2]Centro de Tecnologia de Vacinas - Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, [3]Secretaria de Saúde do Estado de São Paulo, Instituto de Infectologia Emílio Ribas, São Paulo, Brazil

American tegumentary leishmaniases (ATL) have a wide distribution, with an estimated annual incidence of between 600,000 and 1 million new cases, mainly in tropical and subtropical countries. The clinical-epidemiological aspects are fundamental, but laboratory exam data are needed to confirm the diagnosis, mainly due to the varied clinical aspects that are not pathognomonic. A recombinant antigen (rLb6H), identified during the screening of a genomic expression library of *L. (V.) braziliensis* (MHOM/BR/75/M2903) with serum from a patient infected by *L. braziliensis* with mucosal leishmaniasis at the Access to Advanced Health Institute—AAHI, Seattle, USA and was evaluated (2017) and validated (2022) on an ELISA platform for ATL diagnosis, with promising results. This study aimed to produce the rLb6H in Brazil and evaluate its performance on the ELISA platform to diagnose ATL infection. The rLb6H sequence was optimized and analyzed using bioinformatics. The pET24a(+) containing the Lb6H gene was transformed into *E. coli* of the SHuffle T7 Express strain. The induction was conducted at different times and temperatures to evaluate the best condition for protein expression. SDS-PAGE analysis showed that the Lb6H protein presented a band of 76.2 kDa. After lysis, the pellet containing the Lb6H protein was solubilized in a buffer with 8 M urea, and the protein was purified by affinity chromatography on a histidine column. The protein was quantified by using a BCA Protein Assay after dialyzing. After ELISA standardization, 176 serum samples from Brazilian regions were assayed: 93 from ATL patients, diagnosed by direct identification of *Leishmania* infection or PCR, and 83 controls considered healthy by their assessment and clinical exam. The rLb6H-ELISA performance was based on the Receiver Operating Characteristic curve results. In samples from ATL patients, rLb6H-ELISA sensitivity (CI 95%) was 95.6 % (89.1%-98.3%), and the specificity was 96.4% (89.9%-99.0%). Our preliminary evaluation results corroborate previous results, showing that rLb6H produced in Brazil is valuable for possible future use in the routine serological diagnosis of ATL.

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EVALUATION OF THE CROSS-REACTIVITY OF THE RK28 ANTIGEN USED IN THE SEROLOGICAL DIAGNOSIS OF HUMAN VISCERAL LEISHMANIASIS

Bruna R. Dos Santos[1], Ruth T. Valencia-Portillo[1], Silvia M. Di Santi[2], Hiro Goto[1], **Maria Carmen A. Sanchez**[1]

[1]Instituto de Medicina Tropical da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, [2]Núcleo de Estudos em Malária/ Instituto Adolfo Lutz/ Instituto de Medicina Tropical da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Advances in VL diagnosis were driven by the development of lateral flow immunochromatographic tests based on the rK39 antigen, facilitating access to diagnosis and presenting high sensitivity and specificity. On the other hand, the low accuracy observed in East Africa led to the development of rK28, which, although it has high sensitivity, has demonstrated low specificity in regions where other infectious diseases coexist. The present work aimed to evaluate the cross-reactivity of the rK28 antigen compared to rK39 (produced by Access to Advanced Health Institute - AAHI, Seattle, USA), employing samples from patients with malaria from different locations in Brazil. The panel used was composed of serum samples from patients with positive thick blood smear and positive serology (ELISA with MSP1-19) for *Plasmodium falciparum* or *P. vivax*: 55 from patients diagnosed in São Paulo Municipality (15 with *P. vivax* and 40 with *P. falciparum*), and 48 from the State of Pará (*P. vivax*). The samples were tested with rK39 and rK28 antigens on the ELISA platform. In São Paulo, a positivity rate of 40.0% (24.9%-56.7%) was obtained with ELISA-rK28 and 2.5% (0.1%-13.2%) with ELISA-rK39, in *P. falciparum* samples, and 20.0% (4.3%-48.1%) with ELISA-rK28 and 6.7% (0.2%-31.9%) with ELISA-rK39, in *P. vivax*. In samples from Pará (*P. vivax*), positivity was 16.7% (4.5%-30.2%) with ELISA-rK28 and 2.1% (0.1%-11.1%) with ELISA-rK39. Although the coexistence of malaria and visceral leishmaniasis in the patients' places of origin cannot be excluded, the significant difference in positivity between the antigens (Fisher exact test, p=0.0001) indicates the occurrence of cross-reactivity between rK28 and the patients' antibodies with *falciparum* malaria. In the case of patients with *P. vivax*, there was no significant difference between both antigens in the samples from São Paulo (Fisher exact test, p=0.5977), although in Pará, the positivity was significantly higher with rK28 (Fisher exact test, p=0.0305).

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VALIDATION OF A WHOLE BLOOD *TRYPANOSOMA CRUZI* QUANTITATIVE RT-PCR ASSAY ACROSS A RELEVANT RANGE OF PARASITEMIA

Evan Teal, Rachel Alfaro Leone, Caryn Bern, Jeffrey Whitman

UCSF, San Francisco, CA, United States

Detecting acute or reactivated Chagas disease is important in immunocompromised patients, commonly in the setting of organ transplant and HIV co-infection. The US CDC is the only lab accessible to all US

healthcare providers that provides clinical PCR testing. It is expected that new requirements for donor screening will increase the volume of testing that may necessitate more widespread implementation of quantitative PCR (qPCR) assays for Chagas disease. Our study seeks to adapt published PCR primers and probes (minicircle and satellite DNA) to a standard curve of clinically relevant parasite concentrations. Additionally, we aim to evaluate the analytical sensitivity of SYBR green reporter (all amplified DNA) to TaqMan probe (sequence-specific amplification products) to determine if SYBR green may provide more sensitive detection. We will evaluate limits of detection (LoD) and quantification (LoQ) in multiple *T. cruzi* strains relevant to human infection (Dm28c (TcI), Y(TcII), and CL Brenner(VI)). The relevant range of LoQ was determined to be ~0.05-500,000 parasite equivalents per mL (Peq/mL) based on published research in immunocompromised populations. LoQ was determined along an 8-point standard curve with linearity r^2 >0.90 and a cycle threshold (Ct) coefficient of variance <10% for each concentration run in triplicate. We have evaluated 3 technical replicates for minicircle primers with Dm28C DNA, demonstrating acceptable linearity and intra-assay precision by SYBR green and TaqMan methods. SYBR green demonstrated increased analytical sensitivity by lower Ct values at all points across the quantitative range with an average Ct difference of 2.4. These findings suggest that TaqMan probe sequences may not be present in all kDNA amplicons. This may be of limited clinical significance given both are detectable across this range of clinically relevant parasite concentrations. These preliminary findings demonstrate that a whole blood qPCR method quantifying parasitemia can be achieved. Further studies are planned to evaluate whether the observed increase in analytical sensitivity by SYBR is applicable to LoD.

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THE RELATION BETWEEN RECOMBINANT PROTEIN GRA1 AND SEVERITY INDICATORS IN PATIENTS WITH TOXOPLASMOSIS AND HIV/AIDS CO-INFECTION

Luis Canales G.[1], Edith Málaga[2], Ricardo Medrano[2], Brigitte Rivera H.[1], Seichi Mochizuki[1], Stefany Quiñones G.[1], Lynn Pinchi[3], Viviana Pinedo[4], Lilia Cabrera[3], Cesar Ramal A.[5], Hannah Steinberg[6], Robert H. Gilman[7], Nataly Bowman[8], Maritza Calderón[2], Patricia Sheen[1]

[1]Laboratorio de Bioinformática, Biología Molecular y Desarrollos Tecnológicos. Facultad de Ciencias e Ingeniería. Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Laboratorio de Enfermedades Infecciosas - LID. Facultad de Ciencias e Ingeniería. Universidad Peruana Cayetano Heredia, Lima, Peru, [3]Asociación Benéfica Prisma, Lima, Peru, [4]Universidad Nacional de la Amazonía Peruana, Iquitos, Peru, [5]Department of Infectious and Tropical Diseases, Hospital Regional de Loreto, Loreto, Peru, [6]Department of Microbiology and Immunology, University of Illinois, Chicago, IL, United States, [7]Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States, [8]Division of Infectious Disease, School of Medicine, University of North Carolina, Chapel Hill, NC, United States

Toxoplasmosis is a critical opportunistic infection in patients with HIV/AIDS, which faces important challenges in its diagnosis and treatment. In this context, recombinant proteins offer significant advantages in terms of sensitivity and specificity. The GRA1 protein, secreted by *T. gondii,* is key in the life cycle of the parasite and essential for maintaining the parasitophorous vacuole, allowing persistence in the host. It has been established that GRA1 can be a valuable marker for the detection of recent infections of toxoplasmosis. This study investigates the relationship between the serological response in Western blot towards the recombinant protein GRA1 produced in *E.coli* and the immunological markers CD4+, CD8+ and the CD4+/CD8+ ratio, exploring its potential as a biomarker of severity in advanced stages of HIV infection. The results showed that 80.7% of the patients (46/57) were positive for IgG and 31.6% (18/57) for IgM. Mean CD4+ lymphocytes of 63 (27-136) cells/mm3 were recorded. , CD8+ of 764 (385-984) cells/mm3, and a CD4+/CD8+ index of 0.08 (0.04-0.17). The mean log viral load was 4.7 ± 1.0 log10 RNA copies. In addition, three relevant clinical cases are detailed with positive IgM and negative IgG values, indicating a high probability of recent toxoplasmosis infection. The first case describes a patient with severe neurological compromise and altered consciousness (total Glasgow Scale = 9), who did not improve with cotrimoxazole treatment and died after recruitment. The second case involves a patient with myelopathy from the level T10 and disorientation (total Glasgow Scale = 14), who was also positive for HTLV-1. The third case reports a patient with mild IgM positivity, CD4+ in 70 cells/mm3 and symptoms of altered consciousness (total Glasgow Scale = 13), together with a brain tomography compatible with cerebral toxoplasmosis, treated with cotrimoxazole. This antigen has the potential to predict cases of acute infection and reactivation of toxoplasmosis in patients with HIV. Future studies should validate the sensitivity and specificity of GRA1, comparing it with standard tests and increasing the number of samples analyzed.

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DEVELOPMENT OF ISOTHERMAL AND CRISPR-BASED DIAGNOSTICS FOR THE DETECTION OF *BABESIA* PARASITES

Nirmallya Acharyya, Sabarinath Neerukonda, Brendan Elsworth

US Food and Drug Administration, Silver Spring, MD, United States

Human babesiosis is caused by infection of the red blood cells with *Babesia* species parasites and can result in severe disease and even death, especially in immunocompromised or asplenic individuals. In the USA there are ~2,000 cases of human babesiosis annually, primarily caused by *B. microti*, however, due to underdiagnosis the true number of infections has been estimated to be up to 10-fold higher. The number of cases of babesiosis is likely to continue increasing due to the expanding range of the ticks that transmit infection. Further, babesiosis can be transmitted by blood transfusion, although testing is now in place in endemic states. Diagnosis is currently based on the presence of parasites in a blood smear or by PCR which require trained technicians and specialized equipment. Here, we investigate and compare the utility of recombinase polymerase amplification (RPA) and Cas12 or Cas13-based CRISPR assays as a simple isothermal method for the detection of *B. microti* and *B. divergens* nucleic acid. We further investigate the sensitivity and specificity of each assay from different sample types, including lysed whole blood and purified nucleic acids. These methods offer the potential of a simple point-of-care diagnostic with the sensitivity and specificity of PCR and the ability to multiplex for the detection of other tickborne pathogens in the future.

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TOXOPLASMA GONDII IN TERTIARY HOSPITAL, EASTERN SAUDI ARABIA: ROLE OF SEROLOGY AND MOLECULAR DIAGNOSIS AND INSIGHT INTO PREDICTIVE RISK FACTORS

Qasim AlKhaleefah[1], Obeid E. Obeid[1], Nourah Al Qahtani[2], Salma Al Jaroodi[1], **Ayman A. El-Badry**[3]

[1]Department of Microbiology, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia, [2]Department of Obstetrics and Gynecology, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Egypt, [3]Cairo University Kasr Al-Ainy Faculty of Medicine, Egypt & Imam Abdulrahman Bin Faisal University, Saudi Arabia, Cairo, Egypt - Dammam, saudi Arabia -, Egypt

Toxoplasmosis is a potentially life-threatening disease that necessitates accurate diagnosis for treatment, prevention of transmission, and unfavorable consequences. This study is to determine the serological and molecular prevalence of *Toxoplasma gondii* in sera of clinically suspected cases and estimate potential risk factors for the occurrence of Toxoplasmosis. *Toxoplasma*-specific IgG and IgM were detected in 22.4% (32 cases) and 4.2% (6 cases), respectively. 529 bp-repeat elements PCR (RE-PCR) detected *Toxoplasma* DNA in 33.6% (48 cases), and B1-nPCR detected *Toxoplasma* DNA in 23.7% (34 cases) of the study population. All positive cases by the B1-nPCR were also positive by direct RE-PCR, and none of the negative cases by B1-nPCR were positive by direct RE-PCR. RE-PCR revealed a perfect sensitivity (100%) and 87.16% specificity compared to B1-nPCR with substantial agreement. The serological test showed limited sensitivity and moderate specificity with a slight agreement between the serology test and B1-nPCR results. Age distribution of positive

cases showed a peak in the 25-40 years age group. Among patient characteristics (demographic, clinical, and laboratory data and lifestyle habits), patients with chronic diseases, a history of adverse neonatal consequences, pregnant women who had intrauterine growth restriction/ premature rupture of membranes, handled undercooked meat, routinely ate from restaurants were at higher risk of having *Toxoplasma*. In positive *Toxoplasma* patients, there was a statistically significant increase in the risk of neonatal consequences among individuals with chronic diseases. Routine hand washing was a protective habit against toxoplasmosis. The study results emphasized the advantage of using PCR tests coupled with routine serological tests for diagnosing toxoplasmosis in clinically suspected cases, thus helping improve national guidelines for *Toxoplasma* screening.

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CHARACTERIZATION OF LEISHMANIASIS IN THE TOURIST CORRIDOR OF THE AMAZONAS REGION, PERU

Sonia Huyhua[1], Marianella Villegas-Pingo[2], Kevin Rivera[3], Lizandro Gonzales[4], Hugo Valdivia[5], Stella M. Chenet[6]

[1]Facultad de Ciencias de la Salud – FACISA, (UNTRM), Chachapoyas, Peru, [2]Instituto de Investigación de Enfermedades Tropicales, Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru, [3]Facultad de Medicina. Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru, [4]Laboratorio Referencial de Salud Pública Amazonas. Dirección Regional de Salud (DIRESA), Amazonas, Peru, [5]U.S. Naval Medical Research Unit No. 6 (NAMRU-6), Lima, Peru, [6]Instituto de Investigación de Enfermedades Tropicales. Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas (UNTRM), Chachapoyas, Peru

Cutaneous leishmaniasis (CL) is endemic in the region of Amazonas and represents a major public health challenge. In 2023, 314 cases of CL were reported, compared to 284 cases in 2022. It is worth noting that most of the cases were reported in the tourist corridor of "Alto Utcubamba" which includes the provinces of Luya and Chachapoyas. However, a high number of underreported cases is suspected due to the social stigma, the lack of health coverage, and an apparent resistance to the treatment. In this study, we analyzed 24 samples collected in the provinces of Chachapoyas and Luya during 2022 and 2023. Samples were diagnosed as positive to *Leishmania* through a direct smear examination and cultured on blood agar, followed by a FRET-based real-time PCR technique targeting the MPI and 6PGD genes. Results showed 12 positive specimens for *L. (V.) braziliensis* and 11 for *L. (V.) peruviana*; however, one sample was undetermined. The majority of the patients reported u*lcers in the lower limbs with raised edges and a granular bottom*. According to the epidemiological information, most of the patients (10/24) belonged to the ≥ 60 age group with agriculture as their main occupation. Although most of the samples were properly characterized, the difficulty in the identification of one of the samples could be attributed to genetically complex strains, including hybrid. Moreover, *Leishmania* strains, resulting from genetic exchanges, are suggested to cause more severe clinical symptoms and an increase transmissibility. On the other hand, it is important to highlight that some species within the *L. braziliensis* complex, such as *L. (V) braziliensis*, can cause metastasis to destructive mucosal lesions after healing the initial skin lesion. In addition, reports suggest that this species is more virulent because it can cause mucocutaneous leishmaniasis, therefore, it is important to characterize and properly identify the *Leishmania* species circulating in the area, to have a better idea of the prognosis of the disease.

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ASSOCIATION BETWEEN IMMUNE PROFILE AND CHAGAS DISEASE PROGRESSION IN NATURALLY INFECTED RHESUS MACAQUES

Rachel Clear[1], Weihong Tu[1], Kelly Goff[2], Preston Marx[2], Claudia Herrera[1], Eric Dumonteil[1]

[1]Tulane University, New Orleans, LA, United States, [2]Tulane National Primate Research Center, Covington, LA, United States

Chagas Disease is caused by the protozoan parasite *Trypanosoma cruzi*; clinical presentation ranges from asymptomatic to severe cardiac and/ or digestive damage. Previous studies in naturally infected macaques indicated a role for parasite strain composition in disease progression, suggesting differences in immune response between "controller" and "progressor" macaques. In this study, we used RNA-sequence data to analyze Major Histocompatibility Complex (MHC) genes, immunoglobulin (Ig) subclasses, and Ig and T-cell Receptor (TCR) repertoires in eighteen naturally infected macaques and nine uninfected macaques to test for differences in the breadth of the immune response associated with disease progression and parasite strain diversity. MHC molecules are responsible for binding foreign epitopes to induce adaptive immune responses via antigen presentation. The TCR complex is found on the surface of T lymphocytes, and reflects the diversity of antigens presented via MHC molecules during infection. Similarly, IgG diversity can also inform on the differentiation of B cells as a response to infection. Different MHC alleles were observed between the uninfected and infected macaques, with several alleles unique to the progressors. The proportion of Ig subclasses showed limited differences associated with infection. On the other hand, analysis of the Ig repertoire indicated that infection was associated with an increase in IgG diversity together with the expansion of selected IgGs, and this was more pronounced in controller macaques compared to progressors. TCR repertoire was also affected by infection with the expansion of several TCRs, but differences between controller and progressor macaques were minimal. These results provide evidence that MHC genes may play a role in host genetic susceptibility, and that differences in IgG and TCR repertoires may be associated with Chagas disease progression. A better understanding of these processes is needed to improve understanding of disease risk and patient care.

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MOLECULAR EPIDEMIOLOGY OF *TRYPANOSOMA CRUZI* IN EL SALVADOR ELUCIDATED BY MULTI-LOCUS SEQUENCE TYPING USING THIRTEEN HOUSE-KEEPING GENES.

Yuko Nitahara[1], Marvin S. Rodríguez[2], Yu Nakagama[1], Katherine Candray[1], Junko Shimada[3], Yasutoshi Kido[1]

[1]Osaka Metropolitan University, Osaka, Japan, [2]Centro de Investigacion y Desarrollo en Salud, San Salvador, El Salvador, [3]Gunma Univeristy, Gunma, Japan

One of the important factors in controlling infectious diseases is the precise targeting of the foci on which we apply our limited resources. El Salvador, located in the Central America, is endemic of Chagas disease with newly diagnosed patients every year to date. Chagas disease is a zoonotic disease caused by the infection of a single-celled parasite called *Trypanosoma cruzi*. The transmission of *T. cruzi* to humans in this region mainly occurs through contact with blood-sucking triatomine bugs called *Triatoma dimidiata*, locally known as 'chinche'. Although endemic for a long time, little is known about the characteristics of *T. cruzi* lineages circulating in this country. This study focused on illustrating the current distribution of *T. cruzi* lineages in El Salvador by genetically analyzing 145 *T. cruzi* samples from *T. dimidiata* collected from throughout the country. The results of DTU classification showed homogenous genetic characteristics in the country – 99.3% resulted in *T. cruzi* lineage I (TcI). Further analysis based on the sequence data of thirteen housekeeping gene fragments revealed the twelve novel sequence types, which consisted of two major groups based

on phylogenetic analysis. These results suggested persistent area-limited transmission of *T. cruzi*, which may serve as an important insight for the disease control strategy in this region.

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CO-INFECTIONS OF *LEISHMANIA DONOVANI* AND *LEISHMANIA MAJOR* IN BLOOD OF PATIENTS WITH VISCERAL LEISHMANIASIS FROM GARISSA COUNTY, NORTHERN KENYA

Vane Kwamboka Omwenga[1], Cyrus Ayieko[2], Kimita Gathii[3], Clement Masakhwe[3], John Waitumbi[3]

[1]WRAIR-A-Kenya/Maseno university, Kisumu, Kenya, [2]Maseno university, Maseno, Kenya, [3]WRAIR-A-Kenya, Kisumu, Kenya

Leishmaniasis is endemic in many countries, including Kenya. Globally, around 350 million people are at risk of contracting the disease. Despite an increased frequency of visceral leishmaniasis (VL) outbreaks in Northern Kenya (Garissa county) in recent years, there is little data on the genetic structure and epidemiology of *Leishmania* parasites in the region. This study investigated the inter-species diversity and evolutionary relationships of *Leishmania* parasites collected from Northern Kenya (Garissa County) during the 2019 - 2022 visceral leishmaniasis outbreak. A total of 286 blood samples collected from patients suspected of having VL at Garissa Referral County Hospital between 2019 and 2022 were analyzed. *Leishmania* parasites were screened at genus and species level by quantitative real-time PCR (qRT-PCR). To characterize the parasites genotypes, amplicons of Hsp70 (~2000nt) and ITS (1,400nt) genes generated through conventional PCR were fragmented into suitable library sizes, sequenced and analyzed using phylogenetic tools. To deconvolute unexpected observation of mixed infections of *L. donovani* and *L. major*, we designed a deep sequencing assay targeting un-fragmented 350nt region of ITS1 gene. Sequencing was performed on the Illumina MiSeq platform. Sequences were analyzed using the ngs mapper pipeline and Dada2 in R. By qRT-PCR, 128/286 (45%) blood specimens tested positive for *Leishmania* at the genus level. Upon speciation, 48/128 (17%) had mono-infections of *L. donovani*, 2/128 (1%) had mono-infections of *L. major* while 78/128 (27%) had co-infections of *L. donovani* and *L. major*. On sequencing the PCR amplicon libraries, 86/128 Hsp70 and 79/128 ITS gene sequences clustered with *L. donovani* complex. On sequencing the full 350nt ITS fragments, mixed infection of *L. donovani* and *L. major* were detected. This study reveals the complex nature of *Leishmania* epidemiology in Kenya. It also sheds light on the possible inter-species interaction that may have significant implications on diagnosis and pharmaco-therapy.

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EVIDENCE FOR VERTICAL TRANSMISSION OF GENETICALLY DIVERSE *TYRPANOSOMA CRUZI* IN A NATURAL RODENT RESERVOIR POPULATION

Nathaniel L. Gibson[1], Bridget Knudson[2], Bruno M. Ghersi[1], Anna C. Peterson[1], Claudia Riegel[3], Eric Dumonteil[2], Claudia Herrera[2], Michael J. Blum[1]

[1]University of Tennessee Knoxville, Knoxville, TN, United States, [2]Tulane University, New Orleans, LA, United States, [3]New Orleans Mosquito Termite and Rodent Control Board, New Orleans, LA, United States

Chagas disease, caused by the protozoan *Trypanosoma cruzi* (*T. cruzi*), poses a significant health threat in the Americas with 6-8 million people infected by the parasite and 75 million at risk of contracting the disease. While Chagas disease is vector-borne, vertical transmission has played an increasingly significant role in disease transmission. Across Latin America, the monitoring of blood and organ donations coupled with vector control programs has led to vertical transmission becoming the main transmission pathway for spread amongst humans. Studies have found that a high diversity of *T. cruzi* DTUs (Discrete Typing Units) can circulate within human populations, and also that individuals of other mammalian hosts can have high *T. cruzi* DTU diversity. It is less clear how *T. cruzi* prevalence and diversity is sustained in non-human mammals. We hypothesized that vertical transmission may also be a pathway for sustaining pathogen reservoirs and DTU genetic diversity in other mammals, namely urban rodent reservoirs. Leveraging a previous study in New Orleans (LA, USA), we examined 10 *T. cruzi* PCR positive pregnant rodents (Norway rats, black rats, and house mice) and 66 embryos. Fifteen of the 66 (22.7%) embryos were positive for *T. cruzi* by PCR. Genotyping PCR of the *T. cruzi* mini-exon gene and deep sequencing were performed to characterize the DTU structure, demonstrating infections with multiple DTUs such as TcI, TcII and TcV. These findings indicate that vertical transmission in rodent populations can potentially sustain *T. cruzi* infection and multiclonality in urban areas where vector populations might be small or absent. Given the increasing importance of vertical transmission, it would be prudent to conduct further investigations to better characterize the transmission pathway and understand what impact vertical transmission could have on *T. cruzi* prevalence and diversity in other natural reservoir populations. For example, combining diagnostic and genotyping assays with genomic estimates of relatedness among *T. cruzi*-positive hosts could shed further light on vertical transmission in natural populations.

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GENOME ANALYSIS OF *TRYPANOSOMA CRUZI* FIELD ISOLATES OFFERS THE OPPORTUNITY TO STUDY THE EFFECT OF INFECTION CONTEXT ON PARASITE GENETIC DIVERSITY

Jill Hakim[1], Sneider Gutiérrez[1], Louisa Messenger[2], Monica Mugnier[1]

[1]Johns Hopkins University, Baltimore, MD, United States, [2]University of Nevada, Las Vegas, NV, United States

Trypanosoma cruzi is the causative agent of Chagas disease, a neglected parasitic disease that kills 10,000 people each year. Despite the disease's high public heath burden, there has been very little investigation into the parasite's genome, especially in parasite strains infecting human patients. Here, we describe short read whole genome sequencing and assembly of 15 clinically isolated T. cruzi samples from different relevant infection contexts: mothers at time of delivery, patients with Chagasic cardiomyopathy, and patients co-infected with HIV. We have produced gene level assemblies for each sample and resolve multiple putative single copy genes. We observe variable allele frequency at these single copy loci and demonstrate that, even after successive passage in culture, the parasite isolates maintain clonal complexity, and can distinguish heterozygous haplotypes of divergent clones within a single infection. This represents the first comparison of whole genomes from such a wide array of clinical contexts. These results demonstrate the feasibility of large scale *T. cruzi* whole genome studies using even low sample inputs and allows additional investigation of complex parasite infection to uncover genetic features driving clinical manifestation of disease.

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ACCEPTABILITY AND IMPACT OF THE MAGIC GLASSES LOWER MEKONG, A CARTOON-BASED EDUCATION PACKAGE TARGETING SOIL-TRANSMITTED HELMINTHS AND OPISTHORCHIASIS VIVERRINI IN THE LOWER MEKONG BASIN

Suji Yoo O'Connor

National Centre of Epidemiology and Population Health, The Australian National University, Acton, Australia

Helminth infections caused by soil-transmitted helminths and the liver fluke, *Opisthorchis viverrini*, are a major public health concern in the Lower Mekong Basin, impacting health, educational, and socioeconomic outcomes. Infections, often beginning in childhood, are associated with anaemia, malnutrition, cognitive deficit, and in chronic cases of *Opisthorchis viverrini*, cholangiocarcinoma. The primary control strategy for helminthiases is mass drug administration, however this does not prevent reinfection. Therefore, additional strategies aimed at improving sanitation and hygiene and safe eating practices, are needed. Children have been identified as an

important target group for health intervention, with several studies reporting high incidence of helminthiases in pre- and school-aged children. The "Magic Glasses" is a novel cartoon-based helminth education intervention for schoolchildren, that has demonstrated success with improving schoolchildren's knowledge, attitudes and practices surrounding soil-transmitted helminths, in China, the Philippines and Vietnam. A cluster-randomised trial will be conducted to evaluate the acceptability and impact of a new "Magic Glasses" intervention, targeting schoolchildren in the Lower Mekong Basin, including Cambodia, Thailand and Lao PDR. This study will be the first "Magic Glasses" intervention to target multiple countries, and to address *Opisthorchis viverrini* (in addition to soil-transmitted helminths).I will present our findings from the Lower Mekong study, and their implications for a scaling up protocol of the "Magic Glasses" in the Lower Mekong Basin.

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USING PHOTOVOICE AS A COMMUNITY BASED PARTICIPATORY RESEARCH TOOL FOR CHANGING SANITATION AND HYGIENE BEHAVIOURS IN TAABO, COTE D'IVOIRE

Véronique Koffi[1], Roland Bini[2], Clémence ESSE[2], Gilbert Fokou[1], Piet Vaneeuwijk[3]

[1]Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte D'Ivoire, [2]Université Félix Houphouët Boigny, Abidjan, Côte D'Ivoire, [3]Institute of Social Anthropology, Abidjan, Côte D'Ivoire

In Côte d'Ivoire, observable efforts have been made by the government and its partners against NTDs, but this does not contribute in the long term results in efforts to control the disease. Those efforts being jeopardised by the absence of participatory community-based programmes. In contribution to correct that gap, a research program on Community Health Education (CHE) has been designed and implemented alongside chemotherapy and Community Led Total Sanitation (CLTS). TThe objective of this paper is: to show how photovoice, a community based participatory research tool, can be used to change behaviours of communities regarding hygiene and sanitation. This study was based on qualitative approach. Disposable cameras were entrusted to 4 peoples in each of the four selected villages (respecting the criteria of age and sex) to provide pictures on hygiene and sanitation. Pictures generated were discussed during FGDs. The activities were completed with one-on-one interviews with 18 key informants. Photos show les informations, feelings, and realitises of the communities. photovoice were used to explore local perceptions and practices around hygiene, sanitation related to health. The findings illustrate that photovoice was an effective participatory art-based tools for understanding behaviours, creating awareness, arouse action among communities, and engaging with local leaders at the hygiene and sanitation-health nexus.

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IMPACT OF COMMUNITY PARTICIPATORY APPROACHES IN ENHANCING ACCESS TO MASS DRUG ADMINISTRATION FOR TRACHOMA IN A PASTORAL CONFLICT AREA OF KENYA

Paul M. Gichuki[1], Bridget W. Kimani[1], Tabitha Kanyui[1], Collins O. Okoyo[1], Titus Watitu[2], Wycliff P. Omondi[2], Doris W. Njomo[1]

[1]Kenya Medical Research Institute, Nairobi, Kenya, [2]Division of Vector Borne and Neglected Tropical Diseases, Ministry of Health, Nairobi, Kenya

Trachoma, a neglected tropical disease (NTD) is the leading infectious cause of blindness in sub-Saharan Africa. The disease is caused by the bacterium *Chlamydia trachomatis*. In Kenya, trachoma is endemic in 12 out of the 47 counties. In Baringo county, eight rounds of mass drug administration (MDA) have been implemented. Treatment coverage has remaining consistently low in Loyamorok ward of Baringo County, ranging from 62% in 2012, 56.6% in 2020 and 67.6% in 2021.Successful implementation of MDA programmes for NTDs requires community engagement strategies to reach out the local communities. This study sought to identify barriers of community participation and access to MDA in Loyamorok ward, develop and test strategies to be recommended for improved uptake during subsequent MDA. The study adopted a pre-intervention, intervention and post intervention phase design without control groups. Household surveys were conducted during pre-intervention and post intervention phases. Community barriers to MDA access and participation were identified, strategies for improving MDA uptake were developed and tested using participatory approaches prior to the 2023 MDA. Power and gender dynamics, insecurity, terrain and accessibility, ineffective teams and unsupervised swallowing of drugs during MDA campaigns were the barriers identified during the pre-intervention phase. Effective stakeholder's engagement, enhanced social mobilization, community awareness creation for trachoma, effective planning and execution, implementation monitoring of MDA campaigns were the strategies developed and tested during intervention phase. Knowledge about the causes of trachoma increased from 46.9% during the pre-intervention phase to 65.5% during the post intervention phase. The overall MDA coverage in the area increased from 67.6% in the previous MDA to 87% during the 2023 MDA thus meeting the WHO threshold of 80%. The strategies identified, verified and tested by the stakeholders in Loyamorok ward prior to the 2023 MDA had a positive significant impact on MDA treatment coverage.

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SUPPORTING LYMPHATIC FILARIASIS MORBIDITY MANAGEMENT AND DISABILITY PREVENTION (MMDP) ACTIVITIES IN WEST AFRICA: CASE STUDY FROM NIGERIA AND SIERRA LEONE

Moses Oluwaseun Aderogba, Louise K. Makau-Barasa

END Fund, New York, NY, United States

According to the World Health Organization (WHO), neglected tropical diseases (NTDs) affect more than 1 billion people globally. Among these an estimated 882 million people in 44 countries are at risk of Lymphatic Filariasis (LF) and require preventive chemotherapy. Lymphatic filariasis (LF) is a parasitic disease caused by nematodes (roundworms) that are transmitted through the bites of infected mosquitos. Left untreated, adult worms disrupt the lymphatic system and result in fluid retention leading to lymphedema, elephantiasis, and hydrocele. These often painful and disfiguring conditions lead to impairments, reduced economic productivity and discrimination. Morbidity management and disability prevention (MMDP) is an important aspect of the Global Program to Eliminate Lymphatic Filariasis (GPELF). In Africa the burden of LF morbidity remains high due to several factors, among these are lack of timely treatment, stigma, and a higher prevalence of the disease manifesting among economically impoverished populations. Despite the availability of WHO minimum package of care for LF morbidity to countries, LF morbidity management interventions continue to receive low attention from national NTD programs. In this case study, we present secondary data analysis of implementing partners supporting MMDP programs between 2020 and 2023 in Nigeria and Sierra Leone. The analysis focuses on the programmatic and financial reports of LF MMDP activities from five supported implementing partners. We found that the burden of morbidity is inadequately understood, the LF MMDP program is often delayed until endemic implementing units complete five effective rounds of Mass Drug Administration (MDA), there is a shortage of human resources, and services are concentrated in urban areas. Furthermore, the national LF program tends to prioritize assessments over morbidity management, and the cost of providing care to individuals affected remains high, averaging $150 per patient, as of 2023.
We note a need for national NTD programs to address challenges highlighted above to integrate the program into the public health system.

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ASSESSING THE CAPACITY OF HEALTH FACILITIES TO DIAGNOSE, TREAT, AND MANAGE VISCERAL LEISHMANIASIS: EVIDENCE FROM TIATY, BARINGO COUNTY, KENYA

Leah A. Oruko[1], Saraina C. Ulysse[1], Mwatela Kitondo[2], Hellen Nyakundi[2], Richard Wamai[3], Elizabeth Chebet[4], Jane Sarich[5]

[1]Northeastern University, Boston, MA, United States, [2]African Centre for Community Investment in Health, Nginyang, Kenya, [3]Department of Cultures, Societies, and Global Studies, College of Social Sciences and Humanities, Northeastern University, Boston, MA, United States, [4]Chemolingot Sub-County Hospital, Chemolingot, Kenya, [5]Department of Health, Baringo, Kenya

Visceral Leishmaniasis (VL) is a significant threat in Kenya, with 1,573 cases reported in 2022. However, funding for VL within the Ministry of Health is limited. The Kenyan Strategic Plan for VL (2021-2025) aims to enhance healthcare workers' capacity and establish more testing and treatment centers, yet there is no systematic tracking of health facilities offering VL services. This research evaluates health facilities' capacity in managing VL and explores patient experiences in accessing VL health services in Tiaty, amidst challenges of poverty and limited healthcare access. The study adopts mixed methods. Health facility surveys were dispersed across health facilities in Tiaty sub-county, covering 8 level 2-4 facilities from January-April 2024. Household questionnaires and focus group discussions were conducted in 5 village clusters with the highest VL case reports in Tiaty. Furthermore, surveys were administered at the VL treatment center to patients completing VL treatment until May 2024 to assess their experiences. Observations highlight that level 2&3 health facilities lack resources for diagnosing and treating VL, resulting in patient referrals to level 4 hospitals. Approximately 62.5% of facilities fall under the level 2 category, with 75% are managed by the government. 75% of health personnel has received training for VL, yet diagnostic services (rK39 test) are only available in 50% of facilities, and treatment services are provided in just 12.5% facilities. These challenges are exacerbated by supply chain issues, leading to shortages of diagnostic kits and treatment materials in the facilities that offer the services. Villages with high VL cases are located, on average, 13.63 km away from local health centers, negatively impacting health-seeking behavior. 124 household surveys conducted in March 2024 highlighted transportation costs and distance as significant barriers to healthcare access. Despite these challenges, respondents view health services as somewhat effective, highlighting the need for increased staffing and improved facilities closer to communities to improve VL diagnosis, treatment, and management.

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ASSESSING COMMUNITY DRUG DISTRIBUTORS PERFORMANCE IN GHANA; A GENDER BASED APPROACH

Charles Brown-Davies[1], Diana Stukel[2], Irene Dzathor[1], Emmanuel Nyarko[3], Ernest Mensah[3], Maureen Headland[4]

[1]FHI 360, Accra, Ghana, [2]FHI 360, Washington, Ghana, [3]Ghana Health Service, Accra, Ghana, [4]FHI 360, Washington, DC, United States

According to a gender equity and social inclusion (GESI) assessment conducted in 2019 in Ghana men and women indicated that female community drug distributors (CDDs) express themselves very well, are reliable, patient, take more time to explain NTDs and their effects, why take MDA medicines, MDA drug potential side effects and what to do if they occurred. Female CDDs meet their targets and have impressive record-keeping abilities. These findings were disputed and the recommendation to conduct a gender specific assessment of CDDs performance. The main objective of this study was to assess performance differences in male and female CDDs in completion of registers during MDA for Lymphatic Filariasis and Onchocerciasis. Bole, Kwahu East and Sunyani West Districts were randomly selected to represent three Lymphatic Filariasis and Onchocerciasis endemic districts in Ghana whose CDDs were assessed during the study. Based on the total number of CDDs used in the immediate past MDA for the three selected regions a total sample size of 317 CDDs was estimated and adopted for the assessment. This sample size was proportionally allocated to the three selected districts based on their total CDDs in the previous MDA. In each sub district in depth interviews were conducted for 10% of all selected CDDs with a structured questionnaire on Kobo collect software. All Data from the assessment and in-depth interviews was captured and cleaned with MS excel. Basic descriptive statistics were run in MS excel and further analysis done using SPSS version 21. There were differences in the mean percentage scores for the various areas assessed in the registers and the overall assessment for Female and Male CDDs. These differences were not statistically significant. Mean percentage scores for all CDDs across districts showed statistically significant differences. Mean percentage scores for male CDDs across districts showed statistically significant differences. Mean percentage scores for female CDDs across districts showed statistically significant differences. More advocacy is needed in engaging both gender equally in conducting and supporting their communities with MDA.

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MIXED INFECTIONS OF SOIL TRANSMITTED HELMINTHS AND *SCHISTOSOMA MANSONI* AMONG SCHOOL STUDENTS IN KAKAMEGA COUNTY, KENYA

Christine L. Wanjala, Elizabeth Omukunda

Masinde Muliro University of Science and Technology, Kakamega, Kenya

Soil-transmitted helminth (STH) and schistosome infections are a major public health concern affecting mainly School-aged children in poor resource areas. Mass drug administration (MDA) has proven to be an effective approach to reduce worm burden. However, there are cases of recurrent infections in areas where Mass drug administration is not supported by water, sanitation and hygiene (WASH) activities. This Cross-sectional study aimed at assessing the prevalence of soil transmitted helminths and *Schistosoma mansoni* among school aged children in Kakamega County, Kenya. Stool Samples were collected from 278 school aged children from five primary schools within, Lurambi sub-County. Data on risk factors associated with Soil transmitted helminthes and *S. mansoni* infections was obtained using a structured questionnaires. Stool samples were examined for eggs of STHs and S. mansoni using quantitative Kato-Katz technique. The data obtained was analysed using Pearson Chi-square test and multivariate logistic regression analysis. The overall prevalence of intestinal parasite infection was 14.4 % (n=278). Ascaris lumbricoides had the highest prevalence at 11.5%, followed by S. mansoni at 2.1%, whereas Hookworm and *Trichuris trichiura* had the least prevalence of 0.4% each. Highest prevalence of STH was recorded in rural primary school at 8.3% and a mean intensity of 3396 epg. Poor hygiene such as not washing hands/fruits and vegetables before eating (OR: 3.529; CI: 1.0539-11.8175; P-value ≤0.05: OR: 2.3129; CI: 1.831-4.1691; p-value≤ 0.005) were the major risk factors to STH infections. There is still high prevalence of mixed infections with intestinal worms. There is need to intensify utilization of WASH activities to complement the School deworming programmes for successful control of soil transmitted helminthes.

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RISK FACTORS AND ULTRASOUND ASPECTS ASSOCIATED WITH UROGENITAL SCHISTOSOMIASIS AMONG PRIMARY SCHOOL CHILDREN IN MALI WEST AFRICA

Bakary Sidibé[1], Privat Agniwo[1], Safiatou N. Doumbo[1], Assitan Diakité[1], Hassim Guindo[1], Moudachirou Ibikounlé[2], Abdoulaye Dabo[1], Jerome Boissier[3], Jerome Boissier[3], Boris Savassi[3]

[1]Malaria Research and Training Center, Bamako, Mali, [2]University of Abomey Calavi, Cotonou, Benin, [3]IHPE, Perpignan, France

Urogenital schistosomiasis is endemic in Mali and is a major cause of serious morbidity in large parts of the world. This disease is responsible for many socio-economic and public health issues. This study aimed to investigate the impact of the disease on morbidity and to describe demographic and socioeconomic factors about the status of children with

urogenital schistosomiasis in Mali. We conducted a cross-sectional study in November 2021 of 971 children aged 6 to 14 years selected at random from six schools in three districts in the Kayes Region of Mali. Demographic and socioeconomic data were collected on survey forms. Clinical data were collected following a medical consultation. Hematuria was systematically searched for through the use of strips. The search for *Schistosoma haematobium (Sh)* eggs in urine was done via the filtration method. The urinary tract was examined by ultrasound. Associations between each of these variables and disease infection were tested using multivariate logistic regression. The overall prevalence of urinary schistosomiasis detected was 50.2%. The average intensity of infection was 36 eggs/10 ml of urine. The associated risk factors for urogenital schistosomiasis showed that children who bathed used the river/pond as a domestic water source, and who habitually urinated in the river/pond were more affected (P<0.05). Children with farming parents were most affected (P=0.032). The collection of clinical signs revealed that boys had more pollakiuria (58.6%) and dysuria (46.4%) than girls. Ultrasound data showed that focal lesion rates were recorded in all villages with the lowest rate in Diakalel (56.1%). Ultrasound and parasitological findings showed that irregularity and thickening were strongly associated with urinary schistosomiasis (P<0.0001). *Sh* infection was still endemic in the study site despite more than a decade of mass treatment with praziquantel. However, the high percentage of symptoms associated with high intensity reinforces the idea that further studies in terms of schistosomiasis-related morbidity are still needed.

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TREATMENT COVERAGE ACHIEVED UNDER TWO ENHANCED MASS DRUG ADMINISTRATION REGIMENS FOR TRACHOMA IN THE REPUBLIC OF SOUTH SUDAN: ENHANCING THE A IN SAFE (ETAS) TRIAL RESULTS

Tania A. Gonzalez[1], Angelia M. Sanders[1], Yak Y. Bol[2], Stephen Ohidor[3], Andrew R. Deathe[1], Andrew W. Nute[1], Patrick Odongi[3], Lochebe Boniface[3], Stella Abuba[3], James Niquette[3], E. Kelly Callahan[1], Scott D. Nash[1]

[1]The Carter Center, Atlanta, GA, United States, [2]Ministry of Health, Juba, South Sudan, [3]The Carter Center, Juba, South Sudan

The 2022 Enhancing the 'A' in SAFE (ETAS) trial (NCT05634759) evaluated the cost, feasibility, and acceptability of enhanced mass drug administration (MDA) treatments for trachoma in the Republic of South Sudan. Thirty communities in trachoma endemic Kapoeta North County were randomized 1:1 to 2 treatment arms, and an electronic census was conducted in all enrolled communities. The first arm (triple dose) entailed a community-wide MDA, followed by 2 rounds of treatment aimed at children ages 6 months to 9 years, 2 weeks and 4 weeks later. The second arm (biannual) consisted of 2 community-wide MDA campaigns separated by 6 months. The aim of this report is to detail the MDA coverage achieved in the study arms. The triple dose arm included 17,626 participants, including 8,644 (49.0%) children ages 6 months to 9 years. The biannual treatment arm included 16,974 participants, including 7,852 (46.3%) children. In the triple dose arm, 7,390 (85.5%) children were treated during community-wide MDA, and 6,101 (70.6%) and 6,615 (76.5%) received treatment in the second and third child-only rounds. Coverage among children at the community-level in this arm varied from 50.0-95.5% across all rounds. In the biannual arm, 5,583 (74.5%) and 6,354 (80.9%) children were treated during the 2 MDA rounds with a community-level coverage range of 70.1-95.2% across all rounds. Cumulatively in the triple dose arm, 7,959 (92.1%) children received at least 1 dose of MDA (from any round), 6,632 (76.7%) received at least 2 doses, and 5,515 (63.8%) received all 3 doses. In the biannual arm, 7,465 (95.1%) children received at least 1 dose of MDA, and 4,742 (60.4%) received both doses. Families moving to farms and families with cattle most often missed treatment. This trial demonstrated that both treatment regimens achieved similar per-protocol coverage, triple dose (63.8%) and biannual (60.4%), and in both arms over 90% of children received at least 1 dose. Work is needed to improve coverage across each round of treatment, particularly among mobile families, and to determine whether the cost and effort required by these enhanced regimens result in trachoma reductions.

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EFFECTIVENESS OF COMMUNITY HEALTH EDUCATION ON VISCERAL LEISHMANIASIS IN IMPROVING KNOWLEDGE, PRACTICE AND HEALTH SEEKING BEHAVIOR IN TIATY, KENYA

Saraina C. Ulysse[1], Richard G. Wamai[2], Mwatela Kintondo[3], Hellen Nyakundi[3], Leah Oruko[1], Elizabeth Chebet[4], Elijah Plilan[5], Miriam Lotodo[5]

[1]Department of Health Sciences, Bouvé College of Health Sciences, Northeastern University, Boston, MA, United States, [2]Department of Cultures, Societies, and Global Studies, College of Social Sciences and Humanities, Northeastern University, Boston, MA, USA, Boston, MA, United States, [3]African Centre for Community Investment in Health, Baringo County, Kenya, [4]Chemolingot Sub-County Hospital, Baringo County, Kenya, [5]Department of Health, Baringo County, Kenya, Baringo County, Kenya

This project seeks to examine the effectiveness of community health education on visceral leishmaniasis (VL or kala-azar) in improving knowledge, practice and health seeking behavior in Tiaty East and West sub-counties, Baringo county Kenya. A World Health Organization meeting in January 2023 in Nairobi reached a consensus on elimination of VL as a public health problem among East African countries which is now the global disease foci. Kenya's Ministry of Health VL strategic plan stresses health education interventions in community settings. Education is the first step to preventing the occurrence of a disease: knowing what the disease is, how to identify it, where to seek treatment, or how it is transmitted. It is therefore important to assess the efficacy of health education interventions in promoting behavioral changes. However, there is limited research in Kenya where a scoping review of studies in the country found limited research on prevention (less than 4%). We therefore conducted a study in nine villages within Tiaty, where a local nonprofit, African Centre for Community Investment in Health has conducted health education on kala-azar at least twice in the last 10 years. Nine enumerators were used to collect information through the household questionnaires within these villages; each enumerator visited two villages except for one who only visited one. Participants were chosen on the basis of whether they were aware of Kala-azar. Preliminary results of the 184 participants show that 183 are aware of Kala-azar and 171 have implemented some prevention measures for kala-azar after receiving health education. Based on the preliminary results, current health education on Kala-azar has been effective in increasing knowledge of the signs, symptoms and treatments for Kala-azar and promoting better health behaviors.

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SOCIO-ECONOMIC PROFILE OF NEVER TREATED INDIVIDUALS DURING MASS DRUG ADMINISTRATION TARGETING ONCHOCERCIASIS IN HARD-TO-REACH AREAS OF MALI: A CROSS-SECTIONAL STUDY

Yaya Ibrahim Coulibaly[1], Abdoul Fatao Diabate[2], Moussa Sangare[3], Sekou Oumarou Thera[2], Diadje Tanapo[2], Mahamoud Mahamadou Koureichi[2], Siaka Yamoussa Coulibaly[2], Salif Seriba Doumbia[2], Housseini Dolo[2], Yacouba Sangare[4], Dukharmel Nazaire[5], Thomas B Nutman[6], Alison Krentel[7]

[1]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies; Dermatology Hospital of Bamako, Bamako, Mali, [2]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies, Bamako, Mali, [3]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies; School of Epidemiology and Public Health, University of Ottawa, Bamako, Mali, [4]National Onchocerciasis control program, Bamako, Mali, [5]Bruyere Research Institute, Ottawa, ON, Canada, [6]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States, [7]Bruyere Research Institute; Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada

Onchocerciasis operational transmission zone (KA05) failed the last pre-stop survey assessment. After decades of mass drug administration (MDA) implementation in KA05, the never treated population (NT) may

contribute to ongoing transmission. This study sought to understand the demographic and socio-economic profile of individuals never treated during MDA for onchocerciasis. A cross-sectional survey was conducted in the KA05 zone, combining three health districts (HDs): Sagabari, Kita, and Kenieba. The study involved participants aged 18 years and above. validated questionnaire including history of MDA participation, individual characteristics, housing conditions, income and material goods was used to collect data. Based on these characteristics, we adopted a multiple correspondence analysis and a hierarchical ascending classification approach to classify NT. We used these profiles to conduct a multilevel logistic regression approach (individual, household, and health districts) to estimate factors associated with never-treatment. We obtained 3 profiles according to socio-economic (SES) characteristics. Profile 1 (reference group for regression) has the highest SES status in terms of facilities and access to toilets while Profile 3, has the lowest standard of living. Younger age (less than 33 years) and Profile 2 were two characteristics significantly associated with increased likelihood of being NT, with respectively, adjusted ORs (aOR (95% CI)) of 2.77 (2.03 to 3.81) and 4.48 (2.23 to 9.30). The difference between profile 3 and profile 1 (reference) regarding the risk of never treatment was not statistically significant (aOR = 1.18 (95% CI 0.62 to 2.28)). Never treatment during MDA targeting onchocerciasis in hard-to-reach areas of Mali is associated with younger age and profile 2 (midlevel SES status). Further research is needed to understand the underlying factors driving these associations and to develop tailored interventions to improve access to treatment, especially in areas with lower living standards.

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SOCIO-ECONOMIC IMPACT OF 24-MONTH LYMPHEDEMA MANAGEMENT IN AFFECTED PERSONS IN MALI: CROSS-SECTIONAL STUDY

Housseini Dolo[1], Diadje Tanapo[1], Sekou Oumarou Thera[1], Moussa Sangare[1], Abdoul Fatao Diabate[1], Lamine Diarra[1], Michel Emmanuel Coulibaly[1], Lamine Soumaoro[1], Siaka Yamoussa Coulibaly[1], Salif Seriba Doumbia[1], Abdallah Amadou Diallo[1], Ousmane Faye[2], Hamadoun Sangho[3], Seydou Doumbia[1], Thomas B Nutman[4], Yaya Ibrahim Coulibaly[1]

[1]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies, Bamako, Mali, [2]Dermatology Hospital of Bamako, Bamako, Mali, [3]Teaching department of public health and specialties, Bamako, Mali, [4]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States

Lymphedema is a disfiguring complication of lymphatic filariasis that prevents affected individuals from carrying out their activities, contributing to low productivity and social exclusion. During a trial implemented for 24 months (LEDoxy), local hygiene measures improved the quality of life of lymphedema patients. The aim of this study was to assess the socio-economic impact of regular local care based on the hygiene package used during the clinical trial among participants up to 16 months after the trial completion. We conducted a mixed method study with a before-and-after approach in the health districts of Kolondieba and Kolokani from August to December 2021. Quantitative data were collected using a questionnaire through Kobotoolbox platforms. For qualitative data, we used a pre-established interview guide to conduct in-depth interviews and focus group discussions. Quantitative data were analyzed using SPSS V25.0. Fisher's exact test and Student's t-test were used to compare proportions and means, respectively. We performed a thematic analysis approach to analyze qualitative data using Quirkos V2. We investigated 196 lymphedema patients with a median age of 56 years, and a sex ration of 0.15. We observed a reduction in the monthly frequency of acute filarial attacks from 90.8% (178/196) before the trial to 43.9%, (86/196) after the trial ($p<10^{-3}$). Additionally, the average cost of managing acute filarial attacks significantly decreased from US$20 before the trial to US$6, 16 months after the trial ($p<10^{-3}$) per acute attack. Patients reported that the hygiene program reduced social isolation and stigma and improved their ability to work. A patient stated "*We had difficulty walking, but thanks to the LEDoxy study, I can now walk long distances and participate in community activities*". Local hygiene care of affected limb appears to be an effective intervention for reducing the monthly frequency of acute filarial attacks among lymphedema patients, leading to cost savings in managing acute attacks. Further explorations are needed to assess the sustainability and long-term impact of this hygiene-based care.

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SUSTAINABILITY OF LYMPHEDEMA HYGIENE-BASED SELF-CARE WITHIN LEDOXY PATIENTS MORE THAN TWO YEARS AFTER THE CLINICAL TRIAL IN RURAL AREAS, MALI: A CROSS-SECTIONAL STUDY

Abdoul Fatao Diabate[1], Yaya Ibrahim Coulibaly[2], Moussa Sangare[3], Diadje Tanapo[1], Aashka Sood[4], Sekou Oumarou Thera[1], Housseini Dolo[1], Fatoumata Traore[1], Binta Sall[1], Michel Emmanuel Coulibaly[1], Lamine Soumaoro[1], Siaka Yamoussa Coulibaly[1], Salif Seriba Doumbia[1], Abdallah Amadou Diallo[1], Mariana Stephens[5], Fodie Maguiraga[5], Anne Heggen[6], Jamie Tallant[6], Jayla Norman[7], Charles Mackenzie[8], Joseph P. Shott[9], Ute Klarmann-Schulz[10], Achim Hoerauf[11], John Horton[12], Sarah Sullivan[5], Eric A. Ottesen[13], Alison Krentel[14], Thomas B. Nutman[15]

[1]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies, Bamako, Mali, [2]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies of Bamako, Mali; Dermatology Hospital, Bamako, Mali, [3]International Center for Excellence in Research, | University of Sciences, Techniques and Technologies of Bamako, Mali; University of Ottawa, Bamako, Mali, [4]Bruyere Research Institute, Ottawa, ON, Canada, [5]Neglected Tropical Diseases Support Center, Task Force for Global Health, Atlanta, GA, United States, [6]The End Fund, New York, NY, United States, [7]Neglected Tropical Diseases Support Center, Task Force for Global Health, Decatur, GA, United States, [8]Neglected Tropical Diseases Support Center, Task Force for Global Health,Decatur, GA, United States; The End Fund, New York, NY, United States, Decatur, NY, United States, [9]Division of Neglected Tropical Diseases Division, Global Health Bureau, U.S Agency for International Development, Washington, DC, United States, [10]Institute for Medical Microbiology, Immunology and Parasitology (IMMIP), German Centre for Infection Research (DZIF), Bonn-Cologne Site, University Hospital Bonn, Venusberg-Campus 1, 53105 Bonn, Germany,, Bonn-Cologne, Germany, [11]Institute for Medical Microbiology, Immunology and Parasitology (IMMIP), German Centre for Infection Research (DZIF), Bonn-Cologne Site, University Hospital Bonn, Venusberg-Campus 1, 53105, Bonn-Cologne, Germany, [12]Tropical Projects, Hitchin, United Kingdom, Hitchin, United Kingdom, [13]Neglected Tropical Diseases Support Center, Task Force for Global Health, Atlanta, NY, United States, [14]Bruyere Research Institute, Ottawa, ON, Canada, University of Ottawa, Ottawa, ON, Canada, [15]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States

The LEDoxy clinical trial comparing doxycycline plus local hygiene to placebo plus local hygiene on filarial lymphedema management did not confirm the expected ability of doxycycline to reverse or halt the progression the condition. All trial participants received repeated training in hygiene practices of WHO's Essential Package of Care for lymphedema and were provided with hygiene kits over the 24-month trial period. The current study investigated the sustainability and barriers to self-care more than 2 years after the trial completion. A mixed-method study was conducted in the Kolondieba and Kolokani health districts from December 2023 to March 2024. All LEDoxy participants with stages 1-3 lymphedema were invited to participate in this study. Data were collected through questionnaire administration using REDCap platform and analyzed using SPSS 26.0 and NVIVO 14. Additionally, individual in-depth interviews (IDI) were conducted to understand patients' behaviors and experiences regarding lymphedema self-management. Overall, 165 lymphedema patients from LEDoxy were included in the survey. Regarding the sustainability of limb hygiene, 93 (41.9%) patients washed their affected limbs on the day of the survey, 67 (30.2%) the day before, 18 (8.1%) more than two days before, while 44 (19.8%) reported a more distant occurrence. The main difficulties mentioned by participants in maintaining regular hygiene care were lack of financial resources (40.6%), lack of support (4.2%), lack of time (5.5%) and pain during washing (5.5%). Most patients believed that participating in agricultural activities will make affected limbs dirty. Avoiding farming resulted in people believing the LE patient was reluctant to work. Findings show

the sustained impact of high quality training and supervision on routine LE management. Although patients reported barriers to self-management, they were largely able to sustain regular care the two years since the research study. These findings can inform the design of sustainable and well-adapted national self-care programs as part of the morbidity management and disability prevention program in LF elimination.

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MONITORING THE IMPACT OF COMMUNITY-BASED DEWORMING ON SCHISTOSOMIASIS AND SOIL-TRANSMITTED HELMINTHIASIS AMONG SCHOOL-AGE CHILDREN IN WESTERN KENYA: MIDTERM RESULLTS

Florence Wakesho[1], Juma Chitiavi[2], Stella Kepha[3], Wyckliff Omondi[1], Sultani Matendechero[1], Maurice Odiere[4], Irene Chami[5], Ivy Sempele Semplele[5], Alison Ower[5], Joseph Oloo[1], Martin Muchangi[2], Vincent Ouma[2], Jimmy Kihara[4]

[1]Ministry of Health, Nairobi, Kenya, [2]AMREF Health Africa, Nairobi, Kenya, [3]Kenya Medical Research Institute, NAIROBI, Kenya, [4]Kenya Medical Research Institute, Nairobi, Kenya, [5]The End Fund, US, NY, United States

The progress of Kenya's National Breaking Transmission Strategy for interruption of transmission (IoT) for schistosomiasis (SCH) and soil-transmitted helminthiasis (STH) in 4 Kakamega, Bungoma, Vihiga and Trans Nzoia counties of western Kenya (2021-2025) is evaluated through a monitoring and evaluation framework that involves the periodic collection of parasitological data. The midterm evaluation used data from surveys conducted at baseline (689 schools; 41045 School Aged Children (SAC)), 1st sentinel survey (34 schools; 2039 SAC) and at midterm (56 schools; 2804 SAC) after 2 rounds of community-wide MDA, between 2021 and 2023 in wards under MDA . Stool was randomly collected from school-age children in selected schools and examined for SCH and STH infections using Kato-Katz. Prevalence and mean intensity of each helminth species and their 95% confidence intervals (CIs) were calculated. The overall prevalence of *Schistosoma mansoni* was 10.9% (95% CI: 10.3-11.5%), 5.8% (95% CI: 4.9-6.9%) and 4.9% (95% CI: 3.8-6.3%) at baseline, 1st sentinel site survey and at midterm, respectively, with a relative reduction (RR) of 55% ($Z = 11.5$, $P < 0.001$) between baseline and midterm. Overall, 8.1% (95% CI: 7.9-8.4%), 13.5% (95% CI: 12.1-15.1%) and 5.5% (95% CI: 4.7-6.4%) of the children were infected with any STH species at baseline, 1st sentinel site survey and midterm, with a RR of 32.1% ($Z = 4.7$, $P < 0.01$) between baseline and midterm. The mean intensity of *S. mansoni* was 125 epg (114-136) at baseline and 102 epg (77 - 127) at midterm, with a RR of 18.4%. The proportion of Wards with <1% HI *S. mansoni* infections among SAC increased 1.8-fold from baseline to midterm, while Wards with <2% M&HI STH infections increased 1.4-fold. Both the overall prevalence and prevalence of Medium & High Intensity SCH and STH infections reduced at mid-term, but prevalence of infection increased in a few Wards suggesting ongoing transmission. Scaling up of other strategies including behavior change and communication, WASH interventions and snail control to augment MDA coupled with effective treatment coverage will be required to sustain the gains and accelerate the efforts towards IoT.

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ASSESSMENT OF KNOWLEDGE, ATTITUDES, PRACTICES AND FACTORS CONTRIBUTING TOWARDS ONGOING TRACHOMA TRANSMISSION AND MASS DRUG ADMINISTRATION (MDA) COVERAGE IN UGANDA

Joyce Achan[1], Edwin Mayoki[1], Rapheal Opon[2], Stephen Begumisa[1], Stella Agunyo[1], Sharone Backers[1], Alex Rutagwabeyi[1], Charles Kissa[3], Elizabeth Sutherland[4], Danielle Epps[4], Kathryn Crowley[5], Meagan Meekins[4], Jessica Douglas[4], Stephen Otim[6], James Lemukol[6], Denis Olaka[7], Peter Lokwang[7], Alfred Mubangizi[3], Jeremiah Ngondi[8]

[1]RTI International, Kampala, Uganda, [2]Ministry of Health NTD Programme, Kampala, Uganda, [3]Ministry of Health, NTD Programme, Kampala, Uganda, [4]RTI International, Durham, NC, United States, [5]RTI International, Washington, DC, United States, [6]Moroto District Local Government, Moroto, Uganda, [7]Nabilatuk District Local Government, Nabilatuk, Uganda, [8]RTI International, Cambridge, United Kingdom

Moroto and Nabilatuk districts have persistent and recrudescent trachoma, respectively. Past survey failure investigations and Coverage Evaluation Surveys suggest that, while overall MDA coverage is high, there are certain communities and groups that may be more likely to miss MDA. To better understand how these groups and communities may be contributing to ongoing transmission, the study team undertook an assessment to explore the trachoma knowledge attitudes and practice (KAP) among female farmers, male kraal leaders, youth, and village health teams (VHTs) in select communities. Study communities were purposely selected based on historically low coverage or high number of cases of TF, together with other identified social or geographic risk factors. Eight focus group discussions were undertaken and a trachoma KAP questionnaire was administered to 123 individuals living in sample communities and who had missed the most recent MDA. Limited knowledge of trachoma and trachoma prevention was exhibited by female farmers, VHTs, and youth. Many respondents reported rarely undertaking key prevention practices such as washing faces of children at least twice a day; and cleaning children's noses or eyes with a cloth or towel and with water. Instead, respondents reported poor practices such as washing children's faces with saliva and/or with hands or fingers. The findings suggest limited knowledge on the causes and prevention of trachoma, and poor practices towards water, sanitation, and hygiene improvements (WASH), facial cleanliness and seeking trachoma related information to be serious problems, especially among female farmers, youths, and VHTs. It is possible that the low trachoma KAP in these communities may be contributing to ongoing transmission in Moroto and Nabilatuk. Tailored interventions to improve trachoma KAP should be designed for these communities, particularly for women, youth, and VHTs. These include involvement of fellow women, youth and VHT influencers during sensitization and mobilization through local groups that bring them together and enhanced capacity building of VHTs, women and youth leaders.

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TREATMENT COVERAGE FOLLOWING AN ENHANCED MASS DRUG ADMINISTRATION STRATEGY FOR TRACHOMA IN AMHARA REGION, ETHIOPIA: THE CHILD MDA PILOT STUDY

Mohammed F. Shaka[1], Ayalew Shiferaw[1], Eshetu Sata[1], Zebene Ayele[1], Demelash Gessese[1], Adisu A. Dawed[2], Fikre Seife[3], Zerihun Tadesse[1], Anley Haile[1], Kimberly A. Jensen[4], Nicholas A. Presley[4], Tania A. Gonzalez[4], E. Kelly Callahan[4], Scott D. Nash[4]

[1]The Carter Center, Addis Ababa, Ethiopia, [2]Amhara Regional Health Bureau, Bahir Dar, Ethiopia, [3]Ministry of Health, Addis Ababa, Ethiopia, [4]The Carter Center, Atlanta, GA, United States

In Ethiopia's Amhara region, annual mass drug administration (MDA) has been implemented for trachoma since 2007. Despite nearly 15 years of MDA intervention, some districts in the region continue to have persistently high trachoma. Recently, the Ministry of Health of Ethiopia recommended piloting an enhanced treatment strategy encompassing a standard annual MDA, followed by an additional round targeted to children ages 6 months to 9 years (within one month of the initial treatment). In Amhara, two pilot districts, Lasta and Wadilla, in North Wollo zone, received the enhanced MDA strategy. The aim of this study was to determine the self-reported MDA coverage for both rounds of treatment in these districts. MDA coverage surveys were conducted in July 2023, three weeks after the second MDA round, and employed a multistage cluster-randomized sampling design to select participants. Trained data recorders asked respondents if they were offered and swallowed the MDA medications. Sixty clusters comprised of 4,948 individuals from 1,799 households (899 in Lasta, 900 in Wadilla) were surveyed, including 1,651 children ages 1-9 years. The overall self-reported treatment coverage for the community-wide MDA was 82.5% (CI: 73.6 - 88.8%) in Lasta and 77.9% (CI: 67.9 - 85.4%) in Wadilla. During this first round of community-wide MDA, 84.7% (CI: 70.2 - 92.9%) of children from Lasta and 86.9% (CI: 74.9 - 93.6%) of children

from Wadilla received treatment. For the second MDA round targeted only to children, 82.0% (CI: 69.0 - 90.4%) of children from Lasta and 83.1% (CI: 72.8 - 90.1%) of children from Wadilla reported receiving treatment. Of the children surveyed, 82.1% received both rounds of treatment, 12.0% received only one round, and 5.8% did not participate in either MDA. The most common reason individuals reported for not receiving treatment was due to traveling during MDA distribution. This study demonstrated that the additional round of child targeted MDA had an acceptable level of coverage (>80%), which is promising for the feasibility of this strategy and provides important information for the scale-up of enhanced MDA for trachoma throughout Ethiopia.

6676

SAMPLING AND SITE SELECTION STRATEGIES FOR LYMPHATIC FILARIASIS TRANSMISSION ASSESSMENT SURVEYS IN AREAS WITH HIGH SECURITY CHALLENGES: THE BURKINA FASO EXPERIENCE

Mamadou Serme[1], Ouédraogo W. Mathias[1], Zoromé Harouna[1], Christophe Nassa[1], Clarisse Bougouma[1], Ilboudo Adama[1], Ogaobiga Fernand[1], Issa Guiré[2], Yarbanga Mahamady[3], Georges Dimithe[4], Regina Khassanova[4], Dieudonné Naré[4], Micheline Ouedraogo[4], Elisabeth Chop[5], Angel Weng[6], Patricia Houck[6], Yaobi Zhang[7], Benoit Dembele[7], Steven D. Reid[6], Ernest Mensah[8]

[1]The National Neglected Tropical Diseases Program (NTDP), Ministry of Public Health (MOH), Ouagadougou, Burkina Faso, [2]Direction régionale de la Santé et de l'hygiène publique du Centre Est (DRSHP), Tenkodogo, Burkina Faso, [3]Direction régionale de la Santé et de l'hygiène publique de l'Est (DRSHP), Fada N'Gourma, Burkina Faso, [4]Helen Keller International, Ouagadougou, Burkina Faso, [5]Helen Keller International, Washington, DC, United States, [6]Helen Keller International, New York, NY, United States, [7]Helen Keller International, Office for Africa, Dakar, Senegal, [8]FHI 360, Office for Africa, Accra, Ghana

Burkina Faso is one of 35 countries in the World Health Organization (WHO) African region that is endemic for lymphatic filariasis (LF). In June 2000, all health districts (HDs) were classified as endemic, with antigenemia prevalences ranging from 2% to 74%. However, since 2016, Burkina Faso has faced security challenges in some regions, negatively impacting the pursuit of certain LF elimination activities. As a result, several transmission assessment surveys (TAS) have been delayed since 2019 due to insecurity. This is the case for TAS2 surveys in four evaluation units (EUs) in four HDs, and TAS3 surveys in 14 EUs in 14 HDs. In addition, some HDs recently eligible for pre-TAS or TAS are facing security challenges that make it difficult to conduct surveys using the classic methodology recommended by the WHO. This is due to the inaccessibility of localities and major population displacement. The WHO recommends that the National Neglected Tropical Diseases Program document best practices for implementing surveys in areas with high security challenges. In Burkina Faso, participatory approaches were used to assess feasibility, site selection and sampling for pre-TAS and TAS and to develop resilient implementation strategies based on local health workers. Excel forms were used to collect information on security risk and decision algorithm applied to identify eligible sites for the survey. The decision criteria include proportion of target population present, sites where displaced populations are located, the ability to conduct surveys using local actors, and population size. These criteria are reviewed by all the stakeholders at a regional scoping meeting. These sampling strategies were successfully used for pre-TAS and TAS1 surveys in 2023. In 2024, TAS surveys will be conducted in eight EUs across eight HDs using the same approach. However, continuous monitoring of the security situation prior to the start of the surveys is necessary. In addition, special attention should be given to areas that have been excluded due to risk as part of post-stop transmission monitoring.

6677

THE CONTROL AND ELIMINATION OF NEGLECTED TROPICAL DISEASES IN MALI: A SUCCESS STORY

Yacouba Sangaré[1], Modibo Keita[2], Boubacar Guindo[2], Mama Nielé Doumbia[2], Dramane Traoré[2], Fama Kondo[2], Lamine Diarra[2], Fatoumata Koundou Maiga[1], Salif Seriba Doumbia[3], Mahamadou Traoré[1], Massitan Dembelé[1], Cheick Amadou Tidiane Traoré[1], Yacouba Sangaré[1], Lamine Traoré[1], Alex Karl Brown[2], Ouassa Sanogo[2], Benoit Dembele[4], Yaya Ibrahim Coulibaly[3], Steven D. Reid[5], Yaobi Zhang[5], Angela Weaver[5], Achille Kaboré[6], Bolivar Pou[6]

[1]Direction Générale de la Santé et de l'Hygiène Publique, Ministère de la Santé et de Développement Social, Bamako, Mali, [2]Helen Keller International, Bamako, Mali, [3]International Center of Excellence in Research, USTTB, Bamako, Mali, [4]Helen Keller International, Office for Africa, Dakar, Senegal, [5]Helen Keller International, New York, NY, United States, [6]FHI 360, Washington, DC, United States

In Mali, neglected tropical diseases (NTDs) are a major public health problem. Baseline mapping in 2004 showed an average lymphatic filariasis (LF) prevalence of 7.07%. Schistosomiasis (SCH) and soil transmitted helminths (STH) surveys from 2004 - 2005 found an average prevalence of 36.1% and 6.3%, respectively. A 1996-1997 trachoma baseline survey found an active trachoma (TF/TI) average prevalence of 34.9% among children <10 years old and trachomatous trichiasis average prevalence of 2.51% in women >14 years old. The 1974 mapping of river basins in the south and south-east regions showed onchocerciasis (OV) prevalence reaching as high as 84% in one village. From 2005 to 2018, six to 12 mass drug administration (MDA) rounds against LF and STH were conducted, with an average programmatic coverage of 83.5%. For SCH, six to thirteen MDA rounds were carried out, with an average (school-based) coverage of 90%. For trachoma, three to six MDA rounds were carried out, with an average coverage of 85.6%. Over the past 40 years, more than twenty rounds of OV MDA were carried out, with an average coverage of 83.9%. Other strategies implemented include morbidity management, vector control, dissemination of awareness-raising messages, WASH interventions, and capacity-building. Despite over a decade of insecurity, sociopolitical instability, and health crises, Mali is close to achieving its NTD control and elimination objectives. Since 2020, all endemic districts (75/75) have met the criteria to stop LF MDA. In 2021, WHO STH experts confirmed STH is no longer a public health problem. In April 2023, Mali became the 17th country validated by the WHO as having eliminated trachoma as a public health problem. There are two NTDs still being treated by MDA. A SCH data review in 2023 showed that of 1,643 health areas, 16% no longer need MDA, 37% had a prevalence <10% and 18% had a high prevalence >50%. All OV-endemic districts except one (33/34) have done stop MDA surveys (results pending). This progress is the result of strong commitments by health authorities, partnership, and the use of innovative strategies to conduct NTD activities in the challenging operating context.

6678

PRE-STOP OV MDA IN 32 FIRST-LINE VILLAGES IN FOUR OPERATIONAL TRANSMISSION ZONES IN GUINEA

Nouhou Konkouré Diallo[1], Lamine Lamah[2], Abdoul Karim Camara[2], Abdoul A. Diallo[2], Yaobi Zhang[3], Nadia Ben Meriem[3], Benoit Dembele[4], Mamadou Siradiou Baldé[1], Gaston Cherif[1], Angel Weng[3], Steven D. Reid[3], Angela Weaver[3], Achille Kaboré[5]

[1]Ministry of Health, Conakry, Guinea, [2]Helen Keller International, Conakry, Guinea, [3]Helen Keller International, New York, NY, United States, [4]Helen Keller International, Office for Africa, Dakar, Senegal, [5]FHI 360, Washington, DC, United States

Onchocerciasis is a major neglected tropical disease in Guinea. Between 1985 and 2005, onchocerciasis mapping was conducted using the Rapid Epidemiological Mapping of Onchocerciasis (REMO)/skin snip method, supported by the Onchocerciasis Control Program (OCP) in West Africa and later by the African Program for Onchocerciasis Control (APOC). Twenty-four endemic districts were classified as follows: hypo-endemic (nodule prevalence < 20% or microfilariae (mf) prevalence < 40%) in 15

districts; meso-endemic (nodule prevalence 20-39% or mf prevalence ≥ 40% and < 60%) in one district; or hyper-endemic (nodule prevalence ≥ 30% / mf prevalence ≥ 60%) in eight districts. After more than 28 years of annual ivermectin distribution, a pre-stop treatment survey is necessary to determine if these areas can proceed to the stop-MDA survey. A total of 63 first-line villages across four pre-determined operational transmission zones (OTZ) were selected, covering all endemic river basins. The first phase of the survey was conducted in 32 first-line villages. One hundred children aged 5-9 years old per village were selected and dried blood spot (DBS) samples were collected from each child and analyzed using the OV16 rapid diagnostic test (RDT) in the national laboratory. A total of 3,199 children aged 5 to 9 were sampled in 32 villages near *Simulium* breeding sites, (44%) were female. Analysis of the samples revealed that most villages surveyed had zero positive cases and only 8 of the 32 villages surveyed had 2 or more positive cases, with percentages ranging from 2% to 12%. These 8 villages were mostly located in OTZ2 (the forest region) and a few localities near the border with Sierra Leone. Preliminary results indicate that the OTZs may need to be redefined and that some OTZs may qualify for the full stop-MDA survey, pending on the results of the remaining pre-stop villages.

6679

A FOLLOW-UP STUDY IN 2024: SCHISTOSOMIASIS IMPACT ASSESSMENT IN EIGHT DISTRICTS FOLLOWING A DECADE OF MASS DRUG ADMINISTRATION

Ibrahim Kargbo-Labour[1], **Victoria Turay**[2], Sugandh Juneja[2], Amos S. James[2], Alusine S. Kamara[2], Abdulai Conteh[1], Abdulai Koroma[2], Unidiatu Kabia[2], Gandi Kallon[2], Elisabeth Chop[3], Cleo Stern[3], Anna Phillips[4], Angela Weaver[3], Yaobi Zhang[3]

[1]Neglected Tropical Disease Program, Ministry of Health and Sanitation, Freetown, Sierra Leone, [2]Helen Keller International, Freetown, Sierra Leone, [3]Helen Keller International, New York, NY, United States, [4]FHI 360, Washington, DC, United States

The National Neglected Tropical Disease Program in Sierra Leone conducted schistosomiasis (SCH) baseline mapping in all 16 health districts (HDs) between 2008 and 2009. They were categorized as follows: low (≥1 and <10%) prevalence in five HDs; moderate (≥10 and <50%) in five HDs; and high (≥50%) in four HDs. The intestinal species *Schistosoma mansoni* was identified in nine HDs and the urogenital species, *S. haematobium*, was endemic in three (of those nine) HDs. In 2009, annual mass drug administration (MDA) at the district level started by targeting school-aged children (SAC) in six (three high and three moderate) endemic HDs and scaled up in 2010 to include all SAC and at-risk adults in the nine highly or moderately endemic HDs. The five low endemic HDs have received no MDA to date. A subsequent SCH/STH impact assessment was conducted in 2022 in the nine high/moderate HDs to assess the impact of multiple rounds of treatment. In May 2023, a SCH data review evaluated the 2022 SCH impact assessment results, resulting in a revised chiefdom (sub-district) treatment strategy based on updated prevalence estimates. The revised strategy targets either SAC only or community-wide MDA as determined by the new prevalence data. The data review highlighted data gaps in 53 chiefdoms across eight HDs and thus the need to supplement the 2022 survey. A follow-up survey was conducted in 2024 to address these gaps. Results from both surveys indicate a significant reduction in both prevalence and intensity of SCH infection compared to baseline. However, pockets of persistent infection were identified. Survey results from 2022-2024 showed an overall prevalence of 15.4% for *S. mansoni, 5*.4% for *S. haematobium* (haematuria), and 4.5% (urine filtration). Overall, the nine HDs were re-categorized as follows: low prevalence in one HD; moderate in eight HDs; and no high HDs. Over a decade of MDA in Sierra Leone led to a significant reduction in any SCH infection, from an average prevalence of 42.2% at baseline to 19.1% in 2024.

6680

FIX-DOSING IVERMECTIN REGIMENS IN MASS DRUG ADMINISTRATION ACTIVITIES. IS IT TIME TO LEAVE THE DOSING POLE BEHIND?

Adriana Echazu[1], Pedro Emanuel Fleitas[2], Charles Mwandawiro[3], Gabriela Maria Matamoros[4], Wendemagegn Enbiale[5], Áuria de Jesus[6], **Alejandro Javier Krolewiecki**[1]

[1]Instituto de Investigaciones de Enfermedades Tropicales (IIET) - Universidad Nacional de Salta, Oran, Salta, Argentina, [2]Instituto de Salud Global de Barcelona (ISGlobal), Barcelona, Spain, [3]Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [4]Instituto de Investigaciones en Microbiología (IIM), Universidad Nacional Autonoma de Honduras, Tegucigalpa, Honduras, [5]Dermatovenerology Department, College of Medicine and Health Science, Bahir Dar University, Bahir Dar, Ethiopia, [6]Centro de Investigação em Saúde de Manhiça (CISM), Manhiça, Maputo, Mozambique

Ivermectin (IVM) is a critical tool for the control of different Neglected Tropical Diseases. In mass drug administration (MDA) campaigns it is dosed adjusted to body height. Dosing IVM by weight or height has operational disadvantages. In this study we explored alternative dosing regimens for MDA campaigns. To carry out the analysis individual participant anthropometry data of children aged 5 to 15 years was used. 9638 children were included from previous soil-transmitted helminths (STH) clinical trials from endemic areas in Latin-America and Sub-Saharan Africa. The dose in µg/Kg of IVM for each child according to their weight was calculated using four different dosing regimens: 1) Weight-adjusted dose for 200 µg/Kg; 3 mg for children from 15 to 24 kg; 6 mg for 25 to 35 Kg; 9 mg for 36 to 50 Kg; 12 mg for 51 to 65 Kg and 15 mg for 66 to 79 Kg. 2) Height - adjusted dose (WHO dosing pole): 3 mg for 90 to 119 cm; 6 mg for 120 to 139; 9 mg for 140 to 159 cm; and 12 mg above 159 cm. 3) Fixed-dose of 9 mg. 4) Fixed-dose of 18 mg. The proportion of children with correct dose (200 to 600 µg/Kg), above the recommended dose (> 600 µg/Kg) or underdose (< 200 µg/Kg) with each dosing regimen was calculated. Results showed the Fixed-dose IVM 9 mg achieved a higher proportion of correct doses (86%) compared to weight-based (35%) and height-based (66%) regimens, with significantly lower underdosing (4% vs. 55% and 33%, respectively). No children received doses above recommended levels with Fixed-dose of IVM 9 mg or other regimens. Subgroup analysis revealed 87 % correct dosing with Fixed-dose 9 mg for children aged 5 to 13 years old and 93 % with Fixed-dose 18 mg for children aged 14 and 15 years old. The proportion receiving above the recommended dose was 10 % with Fixed-dose 18 mg in children aged 14 and 15 years old. In conclusion implementing a fixed dose IVM regimen based on age would achieve a high proportion of adequate doses, reducing the proportion of underdosing and with little risk of exceeding the recommended dose. Added to the operational advantages of using a single formulation for the entire school population.

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SOIL-TRANSMITTED HELMINTH TRANSMISSION DYNAMICS AND OPTIMAL CONTROL

Roselyn F. Kaondera -Shava, Jeffrey Shaman

Columbia University, New York, NY, United States

Soil-transmitted helminth infections are among the most prevalent neglected tropical diseases, particularly in impoverished regions. These infections affect over 1.5 billion people (about 24% of the global population) and are most common in school-aged children. The diseases impair physical and mental growth in children, thwart educational advancement, and hinder economic development. Soil-transmitted helminth infections are caused by a group of parasitic worms primarily transmitted via soil contaminated with feces from infected individuals. Here, to assess transmission dynamics of helminth infection through the soil in school-aged children, we use a model-inference approach to estimate a key epidemiologic parameter, i.e. the rate at which parasitic worms in the soil infect human population. Further, to explore effective intervention strategies for controlling the spread of these infections, optimal control theory is applied. A dynamic model-inference approach is applied in conjunction with epidemiological data from

the most affected countries in Sub-Saharan Africa and Asia to estimate the rate at which parasitic worms in the soil infect human population. Pontryagian's maximum principle is used to formulate the optimal control problem, where two time-varying control variables are incorporated: the rate of hygiene consciousness through public health education in the susceptible class and the rate of hygiene consciousness in the infectious class. Application of the confirmed system to actual case data is underway and estimates of infection transmissibility to humans and recommendations for optimal control will be reported. The main findings aid in understanding soil-transmitted helminth dynamics and can help guide future public health planning. The disease burden can be significantly reduced or eliminated in affected regions by implementing optimal control measures.

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STRENGTHENING TRACHOMA CONTROL PROGRAMS THROUGH THE INTEGRATION OF LATERAL FLOW ASSAYS FOR SEROLOGICAL MONITORING: A DISTRICT-LEVEL STUDY FROM AMHARA, ETHIOPIA

Ambahun Chernut[1], **Nicholas A. Presley**[2], Getahun Ayenue[1], Paulos F. Yihun[3], Eshetu Sata[1], Fikre Seife[4], Gizachew Yismaw[3], Taye Zeru[3], Tania A. Gonzalez[2], Kimberly A. Jensen[2], Zebene Ayele[1], Fetene Mihretu[1], Zerihun Tadesse[1], E. Kelly Callahan[2], Sarah E. Gwyn[5], Diana L. Martin[5], Scott D. Nash[2]

[1]The Carter Center, Addis Ababa, Ethiopia, [2]The Carter Center, Atlanta, GA, United States, [3]Amhara Public Health Institute, Bahir Dar, Ethiopia, [4]Ministry of Health, Addis Ababa, Ethiopia, [5]Centers for Disease Control and Prevention, Atlanta, GA, United States

Trachoma Control Programs conduct trachoma impact surveys (TIS) to monitor programmatic impact using the field-graded clinical sign trachomatous inflammation–follicular (TF). Recently, programs have begun to collect complementary indicators alongside TF, such as antibody responses to the Pgp3 antigen, to estimate population-level exposure to *Chlamydia trachomatis* (*Ct*). Serological monitoring has been used by the Program in Amhara, Ethiopia, since 2017. Due to the infrastructure needed to perform assays, the Program has relied on an external laboratory in the United States to analyze their samples, which presents logistical challenges and delays. A newly developed lateral flow assay (LFA) is a promising alternative to other serological tests due to its ease of use, high sensitivity (92.6%, CI: 86.4 - 96.2%) and specificity (100%, CI: 94.1 - 100%) compared to the multiplex bead assay, and low laboratory infrastructure needs. In January 2024, the Program in Amhara facilitated a remote LFA training for 3 experienced laboratory personnel at the Trachoma Molecular Laboratory at the Amhara Public Health Institute. The training was held over 3 days and concluded with a competency exam, which all participants passed and were certified. Following certification, participants analyzed dried blood spot samples from a 2023 TIS in Tach Gaynt, a district with considerable trachoma (28.6% TF) despite 14 years of interventions. A total of 2,441/2,539 (96.1%) samples were assayed by the laboratory personnel over 12 working days. They demonstrated high capability to perform LFA, with only 4 (0.2%) invalid samples upon first run, all of which were valid upon retesting. Seropositivity in children ages 1-5 years was 19.9% (CI: 16.2 - 24.2%), which is consistent with Tach Gaynt's high TF prevalence. Individuals ages ≥15 years had high seropositivity (85.7%, CI: 83.8 - 87.4%), indicative of cumulative *Ct* infections from living in endemic areas. The quality of these results and speed at which the samples were analyzed underscore the potential of LFA as a viable option for in-country serological monitoring for Ethiopia and other trachoma endemic countries.

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THE LEISHMANIASES IN ETHIOPIA: A SCOPING REVIEW TO DETERMINE THE SCOPE OF RESEARCH AND REMAINING GAPS

Katherine OBrien[1], Grace Grifferty[1], Hugh Shirley[2], Philip Espinola Coombs[1], Eleni Ayele[3], Mezgebu Silamsaw Asres[3], Ermias Diro[4], Richard Wamai[1]

[1]Northeastern University, Boston, MA, United States, [2]Harvard Medical School, Boston, MA, United States, [3]University of Gondar, Gondar, Ethiopia, [4]University of Washington, Seattle, WA, United States

The leishmaniases are among the group of neglected tropical diseases that cause significant morbidity and mortality. There are mainly two broad categories of the disease: the visceral form, which is deadly, and the cutaneous form, which is disfiguring and stigmatizing. Currently, the East Africa region has the highest visceral leishmaniasis (VL) burden in the world. Ethiopia is one of the East African countries affected by the disease and showed commitment as part of the 2023 Nairobi Declaration for the elimination of VL by 2030. In this endeavor, it is important to identify the scope of existing research, study the available evidence, and identify gaps in research that need priority. This review aims to examine the body of literature on the leishmaniases in Ethiopia and identify remaining research gaps. This scoping review is reported following PRISMA-ScR. The following databases were searched without date restrictions: PubMed, Embase via Embase.com, Web of Science Core Collection, Cochrane CENTRAL, Global Index Medicus, ClinicalTrials.gov, the Pan African Clinical Trials Registry, and PROSPERO. Locally published gray literature will be identified by team members familiar with the Ethiopian setting. Each abstract and full-text will be dually and blindly screened with conflicts resolved by a third reviewer. Included articles must contain an in-depth discussion of the leishmaniases in Ethiopia. Data extracted will consist of study themes, study types, categories, and sub-categories each defined in a comprehensive and previously published codebook developed by this team, with adaptations made to account for the Ethiopia context. There were 8,698 records included in the abstract screen and the full text screen is ongoing. This study will be completed by August 2024 and was registered in OSF on March 2nd, 2024. We plan to disseminate our findings to the appropriate stakeholders in Ethiopia and globally.

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STAKEHOLDER PERSPECTIVES ON THE FEASIBILITY AND ACCEPTABILITY OF A FIXED DOSE COMBINATION OF IVERMECTIN AND ALBENDAZOLE IN GHANA

Ivy Frances Osei[1], **Cornelius Yayele Debpuur**[1], Abraham Rexford Oduro[1], Kwadwo Larbi Opare[2], Allan Brooks[3], Julie Jacobson Jacobson[4], Alejandro J. Krolewiecki[5]

[1]Research and Development Division, Accra, Ghana, [2]Public Health Division, Accra, Ghana, [3]Bridges to Development, Geneva, Switzerland, Geneva, Switzerland, [4]Bridges to Development, Vashon, WA, United States, [5]Mundo Sano, Madrid, Spain, Madrid, Spain

The multi-disciplinary and multi-institutional EDCTP & Swiss government funded project - STOP2030 - seeks to 1) provide an effective treatment against all five species of soil-transmitted helminths, and 2) implement complementary research and activities supporting decisions on potential adoption and scaling up of the fixed-dose combination (FDC) of co-formulated ivermectin (IVM) and albendazole (ALB). A strength of this consortium is the inclusion of a social-science analyses supporting implementation of clinical, regulatory and programmatic developments. Among the complementary planned studies, Kenya and Ghana will explore the acceptability, feasibility and adherence of the FDC of IVM and ALB. As a key component of acceptability evaluation, Ghana Health Service conducted a formative study to explore stakeholders' opinions and perceptions regarding the current management of STH in Ghana, their views on the proposed FDC of IVM and ALB in MDA programs against STH, and the contextual and systemic factors likely to influence the feasibility and acceptability of FDC. The research team conducted 32 key

informant interviews with NTD programme managers at national, regional and district levels, regional and district school health education programme coordinators and schoolteachers, and six focus group discussions with parents of school children in three districts. This analysis highlights challenges (such as availability of adequate logistics for delivery of drugs, community education and sensitization on school deworming) with the current management of STH in Ghana, as well as contextual factors (such as perceptions regarding safety of drugs, and procedures for reporting and managing drug reactions) with implications for the feasibility and acceptability of FDC of IVM and ALB. Findings of this formative study will inform the design of a study that explores the acceptability, feasibility, and adherence of a FDC of IVM and ALB for the control of STH. The results of this formative study, the eventual larger study and the wider STOP2030 project will generate evidence to inform STH control efforts in Ghana, Kenya and beyond.

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SUCCESSES TACKLING PERSISTENCE AND RECRUDESCENCE OF TRACHOMA: KAJIADO COUNTY, KENYA

Samuel Eshitemi[1], Laura G. Senyonjo[2], Esther Andia[1], Michael Kirumba[1], Samuel Njenga[3], Wyckliff Omondi[4], Sarah Gwyn[5], Diana L. Martin[5], Moses Chege[1], Titus Watitu[4]

[1]Sightsavers, Nairobi, Kenya, [2]Sightsavers, Haywards Heath, United Kingdom, [3]KEMRI, Nairobi, Kenya, [4]Kenya Ministry of Health, Nairobi, Kenya, [5]CDC, Atlanta, GA, United States

Trachoma surveys in Kajiado County, Kenya, in 2020 identified a problem of trachoma persistence and recrudescence. Kajiado County is primarily made up of nomadic Maasai communities, who often cross the border to Tanzania and have poor access to adequate water and sanitation, compounded by animal husbandry practices that facilitate *Musca sorbens* (vector for trachoma) breeding. Sightsavers in collaboration with the Kenya MoH, KEMRI and CDC worked to confirm and understand the causes of on-going or recrudescent transmission. Evidence-based programmatic adaptations were made to address the causes and a rigorous monitoring and evaluation framework was put in place to monitor progress (and adapt as necessary) towards elimination targets. Efforts were made to better understand underlying transmission dynamics through enhanced trachoma impact surveys (TIS) adding on testing for *Chlamydia trachomatis (Ct)* infection and anti-*Ct* antibodies (TIS+) in 2021, 2022 and 2024. There has been a clear reduction ($p<0.001$) in *Ct* infection from 6.2%, 3.3% and 2.6% in 2021 to 0.8%, 0.8% and 0.1% in 2024 amongst children 1-5 years in Kajiado West, Central and South sub-counties respectively. Similarly, there is a reduction in clinical indicators (trachomatous inflammation—follicular, TF) from 13.8%, 18.0% and 8.1% in 2021 down to 6.6%, 8.0% and 5.2% in Kajiado West, Central and South, respectively. This has been complemented by an evaluation of anti-*Ct* antibody prevalence data and seroconversion rates over time. The presentation will also outline the key outcome indicators measured as part of the programme performance, including improved real-time reporting of mass drug administration (MDA) coverage and innovative community drug distributor tracking tools, validated through coverage evaluation surveys. Despite this significant progress, geospatial analysis has identified areas with high re-infection rates, six months after MDA. On-going challenges in this area will be outlined, along with plans to protect the significant gains made in tackling persistence and recrudescence of trachoma in Kajiado County, Kenya.

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UNRAVELING CHEMOKINE AND CYTOKINE NETWORKS IN PBMCS CULTURED FROM INDIVIDUALS WITH LEPROSY AND HOUSEHOLD CONTACTS, STRATIFIED BY OPERATIONAL CLASSIFICATION

Lorena Bruna Pereira de Oliveira[1], Pedro Marçal[1], Rafael Gama[1], Thalisson Gomides[1], Marlucy Rodrigues[1], Olindo Martins Filho[2], Joaquim Brito de Souza[3], Alexandre Castelo Branco[4], Jessica Fairley[5], Lucia Fraga[6]

[1]Universidade Vale do Rio Doce, Governador Valadares Valadares, Brazil, [2]Fiocruz/BH, Governador Valadares Valadares, Brazil, [3]Fiocruz/BH, Belo Horizonte, Brazil, [4]Centro de Referencia Endemica e Doenças Especiais (CREDEN-PES), Governador Valadares Valadares, Brazil, [5]Emory University, Atlanta, GA, United States, [6]UFJF/GV, Governador Valadares Valadares, Brazil

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* infectionthat affects the skin, peripheral nerves and nasal mucosa presenting a wide range ofclinical manifestations. Identifying immunological biomarkers applicable as complementarydiagnostic tools for these subgroups as well as to detect subclinical leprosy in householdcontacts would be advantageous. Blood samples (257 individuals, Governador Valadares, Brazil) were collected and tested for immunological assays. Chemokines (CXCL8, CCL2, CXCL9, CCL5,and CXCL10) and cytokines (IL-6, TNF, IFN-ϒ, IL-17, IL-4, IL-10, and IL-2) present in cell culturesupernatants were assessed utilizing the CBA method. Analysis was performed using theFACSVerse, and data were processed through FCAP Array software. Quantitative results wereexpressed in pg/mL, derived from standard curves. Subsequently, integrative networks wereconstructed based on spearman correlations among soluble mediators subsequent to theassessment of the chemokine and cytokine profiles in PBMC cultures from diverse cohorts.Results revealed that the *M. leprae*-stimuli led to a decrease in the number of correlationsbetween soluble mediators as compared to Unstimulated culture (EC = 68 → 62; HHC = 56 → 50and L = 46 → 42). Additionally, when subdivided groups (HHCPB, HHCMB, LPB, and LMB) analyses were performed, an increase in correlations occurred in all groups except for HHCMB when *M. leprae* stimulated the culture. Color map analysis further illustrated that thephenomenon of downregulation was universally observed in the total number of correlations,in the intra-cluster connectivity as well as in the analysis of single patterns of most solublemediators. These findings underscore the intricate interplay of chemokines and cytokines in theimmunological landscape of leprosy. Their complex interactions, modulated by diseaseprogression and antigenic stimuli, unveil the importance of immune responses in leprosypathology, helping elucidate valuable insights into the disease's immunopathogenesis.

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THE POTENTIAL GEOGRAPHICAL DISTRIBUTION OF HANTAVIRUS RODENT HOSTS IN NORTH AMERICA

Abdelghafar Alkishe, Luis E. Escobar

Virginia Tech, Blacksburg, VA, United States

The main way that hantaviruses infect people is through contact with rodent hosts that are infected. These viruses are noteworthy for their zoonotic potential and importance to public health. This study creates a detailed model of 15 hantavirus rodent hosts (that were documented with positive hantavirus from the National Ecological Observatory Network (NEON)) in North America. We used available geospatial data from the Global Biodiversity Information Facility (GBIF). The modeling methodology predicts the spatial distribution of hantavirus rodent hosts across several ecosystems in North America by utilizing sophisticated machine learning techniques, such as Ecological Niche Modelling (ENM). The models are more accurate and ecologically relevant when MERRAclim environmental data are included. The findings of this investigation shed light on potential hotspots of hantavirus rodent hosts, which advances our knowledge of the spatial epidemiology of hantaviruses. Additionally, the modeling approach provides a useful tool for comparing and answering the question of why

more hantavirus cases have occurred in the western United States than in other areas across the country. We provided sets of maps where we highlighted the geographic distribution of each species, a richness map for all 15 species across North America, and a richness map for the most important hosts with high hantavirus prevalence to be compared with a map of human cases on the State level from CDC. The findings of this study have implications for public health planning, enabling more targeted surveillance and intervention strategies to mitigate the risk of hantavirus transmission in North America, especially in the United States where the number of incidents has increased in recent years.

6688

THE ROLE OF LANDSCAPE CHARACTERISTICS IN THE TRANSMISSION OF VECTOR-BORNE DISEASES: CASE STUDY OF PLAGUE

Soanandrasana Rahelinirina[1], Lovasoa Nomena Randriantseheno[1], Mamy Gabriel Randriamanantsoa[2], Sarah Zohdy[3], Romain Girod[1], Mireille Harimalala[1], Minoarisoa Rajerison[1]

[1]Institut Pasteur de Madagascar, Antananarivo, Madagascar, [2]National Plague Control Program, Ministry of Public Health, Antananarivo, Madagascar, [3]US Centers for Disease Control and Prevention, Atlanta, GA, United States

Plague caused by *Yersinia pestis* infection is a virulent vector-borne disease. Despite advances in plague control globally in past decades, Madagascar accounted for 80.5% of the worldwide cases from 2013 to 2018 by WHO. Landscape characteristics may affect the population dispersal of its hosts and vectors and hence the distribution of *Y. pestis*. The identification of spatial patterns of genetic structure of *Y. pestis* is a key factor to understand the dynamics of transmission and spread of the disease. The aim of this study is to examine geographic genetic patterns of *Y. pestis* from small mammal reservoirs and humans in three active plague foci across the central highlands of Madagascar where human plague is reported every year. These areas are separated by high altitudes and distances between 5km to 30km. *Y. pestis* DNAs from rat spleens and human buboes from 2019 to 2022 were extracted and genotyped using single nucleotide polymorphism (SNP) analysis. The North American strain CO92 was used as a reference and *Y. pestis* from 2007 was used to look at population dynamics over time. *Y. pestis* isolates from 23 humans and from 4 rats were analyzed. Two groups y and t were identified using a set of 249 SNPs previously identified. Isolates from humans and rats in the same locality had similar genomic and there was a relationship between genetic and geographic distance. Each group had been persisting over 15 years in these localities. This study highlights the presence of spatial genetic structure of *Y. pestis* at local scales suggesting efficient circulation at smaller geographic scales. Landscapes play a major role in the maintain of plague because of the movement of rodent and their fleas in the short distances in mountainous areas. The characteristics of the micro and macro peridomestic landscape may explain patterns of local transmission of plague. Understanding pathogen population dynamics provides insight into how, where, and when transmission occurs and can inform control decision making.

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UTILIZING A ONE HEALTH APPROACH TO RIFT VALLEY FEVER VIRUS LABORATORY AND FIELD INVESTIGATIONS

Shelby M. Cagle, Olivia Martinez, Nicole Kelp, Rebekah C. Kading

Colorado State University, Fort Collins, CO, United States

The WHO attributes 700,000 deaths each year to vector-borne diseases. Communities living in certain geographic regions or within lower socioeconomic sectors are disproportionately at risk for VBD. Furthermore, the changing climate is rapidly reshaping vector boundaries. Therefore, an integrative approach that considers socioecological dynamics, vector biology, vector control, public health, agriculture, disease kinetics, and other sectors is necessary to reduce the global burden of VBD. We examine the transmission of a high consequence pathogen, Rift Valley fever virus (RVFV), both in the lab and the field to answer the questions: How do ecological factors like temperature impact RVFV transmission in competent mosquito vectors? and What are the risk perceptions of local stakeholders and community members regarding RVFV? To elucidate the effects temperature on virus dissemination and transstadial persistence in naturally infected mosquito vectors: laboratory colony mosquitoes were provided a RVFV-infected blood meal, placed at experimental temperatures (18°C, 28°C and 32°C), monitored for oviposition, survivorship, feeding-rate, and viremia. Oviposition is reduced at 18°C, blood feeding rates and survivorship are reduced at 32°C, indicating a temperature-dependent reduction in vector capacity. Evidence of RVFV vertical transmission in mosquitoes is shown. To further understand RVFV burden of disease, a multinational, transdisciplinary collaboration is underway in endemic regions of Tanzania. The project includes surveillance of humans, livestock, and mosquitoes in vaccine deployment regions, and an investigation of RVF knowledge, attitudes, and practices (KAP) of local stakeholders. Preliminary results of KAP, specifically, risk perceptions and behaviors for RFV will be presented. Ecological factors, such as temperature, can alter vectorial capacity and disease kinetics; whereas social factors, such as individual perceptions and behaviors could limit or exacerbate risk for VBD. Overall, this research will describe the applications of One Health framework to a VBD of global public health concern.

6690

FINANCING, OPERATIONALIZING, AND IMPLEMENTING REGIONAL ONE HEALTH COORDINATION IN SOUTHEAST ASIA

Steven Lam, Hung Nguyen-Viet

International Livestock Research Institute, Nairobi, Kenya

Regional One Health coordination is a promising strategy for addressing shared global health priorities by avoiding duplication and maximizing synergies. Developing coordination mechanisms is urgently needed in Southeast Asia, a recognized hotspot for new zoonoses with the potential to spread globally. The objective of this piece is to identify priority action items for financing, operationalizing, and implementing regional One Health coordination in Southeast Asia. In December 2023, we conducted a 1.5-day workshop to convene 34 experts from government, national research institutes, universities, and international organizations across seven countries in Southeast Asia. This workshop focuses on exchanging experiences in and generating ideas for One Health investment, operationalization, and implementation. Based on their collective experiences, participants agreed on the following 12 action items: 1) leverage existing and emerging funding sources; 2) encourage domestic resource mobilization; 3) cultivate private-public partnerships; 4) develop business cases for One Health; 5) establish a One Health centre for Southeast Asia; 6) develop data governance frameworks; 7) formalize national coordination mechanisms; 8) strengthen engagement in social sciences; 9) strengthen engagement with diverse dimensions of One Health; 10) integrate One Health into national and local frameworks; 11) take stock of past and current initiatives; and, 12) invest in the One Health workforce. The outlined action items serve as ideas for resourcing, operationalizing, and implementing regional One Health coordination in Southeast Asia, with relevance to other regions that are tackling parallel One Health challenges of zoonoses, antimicrobial resistance, and food safety.

6691

UNVEILING ZOONOTIC EXTRAINTESTINAL *E. COLI* BURDEN IN LMICS: A STUDY IN NIGERIA

Yashan Wang[1], Maliha Aziz[1], Edward Sung[1], Daniel Park[1], Cindy Liu[1], Stephen Obaro[2], Nubwa Medugu[3], Bernard Ebruke[3], Lance Price[1]

[1]The George Washington University, Washington, DC, DC, United States, [2]University of Alabama at Birmingham, Birmingham, AL, United States, [3]International Foundation Against Infectious disease in Nigeria, Abuja, Nigeria

The Global Burden of Disease studies estimated that *E. coli* was associated with nearly 1 million deaths globally in 2019, with 80% occurring in low- and middle-income countries (LMICs). 94% of *E. coli* deaths were caused by infections out of the gastrointestinal tract. Previous research underscored the prevalence of foodborne zoonotic strains of *E. coli* in extraintestinal infections in the United States. However, research in LMICs is limited, where factors such as extensive human-animal interaction and inadequate Water, Sanitation, and Hygiene (WASH) conditions may elevate the risk. To understand the burden of zoonotic extraintestinal *E. coli* infections in LMICs, we conducted a study in Nigeria, a West African nation. We analyzed Whole Genome Sequencing data of 122 *E. coli* isolates from humans extraintestinal infections (e. g. bloodstream and urinary tract infections) and included 520 food-animal isolates from Africa as context. We applied a Bayesian latent class model that leverages 17 host-associated (either human or meat) mobile genetic elements to generate probabilistic predictions of the underlying host of the *E coli* isolates, thereby identifying putative spillover strains. The model identified 24.7% of the human extraintestinal *E. coli* infections as food-animal zoonotic. This proportion is significantly higher than previous estimations in the United States, where 8% and 18% of isolates from Arizona and California, respectively, were predicted to be foodborne zoonotic. Our findings indicate that approximately one in four extraintestinal *E. coli* infections in Nigeria may originate from food-animals. Analysis of host-associate elements patterns and major sequence types of zoonotic *E. coli* highlighted geographic variations between African and American isolates. Collecting and analyzing isolates from underexplored regions are imperative to understand the pathogen transmission from food-animals to humans.

6692

ALTERATION OF THE MURINE GUT MICROBIOTA MEDIATES ANTIDEPRESSANT EFFECT OF *MALLOTUS OPPOSITIFOLIUS* EXTRACT

Stella F. Bour[1], Blay Kwofie[2], Kennedy Kukuia[3]

[1]Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon, Accra, Ghana, [2]Department of Medical Pharmacology, College of Health Sciences, University of Ghana, Legon, Accra, Ghana, [3]Department of Medical Pharmacology, College of Health Sciences, University of Ghana,Legon, Accra, Ghana

Major depressive disorder (MDD) is one of the leading causes of disability globally. The treatment of MDD remains an uphill task, but the gut microbiota has been posited as a potential target for the treatment of MDD. We investigated the effect of the hydroethanolic leaf extract of *Mallotus oppositifolius* (MOE) on the gut microbiota of mice and how this contributes to the extract's known antidepressant-like effect. A 7-week chronic unpredictable mild stress (CUMS) procedure was employed in seven (7) groups of mice to induce depression. Oral drug or extract treatment began from the third (3rd) week with MOE (10, 30, 100 mg/kg) and two reference drug groups, fluoxetine (12 mg/kg) and minocycline (40 mg/kg), which have known influence on the gut microbiota. The sixth and seventh groups were the vehicle stressed (VEH-S) and vehicle non-stressed groups (VEH-NS) respectively. Changes in depressive-like behaviours were assessed using sucrose preference test while the forced swimming (FST) test was used to assess sustained antidepressant-effect after treatment discontinuation. Changes in prefrontal cortex (PFC) and hippocampal serotonin (5-HT) levels were also evaluated using enzyme-linked immunosorbent assay (ELISA). The effect of treatment on the profile of the gut microbiota of the various groups was elucidated using 16S rRNA Oxford Nanopore sequencing. MOE and reference drugs reversed the depression-associated reduction in sucrose preference when compared to VEH-S. MOE (with peak effect at 30 mg/kg) reduced immobility while increasing swimming and climbing behaviours in the FST. In addition, MOE reversed CUMS-induced reduction of 5-HT concentration in PFC and hippocampus. The behavioural effects of MOE were associated with shifts in the gut microbiota of CUMS-exposed mice by modifying the relative abundances of depression-related taxa such as Lactobacilli, Desulfovibrio, Parabacteroides. The study has provided seminal evidence that the hydroethanolic leaf extract of *M. oppositifolius* ameliorates CUMS-induced depressive symptoms by modulating the levels of gut microbiota constituents and increasing brain 5-HT levels.

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CUSTOMERS' WILLINGNESS-TO-PAY FOR POULTRY FROM BIOSECURE LIVE BIRD MARKETS IN DHAKA, BANGLADESH

Rebeca Sultana[1], Nadia Ali Rimi[1], Md. Jawwad Kamran[1], Md Mustafizur Rahman[1], Md. Akhtaruzzaman Khan[2], Md. Salahuddin Palash[2], Md. Khaled Saifullah[1], Sayed Masum Billah[1], Ireen Sultana Shanta[1], Kamal Hossain[1], Patrick Webb[3], Beatrice Lorge Rogers[3], Hellen Amuguni[4], Elizabeth Gold[5], Jonathon Gass[6], Sean B. Cash[3], Laura H. Kwong[7]

[1]icddr,b, Dhaka, Bangladesh, [2]Bangladesh Agricultural University, Mymensingh, Bangladesh, [3]Friedman School of Nutrition, Tufts University, Boston, MA, United States, [4]Cummings School of Veterinary Medicine, Tufts University, Boston, MA, United States, [5]John Snow, Inc., Boston, MA, United States, [6]School of Medicine, Tufts University, Boston, MA, United States, [7]School of Public Health, University of California, Berkeley, Berkeley, CA, United States

Bangladesh is a known hotspot for avian influenza circulation. Live bird markets (LBMs) are particularly risky, highlighting the critical need to enhance biosecurity measures. Despite this, little is known about consumers' willingness-to-pay (WTP) for purchasing poultry products from hygienic and biosecure LBMs. This study aimed to examine the WTP of customers to buy poultry from a biosecure LBM in Bangladesh. A total of 600 customers from 60 LBMs in Dhaka, Bangladesh were selected using stratified random sampling and surveyed in June and July, 2023. A set of 17 attributes related to infrastructure, biosecurity practices, and institutional responsibilities to create a biosecure LBM were identified before the survey. The survey asked participants to score each attribute with a 5-point Likert scale according to perceived importance, and state how much they would be willing to pay for those attributes. Washable walkways in LBMs and a regular water supply ranked highest among infrastructure attributes, while separating sick poultry from healthy ones and arranging for separate disposal of dead chickens were most important biosecurity measures. Regular monitoring by market and city corporation authorities ranked highest among institutional attributes. The majority (73%, 439/600) of the customers were willing to pay extra for chicken from an improved biosecure LBM. They were willing to pay BDT 13 (USD 0.12) more per kilogram (kg) for broiler, BDT 17 (USD 0.16) more for *Deshi (Gallus gallus domesticus)*, and BDT 14 (USD 0.13) more for *Sonali* (a cross-breed chicken, similar phenotypic appearance to *deshi* chicken) chicken. Of the customers willing to pay more, 85% (375/439) reported consuming the same amount of chicken at their stated increased price. LBM customers were willing to pay 3-7% more per kg of chicken from a clean and biosecure market. The finding may motivate LBMs stakeholders to improve biosecurity, as customers are willing to pay extra money. Customers' preferences for biosecure LBMs could inform government decision-making on investments and policies for improving LBMs to reduce the risk of spillover of pathogens with pandemic potential.

6694

DISENTANGLING THE EFFECTS OF FINE-SCALE MOBILITY ON LEPTOSPIRAL INFECTION USING GPS TELEMETRY DATA

Pablo Ruiz Cuenca[1], Fabio Neves[2], Max T. Eyre[3], Jonathan Read[1], Federico Costa[2], Emanuele Giorgi[1]

[1]Lancaster University, Lancaster, United Kingdom, [2]Universidade Federal da Bahia, Salvador, Brazil, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom

Human movement significantly influences the transmission dynamics of infectious diseases, particularly those with strong environmental drivers like leptospirosis, a zoonotic bacterial infection associated with mud and water contact. The use of GPS loggers allows a large amount of telemetry data to be collected. Telemetry data offers insights into fine-scale interactions with environmental risk factors, especially useful in complex settings like urban informal settlements. This is crucial in understanding where environmental exposure to leptospirosis occurs, an epidemiological question that remains unclear. In this study, we aimed to characterise people's movements through urban marginalised communities in Salvador, Brazil, quantifying their interactions with three environmental risk factors: domestic rubbish piles, open sewers and a local stream. Our analysis focused on identifying differences in movement patterns between genders, age and leptospirosis antibody status. We used step-selection functions, a spatio-temporal point process model used in animal movement ecology, to estimate selection coefficients. These represent the likelihood of an individual choosing to move in the direction of a specific environmental factor. With 130 participants across four matched study areas wearing GPS loggers for 24 to 48 hours, we recorded locations every 35 seconds during daytime active hours, segmented into morning, midday, afternoon, and evening. We found women were more likely to move closer to the central stream in their community and further away from open sewers than men. This study showcases a novel approach to analysing human telemetry data in infectious disease epidemiology, providing insights crucial for targeted intervention strategies.

6695

A SCOPING REVIEW ON CONTROL STRATEGIES FOR *ECHINOCOCCUS GRANULOSUS*

Tania De La Cruz-Saldaña[1], Javier A. Bustos[1], Nelson Martinez-Merizalde[2], Lizzie Ortiz-Cam[1], Maria Paula Requena[1], Ana Lucia Caceres[1], Carolina Guzman[1], Cesar M. Gaviria[3], Cesar Ugarte-Gil[4], Ricardo Castillo-Neyra[5]

[1]Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Universidad Peruana de Ciencias Aplicadas, Lima, Peru, [3]Universidad Nacional Mayor de San Marcos, Lima, Peru, [4]University of Texas Medical Branch, Galveston, TX, United States, [5]University of Pennsylvania, Philadelphia, PA, United States

Cystic echinococcosis caused by the tapeworm *Echinococcus granulosus (EG)* is a significant public health concern due to its widespread distribution and impact on human health. Cystic echinococcosis is a neglected disease; therefore, it does not receive enough funding and research and programs evaluating interventions are scarce. Our objective was to identify the scientific rationale, objectives, and efficacy of various interventions aimed at reducing, controlling, or eliminating EG in animals and humans, providing a comprehensive overview of the current status of EG interventions worldwide. We mapped all available evidence on interventions for EG up to December 2022. We screened major databases and categorized papers based on type of study, biological mechanism of control, and target populations. We characterized intervention's efficacy and safety outcomes, and associated barriers/facilitators. We assessed study quality. Out of 6080 potentially relevant studies, 40 were deemed appropriate for analysis and included in our review. Ten of these studies reported interventions in humans, 18 in animals, and 12 in animals and humans. Human interventions focused primarily on preventive education aimed at increasing knowledge and awareness. Half of the animal interventions targeted only dogs and the other half targeted dogs and sheep. Interventions involving praziquantel comprised 72% of all interventions. Only two studies focused on sheep vaccination. Among interventions focused on both humans and animals, we found a variety of approaches including education, mass screening, dog population control, slaughterhouse control and surveillance, and praziquantel treatment. The efficacy was varied and will be discussed. The overall quality of the studies was low. Available evidence suggests that interventions with multiple components aimed at animals and humans could achieve EG control. However higher quality evidence is needed. Our study reveals research gaps that need to be addressed to inform future interventions and control programs. Further evidence is needed to assess the sustainability of control measures.

6696

IMPACT OF ANGOLAN ROUSETTE BAT (*MYONYCTERIS ANGOLENSIS*) FORAGING SITE CONSISTENCY ON SPILLOVER POTENTIAL IN THE MOUNT ELGON REGION OF UGANDA

Kalani M. Williams[1], Natalie R. Wickenkamp[1], Emma K. Harris[1], Benard Matovu[2], Betty Nalikka[2], Lillian Nalukenge[2], Micheal Mutebi[2], Aggrey Siya[2], Tanya A. Dewey[1], Kevin Castle[3], Teddy Nakayiki[4], Leonara Rebecca[4], Angella Charity Nassuna[4], Robert M. Kityo[2], Julius J. Lutwama[4], Rebekah C. Kading[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]Makerere University, Kampala, Uganda, [3]Wildlife Veterinary Consulting LLC, Livermore, CO, United States, [4]Uganda Virus Research Institute, Entebbe, Uganda

Angolan rousette bats (*Myonycteris angolensis*) are a potential reservoir for viruses that could be of importance to public health. Our preliminary data suggest these bats host paramyxoviruses and rhabdoviruses. While many bat-associated spillover events are deduced to have occurred at the cave interface, many could not have occurred at caves, and thus must have transpired in locations bats use in the night, likely for foraging. Understanding the consistency of bat nightly foraging behavior across different seasons will illuminate habitat features that are most important to bats, and thus should be targeted for prediction and prevention of viral spillover. In this study, we used GPS tracking to ascertain foraging sites of the frugivorous *M. angolensis* within the Mount Elgon region of Uganda. Through geospatial analysis applications, we tested whether these foraging sites were significantly associated with particular landscape features. GPS data were acquired by suturing GPS units onto bats and taking fixes during periods of high activity over the course of five days in both January (dry season) and May (wet season) of 2023. Using kernel density algorithms to determine foraging hotspots from the distribution of GPS points, our preliminary data suggest foraging hotspots are significantly closer to rivers/streams and protected areas and significantly further from human settlements than would be expected if their distribution was random. Using multi-night data, it was evident that specific foraging locations were visited by multiple bats from the colony, as well as by the same bats over consecutive nights. Foraging ranges were fairly consistent in protected forested areas across seasons, but different foraging locations were identified in populated agricultural sites in wet versus dry seasons. Foraging sites were more variable and more frequently included human settlements during the dry season when endemic fruits are less readily available. These results suggest a seasonal component to resource stress and an associated impact of seasonality on potential for viral spillover due to changes in bat foraging site selection.

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DIVERSE MICROBES HABITING MEDICINAL HERBAL PREPARATIONS EXHIBIT VARIED RESISTANCE TO ESSENTIAL ANTIBIOTICS

Millicent Serwaa Marfo Ogyiri[1], Stephen Yao Gbedema[1], Yaw Duah Boakye[1], Hayford Odoi[2], Theresa Appiah Agana[1], Vivian Etsiapa Boamah[1]

[1]Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, [2]University of Allied Health Sciences, Ho, Ghana

The use of herbal medicine is on ascendency worldwide. This study sought to assess the microbial and heavy metal quality of herbal medicines in the Kumasi Metropolis. Twenty commercially available herbal medicines were sampled from wholesale pharmacies in the metropolis, serially diluted and inoculated on various culture media for microbial growth and count using the pour plate technique. Bacterial isolates were identified by MALDIToF MS, and their Antibiotic Sensitivity patterns determined using the Kirby Buer disc diffusion method, employing breakpoints from the EUCAST guidelines. The samples were digested by the Triple Acid Digestion technique and concentrations of Cadmium, Arsenic and Lead assessed using the MP-AES. All samples were contaminated. Total Aerobic Microbial Counts of $5x10^2$ to $2.38x10^6$ CFU/mL and Total Yeast and Mould Counts of $6.6x10^2$ to $1.71x10^6$ CFU/mL were observed with 45% and 80% of products exceeding the European Pharmacopeia threshold for aerobic count and yeast and mould count, respectively. 87 bacterial isolates comprising 27 species were identified. *Bacillus pumilus* was the predorminant bacterial species (26.13%). *Bacillus cereus* (9.09%), *Pantoea septica, Mixta calida* and *Klebsiella oxycota* were among the least (1.14%). 26 fungal isolates. *Aspergillus* spp. was the most prevalent (46.15%). *Phialophora* spp. and *Fusarium* spp. were the least (1.78%). All bacteria subjected to the Antibiotic Sensitivity Tests exhibited resistance to at least one class of antibiotics. 29 *Enterobacteriaceae* were resistant to ampicillin (10 µg), 46 *Bacillaceae*, resistant to ciprofloxacin (5 µg) and 6 *Pseudomonades*, resistant to ticarcillin (75 µg) and Aztreonam (30 µg). 5 isolates were multidrug resistant. 5% and 40% of products exceeded WHO's daily limits for lead (10mg/kg) and arsenic(5mg/kg), respectively. The presence of a vast array of resistant microorganisms and toxic heavy metals indicates potential contamination of herbal preparations in the Kumasi metropolis. Regulatory authorities should ensure quality assurance for manufacture of herbal medicines is properly enforced.

6698

A ONE HEALTH APPROACH TO TACKLE PLAGUE OUTBREAKS IN DEMOCRATIC REPUBLIC OF THE CONGO: THREE YEARS OF ONGOING EPIDEMICS.

Pascal Adroba[1], Anne Laudisoit[2], Shaun Cross[3], Germain Abhafule[4], Dedha Jean de Dieu[5], Floribert Rekaba[6], Esperance Tshiwedi[7], Mulopo Noella[7], Daniel Mukadi[7], Michael R. Wiley[3], Placide Mbala[7]

[1]Centre de surveillance et de lutte contre la pesteUniversity of Nebraska Medical Center, Bunia, Congo, Democratic Republic of the, [2]Ecohealth Alliance, New York, NY, United States, [3]University of Nebraska Medical Center, Omaha, NE, United States, [4]Centre de Recherche en Maladies tropicales, Rethy, Congo, Democratic Republic of the, [5]Ministry of Health, Rethy, Congo, Democratic Republic of the, [6]University of Monts-Bleus, Kpandroma, Congo, Democratic Republic of the, [7]Institut National de Recherche Biomedicale, Kinshasa, Congo, Democratic Republic of the

Plague is a neglected zoonosis, caused by the flea-borne bacterium *Yersinia pestis*, with mortality rates of around 65% for bubonic plague and around 100% for pulmonary plague if the infection is left untreated. The Ituri endemic plague focus, also known as the Lake Albert focus (6000 km2), is the oldest known focus in Africa. Since 2000, the number of suspect plague cases and outbreak sites has been increasing in range and scope with 9265 suspect cases and 510 deaths (CFR=5.5%). As we all know, a local risk can become global, and ignoring the spread of plague in one of the world's most active hotspots exposes DR Congo and its neighbors to a transnational risk. Moreover, plague outbreaks are unpredictable calling for increased in-country preparedness, detection and response capacities. In the last 20 years, the average annual number of suspect plague cases was 421.1±11.9 (median 155), and the average weekly number of suspected cases was 7.4±21.7 (median 3 cases per week). Between 2021 and 2024, the Rethy health zone alone located in Djugu Territory, has reported 881 cases of human plague. The primary route of infection is likely flea-borne transmission, with domesticated guinea pigs and black rats being significant amplifiers; sylvatic carriers are yet to be identified. Most cases remained classified as suspect due to the absence of confirmatory diagnostic, active surveillance, and funding. However, recent collaborations have allowed for molecular and microbiological *Y.pestis*diagnostics at INRB Goma. Of 55 buboes samples tested, 29 were positive, and 3 full genomes have been generated. To prevent future outbreaks, logistical and technical support have recently focused on public awareness and education in household sanitation and rat consumption risks, free case management, chemoprophylaxis for contact cases, and vector control.

6699

SETTING THE PLATFORM FOR THE ELIMINATION OF STRONGYLOIDIASIS IN AUSTRALIA

Catherine A. Gordon, Darren J. Gray

QIMR Berghofer Medical Research Institute, Brisbane, Australia

Strongyloidiasis is a neglected tropical diseases caused primarily by infection with the roundworm *Strongyloides stercoralis*. While the majority of infections are so-called 'asymptomatic', it can have deadly consequences in cases of immune-compromise leading to hyperinfection and disseminated strongyloidiasis which, untreated, is almost universally fatal. Infections occur globally, although there is little to no surveillance performed, thus the true burden of disease is unknown. While more recently included in the Soil-Transmitted Helminths (STH) by the WHO, traditional diagnostics and treatments for STH are ineffective against *Strongyloides*, further underscoring the urgency of addressing this issue. Estimates based on published literature suggest there may be 600 million infections worldwide, with the majority of these infections occurring in South East Asia (SEA) and the Pacific.While Australia has a low country-wide prevalence, prevalence in endemic communities, particularly in Northern Australia, can be over 30%, and as high as 60%. There is also the added complication of HTLV-I, which is co-endemic in Australia and may be a trigger for more severe disease, and the potential for a zoonotic reservoir in dogs. It is our central thesis that strongyloidiasis is a zoonotic neglected tropical disease of public health importance in Australia and that an integrated interdisciplinary "One Health" approach is required for its elimination. Here we will present an overview of strongyloidiasis in Australia and outline an elimination program we are developing for implementation in remote communities in Northern Australia.

6700

EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF RESPIRATORY SYNCYTIAL VIRUS IN PATIENTS WITH INFLUENZA LIKE ILLNESS IN THE GAMBIA: RESULTS FROM A NEWLY IMPLEMENTED SENTINEL SURVEILLANCE PROGRAM

Amadou Wurry Jallow[1], **Alpha Omar Jallow**[2], Modou Lamin Sanneh[2], Mamadou Malado Jallow[3], Alphonse Mendy[2], Boubacar Diallo[3], Mamadou Aliou Barry[3], Sheriffo Jagne[2]

[1]EDC, MoH, Serrekunda, Gambia, [2]NPHL, Serrekunda, Gambia, [3]Institut Pasteur of Dakar, Dakar, Senegal

Respiratory syncytial virus (RSV) is a major cause of acute respiratory infections in children worldwide and can cause high mortality, especially in developing countries. The Gambia, experiences a high burden of respiratory illnesses among pediatric populations, yet there is limited data on the epidemiology and clinical characteristics of RSV infections. Here, we present results of a newly implemented sentinel surveillance program in two hospitals in the Gambia with a focus on epidemiological and clinical characteristics of RSV infection. From January to December 2023, nasopharyngeal samples were collected from outpatient with influenza-like

illness in two referral hospitals. Clinical and socio-demographic data were obtained using a standardized questionnaire. Collected samples together with the clinical forms were sent to the National Public Health Laboratory (NPHL) on a weekly basis through the Sample Referral Network. Once in the laboratory, samples were tested by targeting 3 respiratory pathogens, including RSV, SARS-CoV2 and influenza A/B viruses using a multiplex RT-PCR. Overall, 148 respiratory specimens were received and analyzed at the NPHL during this pilot phase. Among enrolled patients, 79 (53.4%) were males, 67 (45.3%) were infants aged under 1 year and children above 5 years of age represented 35.1% of all patients. RSV was detected in 14.2%, among which RSV type A was confirmed in 38.1% and RSV type B in 61.9%. RSV detection rates in the different age groups varied significantly with infants aged ≤11 months accounting for 66.7% of positive patients. The highest detection rate of RSV was noted in August (38.1%), which coincide with the rainy season in the Gambia. The most frequently observed symptoms among patients with confirmed RSV infection were cough (90.5%), fever (80.9%) and Dyspnea (52.4%). In summary, our findings from the newly implemented sentinel surveillance program reveal a relatively high prevalence of RSV infection among pediatric patients in the Gambia with co-circulation of both type of RSV. Enhanced surveillance of Severe acute respiratory illnesses in pediatric inpatients in needed.

6701

GENETIC DIVERSITY AND MUTATIONAL PROFILES OF SARS-COV-2 VIRUS IN ADDIS ABABA, ETHIOPIA (2020 TO 2022)

Dejenie S. Teklu[1], Abiy Zegeye[2]

[1]Ethiopian Public Health Institute, Addis Ababa, Ethiopia, [2]Addis Ababa University, Addis Ababa, Ethiopia

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a significant impact on global health and economies. The purpose of this study was to limit the sample area to Addis Ababa and analyze the genetic diversity and mutational profiles of SARS-CoV-2 viruses from 2020 to 2022. SARS-CoV-2 genome sequences were retrieved from the Global Initiative on Sharing All Influenza Data (GISAID) database as of July 19, 2023 only samples collected in Addis Ababa, Ethiopia. A total of 451 high-quality, complete genome sequences were selected for analysis. Nextclade (version 2.14.0) command line pipeline and Pangolin were used for viral genome clade assignment, mutation calling, phylogenetic placement, and lineage designation. The analysis revealed a diverse range of SARS-CoV-2 genetic variants in Addis Ababa, with the Delta variant (66.1%) identified as the predominant strain (Clade 21J: 61.9%, 21I: 1.8% and 21A: 2.4; Pangolin: AY.120: 40.4%, B.1.617.2: 15.5% and others: 10.2%), followed by the Omicron (20.2%) variant (Clade21K: 18.8%, BA.1.1: 11.8). There were a shift from diverse early variants (A, B.1, B.1.480, Alpha, and Beta) to Delta dominance in mid-2021, followed by Omicron's supremacy from late 2021 to mid-2022. A total of 14093 amino acid substitutions were identified (average of 31.2 mutation per sequence). The average substitution rate of amino acids was larger in Omicron variants (45.1) than in Delta variant (30.6). There were four most frequent amino acid substitutions (D614G, T478K, P314L and T3255I) shared between Delta and Omicron variants. Addis Ababa's SARS-CoV-2 landscape transitioned from diverse early variants to Delta dominance in mid-2021, followed by Omicron's predominance from late 2021 to mid-2022. Higher substitution rates in Omicron compared to Delta suggest continued adaptation and emphasize the need for ongoing surveillance and targeted interventions.

6702

RISK FACTORS ASSOCIATED WITH COVID-19 IN-HOSPITAL MORTALITY IN PANAMA

Santiago Hernandez[1], Ana Belén Araúz[2], Neil Rupani[1], Benjamin Jacob[1], Jason Salemi[1], Ismael Hoare[1], Arlene Calvo[1], Ricardo Izurieta[1]

[1]University of South Florida, Tampa, FL, United States, [2]Hospital Santo Tomas. Universidad de Panama, Panama City, Panama

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from China in December 2019 and raised serious concerns worldwide. SARS-CoV-2 was transmitted across Panama in a short period followed by the announcement of the first imported case on March 8th, 2020. This retrospective cohort study aims to examine the epidemiological, clinical, laboratory, medical treatment, and clinical outcomes of patients hospitalized in the Santo Tomas Hospital of Panama City from May 18th, 2020, to November 19th, 2021. A total of 1,526 patients were identified to be SARS-CoV-2 positive through RT-PCR presenting the following characteristics: mean age 54.86 ± 16.60; 61.2% males, 81.4% Panamanians, and 20.2% belonging to the White race/ethnicity. In-hospital mortality was 27.4%. All patients were classified as mild [338(22.2%)], moderate [785(51.4%)], and severe [403(26.4%)] cases, and 331 (21.7%) received invasive ventilation. Hypertension [627(41.1%)] and Diabetes mellitus [425(27.9%)] were the most frequent comorbidities. Laboratory indicators, such as CRP and AST were significantly higher in cases with fatal outcomes. The most frequent acute complications were pneumonia [1,264(82.8%)], acute respiratory distress syndrome [541(35.5%)], and cardiovascular disease [46(3.0%)]. Older age was the risk factor most strongly associated with a fatal outcome (e.g. Age of >75 years vs 18-45 years: odds ratio [OR], 25.7; 95 CI, 13.3, 51.2), followed by exposure to invasive ventilation ([OR] 17.3; 95 CI, 10.8, 28.2), presenting septic shock as an acute complication ([OR] 11.8; 95 CI, 3.55, 47.1) and presenting comorbidities, such as Chronic Kidney Disease ([OR] 5.65; CI, 2.22, 15.1), or HIV ([OR] 3.84; 95 CI, 1.61, 8.92). Additionally, being of Non-white race/ethnicity was a risk factor for death: Mestizo ([OR] 2.02; 1.11, 3.71), Trigueño ([OR] 1.93; 1.16, 3.23). Medical management with non-steroidal anti-inflammatory drugs (OR, 0.67; 95% CI, 0.45, 0.99) was associated with a decreased probability of death. Further collaborative studies are needed to validate our findings with similar studies in other countries of the region.

6703

PULMONARY FUNGAL INFECTIONS AND TUBERCULOSIS CO INFECTION IN YAOUNDE, CAMEROON

Claris Killa[1], Shang Judith[2], Napa Yves[1], Forsab Joseph[3], Gonsu Hortense[1]

[1]The University of Yaounde 1, Yaounde, Cameroon, [2]Centres for disease control and prevention, Atlanta, GA, United States, [3]The University of Buea, Yaounde, Cameroon

Infectious diseases of the respiratory tract are known as respiratory tract infections and are the leading cause of death among all infectious diseases. The objective of our study was to identify the association between Tuberculosis and pulmonary fungal infections in YaoundeWe carried out a transverse and descriptive study from February to June 2021, at the Jamot hospital in Yaounde. A macroscopic, microscopic, fungal culture of the sample (sputum and broncho alveolar liquid) was carried out and a germ tube test, fungal sensitivity test as well as specie identification using the ID 32 C gallery was carried out on the positive cultures as well as microscopy and loop-mediated isothermal amplification done on the samples for *Mycobacterium tuberculosis* identification. Statistical analysis was carried out using the R version 3.6.1 software. The mean was calculated with the aid of the Kruskal Wallis rank sum test. 300 patients participated in this study. They had mean age ±standard deviation of 41.59 ± 17.5 years and extremities of 1 and 91years. The male /female ratio was 2:1. Fungal infection was positive in 127 patients (42.33 %), and Tuberculosis

71 (23.7%). Fungal-TB Co-infection was 46.5%. There is a statistically significant association between Tuberculosis and pulmonary fungal infection.

6704

HOUSEHOLD CONTACT TUBERCULOSIS SCREENING EXPERIENCE AND PREDICTORS OF TUBERCULOSIS DISEASE DIAGNOSIS IN RURAL TANZANIA

Ghassan Ilaiwy[1], Saning'o Lukumay[2], Domitila Agustino[2], Paulo Mejan[2], Kusulla Simeon[2], Estomih Mduma[2], Scott K. Heysell[1], Tania A. Thomas[1]

[1]University of Virginia, Charlottesville, VA, United States, [2]Haydom Global Health Research Center, Haydom, Tanzania, United Republic of

One third of people with TB disease (PWTB) remain undiagnosed, experiencing prolonged illnesses before diagnosis. To close this gap, the World Health Organization and national guidelines recommend TB screening for all household contacts (HHCs) of index PWTB. HHC TB screening experiences vary between countries, and between rural and urban parts within the same country. Therefore, we aimed to characterize the HHC TB screening and explore predictors of TB disease diagnosis among HHCs in Rural Tanzania. We used data from a prospectively enrolled cohort of index PWTB and their HHCs in Haydom, Tanzania. We describe the testing recommended as part of HHC TB screening and use a multivariate regression model to explore predictors of TB disease diagnosis. The cohort enrolled 120 index PWTB with 398 HHCs. 261 HHCs (66%) from 85 households completed TB screening with sputum and chest x-ray recommended for 121 (46%) and 3 (1%) HHCs respectively. 18 HHCs (4.5%) were diagnosed with TB disease, 14 of them with no sputum or CXR recommended. HHCs with TB symptoms and HHCs of index PWTB with pulmonary TB or HIV were more likely to be diagnosed with TB. Only 10 HHCs completed six-months of daily isoniazid TPT out of 61 HHCs who started TPT (16.3%) and 79 HHCs who were eligible (12.7%). The recommended sputum and imaging studies to complete HHC TB screening and short TPT regimens have suboptimal penetration in this rural high-burden setting. Innovative testing and coverage modalities are needed to bridge the gap.

6705

DETERMINATION OF THE LIMIT OF DETECTION OF HETERORESISTANCE OF *MYCOBACTERIUM TUBERCULOSIS* IN TUBERCULOSIS PATIENTS BY NANOPORE SEQUENCING TECHNIQUE FROM GENOMIC DNA AND GENE REGIONS IN SPUTUM SAMPLES AND PRIMARY CULTURES COMPARED TO THE AGAR PROPORTIONS METHOD

Diego Manuel Ramos Lette, Patricia Sheen Cortavarria, Candy Leon, Mirko Zimic, Carlos Barrios, Diego taquiri, Omar Romero, Sonia Huaman

Universidad Peruana Cayetano Heredia, Lima (Lima, Perú), Peru

Heteroresistance in *Mycobacterium tuberculosis* involves the coexistence of resistant and susceptible bacterial subpopulations, potentially leading to inaccuracies in resistance profiling and the emergence of drug-resistant phenotypes. This study aims to detect heteroresistance in *M. tuberculosis* by analyzing direct sputum samples, encompassing both genomic DNA and amplicons, alongside primary cultures. We employed targeted next-generation sequencing (tNGS) and whole genome sequencing (WGS) techniques, comparing our findings against to the gold-standard agar proportion method. DNA yields from sputum varied significantly, ranging from 105 ng to 3.9 µg, underscoring the necessity for optimized DNA extraction and library preparation methodologies. DNA was extracted from saponin-treated sputum to enrich *Mycobacterium* populations, followed by cell lysis using Fastprep. The lysates underwent purification using a dual approach: a non-kit based method utilizing phenol-chloroform and AMPure beads, and a kit-based method. DNA integrity was subsequently assessed via TapeStation. Libraries for sequencing were prepared using Rapid Barcoding and Ligation kits, suitable for both genomic DNA and amplicons. Sequencing metrics will be evaluated using MinKNOW UI software.The non-kit-based extraction yielded significantly higher DNA concentrations (1.2-17 µg) compared to the kit-based method (1-6.7 µg) ($p < 0.05$), with both methods achieving high-quality DNA, as indicated by A260/A280 and A260/A230 ratios (1.7-2.21). DNA integrity index (DIN) values ranged from 1.7 to 6.7, with no significant differences between methods. Regarding DNA integrity, the kit-based method produced longer fragments (13-20 kb), as opposed to the shorter fragments (6-8.5 kb) typical of the non-kit-based method ($p < 0.05$). Nevertheless, both methods generated fragments as short as 400 bp, characteristic of degraded sputum samples. Based on these outcomes, we recommend the non-kit-based method for applications requiring high DNA concentrations, whereas the kit-based method is preferable for obtaining longer DNA fragments.

6706

PRELIMINARY COMPARISON OF ILLUMINA MISEQ AND OXFORD NANOPORE TECHNOLOGIES MINION SEQUENCING METHODS FOR CHARACTERIZATION OF *KLEBSIELLA PNEUMONIAE* ISOLATES

Eungi Yang[1], Vasanta Chivukula[1], Will Overholt[1], Jonas Winchell[2], Maureen Diaz[2]

[1]Centers for Disease Control and Prevention/ ASRT, Atlanta, GA, United States, [2]Centers for Disease Control and Prevention, Atlanta, GA, United States

Klebsiella pneumoniae (KP) is a significant contributor to healthcare-associated infections globally and a leading gram-negative bacterial cause of invasive disease. The burden on healthcare systems may rise due to antimicrobial resistance (AMR) to third generation cephalosporins and carbapenems. Illumina whole-genome sequencing (WGS) is commonly used for KP genomic surveillance. While Illumina sequencing yields high accuracy sequences, the short reads result in fragmented genome assemblies that hinder the contextualization of AMR genes to transmissible elements. It is also costly and requires advanced laboratory infrastructure. In contrast, Oxford Nanopore Technologies (ONT) MinION is suitable for low-resource settings due to its portability and affordability. Its long-read sequences improve resolution of structural variations and generate nearly complete genome assemblies but with lower sequence accuracy. We compared the performance of Illumina and ONT WGS results to characterize key genomic features across 10 KP isolates. Illumina reads were generated with the Illumina DNA prep kit and MiSeq paired end sequencing, then assembled with SPAdes. ONT reads were generated with the Rapid Barcoding kit and R9.4.1 flow cells, basecalled using Guppy, assembled with Flye, and polished using Medaka. Sequence types (STs), K (capsular polysaccharide) and O (lipopolysaccharide) antigen loci, AMR elements, and virulence factors, were extracted using KP-specific genomic tools Kleborate. Results showed 100% concordance in STs, O antigen loci, and virulence factors between Illumina and ONT assemblies. However, discordance was observed in AMR profile of 1 of 10 (10%) isolates and K antigen loci for 3 of 10 (30%) isolates due to missing genes in ONT assemblies. In conclusion, preliminary results suggest that ONT still struggles with base-call errors, potentially affecting the identification of clinically significant features, notably K typing, critical for genomic surveillance. Nevertheless, continual improvements to its basecalling tool and analysis algorithms may enhance its utility for public health genomic surveillance.

6707

RESPIRATORY SYNCYTIAL VIRUS-INDUCED METABOLITES REGULATE MITOCHONDRIAL HETEROGENEITY THROUGH LUNG-BRAIN AXIS

Rohey Njie

Zhejiang Sci- Tech University, Zhejiang, China

Respiratory syncytial virus (RSV) infection established the involvement of metabolites in brain function. This metabolite is an important anti-

inflammatory hormone secreted through the hypothalamic-pituitary-adrenal (HPA) axis. This study is designed to make a follow up studies on our biological pathway of the lung-brain axis, where we found metabolomics and pathological changes in the lungs and brain of mice infected with RSV. The method involved are cell culture and passage (HT-22 cells), CCK-8 analysis, Cell total RNA extraction and qRT-PCR, Western blots and metabolomics analysis. RSV infection induced up-regulation of 16 metabolites in the lung was observed. Twelve up-regulated metabolites were selected their effects were observed on cell proliferation and IL-1β secretion in lipopolysaccharide (LPS)-induced neuronal injury model. The results showed that propanoic acid promoted the proliferation of LPS-treated neurons and inhibited the production of reactive oxygen species (ROS) and the secretion of IL-1β and IL-4. Spermine inhibited the proliferation of LPS-treated neurons and the secretion of IL-1β. Glutaric acid inhibited the proliferation of LPS-treated neurons and promoted the production of ROS and the secretion of IL-1β, IL-6 and IFN-γ. Moreover, propanoic acid inhibited the expression of Drp1 protein and mRNA, and promoted the expression of Mfn2 protein and mRNA. Spermine and glutaric acid promoted the expression of Drp1 mRNA and protein, and inhibited the expression of Mfn2 mRNA and protein. MDIVI-1 treatment inhibited Drp1 expression and promoted Mfn2 expression, thus reversing spermine- and glutaric acid-induced effects. **Conclusion**: This study deciphered possible mechanisms of mitochondrial dynamics imbalance in nerve cells that are driven by spermine and glutaric acid to promote mitochondrial heterogeneity in HT-22 nerve cells.

6708

IMPROVED TUBERCULOSIS DETECTION BY PARTIAL AMPLICON CAPTURE AND RECONSTRUCTION OF PLAMID DNA FRAGMENTS DEGRADED IN URINE

David Evans[1], Megan Pask[1], Jonathan Blackburn[2], Frederick Haselton[1]

[1]Vanderbilt University, Nashville, TN, United States, [2]University of Cape Town, Cape Town, South Africa

Tuberculosis (TB) diagnosis remains a significant challenge. Gold standard culture tests and other common methods such as smear microscopy or the GeneXpert® MTB/RIF PCR assay require sputum samples. However, sputum is often difficult to produce for children and individuals infected with HIV. Urine is an ideal patient sample because it is easily collected in large volumes. There are several WHO approved TB diagnostics that detect proteins in urine but suffer from poor analytical sensitivity. Prior work in the field suggests that TB cell free DNA (cfDNA) is present in urine. However, urine-based assays that target DNA are hindered by dilute concentrations and the presence of DNases that degrade cfDNA into fragments too short to detect by traditional PCR methods. We have developed a novel method to capture and detect small TB DNA fragments from 1 mL urine samples. Synthetic DNA, complementary to the TB biomarker IS6110 gene, was functionalized with dual biotin and used in urine as a fragment capture strand. The bound fragments are extracted by biotin binding to streptavidin coated magnetic beads. The capture strands subsequently act as a template for DNA polymerase to reconstruct the fragments into full length amplicons for detection by commercial PCR kits. This method was evaluated by capturing and detecting known, short synthetic DNA targets spiked into urine. However, we further developed a surrogate clinical sample by spiking a plasmid vector containing full length IS6110 into urine to degraded naturally. This test method represents what occurs in patient samples by incorporating random DNA cleavage in urine and can replicate different clinical circumstances such as the time DNA is exposed to nucleases, poor sample handling, and EDTA preservation. Using this method, we were able to detect as few as 100 copies of fragmented IS6110 DNA in pooled human urine. This method has the potential to improve the sensitivity of urine based TB diagnostics so that children and HIV positive individuals can be tested using a more easily obtained sample specimen without compromising analytical sensitivity.

6709

RISK OF SARS-COV-2 INFECTION AMONG HOSPITAL-BASED HEALTHCARE WORKERS IN THAILAND AT THE MYANMAR BORDER MARCH-JULY 2022

Narumol Sawanpanyalert[1], Nuttagarn Chuenchom[2], Meng-Yu Chen[3], Peangpim Tantilipikara[1], Suchin Chunwimaleung[4], Tussanee Nuankum[1], Yuthana Samanmit[1], Brett W Petersen[4], James D. Heffelfinger[4], Emily Bloss[4], Somsak Thamthitiwat[4], **Woradee Lurchachaiwong**[4]

[1]MoPH Thailand, Nonthaburi, Thailand, [2]Mae Sot General Hospital, Tak, Thailand, [3]Center for Vaccine Equity, Georgia, Georgia, [4]US-CDC Thailand, Nonthaburi, Thailand

The risk of Coronavirus 2019 (COVID-19) infection was investigated during the Omicron wave in 2022 among healthcare workers (HCWs) in a hospital-based setting in Thailand, near Myanmar border. Bivariate and multivariate regression analyses measured the descriptive self-reported adherence to general infection prevention and control (IPC) measures, the risk and factors associated with COVID-19 infection. Among 300 eligible HCWs, 289 (96.3%) provided written informed consent and participated in the study. The median age was 41 years (interquartile range [IQR] 28-48), and 84.1% were female. Of those, 274 HCWs participated in the daily reporting and 27 (9.9%) tested positive for SARS-CoV-2. In the bivariate analysis, nurse assistants (NAs), work locations at the inpatient department (IPD), COVID-19 ward, and acute respiratory infection clinic were associated with increased risk of infection. In the multivariable analysis, working at IPD and COVID ward assignments remained significantly associated with an increased risk of infection, with adjusted RRs of 2.37 (95% CI 1.09-5.15, *p=0.030*) and 5.97 (95% CI 1.32-26.9, *p=0.020*), respectively. NAs were associated with a 3.87 times higher risk of COVID-19 infection (95% CI 0.96-15.6, *p=0.058*), compared to individuals with job titles other than physicians, nurses, and patient caregivers. NAs found high risk of infection, likely due to their frequent and prolong contact with patients and potentially be got COVID-19 infection. It remains unclear whether COVID-19 infection among HCWs was due primarily to exposures during patient care, cross-transmission between HCWs during other activities, or widespread transmission by asymptomatic patients and HCWs. Our findings suggest that HCW's knowledge and attitudes (e.g., disagreeing that caring for COVID-19 patients is stigmatizing, fear of becoming infected), implementing effective IPC strategies, and practicing preventive behaviors are key components of prevention. The importance of prompt detection of COVID-19 and identification of gaps in IPC are an opportunity for improvement the prevention among HCWs in a hospital along the border.

6710

HEALTHCARE FACILITY-BASED INTENSIFIED TUBERCULOSIS CASE DETECTION IN ETHIOPIA: OPPORTUNITIES AND CHALLENGES

Esayas Kebede Gudina[1], Nasir Abdo[2], Demissu Fulas[3], Kolato Gemede[3], Sitota Tesfaye[3], Dereje Adugna[3], Gemeda Abebe[1]

[1]Jimma University, Jimma, Ethiopia, [2]Jimma Zone Health Department, Jimma, Ethiopia, [3]Oromia Health Bureau, Addis Ababa, Ethiopia

Ethiopia is one of tuberculosis (TB)-burden countries with an estimated incidence rate of 164 cases per 100,000 people. Limited healthcare access, low community awareness, inadequate diagnostic infrastructure, and limited screening efforts are major challenges for TB control in Ethiopia. The objective of this study was to evaluate the effectiveness and challenges of facility-based intensified TB case detection in selected health facilities in Ethiopia. The study was conducted in nine health facilities (four hospitals and five health centers) in southwest Ethiopia. Patients and their companions age 18 years and older visiting outpatient units of these facilities were assessed with cough screening tool. Participants with a cough of 14 days or longer (chronic cough) were evaluated as presumptive TB cases with TB symptom screening and sputum GeneXpert examination. Patients already on treatment as confirmed or presumptive TB cases were excluded. A total of 76,988 participants (42,047 patients and 34,941

companions) were included in the survey. Overall, 10,436 (13.6%) reported having a recent cough, of which 2,742 (3.6%) (2,216 patients and 526 companions) had a chronic cough. Among patients with chronic cough, only 1,565 (70.6%) were screened by the treating physician as presumptive TB cases. On the other hand, among the 526 companions with chronic cough, 438 (83.3%) were not willing to be evaluated as presumptive TB cases. In total, 1669 participants were tested with sputum GeneXpert, while the remaining were not tested either because they were unwilling or they had a dry cough. *Mycobacterium tuberculosis* was detected in 76 (4.6%) cases tested with GeneXpert, two of which were among companions. Facility-based TB symptom screening has the potential to improve TB case detection in Ethiopia. However, the lack of a clear strategy at healthcare facilities, along with inadequate level of awareness among patients and healthcare providers, are major hinderances. Improving the capacity of healthcare providers and enhancing health systems for TB screening are essential steps towards advancing the TB elimination agenda.

6711

PROTEOMIC ANALYSIS REVEALS MOLECULAR PATHWAYS UNDERLYING ACUTE KIDNEY INJURY IN COVID-19

Ivy Hurwitz[1], Clinton Onyango[2], Qiuying Cheng[1], Mark Unruh[1], Douglas J. Perkins[1]

[1]University of New Mexico Health Sciences Center, Albuquerque, NM, United States, [2]Maseno University, Maseno, Kenya

Acute kidney injury (AKI) is a severe complication observed in many patients hospitalized with COVID-19. To understand the molecular mechanisms driving AKI in the setting of COVID-19, proteomic analysis was performed utilizing an aptamer-based technology (SomaScan™) on plasma collected from COVID-19 patients who developed AKI (n=17, 42.5%) during hospitalization and those who did not (n=23). There were 125 differentially expressed proteins (DEPs, $P<0.05$), with 74 over-expressed and 51 under-expressed proteins in AKI. Enrichment analysis using MetaCore™ revealed significant enhancement of the Classical Complement (FDR=1.895e-9), Alternative Complement (FDR=1.895e-9), and Lectin-induced Complement (FDR=2.235e-8) Pathways in AKI. Complement system activation can occur directly due to interactions between SARS-CoV-2 and the lectin pathway, as well as through secondary mechanisms such as endothelial injury and cytokine release syndrome. This can contribute to inflammation, tissue damage, and endothelial dysfunction, potentially leading to AKI. Additionally, the dataset showed enrichment of the Blood Coagulation Pathway (FDR=2.729e-5), supporting previous associations between COVID-19 and a hypercoagulable state, which can lead to AKI by impeding renal blood flow and causing ischemia. Furthermore, dysregulation of the Angiotensin System Maturation Pathway (FDR=2.826e-7) was associated with AKI. Dysregulation of the renin-angiotensin-aldosterone system (RAAS) by angiotensin may further be exacerbated by the direct effects of SARS-CoV-2 on ACE2 receptors and secondary inflammatory responses. Overactivation of RAAS can also contribute to AKI by impairing renal perfusion and function. Overall, activation of the complement pathways, coagulation pathway, and angiotensin system in COVID-19 patients with AKI suggests a multifaceted process that involves immune-mediated inflammation, vascular dysfunction, and thrombotic complications. Understanding the molecular mechanisms is crucial for identifying therapeutic targets to mitigate AKI and improve outcomes in COVID-19 patients.

6712

ELEVATED PERIPHERAL BLOOD SARS-COV-2 VIRAL LOADS ARE ASSOCIATED WITH THE DEVELOPMENT OF ACUTE KIDNEY INJURY IN COVID-19 PATIENTS

Alexandra Do[1], Clinton Onyango[2], Shawn Fernandez[1], Mark Unruh[1], Kristan Schneider[1], Douglas J. Perkins[1], Ivy Hurwitz[3]

[1]University of New Mexico Health Sciences Center, Albuquerque, NM, United States, [2]Maseno University, Maseno, Kenya, [3]University of New Mexico Health Sciences Center, ALBUQUERQUE, NM, United States

Acute kidney disease (AKI) is prevalent among COVID-19 patients and is associated with poor clinical outcomes. We previously showed that elevated SARS-CoV-2 viral loads (VLs), particularly in peripheral blood (PB), are an important predictor of severe COVID-19. Here, we examine the relationship between SARS-CoV-2 VLs and the development of AKI in a cohort of hospitalized COVID-19 patients (n= 475) recruited between 4/2020-12/2021 at the University of New Mexico Hospital. Patient demographics, laboratory measures, comorbidities, and major clinical events were collected throughout hospitalization. To ascertain if patients developed AKI, baseline serum creatinine was retrospectively adjusted to the median serum creatinine level. A ratio of >1.5 from peak creatinine to baseline was classified as AKI. SARS-CoV-2 VL dynamics were investigated in the upper respiratory tract (URT) and PB on days 0-3, 6, 9, and 14 by RT-qPCR using the CDC-recommended panel of N1 and RNase P primers and probes. The incidence rate of AKI in the cohort was 29.3% (n=139) with 82.7% (n=115) of these individuals admitted to the ICU and/or died during hospitalization. AKI was more prevalent in patients who were male ($P=0.002$), between 45-64 years ($P=0.037$) and had hypertension ($P=0.032$). Patients who developed AKI had significantly higher URT and PB VLs on the initial sampling days and cumulatively across two weeks. Logistic regression modeling revealed that being male [Odds Ratio (OR)=1.776, $P=0.09$] and higher PB mean VL (OR=1.255 $P=8.10\times10^{-4}$) were predictors of AKI. Mortality across hospitalization was associated with having AKI (OR=6.66, $P=3.02\times10^{-10}$), being male (OR=2.260, $P=0.011$), infected with the Delta variant (OR=0.475, $P=0.038$), higher URT mean VL (OR=1.186, $P=0.005$), and higher PB mean VL (OR=1.717, $P=5.73\times10^{-9}$). These results identify viral load, especially in peripheral blood, as an important predictor for the development of AKI and death. Therapeutic interventions that reduce SARS-CoV-2 in the bloodstream, while also not exacerbating renal impairment, could play a crucial role in improving patient outcomes.

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TRENDS IN RESPIRATORY DISEASES DEATHS BEFORE AND DURING THE COVID PANDEMIC BETWEEN 2010 AND 2021 IN KOMBEWA SUBCOUNTY OF KENYA

Doris W. Njoroge[1], Michal M. Ohaga[1], Peter M. Sifuna[1], Joseph A. Gisaina[1], Janet N. Oyieko[1], Walter 0. Otieno[1], Kirti K. Tiwari[2], Timothy E. Egbo[1], Eric C. Garges[2], Gurdeep S. Buttar[2], Hoseah M. Akala[1]

[1]KEMRI/ Walter reed army institute of research- Africa, KISUMU, Kenya, [2]Walter reed army institute of research- Africa, KISUMU, Kenya

The emergence and rapid evolution of novel infectious pathogens alongside conditions that favor transmission amid rising population, redolent of higher risk of these infection warrant intensified surveillance. This study evaluated the causes of mortality in the Kombewa sub-county, focusing on respiratory infections. The Kombewa Health Demographic Surveillance System collected data on causes of mortality among this population between 2011 and 2021. This was performed using surveys using questionnaires, structural question, and answer sessions, verbal autopsies, and a review of health records to establish causes of death in the region. Demographic information for each participant was collected, and data was archived in an access database and analyzed in the SPSS analysis tool V27. Of 11,209 deaths, 7477 were from known causes, while 3732 were from unknown causes. Respiratory diseases were the main known cause of death at 1351 (17.9%), followed by HIV (14.7%), malaria (10.9%), lifestyle diseases (stroke, hypertension, diabetes, and heart disease) at 775 (10.4%), diarrheal

diseases 557 (7.4%) and other varied causes at 31.4%. Their median age was 57 (interquartile range (IQR) = 27-76 years). Acute respiratory infections, including pneumonia, accounted for 59.1% of the mortality cases, followed by TB with 28.6%. The analysis showed a significant association between age and the cause of death (*p-value* =0.000), however, there was no significant variation in the cause of death between the two periods.. Despite being a malaria-endemic region, respiratory infections were the main cause of death, depicting an increased threat of this infection in the wake of emerging and reemerging respiratory disease pathogens.

6714

CHANGES IN THE RESPIRATORY PATHOGENS TREND IN SEVERE ACUTE RESPIRATORY INFECTION CASES PRE- AND POST-COVID-19 PANDEMIC IN THE KINGDOM OF JORDAN, 2018-2023

Mayar Maged Said[1], Mahmoud Gazo[2], Mohamed AlHawarate[3], Moutasium Hossinate[3], Fatima Thneibat[3], Bassem A. Hamdy[1], Omar Nowar[1], Tamer S. Said[1]

[1]US. Naval Medical Research Unit -EURAFCENT (NAMRU-EAC), Cairo, Egypt, [2]Jordanian Central Public Health Laboratories Directorate, Amman, Jordan, [3]Ministry of Health, Jordan, Amman, Jordan

Detection rates of respiratory pathogens and hospitalization due to respiratory infections were globally influenced by COVID-19 pandemic. In the kingdom of Jordan, a retrospective analysis of the severe acute respiratory surveillance (SARI) data collected from 2018 and 2023, confirmed the pandemic impact on the severe respiratory infections. SARI hospitalized cases increased significantly from 1785 cases pre-pandemic to 5353 cases during the COVID-19 pandemic, to more than 6150 cases post-pandemic. The detection rates of respiratory viruses such as influenza, respiratory syncytial virus (RSV) and rhinovirus(RV), as well as bacteria such as *Bordetella* have been influenced by the pandemic. The first COVID-19case in the kingdom of Jordan was reported in March 2020. During the first 3 months of 2020, there were regular reports of influenza A cases, but as described globally, influenza detection rates dropped to0% in the following months of 2020, until it was detected again in 2021. The percent positivity of influenza A varied: 3.9% (2018), 10% (2019), 3.3% (2020), 0.8% (2021), 4.2% (2022), and 7.7% (2023). The two lineages of influenza B, Victoria and Yamagata, were co-circulating in 2018 with percent positivity of 1.5% and 0.9%, respectively. In 2019 only B/Yamagata lineage was circulating (0.8%), while in2020 only B/Victoria lineage was circulating (1.4%). No influenza B was reported in the kingdom of Jordan in 2021, while in 2022 and 2023 only B/Yamagata lineage was detected with percent positivity of (0.3% and 2.8%, respectively). In 2018, the detection rate of RSV reached 13.6%. However, during the pandemic, RSV detection dropped to 0.5% in 2020 and 2.5% in 2021. Following the pandemic, it increased again to 10.5% in 2022. *Bordetella* cases were reported with percent positivity of 1% in 2023.Our data show that substantial variations in the detection rates of respiratory pathogens were recorded in the kingdom of Jordan between 2018 and 2023. These results highlight the dynamic impact of theCOVID-19 pandemic on respiratory health surveillance in Jordan, emphasizing the need for adaptation to changing patterns.

6715

IL-26 DIFFERENTIALLY AFFECTS THE INFLAMMATORY RESPONSE OF HUMAN MACROPHAGES TO MYCOBACTERIUM TUBERCULOSIS WHOLE CELL LYSATES

Jose Barragan[1], Diana Padilla[1], Jorge Cervantes[2]

[1]TTUHSC El Paso, El Paso, TX, United States, [2]Nova Southeastern University, Fort Lauderdale, FL, United States

IL-26, a proinflammatory cytokine with antimicrobial properties, contributes to host defense against intracellular Mycobacterium tuberculosis (Mtb) and Mycobacterium leprae, reducing bacteria viability even when they are localized inside macrophages. IL-26 can induce autophagy as well as fusion of phagosomes containing bacilli with lysosomal compartments. Interleukin-26 also activates macrophages and facilitates killing of Mtb. We aimed to evaluate the effect of monomeric and dimeric forms of IL-26 in the response of human macrophages to Mtb whole cell lysate containing proteins, lipids and carbohydrates present within the bacterial cell.Human monocytic cell line THP1 which harbor two reporter systems for NF-kB and IRF, were transformed into macrophages with phorbol myristate. Cells were then treated with monomeric and dimeric forms of human IL-26, and then stimulated with Mtb whole cell lysates from various lineages for 24 hours. We observed an increase in NF-kB activation when cells had been treated with IL-26. The effect was more evident in the response to Mtb lysates from strain CDC 1551 in cells treated with IL-26 dimer, and to lysates from HN 878 in cells treated with IL-26 monomer. No changes in IRF activation were observed after treatment with IL-26 nor stimulation with the lysates.IL-26 skews macrophage polarization towards an M1 phenotype by activating NF-κB pathway. IL-26 is a member of the IL-10 cytokine family with, and induces IL-10, an M2 polarization marker. IL-26 induces neutrophil mobilization and accumulation in the lung which is associated with granuloma disruption in active tuberculosis (TB). The lack of IRF activation, which would lead to production of Type I IFNS associated with active TB, may be due to an absence of PAMPS signaling by live mycobacteria from the phagosomal compartment. An aberrant immune response to Mtb ligands from certain lineages may be mediated by IL-26 in human macrophages.

6716

MAPPING UNDIAGNOSED TUBERCULOSIS PREVALENCE IN SUB SAHARA AFRICA: GEOSPATIAL META-ANALYSIS

Haileab Fekadu Wolde[1], Archie C A Clements[2], Temesgen Yihunie Akalu[1], Kefyalew Addis Alene[1]

[1]Curtin University, Perth, Australia, [2]Queen's University, Belfast, United Kingdom

The high burden of undiagnosed tuberculosis (TB) in the community poses a significant challenge for TB control in sub-Saharan Africa (SSA). Interest is increasing in predictive risk mapping for undiagnosed tuberculosis, particularly to scale up early diagnosis and treatment. However, broad geographical analyses are scarce in SSA. We aimed to predict the spatial distribution of undiagnosed TB, including the number of infected people, across SSA. We systematically searched PubMed, CINHAL, Scopus, and PROQUEST from inception to February 20, 2024, for community-based surveys on TB. We extracted data on the prevalence of undiagnosed TB from the surveys and geospatial covariates were obtained from publicly available sources. Bayesian geostatistical model was used to align the data in space and estimate the spatial variation of undiagnosed TB at regional, national, and sub-national levels. Within a Bayesian framework, a logistic regression model was fitted using both fixed covariate effects and spatial random effects to identify drivers of spatial distribution of undiagnosed TB. We identified 66 studies that referenced 233 unique geographical locations from 17 countries. The geospatial analysis showed the mean prevalence of undiagnosed TB ranged from 0.91% in Rwanda to 2.5% in South Africa. It is also estimated there were 0.72 (95% CrI: 0.58 to 1.42) million undetected TB cases in the 17 countries. Substantial national, regional, and local-level variations in the prevalence of undiagnosed TB were also observed. Population density (β: -0.068, 95% CrI: -0.129 to -0.066) was negatively associated with the spatial distribution of undiagnosed TB, while the distance to the nearest health facility (β: 0.332, 95% CrI: 0.273 to 0.482) showed positive association. These findings imply that implementing targeted interventions, such as active case-finding and improving access to health facilities in the identified high-risk areas, could alleviate the burden of undiagnosed TB in SSA. However, additional data collection is necessary to draw further conclusions regarding the prevalence in countries where data is lacking.

6717

DEVELOPMENT OF A NOVEL CELL-FREE CULTURE SYSTEM FOR *IN VITRO* SCREENING OF NEW ANTI-SCHISTOSOMAL MOLECULES USING PURE AND HYBRID *SCHISTOSOMA HAEMATOBIUM*

Koba Privat AGNIWO[1], Ulrich Fabien Prodjinotho[2], Bakary Sidibé[1], Rabiatou Diarra[1], Abdoulaye Dabo[1], Clarissa Prazeres da Costa[3], Niaré Safiatou Doumbo Niare[1], Laurent Dembele[1]

[1]University of Sciences, Techniques and Technologies of Bamako (USTTB), Bamako, Mali, [2]Institute for Medical Microbiology, Immunology and Hygiene, Technische Universitât Mûnchen, Munich, Germany, Munich, Germany, [3]Institute for Medical Microbiology, Immunology and Hygiene, Technische Universitât Mûnchen, Munich, Germany, Bamako, Germany

Schistosomiasis is a worldwide parasitic disease, with 90% of infections occurring in sub-Saharan Africa. The currently available and effective preventive chemotherapy is praziquantel (PZQ). Despite efforts to control and eliminate the disease, it persists in certain regions, particularly in West Africa. The aim of the present work is i) identify the genetic profile of cercariae emitted by snails collected in the Kayes region of Mali; ii) optimize the transformation of *Schistosoma haematobium* cercariae into newly transformed schistosomules (NTS) and into pulmonary, early and late hepatic and adult stages in long-term in vitro culture; iii) evaluate the efficacy of the schistosomicidal activities of two medicinal plants (*Euphorbia hirta and Tamarindus indica*) on *S. haematobium* and its hybrids. Cercaria were obtained by exposing infested snails collected in the Kayes region to sunlight. PCR was used to determine the species (pure or hybrid) of cercariae. The extracts (*Euphorbia hirta and Tamarindus Indica*) were screened before testing their anti-schistosomal activities on NTS previously cultured on: Dulbecco's Modified Eagle Medium (DMEM) and Roswell Park Memorial Institute medium (RPMI). To these media, we added 20% human serum to test the most appropriate conditions for NTS culture. Molecular identification showed that cultivated cercariae were pure *S. curassoni* and hybrids (*S. curassoni x S. haematobium*). We succeeded in transforming 90% of the NTS (45 NTS/50 cercariae). Cultivation of pure and hybrid parasites revealed that parasites develop respectively into adult worms on complete RPMI medium with 20% human serum, and into early liver stages (LiS) on DMEM medium with 20% human serum after 14 days of cultivation. Screening of both plants showed their richness in secondary metabolites, with higher yields for aqueous extracts. Both extracts at a concentration of 500 µg/mL killed NTS at 72 hours post-exposure as also observed for the reference PZQ control.

6718

IDENTIFYING PLATFORMS FOR OPTIMAL DELIVERY OF A NOVEL PEDIATRIC PRAZIQUANTEL FORMULATION FOR SCHISTOSOMIASIS TREATMENT IN HARD-TO-REACH AREAS AND POPULATIONS IN KENYA - WHAT ARE THE KEY CONTEXTUAL FACTORS?

Phyllis Munyiva Isaiah[1], Doris Osei Afriyie[1], Mary Maghanga[2], Donna Obare Ogeto[3], Mary Amuyunzu Nyamongo[2], Peter Steinmann[1]

[1]Swiss Tropical and Public Health Institute, Allschwil, Switzerland, [2]African Institute for Health and Development, Nairobi, Kenya, [3]Ministry of Health, Nairobi, Kenya

A new formulation of praziquantel, arpraziquantel (arPZQ), has been developed for preschool-aged children (PSAC) to fill the treatment gap for this age group in schistosomiasis control and elimination programs. There is now a priority to ensure that the drug reaches all at-risk PSAC in endemic areas, including hard-to-reach areas and populations. This study aimed to determine schistosomiasis treatment-related contextual factors among fishing communities and island populations in the Lake Victoria region (Homa Bay County) in Kenya, and to identify a suitable platform to deliver arPZQ. We conducted a qualitative study using unstructured observations, two case study interviews with parents/caregivers living with disability caring for children ≤5 years,18 focus group discussions (FGDs) with parents/caregivers of children ≤5 years (each with 8-10 participants), and 14 key informant interviews (KIIs) with various government agencies. The data were analyzed using thematic analysis. The results revealed awareness of schistosomiasis among community members but limited knowledge of transmission risk factors. Lake water and open defecation were the main predisposing factors to infection. We observed poor health-seeking behavior in the community due to inaccessibility of quality healthcare services, resulting from health system level, population level, and geographic barriers. Despite these barriers, community members reported positive experiences with previous PZQ mass drug administration (MDAs) and other innovative healthcare programs, and expressed willingness to participate in future MDAs, including with arPZQ. Door-to-door distribution approach by community health volunteers was proposed by parents and key informants as the most feasible platform for community sensitization, mobilization, and arPZQ delivery. To achieve high arPZQ treatment coverage for all at-risk PSAC, and promote ownership and sustainability of the program, the door-to-door approach is the most promising platform to deliver treatment and public health promotion in marginalized hard-to-reach settings in the Lake Victoria Region of Kenya.

6719

LIVER ULTRASOUND FINDINGS BEFORE AND AFTER PRAZIQUANTEL TREATMENT IN UGANDAN PRESCHOOL AGE CHILDREN FROM THE PRAZIQUANTEL IN PRESCHOOLERS (PIP) TRIAL

Sophie Pach[1], Emily Webb[1], Andrew Edielu[1], Roy Nagawa[2], Victor Anguajibi[3], Simon Mpooya[4], Hannah Wu[5], Susannah Colt[5], Patrice Mawa[1], Joachim Richter[6], Jennifer Friedman[5], Amaya L. Bustinduy[1]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]J B International Medical Centre, Kampala, Uganda, [3]China-Uganda Friendship Hospital, Kampala, Uganda, [4]Suubi Medical Centre, Kayunga, Uganda, [5]Center for International Health Research, Brown University, Providence, RI, United States, [6]Germany and Swiss Tropical and Public Health Institute, Basel, Switzerland

Periportal fibrosis is a recognised late-stage manifestation of chronic infection with *Schistosoma mansoni.* Ultrasound changes consistent with schistosomiasis-related morbidity are frequently shown in school age children in endemic areas, with evidence of partial reversibility when treated with Praziquantel (PZQ), the only drug available for the treatment of schistosomiasis. Little is known about the prevalence of periportal fibrosis in preschool age children (PSAC) in endemic areas, or reversibility of ultrasound changes with PZQ treatment. As part of a phase II clinical trial comparing different dosing regimens of PZQ in children age 12-47 months infected with *S. mansoni* in Lake Albert, Uganda ("praziquantel in preschoolers" (PIP) trial), we present results assessing liver ultrasound (US) findings at baseline and at 12 months. Standard ultrasound measures were recorded as per the WHO Niamey Protocol. Children participating in the trial were randomised to receive either (1) 40 mg/kg PZQ at baseline and placebo at 6 months, (2) 40 mg/kg PZQ at baseline and 40 mg/kg PZQ at 6 months, (3) 80 mg/kg PZQ at baseline and placebo at 6 months, or (4) 80 mg/kg PZQ at baseline and 80 mg/kg PZQ at 6 months. Of 283 PSAC seen at both baseline and 12 months, 25 (8.8%) had Image Pattern B with a 'starry sky' appearance at baseline, reducing to 12 (4.2%) at 12 months (p=0.01). 5/283 (1.8%) children had established fibrosis (Image Pattern C) at baseline, and 1/283 (0.3%) had this appearance at 12 months (p=0.22). At baseline 114/283 (40.2%) of PSAC had evidence of periportal thickening as evidenced by abnormally thickened second order portal branches. This reduced significantly to 42/283 (14.8%) at 12 months (p=0.001). Cross-sectional regression analysis of ultrasound results at 12 months showed no significant difference across treatment groups. Incipient schistosomiasis related liver morbidity was detected in the preschool age population enrolled in the PIP trial. There was evidence of susbtantial reversibility of these changes with early praziquantel treatment, with no significant difference based on treatment dose or frequency.

6720

THE IMPACT OF A NEW RAPID DIAGNOSTIC TEST FOR SCHOOL-BASED PREVALENCE MAPPING AND MONITORING AND EVALUATION OF SCHISTOSOMIASIS: A MODELLING STUDY

Joshua M. Chevalier[1], Kyra H. Grantz[2], Sarah Girdwood[2], Thierry Ramos[2], Brooke E. Nichols[2], Shaukat Khan[2], Sarah Hingel[2]
[1]Amsterdam Institute for Global Health and Development, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands, [2]FIND, Geneva, Switzerland

In endemic communities where the prevalence of Schistosoma species infection is ≥ 10%, the World Health Organization (WHO) recommends mass drug administration (MDA) with praziquantel. WHO sampling determines infection prevalence through district-level surveys in school-aged-children (SAC). Recently, the Schistosomiasis Oversampling Study (SOS) has advocated for precision mapping—a two-phase sampling strategy—that would target treatment to the sub-district level. A novel circulating anodic antigen rapid diagnostic test (CAA-RDT) could replace the standard tools for mapping (Kato-Katz and urine-filtration microscopy) to better support precision-mapping and thus more efficient drug distribution. We modeled the ability of a CAA-RDT to correctly classify sub-districts with prevalence above or below 10%, and the associated survey costs, across a range of test sensitivities (60-100%) and specificities (95-100%), district prevalence distributions, and sampling strategies (WHO, SOS) for schistosomiasis mapping or monitoring and evaluation (M&E). We then compared these outcomes to those of Kato-Katz and urine-filtration. High specificity was a key determinant of CAA-RDT performance—with a 97% specificity correctly classifying at least 80% of sub-districts across prevalence settings. A test with 100% specificity and 85% sensitivity correctly classified the most sub-districts (87%) through the SOS sampling strategy. The estimated CAA-RDT cost/SAC was always less than Kato-Katz for prevalence mapping under both sampling strategies—$13.23 (WHO) and $24.98 (SOS phase 1 and 2) for Kato-Katz, versus $12.14 and $19.94 for the CAA-RDT. The cost savings are even greater in settings with both *S. mansoni* and *S. haematobium*, which require Kato-Katz and urine filtration, or for M&E which requires two days of sampling for microscopy. The CAA-RDT could be a valuable diagnostic tool for determining schistosomiasis prevalence and supporting M&E to achieve the WHO target to eliminate schistosomiasis as a public health problem in 78 countries by 2030.

6721

ASSESSMENT OF ALBENDAZOLE SUSCEPTIBILITY IN *FASCIOLA HEPATICA* EGGS FROM ENDEMIC REGIONS OF THE PERUVIAN HIGHLANDS

César A. Murga-Moreno[1], Dayana M. Terrones-Cerna[1], David Ruiz-Pérez[1], Luis I. Alvarez[2], Laura Ceballos[2], Miguel M. Cabada[3], Martha V. Fernandez-Baca[4], César E. Vila-Anticona[5], Ana M. Fernández-Sánchez[1], Rodrigo A. Ore[4], Cristian Hobán[1], Pedro Ortiz[1]
[1]Universidad Nacional de Cajamarca, Cajamarca, Peru, [2]Universidad Nacional del Centro de la Provincia de Buenos Aires, Tandil, Argentina, [3]University of Texas Medical Branch, Galveston, TX, United States, [4]Universidad Peruana Cayetano Heredia, Cusco, Peru, [5]Servicio Nacional de Sanidad Agraria, Junín, Peru

Triclabendazole is the main chemotherapy for the control of fascioliasis around the world. However, albendazole (ABZ) is also indicated for *Fasciola hepatica* infections older than twelve weeks. The frequent use of ABZ has led to increasing resistance in Latin America. The present work describes the susceptibility to ABZ in *F. hepatica* from three endemic regions of the Peruvian highlands, assessed using the Eggs Development Inhibition Test. Adult *F. hepatica* were collected from five naturally infected cattle in each of the main abattoirs from Cajamarca, Junín, and Cusco in Peru. The parasites were maintained for one hour in RPMI medium at 37 °C to allow them to oviposit. Aliquots were pooled for each study area constituting a final concentration of 200 eggs/mL with five repetitions per treatment group. Eggs were incubated in darkness at 25 °C for 12 h with ABZ at 0.5 nmol/mL. Untreated eggs served as controls and were incubated with methanol (1%) under the same conditions. All eggs were then carefully washed to facilitate drug removal and kept in the dark at 25 °C for 15 days. After this period, the eggs were exposed to artificial light (1000 lm) to stimulate hatching of the miracidia. The proportions of hatched/developed and undeveloped eggs were evaluated using an optical microscope. For each repetition, between 100-150 eggs were observed and the ovicidal activity was expressed as a percentage. Data are shown as the mean of five repetitions. The unexposed control egg groups had a mean development rate ≥70%. In the Cajamarca collection the ovicidal activity of ABZ was 79.4%, in Junín 97.5% and in Cusco 97.0%. In conclusion, the susceptibility of eggs exposed to ABZ suggests this drug may be an alternative for the treatment of adult *F. hepatica*.

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SYNTHESIS AND ANTISCHISTOSOMAL STRUCTURE-ACTIVITY RELATIONSHIP PROFILING OF *N*-PYRIDAZIN-3-YLBENZAMIDES

Harrison Banda, Peter Cheuka, Evelyn Funjika
University of Zambia, Lusaka, Zambia

Schistosomiasis is a neglected tropical disease and the second most fatal tropical disease after malaria. By 2021, there were 240 million cases worldwide with 700 million people at risk and 280,000 deaths per annum. *Schistosoma mansoni* and *S. haematobium* species are endemic in Zambia. The drug exclusively remains praziquantel (PZQ), which has been used for over 40 years. This study was based on the structure-activity relationship (SAR) exploration results on Medicines for Malaria Venture's MMV687807 and subsequent SAR explorations e.g. MK1-11. The study introduced an *N*-pyridazin-3-yl heterocyclic ring in lieu of the *N*-phenyl carbocyclic ring thereby editing the *N*-phenylbenzamide (*N*-PhBA) scaffold of MMV687807, MK1-11, etc to the *N*-pyridazin-3-ylbenzamides (*N*-PdzBAs) seeing that *N*-PhBA hits were experimentally found poorly soluble. Six target compounds were successfully synthesized by carbodiimide-mediated amide coupling to the required purity i.e. ≥ 95% cut-off. LC-MS was used as the ultimate criterion of purity and to profile retention time (t_R) while UV-VIS, IR, ^{1}H and ^{13}C-NMR spectroscopy were used for characterization. Compared to the *N*-PhBA hits, *N*-PdzBAs showed much lower potency on *S. mansoni* adult worms and newly transformed schistosomula (NTS) but favourably lower cytotoxicity, better solubility and hydrophilicity. One candidate at 100 µg/mL even at highest dosage only showed 48.33% dead in 72 hrs activity on NTS which was still below the ≥ 50% activity threshold. In addition, other pharmacokinetic properties - measured by both algebraic and *in silico* methods - were found to be better compared to the *N*-PhBAs and calculated solubility (*S*) usually favourably way above the ≥ 100 µM cut-off.

6723

DETECTION OF *SCHISTOSOMA HAEMATOBIUM* CELL-FREE DNA IN URINE SAMPLES STORED ON FILTER PAPERS TO IMPROVE THE DIAGNOSTIC OF URINARY SCHISTOSOMIASIS

Estelle Mezajou Mewamba, Darelle Bethanie Motia, Rachel Morgane Banga Diengue, Loic Edmond Tekeu Mengoue, Rostand Joel Tatang Atiokeng, Arnol Auvaker Zebaze Tiofack, Pythagore Soubgwi Fogue, Gustave Simo
University of Dschang, Dschang, Cameroon

In area under decades of Mass drug administration of Praziquantel, the urine filtration test (UF) currently used to diagnose urinary schistosomiasis lacks sensitivity. As the disease prevalence decreases and the process of elimination is approaching, developing diagnostic tools that could be used to validate the disease elimination, to monitor and evaluate control programs, and also to ensure post-elimination monitoring is becoming essential. This study aimed to improve the diagnosis of urinary

schistosomiasis by detecting cell-free DNA in urine samples stored on filter papers. Urine samples were collected from school-aged children and UF was used to search for *Schistosoma haematobium* eggs. For this study, 119 and 54 urine samples with and without *S. haematobium eggs* were filtered and stored for up to 5 months on Whatman filter papers. DNA was extracted from these filter papers at different time points using cetyl-trimethyl-ammonium bromide (CTAB) and chelex-based method as well as DNA extraction kit. The capacity of filter papers to store *S. haematobium* DNA for several months and the performance of different DNA extraction methods were assessed by PCR. After 3 weeks, 3 and 5 months of storing urine samples on filter paper, specific DNA fragments of *S. haematobium* were amplified on all the 119 (100%) DNA extracts from urine samples found with schistosome eggs; showing that *S. haematobium* cell-free DNA stored on whatman filter paper for up to five months remain detectable with molecular tools. Out of the 54 samples negative by UF, 27 and 23 samples respectively extracted with chelex and CTAB -based method amplified after 3 months of urine storage on filter paper, thus showing the capacity of the molecular tools to detect infections missed by UF. A sensitivity of 100% was recorded for detecting *S. haematobium* DNA in urine samples stored on filter paper. The chelex DNA extraction method appeared less time consuming, cost-effective and easy to perform. It can therefore be used to extract schistosome DNA in urine samples stored on filter paper for molecular diagnostic of urinary schistosomiasis during the elimination and post elimination monitoring.

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FACTORS INFLUENCING THE RESOLUTION OF FEMALE GENITAL SCHISTOSOMIASIS: A LONGITUDINAL STUDY FROM RURAL MADAGASCAR

Valentina Marchese[1], Jean-Marc Kutz[1], Pia Rausche[1], Tahinamandranto Rasamoelina[2], Sonya Ratefiarisoa[3], Ravo Razafindrakoto[2], Myriam Lassmann[1], Fiona Franz[1], Elly Daus[1], Olivette Totofotsy[3], Alexina Olivasoa Zafinimampera[3], André Brito[1], Philipp Klein[1], Anna Jaeger[1], Rivo Solotiana Rakotomalala[3], Zoly Rakotomalala[3], Bodo Sahondra Randrianasolo[4], Irina Kislaya[1], Eva Lorenz[1], Jürgen May[1], Raphael Rakotozandrindrainy[5], Dewi Ismajani Puradiredja[1], Monika Hamp[6], Tarik Gheit[7], Rivo Andry Rakotoarivelo[8], Daniela Fusco[1]

[1]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, [2]Centre d'Infectiologie Charles Mérieux, Antananarivo, Madagascar, [3]Centre Hospitalier Universitaire Androva, Mahajanga, Madagascar, [4]Association K'OLO VANONA, Antananarivo, Madagascar, [5]University of Antananarivo, Antananarivo, Madagascar, [6]Köln-Hohenlind Hospital, Cologne, Germany, [7]International Agency for Research on Cancer, Lyon, France, [8]University of Fianarantsoa, Fianarantsoa, Madagascar

Female genital schistosomiasis (FGS) is the chronic manifestation of *Schistosoma haematobium* infection. Complications include infertility, ectopic pregnancy, and increased risk of HIV acquisition, while the association with HPV infection remains unclear. Schistosomiasis is highly endemic in Madagascar.The objective of this study is to assess the rate of resolution and the factors associated with lesion regression following treatment with praziquantel (PZQ) in women of reproductive age.Enrolment of women in this longitudinal study started in 2021 with a 4-year follow-up with scheduled visits at 12-month intervals (12 +/- 3 months). Follow up will be completed in 2024. The study is implemented at three Primary Health Care Centers (PHCCs) in the rural district of Maravoay. Women were invited to participate in FGS screening by colposcopy (CLP). Each woman screened positive for FGS is offered 40mg/kg praziquantel treatment. FGS diagnosis is confirmed through a blind assessment of CLP images by two specialists. Cervical vaginal lavages (CVLs) are collected to assess the role of sexually transmitted infections, such as HPV. Data collected at recruitment were analyzed to estimate the baseline prevalence of the disease.By February 2024, 1,073 women underwent CLP and CVLs were collected at least once. Specifically, 551 women underwent CLP once, 429 had one baseline and one follow up visit, and 93 had two follow up visits. Among 500 women enrolled in 2021, 302 had a final FGS diagnosis: FGS prevalence was 62.6% (189, 95% CI: 56.9-68.1), and 26.5% (80, 95% CI: 21.6-31.8) of women with FGS were also infected with HPV. Our preliminary data show that Madagascar has a high prevalence of FGS among women of reproductive health. The cohort established in this study will contribute to clarify the role of PZQ treatment in this complicated form of schistosomiasis, informing the clinical management of FGS and the development of targeted public health interventions.

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ACCURATE DETECTION OF FEMALE GENITAL SCHISTOSOMIASIS - A NEGLECTED GYNECOLOGICAL TROPICAL DISEASE

Nilanjan Lodh, Lilianna Buss

Marquette University, Milwaukee, WI, United States

Schistosomiasis is second to malaria as the most devastating tropical parasitic disease in the world. Two main species of Schistosomes, *Schistosoma mansoni*, and *S. haematobium* are predominantly distributed in sub-Saharan Africa, South America, East Asia, and the Middle East. 56 million women are infected with *S. haematobium*, the causative parasite of Female Genital Schistosomiasis (FGS). Schistosomes primarily affect the urinary and intestinal tract, but in FGS parasite eggs can travel and deposit on other tissues such as the female reproductive system resulting in inflammation, causing mechanical blockage, scar tissue, and destruction of anatomical structures. Three-quarters of girls and women with *S. haematobium* infection have FGS making it Africa's most common gynecologic condition. FGS is responsible for up to a three- to four-fold increase in horizontal transmission of HIV/AIDS and likely acts as a cofactor. This study aims to determine FGS infection from field-collected human urine samples from the endemic African country Tanzania via a sensitive and specific molecular approach called loop-mediated isothermal amplification (LAMP). A total of 66 filtered urine samples collected from Tanzania were evaluated via LAMP by amplifying the cell-free species-specific repeat DNA fragment and compared against the PCR amplification. All urine samples were collected after 7-8 days of praziquantel treatment. We have determined the positivity of 14 of 66 urine samples from females with an age range of 17-97 years. All 14 of the samples are LAMP positive, whereas only 4 are PCR positive. LAMP detected *S. haematobium* responsible for FGS from different age groups of females with high sensitivity and specificity. This diagnostic method can be used along with the detection of lessons as hallmark pathophysiology of FGS to develop comprehensive detection and control strategies for FGS in the future.

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DEVELOPING A SIMPLE POINT-OF-CARE LATERAL FLOW ASSAY FOR DETECTION OF *FASCIOLA HEPATICA* DNA IN CLINICAL AND ENVIRONMENTAL SAMPLES

Alejandro Castellanos-Gonzalez

University of Texas Medical Branch, Galveston, TX, United States

Fascioliasis is infection with the liver fluke *Fasciola hepatica*. Lack of data about distribution and burden of fascioliasis in endemic regions is associated with the poor performance of currently available diagnostic methods. Therefore, there is an urgent need to improve the diagnostic of Fascioliasis in endemic areas. Molecular diagnostic methods as real time PCR (RT-qPCR) can detect *Fasciola* DNA in clinical and environmental samples with a high sensitivity and specificity. However, RT-qPCR require expensive equipment, highly trained personnel, and reliable power which may be lacking in endemic locations. In these settings, the ideal diagnostic method for resource constrained areas should be accurate, low cost, portable, and easy to perform and interpret. Lateral flow assays (LFAs) are paper-based point-of-care (POC) diagnostic tools that are widely used because of their low cost, ease of use, and rapid format. We have developed the first rapid PCR-based test to detect Fh DNA in lateral flow (LF) strips. For this assay we have developed a PCR-primers that produce Fh dual-labeled PCR amplicons that can be detected in lateral flow strips. To demonstrate the feasibility to detect Fh in low resource setting, we have used a portable miniPCR equipment. We validated detection of DNA of

F. hepatica (Fh) with miniPCR in LF strips using clinical and environmental samples. Our experiments demonstrated that Fh-miniPCR-LF assay has high sensitivity and specificity (comparable to standard RTqPCR assay) and the assay can be performed in less than 1 hr. To validate the new assay, we used clinical samples obtained from an endemic area. Our results showed 100% correlation with qPCR results to distinguish positive and negative samples. In addition, in this work we described a simple and inexpensive DNA extraction method that can be used in combination with the miniPCR to detect *Fasciola* in remote areas. Therefore, our results will be useful to improve diagnosis of *Fasciola* and also to develop similar strategies for detection of other parasitic infections in remote areas.

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ENHANCING DETECTION AND MONITORING OF SCHISTOSOMIASIS USING FLOW, A URINE-BASED ANALYTE PRE-CONCENTRATION TECHNOLOGY

Brianna Mullins[1], Cody Carrell[1], Danielle de Jong[2], Jane K. Maganga[3], Loyce Mhango[3], Peter Shigella[3], Philbert Kashangaki[3], Raymond Kirigiti[4], Madalyn Gill[1], Ryan Shogren[1], John M. Changalucha[3], Govert J. van Dam[2], Jennifer A. Downs[5], Paul L.A.M Corstjens[2], Jay W. Warrick[1]

[1]Salus Discovery, Madison, WI, United States, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Mwanza Intervention Trials Unit/National Institute for Medical Research, Mwanza, Tanzania, United Republic of, [4]Nkoma Health Center, Simiyu Region, Tanzania, United Republic of, [5](i) Center for Global Health, Department of Medicine, Weill Cornell Medicine (New York); (ii) Department of Medicine, Weill Bugando School of Medicine (Mwanza); (iii) Mwanza Intervention Trials Unit/National Institute for Medical Research (Mwanza), New York, NY, United States

Diagnosis of schistosome infection at the point-of-care using a parasite antigen would improve sensitivity of current testing methods, which use urine and stool microscopy, to both increase access to testing and further efforts toward elimination of schistosomiasis. Salus Discovery has developed a new technology, termed Flow, that expands upon the operational concepts of lateral flow assays (LFAs) by enabling pre-concentration of analytes from 20 mL of urine into 100 µL (i.e., up to 200-fold pre-concentration) prior to detection on an LFA. Importantly, Flow can be performed by minimally trained field workers as it requires < 1 min of hands-on time, no pipetting or centrifugation, and can be either read visually or scanned by a portable reader. One schistosome target of interest, the circulating anodic antigen (CAA), is detectable in serum and urine for all major human schistosome species but testing for it still requires time-consuming and resource-intensive sample preparation and/or pre-concentration so is currently limited to being performed in a laboratory. Our team has recently sought to adapt our Flow technology for POC diagnosis of schistosomiasis using CAA quantified in bio-banked urine samples collected from 30 individuals in an *Schistosoma haematobium* endemic region in north-western Tanzania. Results from this recently published limited clinical study with a prototype (i.e., non-optimized) Flow device indicate that the assay will achieve sensitivity and specificity as targeted in the WHO target product profile (TPP). We've since optimized the Flow device and are currently evaluating its performance using fresh urine samples collected from over 100 individuals in the same *S. haematobium*-endemic region in Tanzania. Participant positivity is determined by quantitative laboratory-based serum and urine CAA testing and results are being compared to urine egg counts. We expect to complete all field testing by June 2024 and will be able to present the results for the performance of the optimized Flow device at the ASTMH conference in November 2024.

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RISK FACTORS FOR SCHISTOSOMIASIS CURE FAILURE/ REINFECTION AMONG PRE-SCHOOL-AGED CHILDREN 12 MONTHS AFTER TREATMENT IN UGANDA

Racheal Nakyesige

MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda

Schistosomiasis is caused by blood flukes called Schistosoma and poses significant health risks, especially for young children. Transmission occurs via contact with contaminated fresh water. Praziquantel (PZQ) is an effective treatment, but in highly endemic regions like the Lake Albert region of Uganda, both cure failure and reinfection following PZQ are common. There are limited data on PZQ cure failure/reinfection rates among preschool-aged children (PSAC). Various factors such as genetics, environment, water contact frequency, and socio-economic conditions may contribute to cure failure/reinfection. A secondary analysis of the Praziquantel in Pre-Schoolers (PIP) trial data was conducted, involving children aged 12-47 months positive for S. mansoni at baseline. Schistosomiasis infection was assessed via stool Kato-Katz (KK) microscopy at baseline, Week 4 and 12 months post-PZQ. Children received either 40 mg/kg or 80 mg/kg PZQ at baseline and received either a repeat dose or placebo after 6 months. Cure failure/reinfection was determined by the proportion of children positive by KK 12 months post-baseline treatment. After adjusting for treatment arm, logistic regression showed that odds of cure failure/reinfection was higher among children aged 2.1-3 (OR=2.8, CI 1.45, 5.55 p=0.002) and >3years(OR=3.1 CI1.6,5.73 p=0.001) and with more frequent visits to Lake Albert (OR= 3.3 CI 1.89, 5.9 p=<0.001). Those with better educated parents had lower odds of cure failure/reinfection at 12 months (OR=0.37, CI 0.23, 0.56 p=<0.001). Malaria or HIV co-infection, anemia, feeding practices, and latrine type showed no significant relationship with cure failure/reinfection risk. As PSAC grow, contact with contaminated water sources increases, emphasizing the importance of clean water and latrine access to reduce reinfection risk. Targeted interventions are crucial for schistosomiasis control in PSAC. Findings for how Treatment impacts reinfection risk by 12 months post PZQ will be published separately.

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INVESTIGATING THE PREVALENCE, INTENSITY, AND CONTRIBUTING FACTORS OF *SCHISTOSOMA MANSONI* INFECTION IN ALMATA DISTRICT, TIGRAY, NORTHERN ETHIOPIA

Gessessew Bugssa Hailu[1], Nega Berhe Belay[2], Prof. Tilahun Tekelehaymanot[2]

[1]Department of Medical Parasitology and Entomology, Biomedical Sciences Division, College of Health Sciences, Mekelle University, Mekelle, Ethiopia, [2]Aklilu Lemma Institute of Pathobiology, Addis Ababa University, Addis Ababa, Ethiopia

Intestinal schsitosomiasis caused by *Schistosoma mansoni* continues to be a significant public health problem in Ethiopia. Hence, this study aimed to investigate the prevalence, intensity and contributing factors of *S.mansoni* infection in Almata district, Tigrai, Northern Ethiopia. A community based cross sectional study design was employed and 1762 participants were enrolled from five clusters in Alama district. Questionnaire was used to assess socio-demographic and other risk factors. Stool sample was collected and examined using Katho katz technique to investigate eggs of *S.mansoni* and determine intensity of infection. The data were analyzed using SPSS version 25. The survey included 941 (53.4%) females and 821 (46.6%) males. Participants' ages varied from 5-80 years, with a median age of 25 years (IQR=27). In this study, the overall prevalence of S.*mansoni* among study participants was 379 (21.5%) and males were predominantly infected, 204 (11.6%), than their female counter parts with statistically significant difference (χ^2= 10.146, P-value=0.001). The proportion of infection was higher among participants lying in the age groups 10-14 and 20-29 years accounting for 7.4% and 3.3% of the infection, respectively. The mean egg count among the infected study participants was 146.82 eggs per gram of feces (epg) + (243.17 SD), and majority 249 (65.7%) had

light (1-99 epg) followed by 106 (28.0%) moderate (100-499 epg) infection. The overall intensity of *S.mansoni* infection was higher among males (180 EPG) than females (108.2 EPG). Factors such as being in Waja cluster (AOR:8.9; 95% CI, 3.5-23.2; P< 0.001); lying in the age groups 10-14 (AOR:6.0, 95% CI: 3.1-11.7, P<0.001), 15-19 (AOR:5.8, 95% CI:2.8-12.2, P<0.001), and 20-29 (AOR:3.5, 95% CI:1.8-6.8; P<0.001) years old; having direct contact with water while crossing (AOR: 2.4, 95% CI: 1.5-3.8, P<0.001); and swimming (AOR: 1.4, 95% CI: 1.01-2.0, P=0.035) were shown to be significantly associated with *S.mansoni* infection. This study indicated that there is a notable burden of the disease in the area and implementing public health interventions are recommended.

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NOVEL INTERVENTION STRATEGIES FOR SCHISTOSOMIASIS ELIMINATION

Lydia Trippler[1], Said Mohammed Ali[2], Naomi Chi Ndum[1], Jan Hattendorf[1], Saleh Juma[3], Shaali Makame Ame[4], Fatma Kabole[4], **Stefanie Knopp**[1]

[1]Swiss Tropical and Public Health Institute, Allschwil, Switzerland, [2]Public Health Laboratory - Ivo de Carneri, Pemba, Tanzania, United Republic of, [3]Zanzibar Ministry of Health, Pemba, Tanzania, United Republic of, [4]Zanzibar Ministry of Health, Unguja, Tanzania, United Republic of

Elimination of schistosomiasis as a public health problem by 2030 is a declared goal of the WHO. Pemba Island, Tanzania, achieved this goal in 2017 and now proceeds towards transmission interruption. The existing spatial heterogeneity of *Schistosoma haematobium* infections calls for targeted interventions. In the SchistoBreak project, implemented from 2020-2024, new adaptive intervention approaches were investigated for their contribution to elimination. In low prevalence areas, a new schistosomiasis surveillance-response approach, including test-treat-track-test-treat (5T) and snail control activities, was assessed for its sensitivity and potential to prevent recrudescence. In hotspot areas, the impact of a multidisciplinary intervention package, consisting of mass drug administration, behavior change communication, and snail control measures was investigated. Annual school- and household-based cross-sectional surveys were conducted to monitor *S. haematobium* prevalence and infection intensities, schistosomiasis-related knowledge, attitudes and practices, and economic status. Each year, more than 6000 individuals were surveyed. The 5T strategy was very useful to identify and treat infected individuals. Across the 3 years of implementation, the surveillance-response approach showed a sensitivity of 43% and the low prevalence levels were mostly maintained. In hotspots, prevalences were significantly reduced in schoolchildren and showed a decreasing trend in the community in Year 1 and 3, but slightly increased in Year 2. Hotspot areas were hallmarked by a large number of poor and rural households, and waterbodies containing *Bulinus*. Behavior change communication significantly improved knowledge and attitude scores of exposed schoolchildren. The overall prevalence remained ~1% across all years, with heavy intensities ≤0.3%. The novel adaptive intervention approaches did not result in interruption of transmission within 3 years. Yet, important insights and evidence were generated that can inform control program decisions and the development of schistosomiasis elimination guidelines.

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SOCIO-ENVIRONMENTAL FACTORS AFFECTING THE RISK OF HUMAN FASCIOLIASIS IN CENTRAL VIETNAM

Yi-Chen Wang[1], Thi Lien Hanh Nguyen[2], Hong Quang Huynh[2], Yiding Ran[1]

[1]National University of Singapore, Singapore, Singapore, [2]Institute of Malariology, Parasitology and Entomology Quy Nhon, Quy Nhon, Vietnam

Fascioliasis, infected by consuming contaminated vegetables and water with *Fasciola* parasites, has caused public health concerns in Central Vietnam, which accounts for 93% of the national prevalence of the disease. Scant attention, however, has been paid to the influences of socio-environmental factors on the infection risk. To bridge the research gap, a cross-sectional survey was conducted in 2023, involving 2,500 participants from 10 communes in four Central Vietnam provinces for ELISA-based blood test for infection status. A subset of these participants was also invited for questionnaire surveys to understand their knowledge about fascioliasis, eating and living habits, and practice to prevent the infection. Household locations were collected using smart phones with Global Positioning Systems capabilities to analyze possible environmental influences of land uses, derived from the Sentinel-2 remote sensing products, on infection risk. The results showed that the associated social risk factors were gender as female (OR=2.395, 95% CI: 1.78-3.22), occupation as farmer (OR=7.57, 95% CI: 2.24-25.59), eating raw vegetable (OR=1.80, 95% CI: 1.20-2.69), and drinking unboiled water (OR=2.935, 95% CI: 2.19-3.93). Importantly, participants with higher knowledge scores did not effectively implement preventive practices. Geospatial analysis of environmental factors showed that individuals' homes surrounded by forest might be less susceptible to infection. Nevertheless, association with water was not consistent across all areas, with some closer to waterbodies more likely to be infected. This study underscores the need for tailored intervention measures that consider specific socio-environmental characteristics of each area, to develop effective risk mitigation plans for foodborne trematode infection.

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DIET OF SCHISTOSOME VECTORS INFLUENCES INFECTION OUTCOMES

Joshua T. Trapp[1], Wesley Yu[1], Johannie Spaan[1], Tom Pennance[1], Fredrick Rawago[2], George Ogara[2], Maurice Odiere[2], Michelle Steinauer[1]

[1]Western University of Health Sciences, Department of Basic Medical Sciences, Lebanon, OR, United States, [2]Kenya Medical Research Institute, Centre for Global Health Research, Kisumu, Kenya

Schistosome parasites cause chronic infections in their vector hosts, freshwater snails, and continually produce infectious cercariae throughout the snail's life. The resource-intensive nature of this relationship suggests that snail diet could greatly impact the disease dynamics of the system. Enhanced nutrition could favor snail immunity, or could favor establishment and reproduction of the parasite. Our study aimed to determine the effect of diet on: (1) snail susceptibility to infection and (2) cercaria production. We fed *Biomphalaria sudanica* snails either a strict lettuce (low nutrient) or pellet (high nutrient) diet for two generations before exposing them to *Schistosoma mansoni*. We used two parasite strains, one that is incompatible and another that is compatible with the snails. When exposed to incompatible parasites, diet did not affect snail susceptibility, as few snails were infected overall. When challenged with the compatible parasites, snails fed the high nutrient diet were more susceptible to infection than their low nutrient fed counterparts. The high nutrient fed snails also produced more cercariae than low nutrient fed snails, but this advantage was lost after the initial assessment at 8 weeks. To determine how diet effects cercariae production post-infection, infected snails were either kept on their initial diet or switched to the other diet. This experiment showed that snails switched from a low to high nutrient diet produced more cercariae than those remaining on the low nutrient diet and similar numbers to those remaining on the high nutrient diet. Unexpectedly, the high to low nutrient group initially produced more cercariae relative to controls, but the pattern reversed after initial assessment. This study showed that resources can impact the susceptibility of the vector snail and the reproductive capacity of intramolluscan schistosomes, with higher nutrients favoring parasite establishment and reproduction, highlighting the plasticity of susceptibility phenotypes. This data can aid predictions of how future environmental changes and resource availability may impact schistosomiasis transmission.

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FACTORS ASSOCIATED WITH NATURAL INFECTION BY *FASCIOLA HEPATICA* IN THE MAIN DAIRY BASIN OF CAJAMARCA IN NORTHERN PERU

Cristian Hoban[1], César A. Murga-Moreno[1], Dayana M. Terrones-Cerna[1], David Ruiz-Pérez[1], Ana M. Fernández-Sánchez[1], Jhover Díaz[1], Sandra Quispe[1], Miguel M. Cabada[2], **Pedro Ortiz**[1]

[1]Universidad Nacional de Cajamarca, Cajamarca, Peru, [2]University of Texas Medical Branch, Galveston, TX, United States

Cajamarca is an important region of Peru for dairy production. Dairy animals in this area are often affected by fascioliasis caused by *Fasciola hepatica*. Fascioliasis negatively affects the productivity parameters of livestock. This study aimed to estimate the prevalence of natural *F. hepatica* infection in cattle and determine animal husbandry factors associated with the infection. Fecal samples from cattle in farms in the Cajamarca Region, Peru were collected between March 2023 and March 2024. Animals were raised in extensive rearing conditions. Cattle demographics and wellbeing using a score based on body condition (5 points maximum) were evaluated. Samples were analyzed using the simple sedimentation technique for differential egg counting. 606 cattle from 97 farms were included in the study. The prevalence of *F. hepatica* infection was 27.7% ($I.C._{95\%}$ 24.1 - 31.3%) (168/606). The mean intensity of infection was 6.1 (S.D. 9.9) eggs per gram (e.p.g.) of stool and 84.5% had infection intensities ≤10 e.p.g. which are considered low. Most *F. hepatica* positive animals were female (75%), adults (51.8%), and had a wellbeing score between 2.5 and 3 points (86.3%). The most common breed was creole (41.1%). There was no statistically significant association between *Fasciola* infection status and demographic/wellbeing score characteristics. The chronic infection of cattle by *F. hepatica* at the low intensity encountered did not appear to affect the general condition of the animals or be influenced by the other variables analyzed.

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ENVIRONMENTAL DNA OF SCHISTOSOME PARASITES REVEALS POSSIBILITY OF WIDENING THE SNAIL VECTOR SPECTRUM IN ENDEMIC AREAS UNDER CLIMATE CHANGE CONDITIONS IN NIGERIA

Chiaka I. Anumudu[1], Attah A. Amos[1], Cephas A. Akpabio[1], Pearl U. Ofoegbu[2]

[1]Cellular Parsitology Programme, Department of Zoology, University of Ibadan, Ibadan, Nigeria, [2]Federal University of Technology Owerri, Owerri, Nigeria

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Climate change has a significant impact on schistosomiasis, leading to changes in cercariae shedding patterns, changes in the range of definitive hosts for schistosome species, and an increase in the number of countries at risk. Therefore, it's important to broaden the range of techniques used to find possible sites of transmission for schistosomiasis surveillance in endemic communities. This includes detecting parasite and schistosome environmental DNA (eDNA). In October and December of 2023, and February 2024 seven locations in Asamu, Ile-tun tun, Alagbon, and Eleyele in Southwest Ibadan, Oyo State, Nigeria, were sampled for schistosome snail intermediate hosts, *Bulinus* and *Biomphalaria* species. Snails were examined morphologically with a stereomicroscope and molecularly by qPCR. Water samples were also analysed by qPCR for eDNA of snail vectors *Bulinus* and B*iomphalaria*, and *Schistosoma spp*: *haematobium* and *mansoni.* Ct values were determined for each sample and the ultimate DNA quantity of the target samples ascertained. A total of 268 snails and 7 water samples were collected from the study sites. Microscopic morphological analyses revealed the presence of *Bulinus* (5) and *Biomphalaria (3)* species, with the majority being *Radix natalensis* (*Lymneae natalensis*), *Melanoides tuberculate, Indoplanorbis exustus, Physa acuta* and *Aplexia waterloti.* Standard cercarial shedding was negative. Water samples from the sites were negative for the eDNA of *Bulinus* and *Biomphalaria* species but were positive for *Schistosoma haematobium* and *S. mansoni*. The qPCR amplification success for parasites in the snail samples was 79% and 89.5%, respectively. The other snails from the sites were positive for schistosome spp. DNA, indicating the snails may be vectors. *Lymnea natalensis* from Asamu (100-120%) had the highest amount of *S. mansoni* DNA , while *Aplexa waterloti* had the highest amount of *S. haematobium* (>100%). These data correspond to similar reports from some African countries, of deviations from schistosome normal cercarial shedding pattern and snail host spectrum. Our data can be used to develop schistosomiasis monitoring in endemic areas.

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SUITABLE COMMUNICATION STRATEGIES PRIOR TO THE INTRODUCTION OF A NOVEL PEDIATRIC TREATMENT OPTION < SCHISTOSOMIASIS IN KENYA

Janet Mbinya Masaku[1], John M. Gachohi[2], Alice Sinkeet[3], Mary Maghanga[3], Florence Wakesho[4], Wyckliff Omondi[4], Jennifer Burrill[5], Ashley Preston[5], Lisa Sophie Reigl[6], Isabelle L. Lange[6], Andrea S. Winkler[6], Sammy M. Njenga[1], Mary Amuyunzu Nyamongo[3]

[1]Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [2]Jomo Kenyatta University of Agriculture and Technology (JKUAT), Nairobi, Kenya, [3]African Institute for Health and Development (AIHD), Nairobi, Kenya, [4]Ministry of Health Kenya, Division of Vector Borne Diseases and Neglected Tropical Diseases (DVBD/NTDs), Nairobi, Kenya, [5]Unlimit Health, London, United Kingdom, [6]Technical University of Munich (TUM), Munich, Germany

Approximately 50 million preschool-age children (PSAC) in Africa need treatment for schistosomiasis but are excluded due to lack of a suitable child-friendly medication. The Pediatric Praziquantel Consortium has developed arpraziquantel, a novel paediatric treatment option for PSAC. In advance of its roll-out, we conducted a social science study to inform implementation. We conducted a cross-sectional study in four villages in two purposively selected Kenyan counties: Homa Bay and Kwale. We conducted 17 in-depth interviews with community opinion leaders, 21 parents/guardians of PSAC and 28 healthcare workers. Ten focus group discussions were held with parents/guardians of PSAC and seven with community health volunteers (CHVs). The aim was to gather information on preferred sources of information about the new drug prior to pilot roll-out. Thematic data analysis was performed. Participants indicated that their traditionally prefered methods of receiving information on treatment programmes for other diseases for PSAC were CHVs, health facilities, radio, road shows and community meetings. Caregivers appreciated those platforms and stated they would, in addition, like to receive information about the PSAC schistosomiasis medication through village leaders, schools, and religious gatherings. Messages to participants during sensitization should include information on the disease effects, signs and symptoms, myths and misconceptions, how to administer the new drug, it's safety and possible side effects. Participants preferred sensitization, shortly before and during the intervention. Our results demonstrate that community members obtain health information concerning their children from multiple sources. To reach audiences with preferences for different information sources and message formulations, we recommend designing a sensitization strategy that employ a variety of channels. Emphasis on key messaging about the drug's safety is needed to build trust in advance of its roll-out

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ENDEMIC COUNTRY LABORATORY QUALIFICATION OF *SCHISTOSOMA HAEMATOBIUM* ANTIBODY BIOMARKERS IN KENYA

Maria Ulke Colman[1], Isaac Onkanga[2], Joshua Kivuthi[2], Maurice Royal[1], Yong Wang[1], Sylvia Ossai[1], Machi Shiiba[3], Kimberly M. Won[1], Maurice Odiere[2], Sukwan Handali[1], William E. Secor[1]

[1]CDC, Atlanta, GA, United States, [2]Kenya Medical Research Institute (KEMRI), Kisumu, Kenya, [3]Emory School of Public Health, Atlanta, GA, United States

In response to the World Health Organization's 2021-2030 Roadmap for Neglected Tropical Diseases emphasis on the need for improved

diagnostic tests, we explored several strategies to identify recombinant antigens suitable for *Schistosoma haematobium*-specific antibody tests. We utilized serum epitope repertoire analysis (SERA), a platform that uses a 12-amino acid peptide library display followed by next generation sequencing with proprietary informatics to screen unique reactivity to sera. We identified two candidate diagnostic peptides. One peptide mapped to *S. haematobium* saposin (SAP)-1 protein. Because the Sh_SAP1 protein sequence is short, we used the whole protein sequence without its signal peptide to express the protein. The other peptide mapped to a hypothetical protein which was not suitable for expressing as a whole protein. Instead, we created a synthetic protein consisting of four repeats of the peptide sequence (rSh_quadruplet). The rSh_SAP1 ELISA, which detects specific IgG1 antibody, had a sensitivity 85% and a specificity of 97%. The rSh_quadruplet ELISA, which detects specific IgG4 antibody, had a sensitivity of 81% and a specificity of 96%. Further evaluation of the ELISAs was done using a different sample set (50 egg positive persons and 52 controls) in Kisumu, Kenya, an endemic country laboratory. The ELISAs conducted in Kisumu mirrored the results from CDC Atlanta labs, meeting or closely approaching the sensitivity and specificity targets of the WHO schistosomiasis target product profile for interruption of transmission and surveillance. We also evaluated samples from 37 individuals at baseline, 6 months, and 12 months after praziquantel treatment using the rSh-quadruplet ELISA, anticipating IgG4 responses would be most likely to decline. Serum samples from participants who were *S. haematobium* egg positive at baseline had lower specific IgG4 antibody levels after 12 months ($p < 0.0001$), although some samples showed an increase at 6 months, followed by a decrease after 12 months. These antigens have the potential to fulfill unmet programmatic needs for schistosomiasis programs.

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ETIOLOGY OF ANEMIA IN THE CONTEXT OF *SCHISTOSOMA MANSONI* INFECTION AMONG PRE-SCHOOL AGED CHILDREN FROM LAKE ALBERT, UGANDA

Alexandra Burgess[1], **Susannah Colt**[1], Andrew Edielu[2], Hannah Wu[1], Patrice Mawa[3], Rachael Nakyesige[3], Gloria Kakoba Ayebazibwe[3], Kanika Men[1], Emily Webb[2], Amaya Bustinduy[2], Jennifer Friedman[1]

[1]Center for International Health Research, RI Hospital and Alpert Medical School of Brown University, Providence, RI, United States, [2]London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Medical Research Council-London School of Hygiene & Tropical Medicine Research Unit, Entebbe, Uganda

There is a significant global burden of disease due to anemia among young children. Among older children and adults, schistosomiasis has been shown to cause both iron deficiency anemia (IDA) and non-iron deficiency anemia (NIDA), the latter largely due to anemia of inflammation, yet this has not been studied in young children. In this study, 345 Ugandan children aged 12 to 48 months infected with egg patent *Schistosoma mansoni* were recruited from villages along Lake Albert, Uganda. Infection intensity was determined by Kato Katz quantifying egg counts per gram of stool (EPG). WHO age-adjusted cutoffs for hemoglobin (< 11 g/dL) were used to determine the presence of anemia. Among anemic children, serum ferritin levels were used to classify children as having IDA (≤ 30 ng/mL) or NIDA (> 30 ng/mL). CRP was measured as a non-specific marker of inflammation. We employed multivariate regression models to assess the relationship between S. *mansoni* infection intensity and anemia etiology. Overall, 23.5% of children had IDA and 32.5% had NIDA. Higher continuous *S. mansoni* EPG was associated with higher odds of IDA (OR 1.36, 95% CI 1.12-1.65, p=0.002) and NIDA (OR 1.23, 95% CI 1.03-1.46, p=0.019) compared to no anemia, after adjusting for age, sex, SES, and malaria. CRP was significantly higher among individuals with NIDA (5.0 mg/L) compared to both no anemia and IDA (0.7 and 1.5 mg/L respectively, $p < 0.0001$). Occult blood loss in stool was significantly more common among children with IDA compared to no anemia (42.1% v. 20.7%, p=0.003). Anemia in pre-school aged children with schistosomiasis is due to both IDA with occult blood loss and NIDA with ongoing immune activation and systemic inflammation. Despite the fact that the WHO recommends including children ages 1-4 in mass drug administration (MDA) campaigns, most are still excluded due to a) limited dissemination of this recommendation, b) lack of widely available pediatric formulation, and c) provision of school rather than community based MDA, missing pre-school aged children. Efforts should be made to better include this vulnerable age group to mitigate morbidity.

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TCBS POSITIVE VIBRIO SPECIES IN WATER SAMPLES OF PRE-URBAN AND PERI-URBAN MAPUTO, MOZAMBIQUE

Matthew Cappiello[1], Henrique Velasco[2], Inacio Mandomando[3], Sanjay Mehta[4]

[1]Loma Linda University Medical Center, Loma Linda, CA, United States, [2]Instituto Comercial de Maputo, Maputo, Mozambique, [3]Centro de Investigação em Saúde de Manhiça, Maputo, Mozambique, [4]University of California San Diego, La Jolla, CA, United States

Despite Maputo's exponential expansion in the last few decades, Mozambique's capital still experiences challenges providing clean water and stable housing to thousands of inhabitants lining its periurban neighborhoods. We performed an observational cross-sectional analysis of data from periurban residential areas of Maputo in spring 2014, prior to the implementation of the Maputo Urban Transformation Project. It was hypothesized that water samples would exhibit increased risk for bacterial contamination, including diseases with epidemic risk such as Vibrio cholerae. Water runoff samples from informal settlements (n=89) were collected in the 25 de Junho A and Inhagoia neighborhoods of Maputo, with locations informally geotagged and labeled by location type (residential runoff, agricultural runoff, piped water), point-of-care pH and oxidation reduction potential, and thiosulfate-citrate-bile salts-sucrose (TCBS) agar growth. A total of 33 samples (37%) were TCBS positive, with positive specimens seen in all three location types including piped drinking water. Spatial analysis was performed using ArcGIS in order to map cluster and outlier cases, as well as hot and cold spots for positive specimens. A cluster of 25 specimens was described as a hot spot with 99% confidence, proximal within a simultaneous distance of 0.3km to an Infulene River wastewater treatment placement as well as a central factory for a local 2M beer brewing company. These studies suggest that Vibrio species and other gram-negative coliform bacteria remain endemic and prevalent in Maputo informal settlement housing. As risk amplifiers such as natural disasters place Maputo's settlements at risk for outbreaks of enteric disease, future studies should assess point-prevalence sites of Vibrio cholerae. These studies could consider high-risk zones such as clusters near industrial sites, as well as water, sanitation, and hygiene interventions that can accompany the Urban Transformation Project's changes.

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WATER QUALITY AND OCCURRENCE OF ENTERIC BACTERIA AND VIRUSES IN ASIPA RIVER, OYO STATE, WESTERN NIGERIA

Olatunji Matthew Kolawole[1], Oluwasanmi A. Adeyemi[2], Modupe O. Jimoh[3]

[1]University of Ilorin, Ilorin, Kwara state, Nigeria, [2]Ajayi Crowther University,, Oyo, Oyo state, Nigeria, [3]University of Warwick,, Conventry,, United Kingdom

Epidemiological evidence substantiates the fatality rates associated with poor Water, Sanitation, and Hygiene (WaSH) practices, in developing nations like Nigeria. The investigation aimed to evaluate the water quality and distribution of enteric bacteria and viruses in Asipa River in Oyo, Nigeria. This study assessed the Knowledge Attitude Practices and Beliefs (KAPBs) of the residents' utilization of Asipa River, investigated the physicochemical characteristics, identified the genotypic variants of enteric organisms isolated, and evaluated the impact of Zinc Oxide Nanoparticles (ZnO-np) treatment on water samples. Six hundred structured questionnaires were utilized to evaluate the KAPBs. Standard procedures were employed to determine the water samples' physicochemical characteristics, total and thermotolerant coliforms. Polymerase Chain Reaction and Sanger sequencing were employed for molecular identification, while ZnO-np

treatment was conducted using established protocols. Results revealed 26.4% of the participants observed sewage disposal within the river, 51.8% utilized the river for domestic and irrigation activities, and 60.2% reported diarrhea from the associated use of the river. The concentrations of dissolved oxygen and chemical oxygen demand (mg/L) varied between 1.2 and 6.4 and 30 and 75, respectively, beyond the limitations set by the World Health Organization. The total and thermotolerant coliform counts (CFU/100mL) ranged from 5.0 x 10^2 to 1.3 x 10^4, and 2.0 x 10^2 to 8.5 x 10^3, respectively. Forty-three bacteria were confirmed and sequences were deposited at the National Centre for Biotechnology Information, USA, and assigned accession numbers. Distribution of enteric viruses reported Sapovirus, Human rotavirus, and Astroviruses presence in 44%, 22%, and 33% respectively in the water samples. ZnO-np treated water significantly reduced in physicochemical parameters ($p<0.05$). Conclusively, Asipa River is contaminated with enteric bacteria and viruses that are of public health significance requiring treatment, implementation, and monitoring for regulatory compliance.

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LATRINE AVAILABILITY AND UTILIZATION ASSESSMENT IN PRIMARY SCHOOLS OF MERHABETE, ETHIOPIA: A MIXED METHOD STUDY

Awraris Hailu Bilchut[1], Esmael Habtamu Ali[2], Nigus Taddese[1], Melese Kitu[2], Fikreab Kebede[3], Ian Fetterman[4], Hadley Burroughs[4], Catherine E. Oldenburg[4], Thomas M. Lietman[4]

[1]Debre Berhan University, Debre Berhan, Ethiopia, [2]Eyu-Ethiopia, Bahir Dar, Ethiopia, [3]Federal Ministry of Health, Disease Prevention and Control, Addis Ababa, Ethiopia, [4]F.I. Proctor Foundation, University of California, San Francisco, San Francisco, CA, United States

While the vast majority of previously trachoma-endemic districts have been controlled in the past two decades, a few hot spots remain. Merhabete District in Ethiopia still has active disease (TF) prevalence ranging from 30-50% in children. As hygiene and sanitation are thought to play major roles in transmission, we assessed latrine availability and utilization at primary schools in the district. A simple random sample of 20 schools was chosen in the Kebele Elimination of Trachoma for Ocular Health (KETFO) study catchment area. At each school, two students, two teachers, and one school principal participated, for a sample size of 100. In-depth interviews were conducted to identify factors that influence latrine utilization. Latrines at each school were observed for availability and utilization with a checklist. Qualitative and quantitative data were analyzed in ATLAS.ti 24 and SPSS, respectively. Among the 20 schools, one, nine, and 10 had zero, one, and two latrines, respectively. In schools with latrines, 79% (15/19) had improved pit latrines, 53% (10/19) had latrines that needed maintenance, and 45% (9/20) had piped water. 47% (9/19) of latrine pits were covered in feces, and 74% (14/19) had feces present outside of the toilet around the latrine compound. The overall latrine utilization at schools was 26% (5/19). 68% (58/85) of participants said that latrine use reduces communicable diseases: trachoma (68%) and diarrhea (59%) were the most frequently cited. Challenges faced in latrine utilization were absence of functioning toilets, inadequate toilets, water shortage, and lack of knowledge on toilet use. Solutions proposed included providing water and soap to the schools through community contributions, building and renovating appropriate toilets through partner mobilization, raising awareness on latrine utilization, and hiring toilet cleaners and school guards. In the study area, the utilization of latrines at schools is influenced by multiple factors including absence of functioning toilets. Stakeholders including MOE and MOH should collaborate to provide appropriate hygiene facilities and raise knowledge about toilet use.

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INTERACTIONS BETWEEN WATER, SANITATION, AND HYGIENE (WASH) AND MOSQUITO DYNAMICS IN WESTERN KENYA: IMPLICATIONS FOR DIARRHEAL AND MALARIA DISEASES

Noriko Tamari[1], Maurice Agawo[2], Heidi E. Brown[1], Luigi Sedda[3], Gary L. Christopherson[1], Katherine D. Ellingson[1], Stephen Munga[4], Kacey C. Ernst[1]

[1]University of Arizona, Tucson, AZ, United States, [2]Maseno University, Kisumu, Kenya, [3]Lancaster University, Lancaster, United Kingdom, [4]Kenya Medical Research Institute (KEMRI), Kisumu, Kenya

Despite the implementation of Water, Sanitation, and Hygiene (WASH) and malaria vector control programs, diarrheal illness and malaria are the leading causes of morbidity and mortality among children under 5 years in Kenya. Since the transmission of diarrhea and malaria may interact with each other through outdoor latrines, we conducted a novel study on integrating WASH practices with mosquito dynamics. Our aim was to evaluate the risk posed by the use of outdoor latrines on diarrheal illness and malaria in a malaria-endemic area of western Kenya. The specific aims were to 1) explore factors associated with outdoor latrine use during the daytime, at night, and early morning, 2) examine the impact of latrine use behaviors on the risks of diarrheal and malaria diseases, and 3) explore factors influencing the abundance of adult *Anopheles* mosquitoes in latrines and houses. We conducted cross-sectional population-based surveys and malaria tests for individuals aged 4 years or older (n=531). Additionally, monthly mosquito sampling was carried out in paired houses (n=50) and outdoor latrines (n=50) using Prokopack aspirators from July 2023 to March 2024. Latrines were more frequently used by adults than children, for defecation than urination, and during the daytime and early morning than at night. A generalized linear mixed models (GLMMs) showed that individuals who felt safe between houses and latrines used latrines more at night than those who did not (urination: aOR=6.65, 95%CI: 1.95, 22.69; defecation: aOR= 5.00, 95%CI: 2.33, 10.71). No association was observed between latrine use and diarrheal or malaria diseases (diarrhea: aOR=0.77, 95%CI: 0.38, 1.57; malaria: aOR= 1.42, 95%CI: 0.74, 2.75). The negative binomial GLMMs showed that pit latrines, having bath space, and iron walls increased abundance of *An. gambiae s.l.* in latrines compared to ventilated improved pit latrines, non-bath space and brick/cement. Only pit latrines increased the abundance of *An. funestus s.l*. No significant factors were associated with the abundance of *Anopheles* mosquitoes inside houses. Further studies will be necessary to achieve a comprehensive understanding.

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HOUSEHOLD RISK FACTORS ASSOCIATED WITH HOSPITALIZED DIARRHEAL PATIENTS IN ULAANBAATAR, MONGOLIA

Amber N. Barnes[1], Uyanga Baasandavga[2], Anu Davaasuren[2], Battsetseg Gonchigoo[2], Greg C. Gray[3]

[1]University of North Florida, Jacksonville, FL, United States, [2]Institute of Veterinary Medicine, Ulaanbaatar, Mongolia, [3]Division of Infectious Diseases, School of Medicine, University of Texas Medical Branch, Galveston, TX, United States

Diarrheal disease is common in Mongolia yet risk factors for infection and hospitalization are not well understood. This study examined hospitalized diarrheal patients (n=120) at the National Center for Communicable Diseases (NCCD) in Ulaanbaatar. From February 2017 to January 2018, medical staff administered a questionnaire to patients or caregivers. Patients were largely from Tov province, including Ulaanbaatar (n=115; 95.8%), female (n=62; 51.7%) and male (n=58; 48.3%), and aged ≤ 1 year to 27 years. Prior illness duration was primarily 2-4 days (n=79; 65.8%). Symptoms included headache (n=28; 23.3%), fatigue (n=12; 10%), nausea (n=11; 9.2%), abdominal cramps (n=19; 15.8%), weight loss (n= 95; 79.2%), vomiting (n=18; 15%), fever (n=99; 82.5%), and diarrhea (n=117; 97.5%). Patient were using antibiotics (n=88; 73.3%), antiparasitic drugs

(n=93; 77.5%) and/or home remedies (n= 55; 45.8%). Housing included ger/yurt (n= 38; 31.7%), house (n=38; 31.7%), and apartment (n=44; 36.7%). Household animal ownership was not common (n=14; 11.7%). Most households used piped water (n=45; 37.5%), well water (n=31; 25.8%), tanker truck (n=14; 11.7%), or a combination of drinking water sources. Sanitation varied between flush/pour flush toilet (n=31; 25.8%), pit latrine w/slab (n=47; 39.2%), pit latrine w/o slab (n=1; 0.8%), composting/biotoilet (n=3; 2.5%), bucket/container (n=5; 4.2%), bury (n=3; 2.5%), or multiple services. One household also used open defecation (n=1; 0.8%). Reported handwashing differed by activity with 18.3% (n=22) of patients or caregivers washing hands before cooking, 22.5% (n=27) before feeding a child, 54.2% (n=65) before eating, 3.3% (n=4) after animal contact, and 26.7% (n=32) after bathroom visit. Households reported consumption of raw or undercooked meat (n=21; 17.5%), unpasteurized milk/milk products (n=22; 18.3%), unwashed/raw vegetables (n=7; 5.8%), and unwashed/raw fruit (n=20; 16.7%). Recognizing risk factors for diarrheal disease, particularly in children, can lead to prevention efforts to reduce hospitalization and household illness.

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MERCURY LEVELS IN HAIR OF PREGNANT WOMEN IN TUMBES, PERU: A CROSS-SECTIONAL STUDY

Sofia I. Chapela-Lara[1], Olivia Arar[1], Lauralee Fernandez[1], Denys Villareal-Palacios[2], Percy Vilchez-Barreto[2], Ricardo Gamboa-Moran[2], Sarah E. Rothenberg[3], William K. Pan[4], Seth E. O'Neal[1]

[1]Oregon Health and Science University - Portland State University, School of Public Health, Portland, OR, United States, [2]Centro de Salud Global - Tumbes, Tumbes, Peru, [3]Oregon State University, College of Health, Corvallis, OR, United States, [4]Duke University Global Health Institute and Nicholas School of Environment, Durham, NC, United States

Mercury, a potent toxicant posing serious risks to human health, particularly for pregnant women and young children, is widely present in the environment due to artisanal and small-scale gold mining (ASGM). The Puyango-Tumbes River, the main source of freshwater for the Tumbes region of Peru, is known to be contaminated with Hg from ASGM sites upstream in Ecuador. This study aimed to characterize hair total mercury (THg) concentrations among 148 pregnant women across 24 communities in Tumbes. Through purposeful sampling, we classified communities into three exposure risk zones. The Puyango-Tumbes watershed group included communities located within 5 km of the Puyango-Tumbes River, where river water is used for irrigation and freshwater fish consumption is common. The Coast group included a Pacific Coast fishing district approximately 30 km from the Puyango-Tumbes River mouth, where there is potential mercury exposure from seafood. The Zarumilla group comprised non-coastal communities in a different watershed unaffected by mining. The mean THg concentration was 2.08 µg/g ± 1.36, with 45% of participants (67/148) exceeding exposure limits (> 2.0 µg/g). The median THg level was 1.84, with an interquartile range (IQR) from 1.01 to 2.83. Median THg levels varied significantly among regions, with the Puyango-Tumbes River group showing the highest levels (2.72 µg/g; IQR 1.66, 3.55) compared to Zarumilla (1.61 µg/g; IQR 0.67, 2.63; p = 0.001) and to the Coast (1.71 µg/g; IQR 1.13, 2.50; p = 0.01), suggesting a higher probability of mercury exposure for pregnant women residing near the Puyango-Tumbes River. This association remained significant after controlling for potential confounding factors. Our findings underscore the importance of identifying high-risk regional populations and ensuring continuous biomonitoring of the Puyango-Tumbes River watershed.

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A MECHANISTIC MODELING APPROACH TO ASSESSING THE SENSITIVITY OF OUTCOMES OF WATER, SANITATION, AND HYGIENE INTERVENTIONS TO LOCAL CONTEXTS AND INTERVENTION FACTORS

Andrew F. Brouwer[1], Alicia NM Kraay[2], Mondal H. Zahid[1], Marisa C. Eisenberg[1], Matthew C. Freeman[3], Joseph NS Eisenberg[1]

[1]University of Michigan, Ann Arbor, MI, United States, [2]Bill & Melinda Gates Foundation, Seattle, WA, United States, [3]Emory University, Atlanta, GA, United States

Diarrheal disease is a leading cause of morbidity and mortality in young children. Water, sanitation, and hygiene (WASH) improvements have historically been responsible for major public health gains by reducing exposure to pathogens, but many individual interventions have failed to consistently reduce diarrheal disease burden. Analytical tools that can estimate the potential impacts of individual WASH improvements in specific contexts would support program managers and policymakers to set targets that would yield health gains. To understand the impact of WASH improvements on diarrhea, we developed a disease transmission model to simulate an intervention trial with a single intervention. We accounted for contextual factors, including preexisting WASH conditions and baseline disease prevalence, as well as intervention WASH factors, including community coverage, compliance, efficacy, and the intervenable fraction of transmission. We illustrated the sensitivity of intervention effectiveness to the contextual and intervention factors in each of two scenarios in which a 50% reduction in disease was achieved through a different combination of factors (higher preexisting WASH conditions, compliance, and intervenable fraction vs higher intervention efficacy and community coverage). Achieving disease elimination depended on more than one factor, and factors that could be used to achieve disease elimination in one scenario could be ineffective in the other scenario. Community coverage interacted strongly with both the contextual and intervention factors. For example, the positive impact of increasing intervention community coverage increased non-linearly with increasing intervention compliance. Additionally, counterfactually improving the contextual preexisting WASH conditions could have a positive or negative effect on the intervention effectiveness, depending on the values of other factors. When developing interventions, it is important to account for both contextual conditions and the intervention parameters. Our modeling approach can provide guidance for developing locally specific policy recommendations.

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EXPLORING PERCEPTIONS AND UNDERSTANDING OF ORAL HEALTH: A STUDY ON ORAL GINGIVITIS AMONG UNDERGRADUATE STUDENTS IN IBADAN

Olufemi Adebayo Adedokun[1], Kazeem Olabamiji Balogun[2], Damilola Opeyemi Olatunji[2], Moses Akinjide Afolabi[2], Mosunmola Olufunke Adedokun[3], Caroline Chidinma Nwoko[4]

[1]University of Ibadan Research Foundation, Ibadan, Nigeria, [2]Adekunle Ajasin University Akungba Akoko, Ondo, Nigeria, [3]University of Ibadan, Ibadan, Nigeria, [4]Adekunle Ajasin University Akungba Akoko, Ibadan, Nigeria

Abstract:Assessing oral health is crucial for organizing community-based programs aimed at promoting the health system. This includes evaluating the knowledge, attitude, and practices related to oral hygiene. Despite its importance, oral health often receives less attention in tertiary education settings. Gingivitis, characterized by gum inflammation, is an early stage of periodontal disease primarily caused by poor oral hygiene practices.A cross-sectional survey was conducted among undergraduate students in Ibadan, using a carefully structured questionnaire. The survey targeted undergraduate students, employing a descriptive survey design without manipulating variables. Closed-ended questions were utilized to assess students' knowledge, beliefs, and attitudes towards oral hygiene and gingivitis.The survey revealed that 67.1% of students strongly disagreed with having prior knowledge about oral gingivitis, while 1.3% disagreed

and 31.6% agreed. Additionally, 91.6% of students strongly disagreed with having been diagnosed with oral gingivitis, indicating a lack of engagement in preventive oral hygiene practices despite awareness of the condition. The majority of students believe they have adequate knowledge about oral hygiene and gingivitis. However, their lack of engagement in preventive practices suggests a gap between knowledge and behavior. Efforts are needed to bridge this gap and promote better oral health practices among tertiary students.

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USE OF THE HOUSEHOLD WATER INSECURITY ACCESS SCALE TO EVALUATE RURAL WATER DELIVERY IN SMALL COMMUNITIES

Gwenyth Lee[1], Gustavo Huera[2], Andrea Sosa[3], Samuel B. Schlesinger[4]

[1]Rutgers, The State University of New Jersey, New Brunswick, NJ, United States, [2]Fundación ALTROPICO, Quito, Ecuador, [3]University of Michigan, Ann Arbor, MI, United States, [4]Green Empowerment, Portland, OR, United States

Community-managed water systems play an important role in providing safely managed water to small and remote rural communities. New projects using this model continue to be implemented despite recent movement towards “professionalization” of water services. However, evaluating the efficacy of these projects at a community level may be challenging when the small number of households, or limited funds for long-term monitoring, limit statistical power to demonstrate health impacts. The household water insecurity access scale (HWISE), an experiential measure of water availability, accessibility, use, acceptability, and reliability, has been linked to health and social outcomes in research, and there is increasingly interest in its usefulness for project monitoring and evaluation. In 2023, the organization Green Empowerment and local partners integrated the HWISE into baseline evaluation surveys from 14 Ecuadorian communities across three regions of the country (coast, highland, and Amazon) where community-managed system are under development. Surveys were conducted in three languages (Spanish, Kichwa, and Cha’palaa). Communities either lacked piped water and were therefore reliant on rainwater, spring water, or surface water, or had highly unreliable, rudimentary piped water systems. The 4-question version of the HWISE (HWISE-4) retained the moderate internal consistency and limited floor and ceiling effects of the 12-question version (HWISE-12), making it a feasible and acceptable option for rapid community assessment, with similar performance for Spanish- and non-Spanish-speaking households. Community of residence explained 28.2% of variation in HWISE-4 scores, while region, survey language, and reported primary water source explained 20.2%, 18.9%, and 4.9% of variation respectively. Households with rudimentary piped water had mean HWISE-4 scores that were 0.9 points lower than communities that relied on surface water (the reference category) (95% CI: -2.2, 0.4). In the next phase of work, we will evaluate changes in HWISE scores as the same households gain access to safely managed water systems.

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MENSTRUAL MATERIAL DISPOSAL PRACTICES WITHIN THE GHANAIAN SOCIOCULTURAL CONTEXT: A QUALITATIVE STUDY

Sitsofe Gbogbo[1], Israel Wurusah[1], Emmanuel Gbogbo[1], Wisdom Axame[1], Priscilla Klutse[1], Robert Dowou[1], Paramount E. Nelson[1], Ishmael Boateng[1], Sarah O. Mantey[1], Nuworza Kugbey[2], Victor C. Doku[3], Frank E. Baiden[1], Fred N. Binka[1]

[1]University of Health and Allied Sciences, Ho, Ghana, [2]University of Environment and Sustainable Development, Somanya, Ghana, [3]King’s College London, London, United Kingdom

Menstrual material disposal is a critical area of concern in management of menstruation. Disposal practices significantly vary across different nations and contexts with implications for environmental pollution and health hazards linked with improper disposal. While good menstrual hygiene practices culminate in having access to safe and convenient facilities to dispose off used menstrual management materials, disposal practices in the Ghanaian context are influenced by sociocultural beliefs which have not been explored empirically. This study explored the sociocultural beliefs underlying disposal of used menstrual materials among senior high school girls in the Volta region of Ghana. The study utilized descriptive qualitative research approach grounded in in-depth interviews to gather data from adolescent girls in senior high schools across five districts in the Volta region. In all, 25 in-depth interviews were conducted, transcribed verbatim and thematically analysed using MAXQDA version 2024. The findings project varied ways by which adolescent schoolgirls dispose off used menstrual materials. The main disposal practices include dumping into dustbins, latrines and pits, burying, and burning. The choice of menstrual material disposal methods was influenced by social or cultural beliefs. These beliefs included using menstrual materials for rituals and, in some cases, a fear of the unknown consequences of open-place disposal. Participants who disposed of materials in bins were generally unconcerned about what happened to them afterwards. Conversely, those who chose methods like pit latrines, burying, or burning were likely motivated by a desire to prevent their materials from being used in rituals. This study illuminates the varied disposal methods used by adolescent schoolgirls for menstrual materials. Their choices are influenced by a range of factors, primarily social and cultural beliefs, along with concerns about personal risks. However, environmental considerations appear to be a less significant factor for these participants.

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ISOTHERMAL AMPLIFICATION AND COLORIMETRIC DETECTION OFV*IBRIO CHOLERAE* IN ENVIRONMENTAL MATRICES

Michelande Adolphe

Méditerranée Infection (IHU)/ Aix-Marseille Université, Marseille, France

Vibrio cholerae, cholera pathogen, which causes acute and fatal enteritis through consumption of contaminated food and water. Apart from aquatic habitats, *V. cholerae* can be found in other environmental media. In this study, we report an integrated detection protocol DNA extraction applicable in field with matrix alkaline lysis and loop-mediated isothermal amplification (LAMP) targeting the Rpob gene of *V. cholerae* with colorimetric reading in one hour. And Different environmental samples in France at Marseille: soil, plants, sea water, tap water and effluents were infected with suspensions bacterial (1 McFarland) of *V. cholerae* (Collection of Strains of the Rickettsia Unit ‘’CSUR” (IHU Méditerranée Infection, Marseille, France) and the same samples were infected with *V. alginolyticus*, and *E. coli* were used as negative controls to test the feasibility of our LAMP system. The LAMP assay reveals 100% specificity for *V. cholerae* by testing three non-*cholera Vibrio* species and four *Enterobacteriaceae* in culture as negative controls. Environmental samples containing *V. cholerae* showed positivity to the LAMP-*V. cholerae* protocol at a 1/50 dilution in one hour. This work contributes to the development of diagnostic tests for *Vibrio* Spp. pathogens mainly *V. cholerae*; and can be used in low-income countries for rapid screening purposes for other environmental disease. This study shows that the methods used are applicable in the field and contribute to the advancement of the diagnosis of environmental pathogens. And loop-mediated isothermal amplification (LAMP) method is effective for detecting very low numbers of bacteria in environmental samples, with the addition benefit of being inexpensive to realize in the field.

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INDICATORS OF DRINKING WATER ACCESS AND ESCHERICHIA COLI CONCENTRATION IN HOUSEHOLD DRINKING WATER IN MADAGASCAR

Amanda Seyler[1], Fabiola Aparicio-Ting[2], John D. McLennan[3]

[1]Department of Anthropology and Archaeology, University of Calgary, Calgary, AB, Canada, [2]Department of Community Health Sciences,

Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [3]Departments of Psychiatry and Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Diarrheal diseases are a leading cause of morbidity and mortality in Madagascar, and *Escherichia coli* (*E. coli*) is one of the most common causes of diarrheal disease in children under five. Moreover, at least 80% of drinking water samples from Malagasy households have been found to be contaminated with *E. coli*, resulting in most households failing to meet the standard for safely managed drinking water as described in Sustainable Development Goal 6. Identifying relevant factors linked to contamination may inform initiatives to improve access to safer drinking water. This cross-sectional study aimed to determine whether different aspects of "access" to drinking water were associated with *E. coli* contamination in household drinking water in Madagascar, specifically (*i*) the use of an improved water source; (*ii*) time to get water; and (*iii*) perceived water sufficiency. The concentration of *E. coli* in household drinking water samples was available from 3,116 households from the sixth round of the nationally representative 2018 Madagascar Multiple Indicator Cluster Survey. Multinomial logistic regression modelling was used to investigate the association between water access variables and different concentrations of *E. coli* in water samples. The use of an unimproved water source significantly increased the odds of higher *E. coli* concentration in drinking water samples, whereas perceived insufficiency and increasing time to get water did not. Several additional contextual variables in the final model were found to increase the odds of *E. coli* concentration, including lower household wealth, rural residence, not treating drinking water at the household level, lacking improved sanitation facilities, and living in certain regions (East Coast, Tsaratanana Massif). A priority continues to be the reduction in reliance on unimproved sources for drinking water in Madagascar, as 54% of the population is dependent on surface water and unimproved wells and springs. Further inquiry is needed to understand the seeming lack of relationship between the risk of *E.coli* contamination and perceived water sufficiency and duration of time to obtain water.

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EVALUATION OF THE ANTIBACTERIAL SUSCEPTIBILITY PATTERN OF VIBRIO SPECIES ISOLATED FROM PERIWINKLES AND AQUATIC SNAILS SOLD AT UMUAGWO MARKET IN IMO STATE, NIGERIA

Ogechi Innocentia Nwachukwu, Chinyere Ukaga, Chika Maureen Ezenwa, Treasure Njidieka Njoku-Obi
Imo State University, Owerri, Imo State, Nigeria, Owerri, Nigeria

Vibrio species occur in both marine and fresh water habitats and in association with aquatic animals. They are human pathogens and account for a significant proportion of human infections such as gastroenteritis. This study was carried out to evaluate the antibiogram of *Vibrio* species isolated from 60 samples of periwinkles and aquatic snails sold at Umuagwo market. The body surfaces of the samples were analyzed on thiosulphate citrate bile salt sucrose (TCBS) agar using standard microbiological method. Antibacterial susceptibility test was carried out using agar diffusion (Kirby Bauer) method. A total of 60 *Vibrio* belonging to six species was isolated. The frequency of occurrence showed that *V. cholerae* was the most predominant 20(33.3). It was followed by *V. vulnificus* 12(26.8%), *V. fluvalis* 8(16.6%), *V. mimicus* 7(16.6%), *V. alginolyticus* 7(13.3%) and *V. parahaemolyticus* 6(13.3%). There was no significant difference ($P<0.05$) in the frequency of occurrence of *Vibro* species on periwinkle and aquatic snail. Antibiogram testing showed that *V. cholerae* was sensitive to ciprofloxacin, pefloxacin and streptomycin. It was resistant to ampicillin, gentamycin, ceporex and ofloxacin. *V. fluvalis* was sensitive to ciprofloxacin, gentamycin and ofloxacin. It was resistant to ampicillin. *V. alginolyticus* was sensitive to ciprofloxacin, septrin and augumentin. It was resistant to ampicillin. *V. mimicus* was sensitive to ciprofloxacin, septrin, ceporex and ampicillin. *V. vulnificus* was sensitive to ciprofloxacin, ceporex and ampicillin. It was resistant to septrin. *V. parahaemolyticus* was sensitive to ciprofloxacin, ceporex and ampicillin. It was resistant to septrin. There was significant difference ($P>0.05$) in inhibition zone diameter between the test organisms. Sea foods like periwinkle and aquatic snail should be properly cooked and not eaten raw or undercooked to avoid *Vibrio* food borne disease.

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SOCIOECONOMIC AND COMMUNITY DRIVERS OF SAFE HOUSEHOLD WATER AND SANITATION: A MIXED METHODS ANALYSIS IN NORTHERN ECUADOR

Molly K. Miller-Petrie[1], Nicolette A. Zhou[2], Kelsey J. Jesser[2], Caitlin Hemlock[2], Christine S. Fagnant-Sperati[2], William Cevallos[3], Gabriel Trueba[4], Gwenyth O. Lee[5], Joseph N.S. Eisenberg[6], Karen Levy[2]
[1]Department of Epidemiology, Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, United States, [2]Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, United States, [3]Centro de Biomedicina, Universidad Central del Ecuador, Quito, Ecuador, [4]Instituto de Microbiologia, Universidad San Francisco de Quito, Quito, Ecuador, [5]Rutgers Global Health Institute, Rutgers University, New Brunswick, NJ, United States, [6]Department of Epidemiology, University of Michigan, Ann Arbor, MI, United States

Large-scale household (HH) water, sanitation, and hygiene (WASH) interventions have had limited success. This finding may be partially explained by a lack of understanding of community priorities, limiting acceptability and uptake. Further, obtaining and maintaining HH WASH solutions (e.g., latrines, cisterns) places a financial and labor burden on individuals, and may be insufficient without community-level WASH infrastructure. We integrated quantitative data from household surveys (n=526) and qualitative data from thematically coded interviews (n=33) in 10 communities in northern Ecuador participating in the ECoMiD cohort study. Considering safe HH WASH as presence of improved water and sanitation in the home; safe community WASH as >85% safe HH WASH, and wealth based on asset data, we found that in communities without safe WASH, wealthy houses had 23% higher levels of safe HH WASH compared to poor houses in the same communities; this difference narrowed among houses in communities with safe WASH, where wealthy houses had just 10% higher levels, indicating that access to community infrastructure may mitigate inequalities in wealth in terms of safe HH WASH. We used multivariate logistic regression to estimate the effect of wealth on HH WASH, adjusting for location and maternal education, with a random effect on community. Wealthy houses had 3.7 (95%CI 1.8-8.8) times the odds of having safe HH WASH compared to non-wealthy houses. The burden of household WASH expenditures was considered high by all interviewees, particularly costs of drinking water and labor to obtain water in the absence of piped systems or rain. Piped systems were viewed as unreliable and contaminated; more wealthy households reported bottled water as the primary household drinking source compared to non-wealthy (51% vs 43%), despite higher access to piped systems among the wealthy (75% vs 49%). Interviewees expressed reluctance to invest in WASH in houses that were not owned or in informal settlements; and concern about installing cisterns in flood prone areas. Understanding these relationships is crucial to improve uptake and acceptance of future WASH interventions.

6752

MOXIDECTIN PLUS ALBENDAZOLE FOR LYMPHATIC FILARIASIS: EFFECTS THROUGH 36 MONTHS POST-TREATMENT

Benjamin Koudou[1], Catherine Bjerum[2], Allassane Outtara[1], Paskal Toki Gabo[3], Charles Goss[4], Daphne Lew[4], Christopher King[2], Peter Fischer[4], Gary Weil[4], Philip Budge[5]
[1]Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte D'Ivoire, [2]Case Western Reserve University, Cleveland, OH, United

States, [3]Centre Hospitalier Régional d'Agboville, Agboville, Côte D'Ivoire, [4]Washington University in St. Louis, St. Louis, MO, United States, [5]Washington University School of Medicine, St. Louis, MO, United States

The Moxidectin for LF study is a 3-year, randomized clinical trial comparing moxidectin + albendazole (MoxA) to ivermectin + albendazole (IA) and moxidectin + DEC + albendazole (MoxDA) to ivermectin + DEC + albendazole (IDA) for Bancroftian filariasis. The IA group was treated annually, while the MoxA, IDA, and MoxDA groups received a single dose at enrollment and were not retreated unless they were microfilaremic at 24 months post-treatment. We have previously reported that all three alternative treatments were superior to annual IA at 12 and 24 months. We now report efficacy data out to 36 months post-treatment. Thirty-six-month data are available for 73/96 (76%) participants with >40 microfilariae (Mf) per mL of blood at baseline. A modified intention to treat (mITT) analysis among these participants shows that 12/13 (92%) persons treated with MoxA were amicrofilaremic at 36 months, compared to 18/19 (95%) after IDA, 20/21 (95%) after MoxDA, and 12/17 (71%) after 3 annual doses of IA (Fisher's exact p=0.093). Two of sixteen (12%) MoxA participants required retreatment for microfilaremia at 24 months, as did 2/23 (9%) IDA and 2/25 (8%) MoxDA participants. Clearance of filarial antigen, measured by Filariasis Test Strip occurred in 1/18 (6%) IA, 3/14 (21%) MoxA, 2/19 (11%) IDA, and 9/22 (41%) MoxDA participants (Fisher's exact p=0.031). Among those with adult worm nests detected by scrotal ultrasound at baseline, 7/8 (88%) IA, 3/9 (33%) MoxA, 1/8 (13%) IDA, and 2/11 (18%) MoxDA participants had worm nests detected at 36 months (Fisher's exact p=0.005). Although preliminary, these data suggest that single-dose MoxA, like IDA and MoxDA, resulted in sustained amicrofilaremia out to 36 months in most participants. Complete results adjusted for baseline characteristics and infection intensity for all participants will be presented at the meeting. Results from this trial suggest that mass drug administration with MoxA could accelerate LF and onchocerciasis elimination in Africa.

6753

STRINGENT APPLICATION OF THE ESSENTIAL PACKAGE OF CARE WITH OR WITHOUT ADDITIONAL TREATMENT WITH DOXYCYCLINE IN PATIENTS WITH ADVANCED STAGES (4 - 6) OF FILARIAL LYMPHEDEMA

Ute Klarmann-Schulz[1], Sarah M. Sullivan[2], Yaya I. Coulibaly[3], Alexander Y. Debrah[4], Thishan C. Yahathugoda[5], Akili Kalinga[6], Suma Krishnasastry[7], Jennifer Nadal[8], Charles Mackenzie[2], John Horton[9], Eric Ottesen[2], Achim Hoerauf[1]

[1]Institute for Medical Microbiology, Immunology and Parasitology (IMMIP), University Hospital Bonn, Bonn, Germany, [2]Neglected Tropical Diseases Support Center, Task Force for Global Health, Atlanta, GA, United States, [3]International Center for Excellence in Research, Bamako, Mali, [4]Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Faculty of Allied Health Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana, [5]Filariasis Research Training and Service Unit, Department of Parasitology, Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka, [6]National Institute for Medical Research (NIMR), Dar es Salaam, Tanzania, United Republic of, [7]Filariasis Research center, Govt. T. D. Medical College, Alappuzha, Kerala, India, [8]Institute for Medical Biometry, Informatics and Epidemiology (IMBIE), University Hospital Bonn, Bonn, Germany, [9]Tropical Projects, Hitchin, United Kingdom

Here, we report on a pilot trial with the aim to assess the efficacy of stringent hygiene measures using the Essential Package of Care with or without additional administration of doxycycline for the treatment of advanced stage (4 - 6) of filarial lymphedema (LE). The trial was carried out in Ghana (GH), India (IN), Mali (ML), Sri Lanka (LK) and Tanzania (TZ), as an add-on to 5 RCTs with the same aim, but with patients LE stage 1-3. Participants were randomized to receive either 200mg doxycycline (DOX) or matching placebo (P) for 6 weeks. Data were aggregated from the 5 country study sites. In total, 171 participants (GH: 58, IN: 20, ML: 19, LK: 19, TZ: 55) were included. Participants were followed up for two years after treatment onset with main follow-up assessments for stage and hygiene changes at 6, 12, 18 and 24 months and for acute adenolymphangitis (ADL) every 2 months. Quality of life (QoL) was assessed using the WHODAS 2.0 score every year. Multivariable analyses were performed to account for country and stage differences. Of the 171 participants, 89 were treated with DOX and 82 with placebo. In the DOX group, 13 (14.6%) participants had stage 4 or 5, whereas 76 had stage 6; in the placebo group, 22 (26.8%) presented with stage 4 or 5 and 60 with stage 6 (p = 0.058). After 24m, 16/82 (19.5%) of the DOX and 19/77 (24.7%) of the P group showed LE stage improvement, whereas only 1/82 (1.2%) and 8/77 (10.4%) showed progression, respectively. The significant influencing factors for progression were stage 4 or 5, ADL during the previous 6m, poor hygiene of the legs and less time lived in the endemic area. The median time to first attack was 12m for P and 14m for DOX (p = 0.42). In both DOX and P groups, there was a better QoL over time, indicated by a decrease of the QoL score from 20.7±1.4 at baseline to 9.1±1 at 24m (p <0.001). ADL during the previous 6m, body weight and poor hygiene of the legs were the most important factors affecting QoL. Overall, the results of this pilot trial suggest that there is good news also for patients with advanced LE stages that they benefit from stringent application of the Essential Package of Care for LE as recommended by WHO.

6754

EVIDENCE OF RENEWED ONCHOCERCIASIS TRANSMISSION AFTER TREATMENTS STOPPED IN 2017 IN THE METEMA SUB-FOCUS OF ETHIOPIA

Yewondwossen Bitew[1], Emily Griswold[2], Jenna E. Coalson[2], Aderajew Mohammed[1], Mitiku Adugna[3], Fetene Mihretu[3], Kadu Meribo[4], Tewodros Seid[1], Tekola Endeshaw[1], Desalegn Jemberie[1], Fikresilasie Samuel[1], Firdaweke Bekele[1], Tadesse Asmare[1], Henok Birhanu[1], Adane Yayeh[1], Geremew Haileyesus[1], Gedefaw Ayenew[3], Yihenew Wubet[3], Anley Haile[1], Fikre Seife[4], Zerihun Tadesse[1], Frank O. Richards[2], Gregory S. Noland[2]

[1]The Carter Center, Addis Ababa, Ethiopia, [2]The Carter Center, Atlanta, GA, United States, [3]The Carter Center, Bahir Dar, Ethiopia, [4]Federal Ministry of Health, Addis Ababa, Ethiopia

The Metema sub-focus is part of the Galabat-Metema international cross-border onchocerciasis (OV) transmission zone between Sudan and Ethiopia. The Metema sub-focus includes Metema, West Armachiho, Tegedie, Chilga, and Gendewuha and parts of Quara and Alefa districts of Amhara region, Ethiopia. Annual or semi-annual ivermectin mass drug administration (MDA) for OV occurred between 2003-2017. Ethiopia and Sudan made a coordinated decision to stop MDA from 2018 after both sub-foci met WHO Stop-MDA thresholds in 2017. The Wudi Gemzu hotspot in Metema was exempted and has since received MDA up to four times a year. During post-treatment surveillance (PTS), entomological evaluations of blackfly pools for parasite O-150 DNA by PCR were done to monitor for renewed signals of transmission. In 2021, 1068 *Simulium damnosum* flies were collected using human landing catch from 6 sentinel sites across the sub-focus. All flies were pooled for testing; 3 of 14 pools were positive, giving a prevalence estimate of 6 infective flies per 2000 (95% upper confidence limit [UCL] 17.7). We followed up with serological testing of 3,836 children less than 10 years old selected by multistage stratified sampling between April and March 2023 using ELISA for Ov16 antibodies, indicating exposure to the parasite. The seroprevalence was 2.3% (95% CI 0.3%-9.2%). Qualitative data identified intense internal conflict, displacement, and human immigration from known endemic areas as major issues during the PTS period. The results confirmed that transmission of onchocerciasis has re-occurred in the Metema sub-focus, representing one of the first global examples of OV PTS failure 5 years after stopping MDA. The program will reinitiate MDA in the sub-focus and investigate whether there was reintroduction of parasites through infected fly or human population movement, whether there was recrudescence from undetected parasites at the time of Stop-MDA assessments, and what factors contributed to renewed transmission. Elimination was declared in the cross-border Galabat sub-focus in early 2023 after successful PTS, but OV monitoring should continue given developments in Metema.

6755

ASSOCIATION BETWEEN ANATOMICAL HYPOSPLENISM AND *LOA LOA* MICROFILAREMIA IN A RURAL AREA OF THE REPUBLIC OF CONGO: A POPULATION-BASED CROSS-SECTIONAL STUDY (THE MORLO PROJECT)

Cédric B. Chesnais[1], Valentin Dupasquier[2], Elodie Lebredonchel[3], Sébastien D. S. Pion[1], Charlotte Boullé[1], Ludovic G. Rancé[2], Marlhand Hemilembolo[4], Michel Boussinesq[1], Jeremy T. Campillo[5], Francois Missamou[6]

[1]Institut de Recherche pour le Développement, Montpellier, France, [2]Montpellier University Hospital, Montpellier, France, [3]Hôpital Bichat-Claude Bernard, Paris, France, [4]Programme National de Lutte contre l'Onchocercose, Brazzaville, Congo, Republic of the, [5]Inserm, Montpellier, France, [6]Programme National de Lutte contre l'Onchocercose, Br, Congo, Republic of the

Loa loa filariasis (loiasis) is considered a benign disease. However, recent epidemiological data suggest an increased mortality rate in *L. loa* infected individuals, emphasizing the importance of studies on the morbidity associated with loiasis. As case-reports suggest anatomical lesions in the spleen among individuals infected with *L. loa*, we aimed at investigating the relationship between *L. loa* microfilarial density (MFD) and spleen volume. In 2022, we enrolled 990 subjects, with one-third being microfilaremic, in a prospective cohort in a general population in the Republic of Congo. At baseline, parasitological assessment, search for Howell-Jolly bodies (HJB), and spleen ultrasonography (US) were performed. Nested analyses of the baseline data from this cohort revealed that, after adjusting for age and sex, individuals with 1-8000 microfilariae (mf)/mL and >8000 mf/mL had a decreased spleen volume of 30.8 and 46.5 mL, respectively (P = 0.010 and 0.008, respectively). Additionally, a model run to explain the presence of a spleen volume <150 mL (the lower limit of normal volume range) demonstrated that individuals with *L. loa* MFD of 1-8000 mf/mL and >8000 mf/mL had adjusted Odds Ratios (aOR) of 1.9 (P = 0.042) and 4.2 (P = 0.016), respectively, when compared to amicrofilaremics. Given that a spleen volume <80 mL is associated with a significantly increased risk of death in patients with severe pneumonitis, further analysis was conducted using 80 mL as a cut-off. Compared to amicrofilaremic individuals, subjects with >35,000 mf/mL had an adjusted OR (aOR) of 14.9 (P = 0.032) to have a spleen volume <80 mL. Interestingly, HJB were also significantly associated with these small spleens (aOR = 3.7, P = 0.017), supporting the hypothesis of potential dysfunction of these spleens. In conclusion, our findings suggest a possible link between loiasis and the development of anatomical hyposplenism, potentially leading to spleen dysfunction. These results imply that loiasis may contribute to an increased risk of bacterial infections and associated mortality in Central Africa.

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IMPACT OF TRIPLE-DRUG MASS DRUG ADMINISTRATION ON THE SEROPREVALENCE OF ANTIBODIES TO LYMPHATIC FILARIASIS IN SAMOA

Harriet Lawford[1], Helen Mayfield[1], Filipina Amosa-Lei Sam[2], Satu Viali[2], Tito Kamu[3], Robert Thomsen[4], Colleen Lau[1]

[1]UQ Centre for Clinical Research, The University of Queensland, Brisbane, Australia, [2]National University of Samoa, Apia, Samoa, [3]Tupua Tamasese Meaole Hospital, Apia, Samoa, [4]Ministry of Health, Apia, Samoa

In August 2018, Samoa was the first country to distribute triple-drug mass drug administration (MDA) to interrupt lymphatic filariasis (LF) transmission. Point-of-care tools to detect filarial antigen (Ag) are used by programmatic surveys but evidence suggests antifilarial antibody (Ab) markers may be more sensitive measures of transmission. We aimed to assess the utility of Abs as a surveillance tool by comparing LF Ag and Ab seroprevalence at baseline and 6-months post-MDA in Samoa and identify risk factors for seropositivity. A community-based serosurvey of participants ≥5 years old took place immediately post-MDA in 2018 and 6-months post-MDA in 2019 in 35 primary sampling units (30 randomly selected and five 'suspected hotspots'). Alere™ Filariasis Test Strips were used to detect Ag and multiplex bead assays to measure seropositivity to *Bm14* Ab, *Wb123* Ab and *Bm33* Ab. Seroprevalence was adjusted for study design and standardised for age and gender. Overall 3795 participants (mean 20.7 years; 49% male) were surveyed in 2018 and 4052 (mean 20.4 years; 48% male) in 2019. At follow-up, seroprevalence did not change significantly for Ag (3.7% vs 4.6%; *P*-value 0.66) or *Bm14* Ab (20.3% vs 18.5%; *P*-value 0.12) but increased for *Wb123* Ab (32.2% vs 43.6%; *P*-value 0.04) and *Bm33* Ab (51.5% vs 95.8%; *P*<0.001). Risk factors for seropositivity at follow-up were age ≥10 vs 5-9 years (aOR: Ag=3.73, *Bm14*=3.77, *Bm33*=4.28, *Wb123*=2.78), male gender (aOR: Ag=4.42, *Bm14* Ab=2.27, *Wb123* Ab=1.43), 'suspected hotspot' residents (aOR: Ag=3.44, *Bm14*=1.98, *Wb123*=2.38) and Savai'i residents (aOR: Ag=3.44, *Bm14*=2.10, *Bm33*=2.83). Contrasting seroprevalence trends were seen for Ag and each Ab from baseline to follow-up. The interpretation of increased *Wb123* Ab and *Bm33* Ab seroprevalence is unclear but may suggest these Ab are detecting increased transmission signals that are not picked up by Ag. Individual LF seromarkers may provide different information about an individual's infection status and population level transmission. Further research into Ab kinetics is needed to determine the utility of monitoring Ab and define target Ab thresholds for LF elimination.

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EVALUATION OF THE EFFECT OF ONE ROUND OF MASS DRUG ADMINISTRATION WITH IDA ON HUMAN *BRUGIA MALAYI* INFECTIONS IN BELITUNG DISTRICT, INDONESIA

Taniawati Supali[1], Yenny Djuardi[1], Sudirman Surdirman[1], Elisa Iskandar[1], Rahmat Alfian[1], Yossi Destani[1], Emanuele Giorgi[2], Peter U. Fischer[3]

[1]Department of Parasitology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, [2]Faculty of Health and Medicine, Lancaster University, Lancaster, United Kingdom, [3]Division of Infectious Diseases, Washington University School of Medicine, Saint Louis, MO, United States

In Belitung District, that is located close to Sumatra Island, lymphatic filariasis (LF) is caused by zoonotic *Brugia malayi*. The district received mass drug administration (MDA) with DEC and albendazole (DA) from 2005-2010 and passed three transmission assessment surveys (TAS). After post TAS-3 surveillance indicated microfilaremia in adults, we conducted in June of 2022 a district-wide survey using the IDA (Ivermectin DA) impact survey design of WHO. More than 30 clusters of adults from 26 villages were examined for night blood microfilariae (Mf) by three-line blood smear. Mf-positive subjects were detected in 16 villages (62%) with the highest rate of Mf-positives in Lassar village (4.8%, 40/833). The overall Mf-rate was 2.7% (121/4417) and older males were more likely to be Mf-positive compared to other population groups. MDA with IDA was conducted by the local health authority in October 2022 with a reported coverage of 90.3%. We conducted a follow-up IDA impact survey in June of 2023. Survey clusters were selected based on geospatial modelling using Mf data from the previous year to focus on communities with high predicted transmission risk. During follow-up Mf-positive individuals were detected in 9 of 13 villages (69%). The overall Mf-rate was 0.84% (35/4174). Eleven villages were re-examined 2023 and the Mf-rate decreased in all of them except for one compared to 2022. These mid-term results indicate that IDA MDA can be highly efficient to clear zoonotic *B. malayi* despite more stringent IDA impact survey design and oversampling. At the same time *B. malayi* infection has been also found in animals in the area (cats, dogs, macaques) and genomic studies indicate exchange of parasites between human and animal populations. This is an additional risk for the elimination of LF in the area and high coverage MDA with intensified evaluation of MDA and post MDA surveillance is needed. Areas with zoonotic *B. malayi* infection may need to be declared by WHO to special intervention zones that need special attention.

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INVESTIGATION OF POTENTIAL ONCHOCERCIASIS HOTSPOTS IN PARTS OF ENUGU SOUTHEAST NIGERIA THAT ARE UNDER POST TREATMENT SURVEILLANCE

Adamu Sallau[1], Jenna E. Coalson[2], Lazarus Nweke[1], Emmanuel Miri[1], Emmanuel Emukah[1], Cephas Ityonzughul[1], Lindsay Rakers[2], Emily Griswold[2], Solomon Adelamo[1], Samuel Ifeanychukwu[1], Ifeoma Otiji[3], Ebere Ogbodo[3], Andrew Obasi[1], Egeonu Attamah-Isiani[1], Chukwuemeka Makata[4], Fatai Oyediran[4], Bertram E.B. Nwoke[5], Frank O. Richards[2], Gregory S. Noland[2]

[1]The Carter Center, Jos, Nigeria, [2]The Carter Center, Atlanta, GA, United States, [3]State Ministry of Health, Enugu, Nigeria, [4]Federal Ministry of Health, Abuja, Nigeria, [5]Imo State University, Owerri, Nigeria

In December 2022 the Nigeria Onchocerciasis Elimination Committee (NOEC) approved the cessation of mass drug administration (MDA) in Enugu state, Nigeria, after surveys indicated that it met WHO's serological and entomological criteria for interruption of onchocerciasis transmission. Shortly after, a publication by Ekpo and colleagues reported parasitological evidence (55% prevalence of nodules by physical examination and 41% microfilaria [mf] prevalence in skin snip microscopy) of persistent *Onchocerca volvulus* from concurrent studies in 225 adults in 6 villages in Enugu. NOEC thus advised a follow-up study be conducted in the same 6 villages and 12 neighboring villages in three local government areas (LGAs) of Enugu to confirm if there were onchocerciasis hotspots with ongoing transmission. We tested 1,434 children aged 5-9 years for Ov16 antibodies by ELISA and examined 1,539 adults (18+ years) for nodules and tested their skin snips for mf by microscopy. Skin snips from 12 Ov16 positive children were tested for mf by PCR; the resulting 5 positives gave a prevalence estimate in children of 0.35% (95% CI 0.11%-0.81%). In adults, prevalence of nodules was 11% and of skin mf was 1.36% (95% CI 0.78-1.94%). No adults had skin mf and no children were Ov16 positive in the villages of one LGA. These results indicated hypoendemic onchocerciasis in contrast to the high prevalences reported by Ekpo et al. (2022). These findings validate NOEC's recommendation that Enugu be classified as "transmission interrupted" and stop MDA, but the two LGAs with Ov16 or mf positives may be hotspots. Blackfly collections are ongoing, and they will be tested for parasite DNA to confirm transmission status. We recommend twice per year MDA in the potential hotspots to ensure transmission interruption.

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MITIGATING COLONIZATION WITH CARBAPENEM-RESISTANT ORGANISMS AMONG NEONATAL INTENSIVE CARE UNIT ADMISSIONS: EVALUATING THE EFFECTIVENESS OF INFECTION CONTROL INTERVENTIONS

Fahmida Chowdhury[1], Gazi Md. Salahuddin Mamun[1], Sanzida Khan[1], Syeda Mah-E-Muneer[1], Aminul Islam[1], Dilruba Ahmed[1], Debashis Sen[1], Md. Golam Dostogir Harun[1], Lisa P Oakley[2], Gemma Parra[2], Ashley Styczynski[2]

[1]icddr,b, Dhaka, Bangladesh, [2]Centers for Disease Control and Prevention (US-CDC), Atlanta, GA, United States

Antimicrobial resistance (AMR) is the global leading cause of death from infections, particularly affecting low- and middle-income countries. Colonization with carbapenem-resistant organisms (CRO) increases the risk of infections with CRO. In an interim analysis of a prospective cohort study, we found 77% (141/182) of neonates in a neonatal intensive care unit (NICU) of a tertiary-care hospital in Bangladesh were colonized with carbapenem-resistant *Klebsiella pneumoniae*, with 63% (89/141) acquiring colonization >48 hours after hospitalization. We aimed to assess the impact of infection control (IC) interventions on CRO colonization among neonates admitted to the NICU. From July 2023 to March 2024, we enrolled 529 neonates: 360 before the intervention and 169 after. Neonates were assessed for CRO colonization using rectal swabs collected on admission, days 3 and 7, and weekly thereafter. Swabs were plated on mSuperCARBA to assess colonization with carbapenem-resistant organisms (CRO, not differentiated to date). Positive blood cultures collected from patients with suspected sepsis underwent testing using VITEK® 2. Our IC interventions targeted hand hygiene (HH) and environmental cleaning (EC), including staff training on proper HH techniques and more frequent cleaning of high-touch surfaces, as well as regular audits to measure compliance with HH and EC. We conducted descriptive analyses using Pearson's Chi-square test. Compliance with HH improved from 13% to 28% following the interventions, while environmental cleaning improved from 9% to 43% based on fluorescent markers. Over the same time, CRO colonization decreased from 93% (333) to 80% (135) ($p<0.001$). Overall bacterial blood culture positivity remained stable at 54% (51/95) vs. 57% (30/53) ($p=0.87$). After implementing IC interventions, we observed a decrease in CRO colonization among NICU patients, though blood culture positivity was unchanged. Results suggest that even modest improvements in IC practices may have a role in curbing CRO transmission in high-risk settings.

6760

URBAN SANITATION UPGRADES IN MAPUTO, MOZAMBIQUE ASSOCIATED WITH REDUCED DETECTION OF ENTERIC PATHOGENS IN FECAL SLUDGES

Gouthami Rao[1], Márcia Chiluvane[2], Yarrow Linden[1], Jack Dalton[1], Drew Capone[3], Amanda Lai[1], David Holcomb[1], Erin Kowalsky[1], Elly Mataveia[2], Victória Cumbane[2], Vanessa Monteiro[2], Edna Viegas[2], Joe Brown[1]

[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Instituto Nacional de Saúde, Maputo, Mozambique, [3]Indiana University, Bloomington, IN, United States

Environmental surveillance of pathogens has gained prominence in monitoring of SARS-CoV-2 infections, to assist in polio eradication, and increasingly in detection of a wide range of other targets to support public health programming. Because wastewater and fecal sludges represent excreta from many individuals, these matrices may also be useful in understanding the effects of interventions aimed to prevent infections. Here, we examine the utility of enteric pathogen detection in fecal sludges as an endpoint in a controlled health impact trial of urban sanitation upgrades in Maputo, Mozambique. We collected 50 fecal sludge samples from an intervention arm receiving upgraded shared latrines and 47 from a comparable control arm using existing poor-quality latrines between March 2022 and April 2023. We extracted total nucleic acid using the QIAamp 96 Virus kit and processed extracts using a customized TaqMan Array Card for RT-qPCR analysis. Overall, we observed a statistically meaningful impact of sanitation upgrades on the percent reduction of *Ascaris lumbricoides* (30%), *Trichuris trichiura* (17%), *Campylobacter jejuni/coli* (11%), enteroaggregative *E. coli* (30%), enteropathogenic *E. coli* (28%) and enterotoxigenic *E. coli* (16%) in the intervention arm ($p<0.05$) relative to control sites for fecal sludge samples. Results are consistent with similar reductions for bacterial and helminth targets observed in stool samples from children under 5 among those served by sanitation interventions compared with comparable controls lacking these upgrades. Detection of enteric pathogens in fecal sludges is a compelling option for further consideration as an outcome measure in water, sanitation, and hygiene (WASH) health impact trials.

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EFFECTS OF HOUSEHOLD CONCRETE FLOORS ON MATERNAL AND CHILD HEALTH (CRADLE TRIAL): A RANDOMIZED CONTROLLED TRIAL

Farjana Jahan[1], Mahbubur Rahman[1], Suhi Hanif[2], Afsana Yeamin[1], Abul Kasham Shoab[1], Zahid Hayat Mahmud[3], Fahmida Tofail[4], Rashidul Haque[5], Ayse Ercumen[6], Jade Benjamin-Chung[2]

[1]Environmental Health and WASH, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, [2]Department of Epidemiology & Population Health, Stanford University, California, CA, United States, [3]Laboratory of Environmental Health, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, [4]Nutrition Research Division, International Centre for Diarrhoeal Disease

Research, Bangladesh, Dhaka, Bangladesh, [5]Infectious Diseases Division, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [6]Department of Forestry and Environmental Resources, North Carolina State University, Raleigh, NC, United States

Early life soil-transmitted helminth infection (STH) and diarrhea are associated with growth faltering, anemia, impaired development, and mortality. Exposure to fecal contamination in soil inside the home may be a key contributor to enteric infections, and a large fraction of rural homes in low-income countries have soil floors. We present the protocol of The Cement flooRs AnD chiLd hEalth (CRADLE) trial, which will measure the effect of installing concrete floors in homes with soil floors on child STH infection and maternal and child health outcomes in rural Bangladesh. Our study site is Sirajganj district, a climate vulnerable region, where 66% of households have mud floors. We conducted a pilot study on the prevalence of STH among 6-24 months of children in Chauhali sub-district of Sirajganj (N= 50 households). The prevalence of any STH (*Ascaris lumbricoides*, *Necator americanus*, or *Trichuris trichiura*) was 27% using qPCR. Households with a pregnant woman, a soil floor, no plan to relocate for 3 years, and walls that are not made of mud will be eligible. We will individually randomize 800 households to intervention or control (1:1) within geographic blocks of 10 contiguous households with 100m buffers between households. We will install concrete floors when the birth cohort is in utero and measure outcomes at child ages 3, 6, 12, 18, and 24 months. The primary outcome is the prevalence of any STH infection detected by qPCR at ages 6, 12, 18, or 24 months in the birth cohort. Secondary outcomes include household floor and child hand contamination with *E. coli*, extended-spectrum beta-lactamase producing *E. coli*, child diarrhea, growth, and cognitive development; maternal stress, quality of life, discretionary time, executive function, and depression; and cost-effectiveness. Laboratory staff and data analysts will be blinded; participants will be unblinded. The trial's design and outcomes will be disseminated among local stakeholders from both the private and public sectors. The trial is expected to generate evidence about whether replacing soil floors with concrete is an effective health intervention in rural Bangladesh and similar settings.

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EFFECTS OF A WATER, SANITATION, AND HYGIENE PROGRAM ON DIARRHEA AND CHILD GROWTH IN THE DEMOCRATIC REPUBLIC OF THE CONGO: A CLUSTER-RANDOMIZED CONTROLLED TRIAL OF THE PREVENTATIVE-INTERVENTION-FOR-CHOLERA-FOR-7-DAYS (PICHA7) PROGRAM

Christine Marie George[1], Presence Sanvura[2], Jean-Claude Bisimwa[2], Kelly Endres[1], Alves Namunesha[2], Willy Felicien[2], Jamie Perin[1], David Sack[1], Camille Williams[1], Raissa Boroto[2], Gisèle Nsimire[2], Feza Rugusha[2], Freddy Endeleya[2], Pacifique Kitumaini[2], Claude Lunyelunye[2], Emmanuel Buhendwa[2], Brigitte Munyerenkana[2], Jessy Timsifu[2], Pascal Kitumanini[2], Blessing Muderhwa Banywesize[2], Justin Bengehya[3], Ghislain Maheshe[2], Cirhuza Cikomola[2], Alain Mwishingo[2], Lucien Bisimwa[2]

[1]Johns Hopkins School of Public Health, Baltimore, MD, United States, [2]Université Catholique de Bukavu, Bukavu, Congo, Democratic Republic of the, [3]Division Provinciale de la Santé Sud Kivu, Ministère de la Santé, Bukavu, Congo, Democratic Republic of the

We aimed to assess whether the Preventative-Intervention-for-Cholera-for-7-Days (PICHA7) program reduced diarrhea and improved child growth in the Democratic Republic of the Congo (DRC). The PICHA7 cluster-randomized controlled trial enrolled diarrhea patient households in urban DRC. Diarrhea patient households were randomized to one of two arms: one in-person visit for the standard message given by the DRC government to diarrhea patients on oral rehydration solution use (standard arm); or this standard message and the PICHA7 program with quarterly in-person visits and weekly voice and text mobile health (mHealth) messages (PICHA7 arm). The primary outcome was self- or caregiver-reported diarrhea in the past two weeks assessed monthly for 12 months. The secondary outcomes were diarrhea with rice water stool (cholera symptom), health facility visits for diarrhea, stunting, underweight, and wasting over 12-months. Analysis was by intention to treat. This trial is registered at ClinicalTrials.gov, number NCT05166850. Between 22 December 2021 and 20 December 2022, 2334 participants were randomly allocated to two arms: 1138 to the standard arm and 1196 participants to the PICHA7 arm. For all age groups (children and adults), diarrhea prevalence during the 12 month surveillance period was significantly lower among participants in the PICHA7 arm (Prevalence Ratio (PR): 0.39 (95% Confidence Interval (CI): 0.31, 0.48) compared to the standard arm. Participants in the PICHA7 arm had a 52% lower odds of diarrhea with rice water stool (Odds Ratio (OR): 0.48 (95% CI: 0.27, 0.86)), and 56% lower odds of visiting a health facility for diarrhea during the 12 month surveillance period (OR: 0.44 (95% CI: 0.25, 0.77)). Children under five years were significantly less likely to be stunted in PICHA7 arm compared with the standard arm (52% vs. 63%) (OR: 0.65 (95% CI: 0.43, 0.99)) at the 12 month follow-up. All WASH components had high adherence. The PICHA7 program which combines mHealth with in-person visits lowered diarrhea prevalence and stunting in the DRC.

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REDUCED EXPOSURE TO ENTERIC PATHOGENS IN CHILDREN LIVING FROM BIRTH IN HOUSEHOLDS SERVED BY SANITATION UPGRADES IN URBAN MAPUTO, MOZAMBIQUE

Erin Kowalsky[1], Márcia Chiluvane[2], David Holcomb[1], Vanessa Monteiro[2], Victória Cumbane[2], Elly Mataveia[2], Toheedat Bakare[1], Drew Capone[3], Gouthami Rao[1], Sindhuja Damodaran[1], Samuel Pomper[1], Oliver Cumming[4], Edna Viegas[2], Joe Brown[1]

[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Instituto Nacional de Saúde, Mozambique, Maputo, Mozambique, [3]Indiana University, Bloomington, IN, United States, [4]London School of Hygiene and Tropical Medicine, London, United Kingdom

The Maputo Sanitation (MapSan) trial began in 2015 to evaluate the impacts of a shared (private) sanitation intervention in low-income, informal communities in Maputo, Mozambique. The design included four measurement points: immediately before sanitation improvements, and then at 12, 24, and 60 months post-intervention. Children under 5 were enrolled at each of these time points in household clusters served by better sanitation and in a comparable cohort lacking these improvements. At 60 months post-intervention, all enrolled children in the intervention arm have experienced better sanitation from birth through early childhood. From both intervention (n = 552) and control arms (n = 578), we collected stool samples for molecular analysis for 22 primary enteric pathogens of interest, including 13 bacteria, 5 soil-transmitted helminths (STHs), and 4 protozoa, using customized multi-parallel qPCR in Taqman Array Cards. The intervention effectively reduced the prevalence of combined bacterial pathogens detected (0.91 PR, 95% CI: 0.81-1.0) and combined STH infections (0.77 PR, 95% CI: 0.65-0.91), when adjusting pooled pathogen measurements for prespecified covariates and accounting for clustering. Specific targets reduced in the intervention arm compared with controls included *Trichuris trichiura* (0.65 aPR, 95% CI: 0.52-0.82), *Ascaris lumbricoides* (0.82 aPR, 95% CI: 0.68-1.0), *Shigella spp*/EIEC (0.72 aPR, 95% CI: 0.60-0.88), and *Enterotoxigenic E. coli* (0.76 aPR, 95% CI: 0.58-1.00). Results suggest that children living from birth in households served by upgraded sanitation experience reduced exposure to enteric pathogens.

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A CLUSTER RANDOMIZED CONTROLLED TRIAL FOR THE EFFECT OF A WATER, SANITATION AND HYGIENE KIT COMBINED WITH STANDARD OUTPATIENT TREATMENT ON DRINKING WATER QUALITY IN NORTHERN SENEGAL

Laura Braun[1], Serigne Niang[2], Djiby N'diaye[2], Joseph Wells[1], Matar Ba[2], Clara Macleod[1], Albert E. Cabo[2], Yahya Gnokane[2], Francoise Siroma[3], Jean Lapegue[2], Moustapha Seye[4], Antonio Vargas[5], Alexandre Devort[2], Dleynaba N'diaye[6], Oliver Cumming[1]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Action Against Hunger, Dakar, Senegal, [3]Action against Hunger, Dakar, Senegal, [4]LARTES, Dakar, Senegal, [5]Action Against Hunger, Madrid, Spain, [6]Action Against Hunger, Paris, France

Globally, 17 million children are affected by severe acute malnutrition (SAM). Under the Community-based Management of Acute Malnutrition (CMAM), outpatient treatment is now recommended for uncomplicated cases. This moves treatment from generally more controlled hospital settings to the household, where the presence of environmental hazards is often higher. As part of the *Traitement Intégré de la Sous-Nutrition Aiguë* (TISA) trial in northern Senegal, we evaluate the effect of adding a water, sanitation, and hygiene (WASH) kit to standard outpatient treatment programmes (OTP) for uncomplicated SAM on household water quality. The control group received the standard CMAM protocol of care and the intervention group received this plus a "WASH kit", which included an eight-week supply of chlorination tablets, a 20-litre water storage container, soap, and hygiene promotion materials. Household water samples were collected among 445 households (203 control, 242 intervention) between 4-8 weeks after enrolment. Samples were analysed for turbidity, free chlorine residual, and indicators of faecal contamination. Child diarrhoea was reported by the caretaker with a 7-day recall at admission and week 4. The intervention was successfully delivered, with 94 % of intervention households having the WASH kit at week 4, *vs* <0.1% in the control. 72% of intervention households reported treating their water, *vs* 7% in the control, which was validated by the significantly higher median residual chlorine of 0.5 mg/l (IQR 0.1 - 1.61) compared to 0.1 mg/l (IQR 0.1 - 0.1) in the control. As a result, mean *E. coli* contamination was significantly reduced from 252 CFU/100ml in the control to 94 CFU/100 ml in the intervention. Child diarrhoea was reduced by 15.6% in the intervention arm, *vs* 4.3% in the control. Improved water quality in the intervention arm may reduce exposure to waterborne pathogens, thereby improving recovery rates for children undergoing outpatient treatment for SAM. Nonetheless, the water contamination remained at medium risk in the intervention arm.

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DRINKING WATER QUALITY AND ACCESS IMPACTS ON INFANT GUT MICROBIOME COMPOSITION IN MOZAMBICAN INFANTS

Courtney Victor[1], Konstantinos T. Konstantinidis[2], Sandy McGunegill[1], Rassul Nalá[3], Jedidiah S. Snyder[1], Matthew C. Freeman[1], Karen Levy[4]

[1]Emory University, Atlanta, GA, United States, [2]Georgia Institute of Technology, Atlanta, GA, United States, [3]Ministry of Health (Instituto Nacional de Saúde), Marracuene, Mozambique, [4]University of Washington, Seattle, WA, United States

The gut microbiome influences immune function, infection resistance, cognitive function, and growth. Gut microbiome composition is influenced by early environmental exposures such as delivery mode and diet, but gaps exist in our understanding of the impact of other environmental factors, notably drinking water, on the gut microbiome. To explore if drinking water quality and continuous access to a safe water supply impact gut microbiome composition during early life, we analyzed 16S rRNA gene amplicon sequences from 1200 child fecal samples from a birth-cohort study in Mozambique. We assessed microbiological water quality and access at each child's household at 3, 6, 9, and 12 months of age. We found that increased access to water was associated with an increase in alpha diversity, a measure of sample species richness and evenness, based on multiple metrics. For example, access to an improved water source on the premises was associated with an increase in Shannon's alpha diversity (RR=1.63, p <0.01). Among children living in households where E. coli was not detected in drinking water, differences in community composition between samples (beta diversity) were higher compared to children in households where E. coli was detected (p <0.01). Similarly, among children who did not have access to basic water, water on the premises, and sufficient quantities of water when needed, we found higher dissimilarity in beta diversity compared to children who did have such access (p <0.01 for all variables). Feature-wise association tests revealed differentially abundant taxa in each group across each water quality and access variable assessed, highlighting potential biomarkers associated with water quality and access. We found a null relationship between alpha diversity and microbiological water quality, as defined by the prevalence of E. coli in source (RR=0.93, p=0.68) or stored water (RR=1.05, p=0.71). This study is among the first to evaluate drinking water quality and access as an environmental exposure on the child gut microbiome and contributes valuable information on acute and chronic health outcomes associated with early perturbations to the gut.

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GENOME-WIDE ASSOCIATION STUDY OF AN AFRICAN SNAIL VECTOR OF SCHISTOSOMIASIS IDENTIFIES GENES ASSOCIATED WITH RESISTANCE TO INFECTION BY *SCHISTOSOMA MANSONI*

Tom Pennance[1], Jacob A. Tennessen[2], Johannie M. Spaan[1], Tammie McQuistan[1], George Ogara[3], Fredrick Rawago[1], Martin W. Mutuku[4], Gerald M. Mkoji[4], Eric S. Loker[5], Maurice R. Odiere[3], **Michelle Steinauer**[1]

[1]Western University of Health Sciences, Lebanon, OR, United States, [2]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [3]Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya, [4]Centre for Biotechnology Research and Development, Kenya Medical Research Institute, Nairobi, Kenya, [5]University of New Mexico, Albuquerque, NM, United States

Schistosomiasis, afflicting hundreds of millions of people worldwide, potentially could be controlled by blocking transmission to their freshwater snail vectors. Most infection of *Schistosoma mansoni* occur in sub-Saharan Africa, where they are vectored by *Biomphalaria sudanica* and related species. In contrast to the neotropical vector, *B. glabrata*, there has been little genomic work on African snails; therefore the genetic basis of African snail-parasite interaction is completely unknown. We performed a genome-wide association study (GWAS) of infected (N=493) and uninfected (N=295) *B. sudanica* originating from the shoreline of Lake Victoria. Pools were sequenced and variable regions SNPs assessed. Allele counts of infected vs. uninfected phenotypes at each SNP were compared to identify those with significant associations to the resistance phenotype. An amplicon panel was designed to validate SNPs in an independent group of infected (N=126) and uninfected (N=100) snails. Additive regression and a Fisher's exact test dominance model were used to identify significant hits. We observed population structure, namely two distinct clusters, within our *B. sudanica* data, which were accounted for in downstream analyses. Following validation, several genomic loci in two unlinked genomic regions of *B. sudanica* were associated with schistosome resistance. Both genomic regions occur on linkage groups previously tied to schistosome resistance in *B. glabrata*, but several megabases away from these known loci and thus representing different genes. Both regions are high in nucleotide diversity and contain several duplications, suggesting they are evolutionarily dynamic. Characterized genes associated with parasite resistance tended to contain transmembrane and other functional binding domains, suggesting a potential role in pathogen recognition. These results provide a first glimpse into the innate immune system of the major schistosome vector *B. sudanica*, informing future studies aimed at predicting/manipulating the vector competence of the snail host.

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GENERATING THE GENERATOR: A GIANT COMPLEX ESSENTIAL FOR MITOCHONDRIAL BIOGENESIS IN *PLASMODIUM FALCIPARUM*

Ijeoma Okoye, Ian Lamb, Swati Dass, Joanne M. Morrisey, Michael W. Mather, Akhil B. Vaidya

Drexel University College of Medicine, Philadelphia, PA, United States

Although the *Plasmodium falciparum* mitochondrion is a validated antimalarial drug target, many *P. falciparum* mitochondrial proteins remain uncharacterized. We aimed to define the roles of a newly identified mitochondrial protein, PF3D7_0707400, in *P. falciparum* parasites, particularly in mitochondrial biogenesis. Bioinformatic analyses revealed PF3D7_0707400 to be an ortholog of ATAD3A (ATPase associated with diverse cellular activities), hence we refer to it as *Pf*ATAD3. To achieve our aim, we employed a CRISPR-Cas9 TetR-DOZI genetic approach to generate TOM22-mNG (Translocator of Outer Mitochondrial Membrane 22-mNeonGreen)/*Pf*ATAD3-3xHA-TetR transgenic parasites where expression of *Pf*ATAD3 can be regulated using anhydrotetracycline (aTc). We show that *Pf*ATAD3 is essential for asexual parasite development as parasites not expressing *Pf*ATAD3 are arrested at 72 hours and ultimately die by 96 hours. Northern blots of total RNA isolated from *Pf*ATAD3-knockdown parasites demonstrate a reduction in COX 1 and Cyt b mitochondrial mRNA transcripts as well as small mitochondrial ribosomal RNAs as early as 24 hours after *Pf*ATAD3 knockdown, with minimal to no COX 1, Cytb, and mitoribosomal RNA transcripts present at 72 hours after *Pf*ATAD3 knockdown. Through live cell scanning confocal imaging of parasites at 48 hours post-*Pf*ATAD3-knockdown, we observe a destabilization of the mitochondrial membrane potential in about 60% of *Pf*ATAD3-knockdown parasites as MitoTracker is unable to accumulate in the mitochondria of these parasites and consequently, diffuses across their cytosol. Furthermore, large-pore composite gel electrophoresis revealed *Pf*ATAD3 to be present in a ~ 4MDa complex indicating the presence of multiple interacting partners by which *Pf*ATAD3 is likely to be performing its essential functions in *P. falciparum* mitochondrial physiology. We are in the process of identifying these interacting partners through proteomic and structural analyses.

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A DRUGGABLE AGC KINASE CLRK MEDIATES TEMPORAL REGULATION OF CYCLIC NUCLEOTIDE SIGNALING AND CONTROLS PARASITE EGRESS AND INVASION

Deepti Sarkar, Ravi Kumar Narayanasamy, Luciana Ribeiro Dinis, Abhai Tripathi, Isabelle Coppens, Prakash Srinivasan

Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States

Cyclic nucleotide signaling orchestrates crucial transitions in the *Plasmodium* life cycle. Therefore, its precise regulation is vital to prevent temporal dysregulation of subsequent pathways such as activation of kinases and proteases critical for parasite egress and invasion. Here, we identify an AGC family kinase and elucidate its function as a negative regulator of cyclic nucleotide signaling. Conditional deletion of CLRK (Cyclic Nucleotide Level Regulating Kinase) resulted in elevated levels of cGMP and cAMP, prematurely activating Sub1, a protease, and untimely processing of many downstream substrates. Loss of CLRK also disrupted MSP1 processing, essential for timely parasite egress. Notably, CLRK-null merozoites exhibited an inability to breach the RBC membrane during egress. Furthermore, through chemical genetic approaches, we identified small molecule inhibitors targeting CLRK, effectively blocking schizont development and merozoite invasion. Lastly, using conditional genetic and chemical genetic approaches we demonstrate an important role for CLRK during the sexual stages of the parasite life cycle. Overall, our findings implicate CLRK as a pivotal regulator of cyclic nucleotide signaling in *Plasmodium*, governing key transitions throughout the parasite life cycle and underscores its potential as a promising therapeutic target.

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INCREASED DUFFY BINDING PROTEIN 1 EXPRESSION CORRELATES WITH *PLASMODIUM CYNOMOLGI* GROWTH IN CONTINUOUS CULTURE

Wayne Cheng[1], Magdalena Argomaniz[1], Caitlin C. Cooper[1], Amadis Vivas[1], Saniya Sabnis[1], Sarah G. Roberson[1], Celia L. Saney[1], Mary R. Galinski[2], Steven P. Maher[1], Dennis E. Kyle[1], Chester J. Joyner[1]

[1]University of Georgia, Athens, GA, United States, [2]Emory University, Atlanta, GA, United States

A continuous culture system would revolutionize *Plasmodium vivax (Pv)* research but remains elusive. *P. cynomolgi (Pcy)* is a closely-related nonhuman primate malaria parasite that shares many biological traits with *Pv* except that *Pcy* preferentially, but not exclusively, invades and develops within reticulocytes. This difference has supported the adaptation of *Pcy* lines that grow in culture, but the mechanisms that enable continuous culture are undefined. Here, we generated a new line of the *Pcy* Berok strain, termed DC line, to grow continuously in culture and performed whole genome sequencing of parasites collected during adaptation to identify the genetic changes that promote growth in culture. Minimal single nucleotide variants emerged during adaptation. Structural variations comprised of insertions and deletions (INDELs) were more common and suggested that a subpopulation of parasites was selected for during adaptation versus de novo mutations that led to improved growth. INDELS were present in many genes associated with the parasite's metabolism, consistent with the nutrient-limited environment of culture. Interestingly, the DC line also had additional copies of the Duffy binding protein 1 gene that was associated with increased gene expression. Duffy antigen receptor for chemokines (DARC) is the ligand for DBP1, and the loss of this receptor has been shown to restrict *P. yoelii* to invading reticulocytes. Thus, we hypothesized that overexpression of DBP1 by the DC line may alter the invasion preference from reticulocytes to normocytes, enabling the parasite to grow effectively in culture. Indeed, invasion assays showed that the WT line preferentially invaded and developed within reticulocytes whereas there was no preference for the DC line. In summary, these data indicate that metabolic changes and alterations in invasion ligand expression through copy number variation support continuous growth of *P. cynomolgi* in culture. This information may help adapt additional *Pcy* strains to culture and inform efforts for culturing *Pv*.

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TISSUE COLONIZATION AND INFECTION ESTABLISHMENT OF *TRYPANOSOMA BRUCEI BRUCEI* AT THE BITE SITE

Hang Thi Thu Nguyen, Daniel Bruzzese, Erick Awuoche, Brian Weiss, Serap Aksoy

Yale university, New Haven, CT, United States

Trypanosoma brucei parasite is known for causing diseases in humans and animals, leading to significant public health and economic burdens. Transmission of parasites occurs when epimastigote parasites colonize the Tsetse fly's salivary glands, transitioning into metacyclic parasites capable of infecting mammals. These metacyclic parasites transform into bloodstream form parasites upon entering the mammalian host, evading the immune system. Despite extensive research on systemic immune responses of the mammalian host to trypanosome infections, understanding the establishment of infection at the bite site remains largely unexplored. To understand early infection dynamics, our group focuses on targeting metacyclic parasites introduced into the host at the bite site. Single-cell RNA sequencing of parasites isolated at the bite site holds promise for unraveling infection establishment. However, the challenge lies in separating parasites from host cells or tissues without altering their transcriptomes. To address this challenge, we developed a transgenic parasite expressing a fusion protein containing tdTomato, red-shifted firefly luciferase, and the TY1 tag. These parasites, sorted based on tdTomato expression, were evaluated for infectivity in tsetse flies and their ability to transmit to mice. Following infection initiation, Fluorescence-Activated Cell Sorting (FACS)

was used to isolate tdTomato-expressing parasites from mouse skin tissue at various time points for single-cell RNA sequencing.The transgenic strain demonstrated stability under culture conditions, high infectivity towards tsetse flies, and efficient transmissibility to mice via natural fly bites or needle injection of isolated parasites. Sorting parasites based on fluorescent signals enabled the collection of samples at multiple post-infection time points. Single-cell RNA sequencing of these sorted parasites provided insight into the transcriptomic profiles during differentiation from metacyclic to bloodstream form trypanosomes, facilitating the study of trypanosome infection establishment at the bite site.

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BROKERED DESIGN: COMMUNITY-DRIVEN LEARNING FOR MALARIA ELIMINATION IN THE DOMINICAN REPUBLIC

Karla Estudillo Fuentes[1], Luccene Desir[2], Victoria Krauss[2], Gregory Noland[2], Karen Hamre[2], Nicole Michelen Strofer[3], Domingo Cabral[4], Jose Luis Cruz Raposo[5], James Lavery[1]

[1]Human Engagement Learning Platform, Hubert Department of Global Health, Rollins School of Public Health, Emory University,, Atlanta, GA, United States, [2]The Carter Center, Atlanta, GA, United States, [3]Malaria and Neglected Tropical Diseases Program, Clinton Health Access Initiative, Santo Domingo, Dominican Republic, Santo Domingo, Dominican Republic, [4]Centro de Prevención y Control de Enfermedades Transmitidas por Vectores y Zoonosis, Ministerio de Salud y Asistencia Social, Santo Domingo, Dominican Republic, [5]Centro de Prevención y Control de Enfermedades Transmitidas por Vectores y Zoonosis, Ministerio de Salud y Asistencia Social, Dominican Republic, Santo Domingo, Dominican Republic

Effective community engagement is crucial for achieving the ambitious goal of malaria elimination. *Brokered Design* (BD) is a novel strategy for program co-design and organizational learning, initially developed by the Human Engagement Learning Platform at Emory University in collaboration with The Carter Center, to address declining participation in Mass Drug Administration (MDA) for lymphatic filariasis elimination in Haiti. In January 2024 BD was adapted to malaria elimination efforts in the Dominican Republic (DR). The first co-design round of BD occurred in the San Juan and Azua regions, employing a rapid assessment through community conversations to inform a communications strategy for a Reactive Drug Administration (RDA) implementation in response to a malaria outbreak in these regions in early 2024. The conversations engaged 36 people including community health workers, non-Spanish-speaking agricultural workers, and other community members. Key insights included the importance of recognizing and safeguarding close relationships within the community, incorporating community partners into engagement strategies, respecting all community members, favoring in-person communication channels, providing comfortable settings for conversations with community members, ensuring inclusivity and fairness of communications, and explaining and justifying the health interventions. These insights support the Ministry of Health (MOH) in their developing communications strategy. Consequently, initiatives were undertaken to hire ethnically diverse health workers, involve community groups in strategy implementation, and shape key intervention messages with the national communications team. The rapid assessment served as an initial step in a broader application of BD to support organizational learning for CECOVEZ (DR MOH's tropical diseases center) and its partners to align health intervention designs and implementations with the interests of community stakeholders. We describe subsequent applications of the BD method in the MOH's implementation of RDA in the DR and highlight other potential applications of the method in global health programs.

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ACCELERATING PROGRESS TOWARDS THE ELIMINATION OF MALARIA AND OTHER VECTOR-BORNE DISEASES: ENGAGING WOMEN IN VECTOR CONTROL, THE PAN-AFRICAN MOSQUITO CONTROL ASSOCIATION (PAMCA) EXPERIENCE

Damaris Matoke-Muhia, Jessy Goupeyou-Youmsi, Rosalia Joseph, Christina Sudi, Emma Orefuwa

Pan Africa Mosquito Control Association, Nairobi, Kenya

Despite the progress made in the control of vector-borne diseases (VBDs), the burden of VBDs remains significantly high in tropical and subtropical regions. The ccomplexity of global health problems demands involvement and leadership that represents pluralism in society. The Pan-African Mosquito Control Association (PAMCA), through its Women in Vector Control (WiVC) program seeks to strengthen women's participation and leadership in VBDs control and elimination initiatives in Africa as per the SDG goal 3. In 2021 - 2023, PAMCA WiVC successfully hosted and co-organized trainings including effective communication and leadership skills, proposal, and manuscript writing, safeguarding, among others. A total of 95 women from 29 countries in Africa were trained. Further, the program rolled out a structured mentorship program "LiftHer2", where 42 mentees and 30 mentors in cohorts 1 and 2, of a 12 month period each, were enrolled. To increase visibility and networking, 17 women in early, mid and senior career level from 11 countries in Africa were recognized and awarded for their excellent work and contribution to VBDs. Ten early-career women received travel sponsorship to attend and present their research work during the 8th and 9th PAMCA annual conference in 2022 and 2023, respectively. Enrollment or recruitment to program activities was done through a competitive process, external evaluation and regional balance consideration. Monitoring and evaluation of the program indicate that several women who participated in the activities advanced in their careers, with 6 successfully completing their PhDs, several enrolled for post graduate studies, while others secured new jobs or received promotions at their workplace. The WiVC program has showcased that training, mentorship and recognition of excellence are important in empowering, enhancing leadership roles and addressing VBDs in Africa. The program has immensely contributed to the pool of skilled and knowledgeable African women with capability and confidence to address VBDs, thus contributing to the sustainability of vector control initiatives and elimination programs in the continent.

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ADDRESSING HEALTH DISPARITIES AMONG TRANSGENDER WOMEN IN THE MIDDLE EAST: APPLYING THE ADAPT-ITT MODEL TO REFINE AND ENHANCE A COMMUNITY-BASED HIV INTERVENTION

Sasha Abdallah Fahme[1], Rachel Kaplan[2], Leah Zraika[3], Parya Saberi[2]

[1]Weill Cornell Medicine, New York, NY, United States, [2]University of California San Francisco, San Francisco, CA, United States, [3]Helem Lebanon, Beirut, Lebanon

The Middle East is one of two world regions with increasing HIV incidence. HIV risk and mental health morbidity are high among transgender women in Lebanon, a complex humanitarian setting. Our previous single-group feasibility study of the culturally specific, transgender women-led intervention, 'Baynetna,' demonstrated improved access to HIV testing and mental health outcomes compared to standard of care, but gaps were still observed in HIV prevention and among refugees suffering from traumatic war events and violence. We therefore sought to refine and enhance this intervention by incorporating data on transgender women's lived experiences of health and social disparities in preparation for a full randomized-controlled trial. Applying the ADAPT-ITT model, we conducted focus group discussions (FGDs) with transgender women to gather information on HIV prevention disparities as well as unmet mental health needs related to war trauma and transphobic violence. Based on

these data, we produced a draft of the adapted intervention, consulted with topical experts who provide care to this community, and integrated their feedback into a refined draft intervention. We then theater-tested the enhanced intervention content in FGDs with transgender women and incorporated their opinions into the final intervention. A total of 27 transgender women from Palestine (4%), Syria (30%), and Lebanon (66%) participated in the FGDs. The overwhelming majority experienced extreme poverty and shelter insecurity and did not have health insurance. FGDs demonstrated: poor knowledge of and access to HIV prevention; internalized and experienced HIV and gender identity stigma; traumatic experiences of transphobic and political violence; and refugee-host tensions within the transgender community. Interactive content on HIV and gender identity stigma, HIV prevention, human rights, and community solidarity were adapted and added to the intervention following consultation with topical experts. All theater-testing participants (n=14) regarded the new content as beneficial, appropriate, and feasible for incorporation into the broader intervention.

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TOWARDS INCLUSIVE HEALTHCARE: UNDERSTANDING CAREGIVER PERCEPTION ON THE USE OF A DIGITAL TOOL BY CLINICIANS TO MANAGE SICK CHILDREN IN PRIMARY HEALTHCARE SETTINGS OF TANZANIA: A MIXED METHOD STUDY

Geofrey I. Ashery[1], Ibrahim E. Mtebene[1], Alexandra V. Kulinkina[2], Godfrey A. Kavishe[3], Rainer Tan[4], Chacha D. Mangu[5], Lameck L. Luwanda[1], Peter Agrea[5], Nyanda E. Ntinginya[6], Honorati M. Masanja[1], Valérie D'Acremont[4], Sabine Renggli[1]

[1]Ifakara Health Institute, Dar es Salaam, Tanzania, United Republic of, [2]Swiss Tropical and Public Health Institute, Basel, Switzerland, [3]National Institute of Medical Research, MMRC, Mbeya, Tanzania, United Republic of, [4]University of Lausanne, Lausanne, Switzerland, [5]National Institute for Medical Research, MMRC, Mbeya, Tanzania, United Republic of, [6]National Institute for Medical Research, Mbeya, Tanzania, United Republic of

With ongoing global digitalization, more and more digital tools are being used to provide health services. So far, most research on perception of digital healthcare tools has been done in settings with high levels of digital literacy or from a healthcare provider's perspective. Little is known about how digital tools are perceived by caregivers with low levels of digital literacy who seek care for their sick children. We investigated caregivers' perception of the use of a tablet-based clinical decision support algorithm to manage sick children in rural and peri-urban primary healthcare settings in Tanzania using a mixed-method approach. 222 surveys and 18 focus group discussions with caregivers of children, who were managed using the digital tool, were conducted in the vicinity of nine primary healthcare facilities in Morogoro and Mbeya region, Tanzania. 67% of caregivers interviewed did not use smartphones regularly and 82% had never received any services with smartphones or tablets before, confirming low levels of digital literacy and penetration of such tools. Survey results showed that perceived quality of care increased (81.5%), interaction between caregiver and provider improved (79.7%), caregivers trusted the digital tool (81.1%), and usage of the tool would not negatively influence future healthcare seeking (98.2%). Focus group discussions confirmed the caregivers' overall positive perception of the digital tool. The positive perception of caregivers on using a digital tool to manage sick children in primary healthcare settings suggests that such tools may be used even in settings with low levels of digital literacy.

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DECOMPOSITION ANALYSIS OF CHANGE IN THE BURDEN OF NEGLECTED TROPICAL DISEASES, 1990-2021

Ewerton Cousin, Cathleen Keller, Joanna Whisnant, Stephanie R. M. Zimsen, Taren Gorman, Olivia Nesbit, Lydia Plante, Michael Celone, Quince Hara, Jonathan F. Mosser

Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, United States

The global burden of neglected tropical diseases (NTDs) has decreased significantly due to factors such as improved sanitation, vector control, and treatment availability. Demographic trends also play an important role in understanding and estimating this burden. We aim to describe the change in the burden of NTDs attributable to demographic changes and disease rates from 1990 to 2021. This analysis includes results of 22 NTDs from the Global Burden of Disease (GBD) Study 2021. We describe the disability adjusted life years (DALYs), defined as the sum of years lived with disability and years of life lost. We present global results within super-region, age and cause levels. To estimate the change in the number of NTDs DALYs due to population growth, change in population age-structure, and change in disease rate, we used the Das Gupta three-factor method. Globally, the number of DALYs due to NTDs decreased by 44.3% (95% UI 48.1 to 45.1) from 1990 to 2021, from 29.5 to 16.5 million (95% UIs 22.5 to 41.4, 12.3 to 21.4). Changes in diseases rates contributed to a decline of 73% in the number of DALYs from 1990 to 2021. On the other hand, population growth contributed to an increase of 33% in the number of DALYs. Changes in population age structure had a small effect, contributing to a decrease of 4% in the number of DALYs. Rates of DALYs decreased across all age groups, with similar decreases spanning age groups from 2 to 70, whereas counts of DALYs increased for ages 70 and up. South Asia had the highest decrease in the number of DALYs, moving from 8.88 million in 1990 to 4.08 million in 2021. Changes in disease rates contributed to a decrease of 96% in the number of DALYs, and population growth contributed to an increase of 43%. The age-standardized rate of DALYs decreased from 791 (503 to 1379) to 230 (156 to 318) per 100,000. Our estimates demonstrate that changes in population and rates of NTDs have significantly varied since 1990, by age, geography and cause. These estimates can be utilized as a resource in consideration of policy and intervention strategies to reach control, elimination, and eradication goals of NTDs.

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SPATIAL ACCESS TO HEALTH SERVICES IN THE TRI-BORDER REGION OF ARGENTINA, BOLIVIA, AND PARAGUAY

Carla Rodriguez Gonzalez[1], Susana Ávila[2], Mariana Fernández[2], Favio Crudo[2], Veronica Andreo[1], Maria Victoria Periago[2]

[1]Instituto Gulich, Cordoba, Argentina, [2]Fundacion Mundo Sano, Buenos Aires, Argentina

Increasing access to healthcare services is one of the key objectives of health systems worldwide, as inadequate access contributes significantly to social health inequities. This challenge is particularly pronounced in regions like the Tri-Border area of Argentina, Bolivia, and Paraguay, which face geographical isolation and marginalized healthcare services. Indigenous communities in this region encounter significant obstacles in accessing healthcare, exacerbated by insufficient infrastructure, primary healthcare coverage, and essential resources such as ambulances. The government of Salta province declared this area a "socio-sanitary emergency" in 2020 due to these challenges, highlighting the urgent need for improved healthcare accessibility. In this context, the main objective of this study was to assess the accessibility to health services for indigenous communities in the Tri-Border region using artificial intelligence tools, spatial analysis, and remote sensing. We used a high-resolution SPOT satellite image provided by the Argentine Space Agency (CONAE) and cartographic data obtained from open data sources. For the analysis, the AccessMod5 tool developed by the World Health Organization was used. First, an accessibility analysis was conducted to calculate the spatial distribution of travel time to/from

medical care centers, followed by a geographic coverage analysis to define the influence zone associated with each healthcare center. The resulting maps revealed isolated regions located more than an hour away from the nearest hospitals as well as disparities in healthcare coverage distribution, underscoring areas with fewer healthcare centers and a pressing need for improved infrastructure. These findings emphasize the critical necessity of enhancing the healthcare system in the region and implementing targeted interventions to ensure equitable access to medical services for indigenous communities. Our findings will be disseminated to regional authorities to inform decision-making and promote enhanced access to healthcare services.

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ASSOCIATION OF BLOOD PRESSURE AND ANTHROPOMETRIC INDICATORS WITH GENE VARIANTS IN ADULTS IN THE KASSENA NANKANA MUNICIPAL AND KASSENA NANKANA WEST DISTRICT OF GHANA

Joseph Alale Aweeya[1], Godfred Agongo[2], Patrick O. Ansah[1], Lord Gowans[3]

[1]Navrongo Health Research Centre, Navrongo, Ghana, [2]C. K. Tedam University of Technology and Applied Sciences, Navrongo, Ghana, [3]Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

Cardiovascular diseases are a global health issue with an increasing burden and are exacerbated by hypertension and obesity. High blood pressure and obesity are partly attributed to genetic variants that are generally not known in sub-Saharan African populations. Genome-wide association studies (GWAS), mainly performed in European, African American, and Asian cohorts, have identified variants associated with blood pressure and anthropometric indices. However, few studies have been performed in sub-Saharan Africans.This study evaluated the effect of single nucleotide polymorphisms (SNPs) in eight candidate genes (*ABCA1*, *LCAT*, *LPL*, *PON1*, *CETP*, *PCSK9*, *MVK*, and *MMAB*) on blood pressure and anthropometric indicators among 1,839 Ghanaian adults. DNA was extracted and genotyped using the H3Africa SNP array. Linear regression models were used to test the association between SNPs and log-transformed blood pressure levels and anthropometric indices, adjusting for sex, age, and body mass index (BMI). In addition, Bonferroni correction was performed to account for multiple testing. One variant of the *PCSK9* gene (rs17111557) was significantly associated with diastolic blood pressure (DBP) at $p = 0.003$ with or without Bonferroni correction and $p = 0.006$ after covariate adjustments. This variant was located in the intronic region of the *PCSK9* gene. The functional prediction of this gene variant suggests an impact on the binding site of transcription factors, thereby altering the rate of transcription. The novelty of this study lies in its ability to identify the rs17111557 variant in the *PCSK9* gene to be associated with DBP.

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USE OF A ONE HEALTH APPROACH TO DETECT EIGHT NOVEL HIGH RISK PATHOGENS IN ACUTE FEBRILE PATIENTS IN NIGERIA

Claire Quiner[1], Jay Samuels[2], Jean Kim[1], Philippe Chebu[2], Cyril Erameh[3], Vivian Kwaghe[4], Lauren Courtney[1], Onyia Ejike[4], Ikponmwosa Odia[3], Eke Ofuche[2], Femi Owolagba[2], Kat Asman[1], Osas Edeawe[3], Ephraim Ogbaini[3], Nankpah Vongdip[4], Victoria Orok[4], Oladimeji Matthew[4], Blessed Okira[4], Jacqueline Agbukor[3], Julius Imoyera[3], Adamu Ephraim[1], Emmanuel Oga[1]

[1]RTI International, Research Triangle Park, NC, United States, [2]APIN Public Health Initiatives, Abuja, Nigeria, [3]Irrua Specialist Teaching Hospital, Irrua, Nigeria, [4]University of Abuja Teaching Hospital, Abuja, Nigeria

The Surveillance of AFI Aetiologies in Nigeria (SAFIAN) study aims to investigate infectious etiologies of acute febrile illnesses (AFIs) which are commonly misdiagnosed and treated as malaria. SAFIAN uses the TaqMan-Array Card (TAC), a customizable tool allowing simultaneous screening of up to 380 targets. Pathogens commonly surveilled in Nigeria include Lassa and dengue virus, and Plasmodium spp. However, climate change, urbanization and transportation networks have increased risk of pathogen spread into new geographic locations. We developed a One Health methodology to assess Nigeria's susceptibility to a list of pathogens by evaluating their transmission potential (TP). The evaluation included transmission route, previous detection, and vector presence and habitat suitability in Nigeria. We applied this methodology to select pathogens for the TAC used in SAFIAN. We identified 8 previously undetected or scarcely detected pathogens, including two Category A pathogens. Rickettsia spp. was detected in 55 participants, despite no previous human molecular detection in Nigeria. Its inclusion in SAFIAN was based on prior molecular detection in its tick vector in Nigeria, whose geographic range was documented to have extended to Nigeria in 2013. Crimean-Congo Hemorrhagic Fever Virus and Brucellosis spp., each detected in 4 participants, were included based on existing seroprevalence among humans and/or cattle. Four arboviruses were detected, O'nyong-nyong(5), Chikungunya(4), Zika(3) and West Nile(1); inclusion was based on human seroprevalence and presence of their vectors. Hepatitis E virus(1) was documented in humans and animals and its transmission to humans, fecal-oral route/contaminated water, is vector-independent, such that transmission could occur anywhere. In Nigeria, these 8 pathogens are not surveilled/routinely tested for and are rarely included in research. The number of unexpected findings with public health significance in a modest sample size of 465 demonstrates the utility of our One Health-based methodology. We recommend a broader consideration of pathogens in research beyond established approaches.

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PATHOGEN ANALYSIS NETWORK FOR DETECTING MICROBES IN REAL-TIME (PANDEMIC)

Jessica D. Wiley[1], Ryan C. Chapman[1], Karla Prieto[1], **Michael R. Wiley**[2]

[1]PraesensBIO, LLC, Omaha, NE, United States, [2]University of Nebraska Medical Center, Omaha, NE, United States

Preparing for emerging biological threats has become increasingly challenging. One of the key components of the first line of defense against a biological threat is our biosurveillance systems. Most surveillance strategies rely on PCR assays, which are inexpensive, fast, and target specific. The disadvantage of using PCR-based methods is that they cannot be highly multiplexed (due to loss of sensitivity), so only a limited number of targets may be detected and monitored within a single reaction. While the BioFire® filmarray® provides panels with up to 14 to 43 targets, it still is sensitive to another disadvantage of PCR-based assays, target erosion. Next-generation sequencing has become a viable complement to PCR-based biosurveillance systems. In metagenomics, unbiased sequencing methods can be applied to known or unknown samples to identify and characterize potential pathogens. Although this unbiased approach offers the advantage of detecting anything, it comes at the cost of sensitivity, generally 100-1000 times lower than PCR. With precision metagenomics, hybrid-capture technology is used to detect a wide range of targets with comparable sensitivity to PCR. A major advantage of this technology is its flexibility (targets can be added to the panel as needed), scalability (the same assay can be used in any health care setting and for any number of patient samples), and ability to detect near-neighbors (probes can capture targets up-to 20% divergent at the nucleotide sequence level). The disadvantages of hybrid-capture are the technical expertise needed to run the assay, longer time-to-answer compared to PCR, and cost of running the assay. We have worked towards simplifying hybrid-capture sequencing and making it more deployable in any laboratory setting. We have developed a platform that includes software for designing probes, protocol for running hybrid-capture on multiple sequencing platforms, and software for the analysis of the data. Precision metagenomics adds another tool to help supplement current biosurveillance systems that rely on PCR and metagenomic sequencing.

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SPATIAL VARIATION IN ENVIRONMENTAL AND SOCIODEMOGRAPHIC DRIVERS OF LEPTOSPIROSIS IN THE DOMINICAN REPUBLIC USING A GEOGRAPHICALLY WEIGHTED REGRESSION

Beatris M. Martin[1], Benn Sartorius[1], Helen Mayfield[1], Angela Cadavid Restrepo[2], Cecilia J. Then Paulino[3], Marie C. Etienne[3], Ronald Skewes-Ramm[3], Eric J. Nilles[4], Colleen L. Lau[1]

[1]Centre fo Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, Australia, [2]School of Public Health, Faculty of Medicine, The University of Queensland, Brisbane, Australia, [3]Ministerio de Salud, Republica Dominicana, Santo Domingo, Dominican Republic, [4]Brigham and Womens Hospital, Harvard Medical School, Boston, MA, United States

Between 1970 and 2012, South America (SA) and the Caribbean region accounted for approximately one-third of all leptospirosis outbreaks reported globally. Annual morbidity per 100,000 residents varied significantly from 3.9 in SA to 50.7 in the Caribbean. Drivers of infection, such as exposure to carrier mammals, contaminated water or soil, differ across geographical areas. This geographical variation is not accounted for in non-spatial models, leading to potential inaccuracies. This study aimed to explore spatial variation at the household level of drivers of leptospirosis seroprevalence in the DR using a geographically weighted regression (GWR) and provide evidence to inform public health interventions. Human infection and socio-demographic data were collected from 2,078 participants in 23 communities in two distinct provinces (Espaillat and San Pedro de Macoris (SPM)), in a 3-stage random cross-sectional serosurvey conducted from Jun-Oct/2012. Based on conceptual risk frameworks for leptospirosis, publicly available remote sensing and census data supplemented the survey. Bivariate mixed-effect models identified variables (p <0.2) for the GWR. In the non-spatial model, significantly higher odds ratio (OR) of leptospirosis seropositivity were observed in older age groups, males, households in a flooding risk area, and increased density of rivers and bare ground within 250 meters of households. Conversely, higher mean value of gross domestic product (GDP) at the community level was associated with lower OR of leptospirosis seropositivity. The GWR identified spatial variation in the effect of each covariate included in the model within and across the two provinces. OR of contact with freshwater varied the most across space (7.8, range 0.8-8.2) with limited variation observed in the OR of GDP while still significantly protective across both regions. Older age groups, males, farmers, and contact with rats were associated with higher ORs of leptospirosis seropositivity in SPM compared with Espaillat. These results and framework can be used to inform more targeted and cost-effective public health actions in the DR and regionally.

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UTILIZATION OF NEAR REAL-TIME ENVIRONMENTAL DATA FOR AN 'EARLY WARNING SYSTEM' TO INCREASE PUBLIC PREPAREDNESS OF THE SEASONALITY AND SPREAD OF LYME DISEASE IN THE UNITED STATES

Patrick H. Kelly[1], Sarah Willis[1], James H. Stark[1], Agustín Estrada-Peña[2]

[1]Pfizer, New York City, NY, United States, [2]Ministry of Health, Madrid, Spain

Quantifying the spatiotemporal spread and risk of Lyme disease (LD) in humans remains a major global challenge. Predictive models can identify environmental associations with LD incidence to better inform risk trends. We demonstrate how environmental data can provide near real-time information on the seasonal onset of LD (seasonal model) and which factors most describe the spread of LD in the United States (US) since 2003 and projected into 2030 (spatial model). Centers for Disease Control and Prevention LD incidence data (2001-2021) in 16 high incidence (>10 cases/100,000 persons) and 18 low-incidence LD jurisdictions were used for the spatial model. Administrative claims data were used to estimate LD incidence (2001-2019) in two high incidence states for the seasonal model. Explanatory variables of climate, normalized difference vegetation index (NDVI), land cover, *Ixodes scapularis* presence, and distribution of tick hosts and reservoirs for *Borrelia burgdorferi* were used to train generalized linear and machine-learning algorithms. The seasonal model found a strong association (R^2=0.90) between daily temperatures (p<0.001) and weekly accumulation of NDVI (p<0.001) with the weekly percentile of reported LD cases. NDVI accumulation (>5) and percentile (25th) of annual reported LD cases accelerated by 3 and 5 weeks, respectively, between 2001-2018 suggestive of increasing LD incidence is in part due to earlier or longer LD seasons (p<0.0001). Spatial models (AUC: 0.98) found the variables that best explained LD spread were mostly (71%) non-climate, including county adjacency of LD cases (22%), *I. scapularis* presence (8.4%), variable forest growth (6.3%), and shrew and skink abundances (5.1% each). By 2030, the model predicted 600 counties (20.5% increase from 2019) categorized as high-incidence LD counties with northward expansion into Canada and westward from US Midwest and Northeast regions. We show how our models utilized as 'early warning systems' could be valuable public health tools to increase public preparedness and uptake of protective measures including vaccination to mitigate increasing global health threats like LD.

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COUNTRIES' PROGRESS TOWARDS GLOBAL HEALTH SECURITY WITH INCREASED HEALTH SYSTEMS RESILIENCE DURING THE CORONAVIRUS DISEASE-19 (COVID-19) PANDEMIC: A DIFFERENCE-IN-DIFFERENCE STUDY OF 191 COUNTRIES

Tyler Y. Headley[1], Sooyoung Kim[2], Yesim Tozan[3]

[1]New York University Abu Dhabi, Abu Dhabi, United Arab Emirates, [2]New York University School of Global Public Health, Department of Public Health Policy and Management, New York, NY, United States, [3]New York University School of Global Public Health, Department of Global and Environmental Health, New York, NY, United States

Research on health systems resilience during the COVID-19 pandemic frequently used the Global Health Security Index (GHSI), a composite index of six categories spanning 37 indicators which score countries' health security and related capabilities. Conflicting results, however, raised questions about the index's validity. This study attempted to clarify these varying results and better characterize the effect of countries' progress towards Global Health Security (GHS) on health systems resilience during the pandemic. We used longitudinal data from 191 countries and a difference-in-difference causal inference strategy to quantify the effect of GHSI scores on countries' essential childhood immunization coverage rates. We divided countries into treatment and control groups for all tested indices by testing cutoff values on a sliding scale to determine the minimum value at which a safeguarding effect was observed. All analyses were adjusted for potential confounders and World Bank governance indicators were employed for robustness tests. While overall GHSI scores prevented declines in childhood immunization coverage rates from 2020 - 2022 (coef: 0.91; 95% CI: 0.41 - 1.41), this safeguarding effect was strongest in 2021 (coef: 1.23; 95% CI: 0.05 - 2.41) as compared with 2020 (coef: 0.74; 95% CI: 0.28 - 1.20) and 2022 (coef: 0.76; 95% CI: 0.06 - 1.46). The coefficient sizes for overall GHSI scores were smaller than the coefficients of many of the GHSI's sub-components, including countries' environmental risks (coef: 4.28; 95% CI: 2.56 - 5.99), biosecurity (coef: 1.87; 95% CI: 0.83 - 2.91), and emergency preparedness and response planning (coef: 1.82; 95% CI: 0.54 - 3.11). Our findings indicate that GHS was positively associated with health systems resilience during the pandemic, that GHS may have had the most significant protective effects in 2021 as compared with 2020 and 2022, and that countries' underlying characteristics, including governance quality, also played a key role in health systems resilience during the pandemic.

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DISTRICT READINESS TO RESPOND TO INFECTIOUS DISEASE PUBLIC HEALTH EMERGENCIES ACCORDING TO THE 7-1-7 TIMELINESS METRICS IN EASTERN UGANDA

Richard Ssekitoleko[1], Herbert Isabirye[2], Benjamin Fuller[3], Margaret R Lawrence[3], Solome Okware[1], Annet Alenyo[1], Immaculate Atuhaire[1], Andrew Bakainaga[1], Elizabeth Mgamb[1], Yonas Tegegn Woldemariam[1], Christopher C. Moore[3]

[1]World Health Organization, Kampala, Uganda, [2]Infectious Disease Institute and the National Public Health Emergency Operations Center, Kampala, Uganda, [3]University Of Virginia, Charlottesville, VA, United States

Among districts in Uganda, there is varying capacity to respond to Public Health Emergencies (PHEs). The WHO categorizes PHEs into 4 levels. Grades 1-3 necessitate a WHO response; ungraded PHEs are monitored. The 7-1-7 timeliness metrics include detecting an infectious disease outbreak in 7 days, notifying authorities in 1 day, and response completion in 7 days. These metrics allow for the assessment of the performance of surveillance, reporting, investigation, and response systems. Required capacities and response components include response initiation, epidemiological investigation, laboratory confirmation, medical treatment, countermeasures, communications and community engagement, and response coordination. We determined; 1) the number of WHO-ungraded PHEs in the Mbale and Teso regions of Eastern Uganda from January-March 2024, and 2) the ability of districts to respond according to 7-1-7 metrics. We identified 5 WHO-ungraded infectious disease outbreaks including anthrax (x2), cholera, measles, and rabies in 5 (19%) of 27 districts in Eastern Uganda. The median (IQR) number of days for detection, notification, and response was 8 (4-24.5), 3 (1.5-11), and 15 (8-19.5), respectively. None of the districts met all 7-1-7 targets due to deficiencies in vaccine access, drug availability, clinician training, and notification, which resulted from poor reporting structures for animal and human teams for zoonoses. Delays in response initiation included laboratory confirmation and putting countermeasures in place. Enhancing public health responses at the district level requires multi-hazard risk assessments, contingency plans, and capacity-building for rapid response teams. Using the 7-1-7 metrics could help districts conduct early action reviews to identify performance setbacks and guide resource allocation. Guiding documents can help districts effectively respond to ungraded PHEs.

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A SUBSET OF CAMBODIAN *PLASMODIUM VIVAX* PARASITES TREATED WITH ARTESUNATE DISPLAY SLOW CLEARANCE AND A DELAYED AND UNIQUE GENE EXPRESSION RESPONSE

Kieran Tebben[1], Virak Eng[2], **David Serre**[1], Jean Popovici[2]

[1]University of Maryland School of Medicine, Baltimore, MD, United States, [2]Institut Pasteur du Cambodge, Phnom Penh, Cambodia

Artemisinin-based combination therapies (ACTs) are the frontline antimalarial drugs for the treatment of malaria infections but the efficacy of artemisinin has been threatened by the rise and spread of resistance in *Plasmodium falciparum* since its emergence in Cambodia in the 2000s. Here, we analyze 158 *P. vivax* infections from Cambodian patients treated with 2 mg/kg/day of artesunate for 7 days. All infections were successfully cleared by day 4. However, 9 of the infections (5.7%) showed parasite clearance time (defined as the slope half-life after regression of log-transformed parasite counts) greater than 5 hours, meeting the WHO definition of artemisinin resistance. We observed no significant association between slow clearance and either patient- (e.g., age, weight) or infection characteristics (e.g., parasitemia, stage composition). We characterized by RNA-seq the parasite gene expression of 15 fast- and 16 slow-clearing infections at baseline and 1, 2 and 4 hours after treatment. While the fast-clearing parasites showed significant changes in gene expression immediately upon treatment (with 408 and 1,463 genes differentially expressed 1 and 2 hours after treatment, respectively), slow-clearing parasites displayed a significantly delayed gene expression response (with no genes differentially expressed one hour after treatment and 1,384 and 2,443 differentially expressed genes 2 and 4 hours after treatment). Many of the genes that changed their expression after treatment in both fast- and slow-clearing parasites were indicative of a global shutdown of transcription and translation, as well as of an overall decrease of proteosome activity (similar to the effects of artesunate on *P. falciparum*). By contrast, many genes only differentially expressed in the slow-clearing parasites were associated with hemoglobin endocytosis (e.g., VSP45, PIP3) and hemoglobin digestion (e.g., falcilysin, vivapain). Overall, our results indicate that some Cambodian *P. vivax* parasites are cleared slowly after artesunate treatment, possibly due to their lower hemoglobin metabolism that would reduce the efficiency of the drug.

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EVALUATION OF AN IMPROVED SYBR GREEN I ASSAY FOR SURVEILLANCE OF ANTIMALARIAL RESISTANCE IN *EX VIVO* AND CULTURED ISOLATES

Agnes C. Cheruiyot, Redemptah Yeda, Farid Abdi, Dennis Juma, Benjamin.Opot@usamru-k.org Opot, Raphael Okoth, Jackline Juma, Risper Maisiba, Maurine Mwalo, Edwin Mwakio, Timothy E. Egbo, Hosea Akala

Kenya Medical Research Institute/ USAMRU-A, Kisumu, Kenya

Malaria morbidity and mortality continues to be a public health concern in endemic regions and has been aggravated by emergence of artemisinin resistance. A SYBR Green I fluorescent based assay has been widely used in drug testing of fresh isolates. However limited studies have reported on parallel evaluation of SYBR green I assay using *ex vivo* and culture adapted isolates. We retrospectively analyzed susceptibility data for six drugs to evaluate SYBR Green I assay ability to produce comparable data in *ex vivo* and cultured isolates. Samples were collected under an approved surveillance protocol between 2018 to 2023 collected from hospital sites in all the six malaria epidemiological zones in the country. Total of 530 isolates were tested, *ex vivo* (330) and 200 tested through adaptation against chloroquine (CQ), quinine (QN), artemether (AT), lumefantrine (LU), artemisinin (AR) and amodiaquine (AMQ). Response curves were obtained from relative florescence units (RFU) using Graph Pad Prism. *Ex vivo* versus cultured isolates data for each drug was compared using Wilcoxon matched paired test. Chloroquine had a median concentration of 9.447ng/ml (4.732-15.79) in isolates tested for *ex vivo* and 15.82ng/ml (9.783-25.41) in cultured isolates, p=0.0001. QN median, 21.41ng/ml (11.93-35.17) in *ex vivo* and 22.45 ng/ml (14.10-40.09) in cultured isolates, p=0.17. AR median, 2.762 ng/ml (1.425-4.302) in *ex vivo* and 3.071 ng/ml (2.029-4.352) in cultured. AT 1.884 ng/ml (1.010-3.241) in *ex vivo* and 1.848 ng/ml (1.164-3.116) in cultured, p=0.91. LU, 9.791 ng/ml (2.196-29.55) in *ex vivo* and 10.57 ng/ml (2.924-25.20) in cultured, p=0.19. AQ, 1.897 ng/ml (0.8870-4.142) in *ex vivo* and 1.199 ng/ml (0.7374-2.870) in cultured isolates p=0.10. Median IC_{50}s in five drugs compared in *ex vivo* versus cultured adapted had no significant variation except chloroquine which had a variation but still within the resistance threshold. Therefore in remote laboratory settings where samples cannot be received and tested within 6 hours of collection, they can be cultured and thereafter drug screening done at a convenient time without compromising on data integrity.

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EMERGING BIOLOGICAL THREATS TO MALARIA CONTROL IN UGANDA: EVIDENCE OF VALIDATED MARKERS OF PARTIAL ARTEMISININ RESISTANCE AND *PFHRP2/3* DELETIONS IN A HIGH TRANSMISSION SETTING

Dr. Bosco B. Agaba[1], Trevor Jye[2], David Smith[3], Prof. Antonio Martin[4], Associate Prof. Beshir Khalid[5], Prof. Moses R. Kamya[6], Prof. Pontiano Kaleebu[7], Prof. Piot Peter[4], Prof. Qin Cheng[8]

[1]Malaria Control Division/London School of Hygiene and Tropical Medicine/ Peter Piot Fellow for Global Health Innovation: Epidemic Preparedness & Response/Mbarara University of Science and Technology, kampala, Uganda, [2]QIMR Berghofer Medical Research Institute, Brisbane, Australia, [3]5Australian Defence Force Malaria and Infectious Disease Institute, Australia, Brisbane, Australia, [4]London School of Hygiene and Tropical

Medicine, London, United Kingdom, [5]London School of Hygiene and Tropical Medicine, London, Australia, [6]Infectious Diseases Research Collaboration, kampala, Uganda, [7]London School of Hygiene and Tropical Medicine/Uganda Virus Research Institute, Entebbe, Uganda, [8]Australian Defence Force Malaria and Infectious Disease Institute, Australia, Brisbane, Australia

Artemisinin-based combination therapy is the recommended treatment option for uncomplicated malaria, however emergency of partial artemisinin resistance threatens their effectiveness. Similarly, P. falciparum histidine-rich protein-2 (HRP2) based Rapid diagnostic tests (RDTs) are extensively deployed, however deletion of the *pfhrp2/3* gene threatens their usefulness. Genomic surveillance was conducted in Karamoja, Lango, Acholi and West Nile regions between 2021 and 2023. Symptomatic patients were screened for presence of parasites with HRP2 and pLDH detecting RDTs. Dried blood spots (DBS) were used to confirm parasite species with a conventional multiplex PCR, *pfhrp2* and *pfhrp3* gene with a real-time multiplex qPCR and *pfk13* mutations by Sanger sequencing with Big Dye Terminator. Regional variations in proportions of *PfK13* mutations were assessed using the chi square or Fisher's exact tests while Kruskal-Wallis test was used to compare absolute parasite DNA levels between wild type and mutants parasites. Overall, 238/240 samples (99.2%) were successfully sequenced. Three mutations were identified; *PfK13* C469Y in 32/238 (13.5%) samples, *PfK13*A675V in 14/238 (5.9%) and *PfK13* S522C in (1/238 (0.42%). The prevalence of *PfK13* C469Y mutation was significantly higher in Karamoja region (23.3%), P=0.007. Majority of parasites in West Nile are of wild type (100%), P=0.002. Relative parasite DNA quantity did not differ between the wild type C469Y and A675V alleles (Kruskal-Wallis test, p=0.6373). Overall, qPCR confirmed single *pfhrp2* gene deletion in 1 out of 416 (0.2%) samples that were confirmed of *P. falciparum* mono-infections. Prevalence of validated markers *PfK13* A675V and *PfK13*C469Y in multiple geographical locations provides additional evidence of emerging threat of artemisinin resistance in Uganda. Findings showed limited threat of *pfhrp2/3* gene deletions suggesting HRP2 RDTs are still useful diagnostic tools. Periodic genomic surveillance is recommended to monitor the proportions of gene deletions and its effect on RDTs as well monitor levels of *PfK13* mutations in parallel with in-vivo therapeutic efficacy studies.

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ARTESUNATE-PYRONARIDINE IS EFFICACIOUS FOR THE TREATMENT OF UNCOMPLICATED *PLASMODIUM VIVAX* INFECTIONS AND BLOCKS TRANSMISSION MORE THAN CHLOROQUINE IN ETHIOPIA.

Migbaru Keffale Bezabih[1], Sinknesh Wolde[1], Misganaw Misganaw[1], Hiwot Teka[2], Bereket Hailegiorgis[3], Natnael Lemessa[1], Legesse Alamerie Ejigu[1], Samuel Girma[2], Mekonnen Tadesse[3], Fikregabrail Aberra Kassa[1], Mikiyas Gebremichael[1], Wakweya Chali[1], Amanuel Shimelash[1], Melat Abdo[1], Addisu Gizat[1], Getinet Habtamu[1], Gudisa Assefa Bayissa[4], Teun Bousema[5], Fitsum G. Tadesse[6]

[1]Armauer Hansen Research Institute (AHRI), Addis Ababa, Ethiopia, [2]U.S. President's Malaria Initiative, USAID, Addis Ababa, Ethiopia, [3]ICAP at Columbia University, Addis Ababa, Ethiopia, [4]Ministry of Health, Addis Ababa, Ethiopia, [5]Armauer Hansen Research Institute (AHRI), Nijmegen, Netherlands, [6]London School of Hygiene and Tropical Medicine, London, United Kingdom

In Ethiopia, *Plasmodium vivax* accounts for approximately 40% of malaria cases. The rapid generation of gametocytes contributes to high infectivity of clinical *P. vivax* patients, even before symptoms arise. The impact of antimalarial treatment on this infectivity and the importance of primaquine to prevent onward transmission remains uncertain. We assessed the efficacy, safety, and transmission-blocking effects of artesunate-pyronaridine (PA) and chloroquine (CQ) in combination with 14 days of primaquine (PQ). *P. vivax* infected patients (n=206) were randomly enrolled in the CQ (n=99) and PA (n=107) arms plus PQ administered starting on day 0 to evaluate efficacy on day 28 or 42. To assess transmission potential in the absence of PQ, additional patients were enrolled to receive delayed PQ starting on day 3 following schizonticidal treatment with CQ (n=15) or PA (n=15). Transmission to mosquitoes was thus evaluated by direct membrane feeding on days 0, 1, 2 and 3 after CQ (n=15), CQ + PQ (n=15), PA (n=15), and PA + PQ (n=15). Treatment success on day 42 was high in both the CQ + PQ (95.3%, 82/86) and PA + PQ (98.0%, 97/99) arms. One early treatment failure was observed in the CQ arm whilst 5 late failures were observed in both arms (CQ, 3/86, PA, 2/99). Asexual parasite clearance was higher in the PA (87.7%, 93/106) than CQ (46.5%, 46/99, *P*=0.001) arm on day 1. Similarly, shorter gametocyte clearance time was observed in PA than the CQ arm (*P*<0.001). Before treatment, 91.7% (55/60) of patients infected mosquitoes. On day 1, 46.7% (7/15) and 13.3% (2/15) of patients still infected mosquitoes in the CQ and PA arm, respectively. In the arms that included PQ, only 26.7% (4/15) patients in the CQ + PQ arm was infectious whilst no infection was observed in the PA + PQ arm. None of the patients infected mosquitoes on days 2 and 3. While both the first line, CQ, and alternative drug, PA, were efficacious for the treatment of uncomplicated *P. vivax* malaria in Ethiopia, PA cleared *P. vivax* asexual parasites as well as gametocytes faster than CQ with indications for a greater transmission blocking effect compared to CQ.

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INTERACTIVE GENETIC EPIDEMIOLOGY TOOLS FOR SURVEILLANCE OF DRUG-RESISTANT MALARIA PARASITE STRAINS

Ethan James Booth, Varanya Wasakul, Tess Verschuuren, Olivo Miotto

Mahidol-Oxford Tropical Medicine Research Unit, Bangkok, Thailand

The rapid emergence and spread of drug-resistant malaria threaten elimination efforts in the Greater Mekong Subregion (GMS). The GenRe-Mekong project, in collaboration with National Malaria Control Programs (NMCPs), conducts genetic surveillance of *Plasmodium falciparum* to monitor drug resistance in the GMS. Translating the generated genetic data into graphic outputs easily interpreted by NMCPs requires extensive analyses, posing a major challenge that demands powerful and intuitive tools. We developed the grcMalaria package for genetic analyses and drug resistance mapping using the R language. The package processes standardized genetic surveillance data, as defined by the SpotMalaria Data Dictionary, using public-domain libraries and data sources. Its companion Web-based interface is based on the R Shiny platform, allowing interactive usage of the R package without requiring programming knowledge. The grcMalaria package turns genotyping data into intuitive geographical maps of drug resistance, allele prevalence, diversity, and relatedness with minimal coding. It also provides clustering analyses that identifies and maps genetically similar strains. Furthermore, the grcMalaria Web application provides easy-to-use access to key features of grcMalaria, bypassing the need for R installation and scripting. The grcMalaria R package and web application offer easy access to crucial information on the spread of drug-resistant parasite strains, and help predict changes in drug efficacy at regional, national, provincial and district levels. These tools render genetic epidemiological analysis accessible, and allow NMCPs to integrate and contextualize their findings within broader regional analyses, strengthening future elimination strategies.

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PARTNERSHIP FOR ANTIMALARIAL RESISTANCE MONITORING IN AFRICA (PARMA) HUBS: LOCALIZATION AND CAPACITY STRENGTHENING FOR AFRICAN RESEARCHERS BY AFRICAN RESEARCHERS

Awa Deme[1], Irene Cavros[2], Mamadou A. Diallo[1], Mouhamad Sy[1], Bassirou Ngom[1], Amy Gaye[1], Aita Sene[1], Djiby Sow[1], Tolla Ndiaye[1], Ibrahima M. Ndiaye[1], Daba Zoumarou[1], Jessica McCaffery[3], Marko Bajic[3], Cassandra Webster[4], Jehan Ahmed[5], Daouda Ndiaye[1]

[1]International Research Training Center on Genomics and Health Surveillance (CIGASS), Dakar, Senegal, [2]U.S. President's Malaria Initiative, Malaria Branch, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [3]U.S. President's Malaria Initiative, Laboratory Science

and Diagnostics Branch, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States, [4]CDC Foundation, Atlanta, GA, United States, [5]PATH, Washington, DC, United States

Therapeutic efficacy studies (TESs) are recommended by WHO to be performed every two years in malaria-endemic countries to evaluate antimalarial therapies. Testing samples collected in a TES helps explain treatment failure at the molecular level and allows for timely revisions to national and global policies. The Partnership for Antimalarial Resistance Monitoring in Africa (PARMA) project trains local scientists in malaria-endemic countries to perform these tests independently.
The first PARMA hub was launched in 2022 at the Centre International de recherche, de formation en Génomique Appliquée et de Surveillance Sanitaire (CIGASS) in Dakar, Senegal to address the growing number of TESs and to center analysis and training on the African continent. During training, researchers learn to perform molecular correction to distinguish recurrent from new infections, sequence samples to characterize molecular markers of drug resistance, and analyze bioinformatic data to identify key mutations. The Senegal PARMA hub has proved to be a meaningful opportunity to build expertise, partnership, and collaboration among TES researchers across Africa. Between 2022 and 2024, the hub generated molecular data for 5 countries, hosted 7 African researchers from 4 countries, and produced standardized high-quality reports for stakeholders. One important challenge is bridging the gap between a country sending researchers for PARMA training and the ability of that country to perform the next TES analysis domestically. Because training is intended to encompass a broad overview of topics, developing expertise requires additional practice at the bench. This also depends on key external infrastructural factors such as availability of equipment and reliable electricity. To bridge the gap, in the next 2-3 years the project aims to leverage existing sequencing instruments and highly multiplexed next-generation sequencing panels to lower costs, improve efficiency, and more easily deploy TES assays in countries without highly equipped labs. At least two additional hubs in sub-Saharan Africa will be set up within five years for greater reach and throughput.

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NEW INSIGHTS ON SELECTION OF MALARIA PARASITES REVEALED BY GENOMES OF OLDEST ARCHIVED *PLASMODIUM FALCIPARUM* POPULATION SAMPLES

Alfred Amambua-Ngwa[1], Mouhamadou Fadel Diop[1], Christopher J. Drakeley[2], Umberto D'Alessandro[1], Dominic Kwiatkowski[3], David J. Conway[2]

[1]Medical Research Council Unit The Gambia at London school of Hygiene and Tropical Medicine, Banjul, Gambia, [2]London school of Hygiene and Tropical Medicine, London, United Kingdom, [3]MRC Centre for Genomics and Global Health, Big Data Institute, Oxford University, Oxford, United Kingdom

Studies of selection on malaria parasites have been driven by the goal of understanding the emergence of resistance to different classes of antimalarial drugs. Investigations on other selective processes and their targets has been overshadowed by that on the evolution of drug resistance. To investigate such processes, *Plasmodium falciparum* genomes were sequenced from malaria-infected blood samples collected in The Gambia between 1966 and 1971, before any drug resistance was detected in West Africa. Genomic complexity within infections was higher than in recently collected samples, consistent with a higher intensity of transmission during this period. Although the overall genomic diversity is similar over time, there were fewer clusters of related parasites among the older samples, suggesting that parasite inbreeding was less frequent. There was no signature of selection on drug resistance loci, but strong signatures of directional selection were seen at several chromosomal locations coding mostly for immune and invasion-related genes. A few of these have also been seen in more recent samples, but some are unique and indicate older selective processes. A genomic scan over time confirms major drug resistance loci have undergone marked changes, but changes are also seen at other loci. The most significant of these are at the *gdv1* locus on chromosome 9 that regulates conversion to sexual transmission stages, and at the *Pfsa1* locus on chromosome 2 and *Pfsa3* locus on chromosome 11, both associated with parasite infections of individuals carrying the HbS haemoglobin variant. These results highlight the significant role of human immune and genetic factors in shaping the evolution of malaria parasites

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A COMPLEX *PLASMODIUM FALCIPARUM* CRYPTOTYPE CIRCULATING AT LOW FREQUENCY ACROSS THE AFRICAN CONTINENT

Olivo Miotto[1], Alfred Amambua-Ngwa[2], Lucas N. Amenga-Etego[3], Muzamil M. Abdel Hamid[4], Ishag Adam[5], Enoch Aninagyei[6], Tobias Apinjoh[7], Gordon A. Awandare[3], Philip Bejon[8], Gwladys Bertin[9], Marielle Bouyou-Akotet[10], Claessens Antoine[11], David J. Conway[12], Umberto D'Alessandro[2], Mahamadou Diakite[13], Abdoulaye Djimdé[13], Arjen M. Dondorp[14], Patrick Duffy[15], Rick M. Fairhurst[15], Caterina I. Fanello[14], Anita Ghansah[16], Deus S. Ishengoma[17], Mara Lawniczak[18], Oumou Maïga-Ascofaré[19], Sarah Auburn[20], Anna Rosanas-Urgell[21], Varanya Wasakul[14], Nina FD White[18], Alexandria Harrott[18], Jacob Almagro-Garcia[18], Richard D. Pearson[18], Sonia Goncalves[18], Cristina Ariani[18], Zbynek Bozdech[22], William Hamilton[18], Victoria Simpson[18], Dominic Kwiatkowski[23]

[1]University of Oxford, Bangkok, Thailand, [2]Medical Research Council Unit The Gambia at LSHTM, Banjul, Gambia, [3]West African Centre for Cell Biology of Infectious Pathogens (WACCBIP), University of Ghana, Accra, Ghana, [4]Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan, [5]Department of Obstetrics and Gynecology, Unaizah College of Medicine and Medical Sciences, Qassim University, Unaizah, Saudi Arabia, [6]Department of Biomedical Sciences of School of Basic and Biomedical Sciences, University of Health and Allied Science, Ho, Ghana, [7]Department of Biochemistry and Molecular Biology, University of Buea, Buea, Cameroon, [8]KEMRI Wellcome Trust Research Programme, Kilifi, Kenya, [9]Institute of Research for Development (IRD), Paris, France, [10]Faculty of Medicine, University of Health Sciences, Libreville, Gabon, [11]LPHI, MIVEGEC, INSERM, CNRS, IRD, University of Montpellier, Montpellier, France, [12]London School of Hygiene and Tropical Medicine, London, United Kingdom, [13]Malaria Research and Training Centre, University of Science, Techniques and Technologies of Bamako, Bamako, Mali, [14]Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Bangkok, Thailand, [15]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, United States, [16]Noguchi Memorial Institute for Medical Research (NMIMR), Accra, Ghana, [17]National Institute for Medical Research (NIMR), Dar Es Salaam, Tanzania, United Republic of, [18]Wellcome Sanger Institute, Hinxton, United Kingdom, [19]Bernhard Nocht Institute for Topical Medicine (BNITM), Hamburg, Germany, [20]Menzies School of Health Research, Charles Darwin University, Darwin, Australia, [21]Institute of Tropical Medicine Antwerp, Antwerp, Belgium, [22]School of Biological Sciences, Nanyang Technological University, Singapore, Singapore, [23]Big Data Institute, Oxford University, Oxford, United Kingdom

The population structure of the malaria parasite *Plasmodium falciparum* can reveal underlying demographic and adaptive evolutionary processes. Here, we analyze population structure in 4,376 *P. falciparum* genomes from 21 countries across Africa. We identified a strongly differentiated cluster of parasites, named AF1, comprising ~1.2% of samples analyzed, geographically distributed over 13 countries across the continent. Members of AF1 carry a genetic background consisting of a large number of highly differentiated variants, rarely observed outside this cluster, at a multitude of genomic loci distributed across most chromosomes. At these loci, AF1 haplotypes appear to have common ancestry, irrespective of the sampling location; outside the shared loci, however, AF1 members are genetically similar to other parasites from the same region. AF1 parasites sharing up to 23 genomic co-inherited regions were found in all major regions of Africa, at locations over 7,000 km apart. Many of the differentiated variants are functionally related, comprising structural variations and single-nucleotide polymorphisms in components of the merozoite surface protein 1 complex, and several other genes involved in interactions with host red blood cell membranes, including invasion, egress and erythrocyte antigen export. This is the first report of a genetic background of such complexity and geographical spread. We coined the term *cryptotype* to denote that AF1 is difficult to detect due to its low frequency, and its recombination with local strains. As AF1 spread across the continent, it appears that the

constellation of mutations remained mostly intact in spite of recombination events, suggesting a selective advantage. We propose that AF1 parasites have adapted to an as yet unidentified evolutionary niche, by acquiring a complex compendium of interacting variants that are otherwise absent from Africa. *In vitro* studies may identify AF1's evolutionary niche, providing new perspectives on host-parasite interactions. It is also possible that other cryptotypes circulate in Africa, and new analysis methods may be needed to identify them.

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UNDERSTANDING GENETIC AND TRANSCRIPTIONAL COMPLEXITY IN MALARIA: INSIGHTS FROM SINGLE-CELL RNA-SEQUENCING IN MALI

Sunil Kumar Dogga[1], Jesse Rop[1], Seri Kitada[1], Yomna Gohar[2], Antoine Dara[3], Dinkorma Ouologuem[3], Fatalmoudu Tandina[3], Sekou Sissoko[3], Arthur Talman[4], Abdoulaye Djimdé[3], Mara Lawniczak[1]

[1]Wellcome Sanger Institute, Hinxton, United Kingdom, [2]Institute of Medical Microbiology and Hospital Hygiene, Heidelberg, Germany, [3]University of Science, Techniques and Technologies of Bamako, Bamako, Mali, [4]MIVEGEC, University of Montpellier, IRD, CNRS, Montpellier, France

Malaria, caused by *Plasmodium* parasites transmitted through mosquito bites, poses a significant threat to human life. Regions with a high prevalence of malaria often exhibit complex infections, where individuals harbour multiple genetically distinct strains of *P. falciparum*, some showing symptoms while others remaining asymptomatic. Our study, employing Chromium 10x single-cell RNA sequencing (scRNA-seq), delved into the circulating sexual and asexual populations of *Plasmodium* parasites among approximately 60 volunteers in Faladie, Mali, sampled during the transmission seasons of 2021 and 2022. Using both short and long-read RNA single cell sequencing techniques, we scrutinised the transcriptional and genotypic diversity of parasites within and between hosts, offering unprecedented insights for the first time into strain-specific patterns within malaria carriers. Leveraging full-length single-cell RNA sequencing (MAS-seq/Kinnex), we explored isoform differences between strains and cell types, revealing an additional layer of transcriptional complexity. Expanding our analysis to include *P. ovale* and *P. malariae*, which are prevalent in Mali, we examined their intraerythrocytic life stages at single-cell resolution for the first time. Our investigation across these species seeks to understand the behaviour of individual strains within complex infections and their potential role in determining the symptomatic status of the hosts and propensity for sexual conversion. Moreover, we made these detailed cell atlases accessible as a valuable resource for the malaria research community via the Malaria Cell Atlas website www.malariacellatlas.org.

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GENETIC VARIATIONS IN *PLASMODIUM FALCIPARUM* INVASION LIGANDS AND THEIR COGNATE HUMAN RECEPTOR VARIANTS IN MALARIA CASES FROM THE GAMBIA

Nora Nghochuzie Nganyewo[1], Martha Anita Martha[1], Mouhamadou Fadel Diop[1], Eniyou C. Oriero[1], Lucas N. Amenga-Etego[2], Alfred Amambua-Ngwa[1]

[1]Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine, Banjul, Gambia, [2]West African Centre for Cell Biology and Infectious Pathogens, Accra, Ghana

The malaria parasite *Plasmodium falciparum* invades the human erythrocytes through ligand-receptor interactions which initiate the clinical signs of malaria. The genes encoding the parasite ligands and human receptors might have experienced some evolutionary changes as a result of these interactions, and this could impact malaria incidence and outcomes. However, variations in parasite ligands and their corresponding receptors in the same individuals have received far less attention even though such studies may be useful in vaccines and drug design, refinement of control strategies as well as provide better understanding of disease development, and progression. To investigate this, a paired study of *P. falciparum* merozoite invasion ligands and their corresponding erythrocyte receptor genes from the same infected individual was carried out using the Nanopore amplicon sequencing approach. Blood samples were collected from 288 malaria-positive individuals from four health facilities in The Gambia. Genomic DNA was extracted from the samples and 12 *P. falciparum* genes: EBA175, EBA181, EBA140, Clag2, Clag8, Rh4, Rh5, merozoite surface protein (MSP)1, MSP6, Duffy binding-like MSP (DBLMSP), erythrocyte binding-ligand 1 (EBL-1), and surface-associated interspersed protein 4.2 (SURFIN4.2), and four human receptors: glycophorin (GP) A, GPB, GPC, and complement receptor 1 (CR1) were sequenced. Moderate to high levels of within-host complexity of infection across sites and high inter-SNP linkage disequilibrium were observed in the DBLMSP and SURFIN4.2 genes of *P. falciparum*, and the human glycophorin B, C, and CR1 gene. There was also a lack of spatial structure between *P. falciparum* from different sites while for the human population, individuals from Basse (Upper River Region) were more distinct from the rest of the population. Analysis of the distribution of variants in receptors identified several SNPs in CR1 and a single variant in GPC associated with severe malaria. These findings suggest that specific host-parasite allelic combinations may determine the infection and severity of malaria.

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DEFINING IMMUNE ESCAPE POLYMORPHISMS IN *PLASMODIUM VIVAX*: INSIGHTS FROM THE ANALYSIS OF ALLELIC TURNOVER OF 16 ANTIGENS IN A LONGITUDINAL COHORT OF PAPUA NEW GUINEAN CHILDREN

Alison Paolo Namuco Bareng[1], Myo Naung[1], Zahra Razook[1], Alicia Arnott[2], Enmoore Lin[3], Benson Kiniboro[3], Moses Laman[3], Leanne Robinson[4], Ivo Mueller[2], Alyssa Barry[1]

[1]Deakin University, Victoria, Australia, [2]Walter and Eliza Hall Institute, Victoria, Australia, [3]Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea, [4]Burnet Institute, Victoria, Australia

Plasmodium vivax, a malaria species causing relapse infection, generates a number of "antigenically distinct strains" that trigger sequential waves of immune escape within hosts. Understanding parasite genetic diversity aids in identifying circulating strains in the population, providing important information in designing broadly efficacious vaccines. However, the exact genetic determinants underlying antigenic diversity remain unknown. This study is one of the first investigations to identify immunologically relevant diversity and polymorphisms in the leading *P. vivax* antigen vaccine candidates. We employed multiplexed long-read amplicon sequencing on 603 samples (paired infection among 126 children) obtained from a longitudinal paediatric cohort in Papua New Guinea. Sequence comparison between paired infections in the same individual was conducted to identify the association between the polymorphic sites and the patient's clinical outcome (symptomatic or asymptomatic infection). Immune escape polymorphisms were defined when the proportion of the polymorphic site associated with a transition to symptomatic infection was significantly varied ($p \leq 0.5$) from those associated with asymptomatic transition. The within-host analysis revealed polymorphisms in blood-stage antigens, including AMA-1, DBP, MSP-1, and CyRPA, significantly linked to symptomatic malaria, suggesting involvement in strain-specific immunity. These polymorphisms also surround residues crucial for merozoite binding and invasion, indicating that they could be maintained by immune selection pressure. Categorising these immune escape polymorphisms into immunologically distinct groups showed widespread distribution of non-vaccine strains, while the Sal-1 vaccine strain had relatively low global frequency, potentially compromising the efficacy of the current vaccine formulations. Overall, this study narrowed down the diversity into immunologically relevant strains, which could guide researchers in their rational selection of antigens or constructs to be considered in designing a highly and broadly effective *P. vivax* vaccine

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SOFTWARE TO ESTIMATE THE PROBABILITY THAT A RECURRENT MALARIA INFECTION IS A REINFECTION, RECRUDESCENCE OR RELAPSE.

Aimee R. Taylor[1], Yong See Foo[2], Michael T. White[1]

[1]Institut Pasteur, Université Paris Cité, Paris, France, [2]The University of Melbourne, Parkville, Melbourne, Australia

A recurrent *Plasmodium falciparum* infection can be caused by a failure to treat a preceding infection (recrudescence) or by a new mosquito inoculation (reinfection). In addition, a recurrent *P. vivax* blood-stage infection can be caused by the activation of latent liver-stage parasites called hypnozoites (relapse). Estimating the cause of recurrence is important; for example, when monitoring antimalarial resistance, in therapeutic efficacy studies of treatments for *P. falciparum*, recrudescence needs to be separated from reinfection; to improve treatment for *P. vivax*, in trials of radical cure treatment regimens, relapses need to be separated from reinfection and recrudescence. We developed an R package that practitioners can use to visually interrogate parasite genetic data used for recurrent state inference, and to estimate the probability that a recurrence is a relapse, recrudescence or reinfection (both Pv3Rs and Pf2Rs inference). The inferential framework is built around the modification of a model used previously to estimate relapse probabilities from genetic data on *P. vivax* infections in clinical trial participants. The original model demonstrated the feasibility of *P. vivax* recurrent state genetic inference, but was limited to data on only a few microsatellite markers and at most two recurrences per participant. The updated model is faster and more powerful. It scales linearly with the number of markers, generating probability estimates from genetic data on the many markers typical of amplicon sequencing data. It is able to directly estimate recurrent state probabilities for participants who experience more than two recurrences. Besides a few edge-cases, which we will describe, the estimates generated by the new model are comparable to those generated previously. In summary, we have built a user-friendly tool for malaria recurrent state inference. To facilitate uptake by practitioners and to promote enhancement by methodologists, we will describe the updates to the underlying model, demonstrate how to use the software, outline current limitations and describe future developments.

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GENETIC REGULATION OF *PLASMODIUM FALCIPARUM* OXIDATIVE STRESS RESPONSES

Camilla V. Pires[1], Jenna Oberstaller[1], Min Zhang[1], Chengqi Wang[1], Thomas Otto[2], Julian Rayner[3], John Adams[1]

[1]University of South Florida, Tampa, FL, United States, [2]University of Glasgow, Glasgow, United Kingdom, [3]University of Cambridge, Cambridge, United Kingdom

Malaria caused by Plasmodium falciparum ranks among the deadliest infectious diseases worldwide, responsible for over 600,000 deaths in 2020. Continuing spread of drug-resistant parasites prioritize the search for new drug targets and understanding resistance mechanisms. Drug treatment, fever conditions, and infected sickle cells induce oxidative stress during the asexual stages. Recently, we demonstrated that oxidative stress compromises the effectiveness of antimalarial drugs, suggesting that prolonged exposure to intraerythrocytic microenvironmental oxidative stress, as would occur in endemic regions with high prevalence for sickle trait and other hemoglobinopathies, may predispose malaria parasites to develop tolerance to the oxidative damage caused by antimalarial drugs like artemisinin. To understand the underlying mechanisms linked to this phenomenon, we used large-scale forward genetic screens of P. falciparum piggyBac-transposon mutants to identify genetic mutants with altered sensitivity to oxidative stress. Comparing results from previous piggyBac genetic screens for dihydroartemisinin, heat-shock, and sickle-trait cell, revealed that the underlying mechanisms important in the oxidative stress inducible tolerance to artemisinin in malaria parasite is central to the other blood stage stress survival responses. The most significant altered parasite metabolic activities linked to increased sensitivity to stress conditions are linked to lipid metabolism, exported proteins, and RNA metabolism similar to changes associated with emerging artemisinin resistance in different field isolates. Further investigations are needed to elucidate how the genetic regulation of oxidative stress responses can lead to artemisinin resistance.

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ASSESSMENT OF STRATEGIES USED IN THE MALARIA ELIMINATION DEMONSTRATION PROJECT FOR THE REDUCTION OF MALARIA IN A TRIBAL DISTRICT OF MADHYA PRADESH, INDIA

Harsh Rajvanshi[1], Farzana Islam[2], Altaf Lal[1]

[1]Foundation for Disease Elimination and Control of India, Mumbai, India, [2]Jamia Hamdard University, New Delhi, India

The Malaria Elimination Demonstration Project (MEDP) in the tribal-dominated, malaria-endemic Mandla district of Madhya Pradesh, India, represents a pioneering public-private partnership aimed at addressing the persistent public health challenge of malaria, which constitutes a significant burden in India, particularly within tribal regions. India, noteworthy for being the only High-Burden High-Impact country in the WHO SEAR to report a decline in malaria cases amid the COVID-19 pandemic, sees approximately 70% of its malaria cases originating from tribal areas. MEDP, a collaborative effort involving the Indian Council of Medical Research, Government of Madhya Pradesh, and the Foundation for Disease Elimination and Control of India, was designed to leverage field-tested malaria elimination strategies, with adaptations to local contexts. The project's multifaceted approach encompassed the T4 strategy (tracking, testing, treating, and tracking treatment efficacy), optimisation of vector control measures such Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS), alongside the deployment of a mobile surveillance tool and community-centric Information, Education, and Communication (IEC) initiatives. The project has published over 24 peer-reviewed manuscripts describing various learnings and findings. This study, employing a mixed-methods cross-sectional design, evaluated the project's impact on malaria case reduction, vector control practices, frontline worker knowledge and practices and identified implementation gaps by the state. Conducted across 71 malaria-reporting villages in Mandla, the study involved a diverse cohort of participants, including healthcare workers, malaria patients, supervisory staff, and technical experts. The findings highlighted notable achievements in case reduction and diagnostic and treatment efficiency among frontline staff and illuminated various challenges. The study uncovers valuable insights into effective malaria elimination strategies, which can be adapted to similar local and global contexts.

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ADVANCING MALARIA ELIMINATION ASSESSMENT IN LORETO, PERU THROUGH THE FREEDOM FROM INFECTION MODEL

Jorge Ruiz-Cabrejos[1], Luca Nelli[2], Bryan Fernandez-Camacho[1], Brian Peña-Calero[1], Jose Luis Barboza[1], Luciana Bartolini-Arana[1], Hugo Rodriguez-Ferrucci[3], Veronica E. Soto-Calle[4], Isabel Byrne[5], Monica Hill[5], Lynn Grignard[5], Kevin Tetteh[5], Alejandro Llanos-Cuentas[6], Chris Drakeley[5], Gillian Stresman[5], Gabriel Carrasco-Escobar[1]

[1]Health Innovation Laboratory, Universidad Peruana Cayetano Heredia, Lima, Peru, [2]School of Biodiversity, One Health and Veterinary Medicine. University of Glasgow, Glasgow, United Kingdom, [3]Universidad Nacional de la Amazonía Peruana, Iquitos, Peru, [4]Dirección de Prevención y Control de Enfermedades Metaxénicas y Zoonosis, Ministerio de Salud, Lima, Peru, [5]London School of Hygiene and Tropical Medicine, London, United Kingdom, [6]Institute of Tropical Medicine Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru

Perú has experienced a substantial decrease in malaria incidence over the past two decades, after intense control programs successfully interrupted transmission in historically endemic regions. In 2023, 90% of malaria cases occurred within Loreto, prompting the National Malaria Elimination Plan to target this region for elimination by 2030. Currently, claims of elimination rely on the absence of reported malaria cases for 36 consecutive months,

following the World Health Organization's (WHO) standard approach, but this method fails to consider limitations and potential underperformance of the surveillance system (SS). This study aims to probabilistically identify areas in Loreto, Perú that are likely to have achieved malaria elimination. We employed a Bayesian modelling approach within the Freedom from Infection (FFI) framework to estimate the probability that malaria transmission is below a critical threshold, defined here as less than 1 case per 10,000 people (PFree). We used passive case detection data (PCD) from 474 health facilities across 53 districts from 2010 to 2022. The primary outcome was PFree measured for both *Plasmodium vivax* (*Pv*) and *P. falciparum* (*Pf*). We defined the threshold for elimination as having a PFree>0.95 for 36 consecutive months in the most recent 3 years (2020-2022) as per the WHO criteria, and compared concordance in classifying facilities as eliminated using the two methods. Overall, PFree values for *Pf* were higher than PFree values for *Pv*. Preliminary results had 24 HFs for *Pf* and 3 HFs for *Pv* with a PFree>0.95 for 36 consecutive months. In contrast, 181 and 126 HFs had zero cases reported for *Pf* and *Pv* respectively. Our results provide a data driven assessment of the progress made towards malaria elimination in the Peruvian Amazon jungle with potential application to others subnational areas in track for malaria elimination in the Region.

6799

COMMUNITY EXPERIENCES AND PERCEPTIONS OF THE BOHEMIA TRIAL OF IVERMECTIN MASS DRUG ADMINISTRATION: A LONGITUDINAL QUALITATIVE STUDY IN KWALE COUNTY, KENYA

Truphena N. Onyango, Khadija Nuru, Karisa Kazungu, Winnie Wangari, Caroline Jones

KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya

The efficacy of ivermectin MDA for malaria control has been tested in clinical trials in sub-Saharan Africa. Multiple individual, social, and operational factors influence uptake and adherence to MDA. For sustained involvement of participants in MDA trials it is essential to understand the local context, including health concerns, previous experiences of MDA, and trial expectations. This knowledge helps develop appropriate community engagement strategies and interpret responses of participants to the trial and the MDA. This paper describes a longitudinal qualitative study undertaken to explore experiences of trial participation and perceptions of effects of ivermectin MDA among participants in the BOHEMIA cluster randomised trial of ivermectin MDA in Kwale, Kenya. Purposive maximum variation sampling was used to select five villages (2intervention and 3 control) involved in the trial. Before the start of the trial social science researchers lived in each village for a period of one month conducting participant and non-participant observations, in-depth interviews and focus group discussions. Just prior to the first round of MDA, the social scientists returned to the villages and stayed there throughout each of the 3 rounds of MDA, conducting participant and non-participant observations of the implementation process; and in-depth interviews on experiences and perceptions of the trial and the effects of the MDA. Observation reports for each village before and during the MDA were developed. 25 IDIs and 18 FGDs were conducted prior to the MDA and 22 IDIs during the MDA. The conduct of the trial (MDA distribution strategy, use of informed consent, detailed checking of eligibility) as well as confidence in the implementing institution, enhanced trust in the trial and the efficacy of the MDA. Poor past experiences with MDA and perceptions of exclusion from community engagement process contributed to unwillingness to participate. In intervention and control arms, the MDA was widely perceived to be effective at reducing mosquitoes and malaria. In the intervention arm the MDA was also perceived to be very effective at killing bedbugs.

6800

REACTIVE CASE DETECTION IN ZANZIBAR, A MALARIA ELIMINATION-TARGETED SETTING EXPERIENCING MALARIA UPSURGES IN 2023

Michael Gulaka[1], Abdulhamid Ramadhan[2], Mohamed Ali Kitwasi[2], Stella Makwaruzi[1], Saidi Mgata[1], Geofrey Makenga[1], Nicodemus Govella[1], Marguerite M. Clougherty[3], Roly Gosling[3], Shija J. Shija[2], Albert Ikonje[4], Sarah-Blythe Ballard[5], Naomi Serbantez[4], Sigsibert Mkude[1]

[1]Population Services International (PSI), Dar es Salaam, Tanzania, United Republic of, [2]Zanzibar Malaria Elimination Program, Ministry of Health, Zanzibar, Tanzania, United Republic of, [3]Population Services International (PSI), Washington DC, WA, United States, [4]U.S. President's Malaria Initiative, U.S. Agency for International Development, Dar es Salaam, Tanzania, United Republic of, [5]U.S. President's Malaria Initiative, U.S. Centers for Disease Control and Prevention, Dar es Salaam, Tanzania, United Republic of

Reactive case detection (RACD) is a malaria elimination intervention that aims to assess malaria transmission among individuals exposed to the same malaria risks as an index case. In Unguja, Zanzibar, in 2023, RACD was conducted by District Medical Surveillance Officers (DMSO) using malaria rapid diagnostic tests (mRDTs) on household members of parasitologically-confirmed malaria cases reported to the national malaria case notification (MCN) system. Positive cases were treated with artemether-lumefantrine. Data were collected using Android tablets and analyzed descriptively. In 2023, 18,283 malaria cases from Unjuja, Zanzibar, were reported to MCN (reference: 4,544 cases in 2022). Household (HH)-level case investigations were conducted for 9,203 (50%) of index cases, and 30,160 household members (including index case) were present during DMSO visits. Of these, 20,957 (70%) were HH members who consented to testing, and 2.5% (530/20,957) tested positive for malaria. HH denominator data were not collected; however, DMSOs reported that HH members, including those at highest risk for malaria infection (adult males), were frequently absent at the time of case investigation. The positivity rate varied across districts: rural Kaskazini A (5.6% [43/766]) and Kati (5.4% [126/2345]) had the highest, while urban Magharibi B (1.3% [68/5195]) and Magharibi A (1.2% [44/3731]) had the lowest. Individuals aged 15-<25 years had the highest positivity rate (3.4% [160/4532]), followed by 5-<15 (3.1% [152/4842]), under 5 (2.3% [56/2458]), and 25+ (1.8% [162/8966]) years. Males had a higher positivity rate (2.8% [272/9892]) than females (2.3% [258/11065]), p=0.055. RACD data demonstrated low coverage of index case HHs and family members, together with low test positivity rates. HH-focused RACD might not be targeting individuals sharing risk factors with the index case. For many, the likely source of infection is outside of the HH, such as the workplace or location of evening activities. As RACD is not a burden reduction tool, higher coverage, better targeted RACD would likely be of more benefit to areas where transmission is closer to zero.

6801

RE-EMERGENCE OF *PLASMODIUM VIVAX* MALARIA CASES IN BORDER AREAS OF MYANMAR AND STRATEGIC EFFORTS TO INTEGRATE NEW TOOLS AT NATIONAL LEVEL FOR ELIMINATION OF *P. VIVAX* MALARIA FROM 2021 TO 2023

Zwe Thihaa Kyaw, Wah Wah Thaw, Kyi Tun Lwin, Soe Htike, Day Naing Aung, Han Lin Aung, Khin Zarli Aye

PATH, Yangon, Myanmar

Despite advances in malaria control, *Plasmodium vivax* malaria remains a problem in border areas of Myanmar. Cases have increased from 43,578 in 2020 to 103,216 in 2022, posing a threat to the country's 2030 elimination goal. The main barriers to addressing *P. vivax* malaria include lack of glucose-6-phosphate dehydrogenase (G6PD) testing before antimalarial treatment, patient adherence to antimalarial treatment, and political instability. This abstract highlights PATH Myanmar's strategic efforts to revise the National Treatment Guideline (NTG) in partnership with the National Malaria Control Program (NMCP), to ultimately reduce the *P.*

vivax malaria case burden in Myanmar. PATH Myanmar has collaborated with the Partnership for Vivax Malaria Elimination (PAVE) to introduce four new tools in Myanmar: primaquine (PQ) treatment counselling, feasibility studies for G6PD testing, PQ shorter regimen, and the establishment of a pharmacovigilance (PhV) working group to raise awareness and knowledge of utilization of tools. PAVE developed an optimized radical cure road map in 2020, followed by the development of PQ adherence counselling tools in 2021. In 2022, PAVE organized the first technical advocacy meeting for use of optimized radical cure tools at the national level and for the introduction of a PhV system for antimalarial medication in Myanmar. In 2023, PAVE advocated to the NMCP for the implementation of operational research for G6PD testing and organized a central-level workshop focusing on PQ adherence counseling and integration of the PQ 7-days regimen into the NTG. Through these strategic efforts, the tools for PQ treatment adherence and counselling are used nationwide, and the PQ 7-days regimen will be integrated into the NTG. Moreover, a PhV system is being developed at the national level. Although operational research for G6PD testing has been delayed due to the political instability in Myanmar, PAVE efforts have successfully encouraged the NMCP to integrate new tools into the NTG to guide reduction of *P. vivax* malaria in Myanmar.

6802

OPTIMIZING LAST-MILE DELIVERY THROUGH THE INTEGRATION OF MALARIA COMMODITIES DISTRIBUTION IN MALAWI

Fikadu Batu[1], Daniel Taddesse Taddesse[1], Lumbani Munthali[2], Lumbani Makwakwa[3], Denver Raisi[1], Elias Mwalabu[1], Charles Nzawa[1]

[1]USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project, Lilongwe, Malawi, [2]Ministry of Health-NMCP, Lilongwe, Malawi, [3]USAID, Lilongwe, Malawi

Efficient supply chain management is crucial for malaria management in Malawi, where 6.4 million cases were reported in 2023, necessitating timely and effective distribution of life-saving commodities. The country's supply of malaria commodities is predominantly funded by the U.S. President's Malaria Initiative (PMI) and the Global Fund (GF), and the historical use of separate storage and distribution systems had become a logistical burden to its National Malaria Control Program (NMCP). Monthly coordination of two plans resulted in duplication, complexity, inefficiency, delays, and higher costs, and recording transactions for two distribution streams at service delivery points meant an increased workload for health facility staff. To address this, the NMCP, supported by the USAID Global Health Supply Chain Program-Procurement and Supply Management (GHSC-PSM) project, in coordination with GF and PMI, facilitated the signing of a Memorandum of Understanding (MOU) in 2022 between the GF project implementation unit (PIU) and GHSC-PSM. The MOU formalized the launch of an integrated distribution mechanism that facilitated visibility of central warehouse inventory data and distribution schedules, and alternated distribution every other month between the two service providers. This initiative resulted in a substantial (30%) reduction in overall distribution costs between October 2022-September 2023, notably in operational, transportation, and personnel expenses. Annual cost savings for the period totaled $133,000 for PMI alone. The reduced frequency in delivery, from 12 to 6 deliveries per year, significantly reduced the workload for health facility staff, while maintaining low stockout rates (<1% for first-line Artemisinin-based combination therapy treatments). These results of substantial cost savings, operational transparency, and improved efficiency in managing malaria commodities validate the integrated system's ability to enhance distribution and provide a basis for potential implementation in similar contexts, especially to optimize limited resources and improve last-mile delivery of health commodities.

6803

EXAMINATION OF PATHOGENS AND FECAL MARKERS IN THE ENVIRONMENT DUE TO INADEQUATE SANITATION SERVICES IN THE ALABAMA BLACK BELT.

Olivia A. Harmon, Megan Lott, Joe Brown

The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

It is estimated that 2.2 million Americans live in homes that lack access to running water or basic plumbing. These shortcomings in access are even more likely to be experienced in Black, Indigenous, and Latino communities when compared to their white counterparts. One region where these inequalities in access to safe and reliable water and sanitation services persist is Alabama's Black Belt. This research aims to get an idea of the microbes present in the environment due to inadequate sanitation infrastructure in a small rural Black Belt community. We collected surface water and soil samples at properties owned by the Auburn Rural Studio and public spaces in the community over January, February, and May of 2023. We collected 125 samples (92 water samples and 33 soil samples) over the course of three months. Of the 125 samples collected 43 were cultured for total coliform, *E. coli*, and Enterococci by IDEXX, and 88 were examined for 48 molecular targets through real-time quantitative PCR using a custom TaqMan Array Card. Of the environmental samples collected and cultured by IDEXX, 43/43 (100%) contained total coliforms, 35/43 (81.4%) contained *E. coli*, and 31/31 (100%) contained enterococci. Of the 88 environmental samples analyzed by TaqMan Array Card, 39 (44.3%) contained gene targets specific to *E. coli* and 67 (76.1%) contained gene targets specific to enterococci. We found *Blastocystis spp.* in 5 of 63 soil samples (7.9%) and 16 of 25 water samples (64%) and *Cryptosporidium spp.* in 20/25 (80%) of surface water samples examined. There was no significant difference in concentration of *E. coli* or enterococci between sites that were impacted and unimpacted by inadequate sanitation in January ($p = 0.561$ for *E. coli* and $p = 0.941$ for enterococcus *Wilcoxon Rank Sum Test*) and February ($p = 0.102$ for *E. coli* and $p = 0.346$ for enterococcus *Wilcoxon Rank Sum Test*). However, the concentration of *E. coli* or enterococci was significantly higher from those samples collected in sites impacted by inadequate sanitation when compared to unimpacted sites in May ($p = 0.0284$ for *E. coli* and $p = 0.0158$ for enterococcus *Wilcoxon Rank Sum Test*).

6804

FECAL EXPOSURE PATHWAYS FOR CHILDREN IN LOW-INCOME, UNPLANNED COMMUNITIES OF URBAN MAPUTO, MOZAMBIQUE USING A QUANTITATIVE MICROBIAL RISK ASSESSMENT FRAMEWORK

Julia Silva Sobolik[1], Elly Mataveia[2], Mahira Amade[2], Cynthia Silva[2], Liliana Dengo-Baloi[1], Laura Braun[1], Oliver Cumming[1], Edna Viegas[2], Jackie Knee[1]

[1]LSHTM, London, United Kingdom, [2]Centro de Investigação e Treino em Saúde da Polana Caniço (CISPOC), Maputo, Mozambique

Enteric pathogen exposures are critical drivers of child mortality in Mozambique with 6.6% of total deaths among children <5 attributed to enteric infections. Despite high prevalence of enteric infections in children, the household transmission pathway(s) driving these exposures are still being explored. To identify the critical exposures for children <24 months in low-income, unplanned communities in Maputo, Mozambique, we collected and analyzed environmental samples (n=574) for culturable *E. coli*: drinking water (source [n=48], stored [74]), food (solid [61], liquid [28]), hands (mother [78], child [76]), surface swabs (floor [75], food preparation area [71]), and soil [63] in the household setting. We estimated daily quantitative *E. coli* exposure doses for a child using a stochastic quantitative microbial assessment (QMRA) model (10,000 iterations, mc2d package) and caregiver-reported food consumption rates. Relative reductions in *E. coli* dose were calculated for water treatment (boiling once daily) and handwashing (uniform distribution: 1-4 times daily, 30-90% efficacy). Among all samples, 251 (44%) were positive for culturable *E. coli*, with the highest concentrations in soil (mean $\log_{10}$: 4.77 per 1g) and child's hands

(mean $\log_{10}$: 3.55 per two hands). The lowest *E. coli* concentration was for source drinking water (mean $\log_{10}$: 1.07 per 100 mL). Using the QMRA model, solid food consumption was the dominant *E. coli* exposure pathway: median 710.5 CFU/day (95th percentile range: 2.3, 2.0 x 10^{5}). The lowest *E. coli* dose was associated with child's hands: median 0.4 CFU/day (95th percentile range: 4.7 x 10^{-4}, 381.6). Simulating single interventions, boiling of stored water reduced the *E. coli* dose by > 99.999% to a median 1.4 x 10^{-4} CFU/day, whereas handwashing resulted in an attenuated dose reduction (22%) to a median 3.1 x 10^{-1} CFU/day. This study underscores the importance of food-mediated fecal exposures among children. Forthcoming enteric pathogen data aims to corroborate the relevant exposure pathways and impact on child health. Evaluation of targeted food interventions to interrupt food-mediated exposures are warranted.

6805

UNDERSTANDING ANTIBIOTIC RESISTANCE, VIRULENCE, AND BIOFILM FORMATION IN *ACINETOBACTER BAUMANNII*: INSIGHTS FROM GORANCHATBARI SUB-CATCHMENT, DHAKA CITY

Mohammad Rafiqul Islam, Mohammad Atique Ul Alam, Md. Sakib Hossain, Amanta Rahman, Ashrin Haque, Md. Foysal Abedin, Md. Hajbiur Rahman, Md. Shafiqul Islam, Zahid Hayat Mahmud

icddr,b, Dhaka, Bangladesh

Increased incidence of hospital acquired infections may be attributed due to the existence of ESBL producing *Acinetobacter baumannii,* a serious health concern for both hospitals as well as community healthcare environment. The biofilm forming capacity makes them a persistent pathogen in these environments. This study aimed to isolate *A. baumannii* positive for ESBL production from environmental samples, characterization of key virulence and ESBL genes, assessment of antibiotic resistance profile and biofilm forming capacity. A total of 21 environmental samples were collected between April-December, 2022. In this study, 56 isolates of ESBL producing *A. baumannii* were investigated. The ESBL producing *A. baumannii* were subjected to PCR to detect resistance and virulence genes. Among those isolates, 71.4% and 5.4% contained bla_{TEM} and bla_{SHV} genes respectively. In the case of virulence factors, 76.8%, 69.6%, 64.3%, 62.5%, 28.6%, 10.7% and 5.4% of the isolates harbored *pgaB*, *bfmS*, *csuE*, *ompA*, *kpsMII*, *fimH* and *bap* genes respectively. Whereas, 26.8% of the isolates were positive for each of *ptk* and *epsA* genes. During the biofilm formation assay, it was observed that 1.8% of the isolates formed strong and 66.1% formed weak biofilm respectively at 25ºC. In addition, at 37ºC, 1.8% of isolates were moderate and 76.8% were weak biofilm formers respectively. Antibiotic susceptibility testing revealed that 8.9% of the studied isolates were found resistant to cefotaxime and 5.4% were to cotrimoxazole. In addition, 87.5% and 91.1% of studied isolates were found intermediately resistant to ceftriaxone and cefotaxime respectively. As indicated by this study, *A. baumannii*, which produces ESBLs, is rapidly migrating from clinical settings into the environment and could serve as a reservoir for antimicrobial resistance. The data could significantly impact how well public healthcare initiatives are implemented. Exposure to them may create a severe threat to public health.

6806

ENVIRONMENTAL EXPOSURES ASSOCIATED WITH ENTERIC PATHOGEN CARRIAGE IN CHILDREN AGED SIX MONTHS IN NORTHERN ECUADOR

Kelsey J. Jesser[1], Nicolette A. Zhou[2], Caitlin Hemlock[1], Molly K. Miller-Petrie[1], Christine S. Fagnant-Sperati[1], April Ballard[3], Paige Witucki[4], Andrea Sosa-Moreno[4], Gabriel Trueba[5], William Cevallos[6], Gwenyth O. Lee[7], Joseph N.S. Eisenberg[4], Karen Levy[1]

[1]University of Washington, Seattle, WA, United States, [2]University of Washington, SEATTLE, WA, United States, [3]Georgia State University, Atlanta, GA, United States, [4]University of Michigan, Ann Arbor, MI, United States, [5]Universidad San Francisco de Quito, Quito, Ecuador, [6]Universidad Central del Ecuador, Quito, Ecuador, [7]Rutgers University, New Brunswick, NJ, United States

Enteric pathogens are a major cause of mortality and morbidity globally, disproportionately impacting populations in low- and middle-income countries with limited access to water, sanitation, and hygiene (WaSH) resources. We identified environmental risk factors associated with enteric infection in 6-month-old infants along an urban-rural gradient in northern Ecuador; communities were grouped as urban, semi-urban, and rural with road or river access. We collected exposure data on household WaSH, animal exposure, floor material, crowding, and fecal contamination of drinking water and hand rinses, as well as covariates including mother and child demographics, child vaccination status, food insecurity, and socioeconomic status. Child stool samples were analyzed for bacterial (n=10), viral (n=6), and parasitic (n=6) pathogens using multiplex TaqMan Array Cards. We utilized multivariate models, elastic net regression, and distance-based statistical methods to explore factors associated with: i) any infection, ii) coinfection, iii) total number of pathogens, and infection with any iv) bacteria, v) virus, or vi) parasite. Among 276 children, most (87%) were positive for at least one pathogen and 71% were positive for multiple pathogens. Bacterial pathogens were most common (81%), followed by viruses (57%) and parasites (8.3%). Factors associated with reduced risk of infection (p<0.05) included: ceramic tile floors, improved hygiene, and unshared household toilet attached to a sewer system. Risk factors included living in a semi-urban or rural community; having unimproved sanitation; and having a drinking water source from a well or surface water. Seasonality was associated with the likelihood of infection, with fewer viral infections and more bacterial infections in the rainy season. We will also report on specific pathogens, for example *E. coli* detection in child hand rinse was associated with *Giardia* infection. Environmental conditions are associated with enteric infection risk, varying by pathogen type. This data suggests areas of focus for future WaSH interventions with the goal of reducing enteric disease burdens.

6807

SOIL-BORNE EXPOSURE TO ANTIMICROBIAL RESISTANT *E. COLI* AND SOIL-TRANSMITTED HELMINTHS THROUGH SOIL FLOORS IN RURAL BANGLADESH

Ayse Ercumen[1], Md. Sakib Hossain[2], Tahani Tabassum[2], Ashrin Haque[2], Amanta Rahman[2], Md. Hajbiur Rahman[2], Claire Anderson[3], Sumaiya Tazin[1], Suhi Hanif[3], Md. Rana Miah[2], Afsana Yeamin[2], Farjana Jahan[2], Abul Kasham Shoab[2], Zahid Hayat Mahmud[2], Mahbubur Rahman[2], **Jade Benjamin-Chung**[3]

[1]North Carolina State University, Raleigh, NC, United States, [2]icddr,b, Dhaka, Bangladesh, [3]Stanford University, Stanford, CA, United States

Floors made of soil are common in low-income countries and are increasingly recognized as an exposure route for childhood infectious diseases, including soil-transmitted helminth (STH) infections. Soil is also a critical reservoir for antimicrobial resistant organisms. We aimed to investigate associations between flooring material and detection of antimicrobial resistant *E. coli* and STH on floors among rural Bangladeshi households. We enrolled 49 households with a child <2 years (28 with soil floors, 21 with concrete floors) in villages of Sirajganj district in northwestern Bangladesh. Field staff identified the room where the child slept to swab a 50 x 50 cm area using a sterile pre-hydrated sponge and sweep floor dust from up to ten 50 x 50 cm areas with a clean brush. Swab samples were eluted from the sponge with sterile water and analyzed using IDEXX QuantiTray/2000 with Colilert-18 and cefotaxime supplementation to enumerate the most probable number (MPN) of cefotaxime-resistant *E. coli*. We detected *Ascaris lumbricoides* and *Trichuris trichiura* with qPCR in floor dust samples and with microscopy in floor swab samples. There was a mean of 8.0 g of dust on soil floors vs. 0.2 g on concrete floors (t-test p-value=0.005) per m^2. We detected cefotaxime-resistant *E. coli* on 86% of soil floors vs. 38% of concrete floors (chi2 p-value=0.001), with a mean $\log_{10}$-transformed MPN of 3.1 on soil floors vs. 1.6 on concrete floors (t-test p-value<0.0005). Using qPCR, we detected *Ascaris* on 18% of soil floors

and none of concrete floors, and *Trichuris* on 29% of soil floors and 31% of concrete floors. Using microscopy, we detected STH on 33% of soil floors and none of concrete floors (chi^2 p-value=0.01). Our findings indicate that soil floors are a source of child exposure to antimicrobial resistant organisms and STH in low-income countries; children can ingest soil from floors via dust or geophagia and indirectly through contaminated hands and objects. Efforts to mitigate infectious diseases and antimicrobial resistance in low-income countries should test flooring improvements to reduce soil-borne exposure to fecal organisms.

6808

ASSOCIATION OF WATER, SANITATION AND HYGIENE (WASH) AND ANIMAL OWNERSHIP TO RELAPSE TO ACUTE MALNUTRITION (AM) FOLLOWING RECOVERY FROM SEVERE ACUTE MALNUTRITION (SAM) AMONG CHILDREN 6-59 MONTHS IN MALI, SOUTH SUDAN AND SOMALIA: A PROSPECTIVE COHORT STUDY

Lauren Eleanor D'Mello-Guyett[1], Sarah King[2], Sherifath Mama Chabi[3], Feysal A. Mohamud[4], Nancy Lamaka[5], John Agong[5], Malyun Mohamed[4], Karim Kone[3], Karin Gallandat[1], Mesfin Gose[5], Mohamed S. Omar[4], Magloire Bunkembo[3], Indi Trehan[6], Anastasia Marshak[7], Khamisa Ayoub[8], Ahmed H. Olad[9], Bagayogo Aliou[10], Heather Stobaugh[11], Oliver Cumming[1]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Centers for Disease Control and Prevention, Atlanta, GA, United States, [3]Action Against Hunger, Bamako, Mali, [4]Action Against Hunger, Mogadishu, Somalia, [5]Action Against Hunger, Juba, South Sudan, [6]University of Washington, Seattle, WA, United States, [7]Tufts University, Boston, MA, United States, [8]Ministry of Health for the Republic of South Sudan, Juba, South Sudan, [9]Federal Ministry of Health for the Federal Republic of Somalia, Mogadishu, Somalia, [10]Ministry of Health and Social Development for the Republic of Mali, Bamako, Mali, [11]Action Against Hunger, Washington DC, DC, United States

In the context of high burdens of acute malnutrition (AM), children recovered from severe acute malnutrition (SAM) may frequently relapse upon returning to households with inadequate water, sanitation and hygiene (WASH) conditions which may increase the risk of infection with enteric pathogens and disease. This study aimed to identify the association of WASH, and animal ownership, to relapse to AM. This prospective cohort study examined the association of WASH-related risk factors, and animal ownership, to relapse to AM over six months among children treated and recovered from SAM in Mali, Somalia, and South Sudan. A total of 1008 children recovered from uncomplicated SAM were recruited and followed for this study. Within six months after initial recovery, 32%, 64% and 21% of children relapsed to AM in Mali, South Sudan and Somalia, respectively. In Mali, the use of multiple drinking water sources led to a 71% increased risk of relapse to AM (aRR1.71, 95% CI:1.21-2.43, p=0.003) and a lack of soap led to a 71% increased risk (aRR1.71, 95% CI:1.03-2.82, p=0.037). In South Sudan, using an unimproved or surface drinking water source was associated with 20% increased risk of relapse to AM (aRR1.20, 95% CI:1.05-1.36, p=0.006), practising open defecation was associated to 14% increased risk (aRR1.14, 95% CI:1.00-1.29, p=0.043) and compounds with observable animal faeces had 13% increased risk (aRR1.13, 95% CI:1.04-1.24, p=0.006). Ownership of sheep (aRR0.57, 95% CI:0.40-0.81, p=0.002) and cattle (aRR0.79, 95% CI:0.72-0.86, p=0.000), was a protective in Mali and South Sudan, respectively. In Somalia, no risk factors for relapse were identified. Our study identified several WASH-related risk factors for relapse to AM including inadequate drinking water sources, practising open defecation, a lack of soap and exposure to animal faeces. Identifying the relative importance of factors for adverse outcomes following initial SAM recovery could help improve the identification of children and communities at greater risk of relapse and inform interventional efforts for post-discharge support to sustain recovery.

6809

COMMUNITY PERCEPTIONS OF OPEN DEFECATION AND SCHISTOSOMIASIS CONTROL: LESSONS LEARNED FROM A RAPID ETHNOGRAPHIC ASSESSMENT STUDY IN THREE ENDEMIC LAKESHORE COMMUNITIES IN MAYUGE, UGANDA

Lucy Pickering[1], Edith Nalwadda[2], Lazaaro Mujumbusi[3], Agnes Ssali[3], Janet Seeley[3], Poppy H L Lamberton[1]

[1]University of Glasgow, Glasgow, United Kingdom, [2]Independent Researcher, Entebbe, Uganda, [3]MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda

Schistosomiasis is a neglected tropical disease, infecting over 240 million people globally, with over 4 million people infected in Uganda. Open defecation in high endemicity areas is a significant driver of transmission. Improved understanding of practices and perceptions of open defecation will help inform how best to reduce it. Data were collected over six weeks in each of three high endemicity communities using rapid ethnographic assessment, comprising 60 individual in-depth interviews, 19 focus group discussions, Village Health Team (VHT)-guided walks, transect walks, and structured observations. Guided walks focused on latrines and open defecation sites. Data were analyzed thematically using iterative categorization. Observations and walks revealed open defecation to be a commonly occurring practice in all communities, coupled with low private and public latrine coverage, and public latrines often described by VHT guides as unusable due to lack of cleanliness or being full. Interviews and focus group discussions supported these findings and further highlighted perceptions of public latrines as costly and dangerous to health when dirty, unequal access to private latrines, and perceptions of *who* engaged in open defecation: accusations ran along existing lines of status and inequality, emphasising children, certain tribes, people who use alcohol and in particular (low status, often itinerant) fishermen. This practice thus sits at the intersection of infrastructure, poverty, logistical and bodily limitations, and accusation as an amplifier of inequality. Reducing schistosomiasis transmission by reducing open defecation therefore requires a multi-scalar response: more public latrines coupled with effective cleaning and emptying, situated sensitively to where people live and work; affordable cost, and; working with communities on the risks of open defecation, why some (are perceived to) choose it, and identifying 'best fit' solutions that people will be willing to take up in order to reduce, even if not eliminate, onward *Schistosoma* transmission risk.

6810

HOST GASTRIC CORPUS MICROENVIRONMENT FACILITATES *ASCARIS SUUM* LARVAL HATCHING AND INFECTION IN A MURINE MODEL

Yifan Wu[1], Grace Adeniyi-Ipadeola[1], Mahliyah Adkins-Threats[1], Matthew Seasock[1], Charlie Suarez-Reyes[1], Ricardo Fujiwara[2], Maria E. Bottazzi[1], Lizhen Song[1], Jason C. Mills[1], Jill E. Weatherhead[1]

[1]Baylor College of Medicine, Houston, TX, United States, [2]Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Ascariasis (roundworm) is the most common parasitic helminth infection globally and can lead to significant morbidity . Children become infected with *Ascaris* spp. via oral ingestion of eggs. It has long been assumed that *Ascaris* egg hatching and larval translocation across the gastrointestinal mucosa to initiate infection occurs in the small intestine. Here, we show that *A. suum* larvae hatched in the host stomach in a murine model. Larvae utilize acidic mammalian chitinase (AMCase; acid chitinase; Chia) from chief cells and acid pumped by parietal cells to emerge from eggs on the surface of gastric epithelium. Furthermore, antagonizing AMCase and gastric acid in the stomach decreases parasitic burden in the liver and lungs and attenuates lung disease. Given Ascaris eggs are chitin-coated, the gastric corpus would logically be the most likely organ for egg hatching, though this is the first study directly evincing the essential role of the host gastric corpus microenvironment. In addition, we show that the gastric corpus

downregulates AMCase and acid in response to repeated *A. suum* infection to reduce larval migration. These findings point towards potential novel mechanisms for therapeutic targets to prevent ascariasis and identify a new biomedical significance of AMCase in mammals.

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COMPREHENSIVE SINGLE CELL RNA SEQUENCING UNVEILS THE TRANSCRIPTIONAL DYNAMICS OF *PLASMODIUM VIVAX* HYPNOZOITE FORMATION

Gigliola Zanghi[1], Lindsay V. Clark[1], Nastaran Rezakhani[1], Wanlapa Roobsoong[2], Jetsumon Sattabongkot[3], Sumana Chakravarty[4], Stephen L. Hoffman[4], B. Kim Lee Sim[4], Stefan H.I. Kappe[1], Ashley M. Vaughan[1]

[1]Seattle Children's, Seattle, WA, United States, [2]Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Bangkok, Thailand, [3]Mahidol Vivax Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, [4]Sanaria Inc., Rockville, MD, United States

On one of the primary objectives of *Plasmodium vivax* malaria parasite liver stage research is to understand the formation, persistence, and activation of hypnozoites, the dormant liver stage parasites that are responsible for recurrent relapses. However, this research faces severe challenges, due to the limited access to *P. vivax* sporozoites. To unravel the molecular pathways governing hypnozoite formation, we adopted a comprehensive strategy. We revisited the utilization of Chesson strain *P. vivax* sporozoites, as well as P. vivax field strains from Thailand, for hypnozoite biology analysis in conjunction with the highly infectable human hepatocyte cell line HCO4. Furthermore, we employed single-cell RNA sequencing to analyze the transcriptional profiles of both oocyst and salivary gland sporozoites as well as a time course of developing liver stage parasites - both schizonts and hypnozoites. Our efforts resulted in the transcriptional profiling of over 50,000 individual sporozoites and 500 liver stage parasites. We have delineated multiple gene expression clusters and, as to be expected, observe stark differences in expression profiles between sporozoites and liver stage parasites. Preliminary analysis indicates an upregulation of genes related to RNA-binding in the hypnozoite population, suggesting a potential regulatory role in hypnozoite formation. Additionally, we have devised a reliable RNA-FISH/IFA protocol capable of specifically identifying transcripts expressed solely in hypnozoites. This multifaceted approach promises a deeper understanding of hypnozoite biology and holds promise for uncovering novel interventions to mitigate relapses.

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PLASMODIUM VIVAX-INDUCED BONE MARROW ALTERATIONS PERSIST LONG AFTER ACUTE PHASE OF INFECTION

Joao Luiz Silva-Filho[1], Jessica RS Alves[2], Anne CG Almeida[3], Erich De Paula[2], Stefanie Lopes[4], Kevin Couper[5], Thomas Otto[1], Gisely Mello[6], Wuelton Monteiro[3], Marcus Lacerda[3], Fabio TM Costa[2], Matthias Marti[1]

[1]University of Glasgow, Glasgow, United Kingdom, [2]University of Campinas, Campinas, Brazil, [3]Tropical Medicine Foundation Dr. Heitor Vieira Dourado, Manaus, Brazil, [4]Fiocruz, Manaus, Brazil, [5]University of Manchester, Manchester, United Kingdom, [6]Tropical Medicine Foundation Dr. Heitor Vieira DouradoUniversity of Glasgow, Manaus, Brazil

Plasmodium vivax (*Pv*) infection can lead to poor clinical outcomes, despite low peripheral parasitaemia. Estimation of total *P. vivax* biomass based on markers in peripheral blood (PB) indicates a "hidden" population outside of circulation. Indeed, recent studies revealed a major *Pv* reservoir in bone marrow (BM) and spleen. The development of *Pv* parasites in the BM raises questions about the locally established host-parasite interactions and their clinical relevance in malaria pathogenesis. Here, we aimed to define *Pv*-induced immune responses in the BM and their effect on BM function and disease development. Matched BM aspirates and PB samples have been collected from a prospective longitudinal cohort of uncomplicated *Pv* patients from Brazil, to investigate parasite and host signatures in the hematopoietic niches of BM compared to blood. So far, we analysed host signatures by combining clinical data and multiplexed profiling of 64 protein markers in matched BM and PB material sampled at hospital admission (day 0), as well as 45 and 60 days after, in comparison to healthy donor BM samples. Luminex results demonstrate that *Pv* infection induces a wide range of host responses in the BM during acute phase, most of which persist long after infection is resolved. Persisting upregulated responses were related to megakaryopoiesis, lymphopoiesis, granulopoiesis, myeloid chemoattraction, neutrophil and endothelial cell activation, inflammasome activation, type II IFN response, Th1 response and T-cell exhaustion/inhibition. Persisting downregulated protein markers were related to BM function, such as hematopoietic quiescence, dendritic cell differentiation. In contrast, persisting responses are largely absent in the PB. Ongoing single cell and bulk transcriptomics of host response and parasite signatures in both compartments will be presented. This study emphasises the relevance to investigate the impact of *Pv* infection in the hematopoietic niches. As such, our work will contribute to a better understanding of *Pv* biology and pathogenesis, and hence to our efforts to reduce the burden of this important human disease.

6813

A HUMAN PLURIPOTENT STEM CELL DERIVED MODEL OF THE NEUROVASCULAR UNIT COMPRISED OF BRAIN MICROVASCULAR ENDOTHELIAL CELLS, ASTROCYTES, AND NEURONS IN CEREBRAL MALARIA

Adnan Gopinadhan[1], Finley Andrew[1], Rylee Anderson[2], Alejandro Soto[1], Jason M. Hughes[2], Andrea L. Conroy[1], Chandy John[1], Scott G. Canfield[2], Dibyadyuti Datta[1]

[1]Indiana University, Indianapolis, IN, United States, [2]Indiana University, Terre Haute, IN, United States

Damage to the blood-brain barrier (BBB) and neurovascular unit (NVU) leading to long-term neurologic impairment in cerebral malaria (CM) remains a poorly understood complication of *Plasmodium falciparum (Pf)* infections. How *Pf*-infected RBCs (*Pf*-iRBCs) sequestered to brain endothelial cells cause damage to neuronal cells without crossing the BBB is unclear. *In vitro* models have advanced our knowledge of CM-mediated BBB disruption, but few have investigated NVU damage. Previously, using induced pluripotent stem cell-derived brain microvascular endothelial cells (iPSC-BMECs) co-cultured with *Pf*-iRBCs, we've demonstrated *Pf*-mediated damage to the BBB. In this study, we have expanded our *in vitro* model of the BBB in CM to include iPSC-derived neurons and astrocytes along with BMECs in co-culture with *Pf*-iRBCs to represent the NVU in CM. Our novel, multicellular model of the NVU represents near *in vivo* like barrier resistance (3800 Ωxcm^2) by transendothelial electrical resistance (TEER) that is 10 times that observed in human primary BMEC based models ($\leq$400 Ωxcm^2). iPSC neurons and astrocytes were characterized using β-tubulin III and GFAP staining. Using HB3var03 parasite strain that binds endothelial surface proteins ICAM-1 and EPCR—key mediators of CM neuropathology, we conducted co-culture experiments up to 9 hours (h). At 6 h post co-culture with *Pf*-iRBCs, there was a significant reduction in barrier resistance of the iPSC-BMEC (1827 Ωxcm^2) compared to uninfected RBC co-culture (2937 Ωxcm^2); which remained low at 9 h (all $P<0.005$). We observed increased sodium fluorescein permeability indicative of a leaky barrier in *Pf*-iRBC co-cultures compared to uninfected RBC co-cultures at 6 h. Breaks in tight junction protein localization further confirmed BBB disruption in *Pf*-iRBC co-cultures at 6 h. Ongoing experiments will identify altered expression of endothelial surface markers and efflux proteins. Our multicellular iPSC-derived model of the NVU with enhanced barrier integrity replicates key features involved in the pathogenesis of CM and can serve as a surrogate to investigate pathogenic stimuli underlying NVU damage in CM.

6814

DIETARY EFFECTS ON THE COURSE OF VISCERAL LEISHMANIASIS IN A MOUSE MODEL

Natalie Jarvis, Grace Gutzman, Yani Chen, Bayan Zhanbolat, Patrick Nuro-Gyina, Jacilara Conceicao, Mary Wilson
University of Iowa, Iowa City, IA, United States

The demographics of leishmaniasis has changed dramatically in endemic regions of Brazil, concurrent with changes in socioeconomic status and consequent shift towards a high-fat high-cholesterol diet (HFHC). With this shift, a novel presentation of cutaneous leishmaniasis due to *L. braziliensis* has emerged in obese patients, characterized by poorer treatment response with higher recurrence rates in obese individuals, s reported previously. A direct link between diet-induced changes in metabolic and immune status and the manifestations of visceral leishmaniasis (VL) has not been established. We hypothesize that diet-induced changes in immunometabolism may also affect the progression and outcome of VL. To address this, we examined the effects of a HFHC and protein-deficient (LP) diet in a murine model of VL. BALB/c mice were maintained on HFHC, LP, or control diets for 4 weeks, then either infected or not with L. *infantum*. The course of infection was monitored by histology and by qPCR to document inflammation and parasite loads. The HFHC diet abrogated the expansion of parasite loads in the liver and caused exacerbated parasite growth in spleens ($P<0.0001$). Mice on a LP diet, in contrast, developed higher parasite loads in livers than control mice ($P<0.0001$). Control mice developed granulomas in the livers as the disease progressed. In contrast, mice on a HFHC diet developed a basal inflammatory response in the liver and failed to develop organized, mature granulomas ($P<0.0001$). Mice on a LP diet had increased numbers of granulomas in the liver ($P<0.0001$). These findings suggested that the basal inflammation of the HFHC diet led to failure to contain the parasite and early dissemination of infection to the spleen. Dietary factors may influence the changing spectrum of VL.

6815

PERSPECTIVES ON EQUITABLE PARTNERSHIPS IN GLOBAL HEALTH

Senait Kebede, Mischka Garel, Michael Chung, Rebecca Martin
Emory Global Health Institute, Emory University, Atlanta, GA, United States

Equitable global health partnerships (EGHPs) are gaining traction amid decolonization global health movements, spotlighting power imbalances rooted in colonial legacies. There is an increased call among global health institutions for a meaningful change that fosters equity, inclusivity, and fairness, and values local knowledge in research partnerships. The Emory Global Health Institute (EGHI) took a methodical approach, with a literature review and an explanatory sequential QUAN-QUAL mixed methods strategy to assess perspectives on EGHPs. A quantitative survey and key informant interviews were conducted among Emory faculty in the US and their partners in low- and middle-income countries (LMICs) engaged in global health research collaborations. Additionally, a decolonizing global health working group was convened to deliberate on the findings and establish priority areas. The literature identified key principles for advancing equitable partnerships: authentic collaboration, inclusion, shared benefits, commitment to the future, responsiveness to inequities, and humility. Survey analysis revealed agreement between US and LMIC partners across 16 out of the 22 indicators with marginal differences in responses with regards to infrastructure, communication, bidirectional training, fair compensation, financial transparency, and sustainability. LMIC partners prioritized capacity strengthening, equity principles, communication, and relationship building, while US participants focused on operational efficiency and equity. The findings are consistent with previous studies in the literature. Based on all the results and discussions the main priorities to advance EGHPs are; establishing tools and frameworks to integrate equity, measure progress, bidirectional capacity building, knowledge sharing, and creating a platform for constructive dialogue to influence policies for fair access to financial and technical resources. The building momentum to advance EGHPs can be furthered and expanded on with collective efforts to implement key principles and actionable steps that center equity in global health practice.

6816

INNOVATION FOR NEGLECTED DISEASES: TWO DECADES OF PROGRESS AND GAPS IN NEW DRUG APPROVALS

Paul G. Ashigbie[1], Rajiv Shah[2], Jonathan M. Spector[1], Thierry T. Diagana[3]
[1]Global Health, Biomedical Research, Novartis, Cambridge, MA, United States, [2]Global Health and Sustainability, Novartis, Basel, Switzerland, [3]Global Health, Biomedical Research, Novartis, Emeryville, CA, United States

Therapeutic innovations have an essential role to play in addressing the burden of neglected diseases. This study analyzes the approval landscape of novel medicines for diseases that disproportionately affect populations in low- and middle-income countries (LMICs) to inform drug research, development, and access strategies. We examined the online databases of 26 medicines regulatory authorities (from the record of World Health Organization-Listed Authorities), the WHO Prequalification Program, and other online platforms for medicines approved between 2003 and 2023. The focus was on 47 diseases identified by WHO, the Access to Medicines Foundation, or Policy Cures Research to be priority health conditions in LMICs. Inclusion criteria were new chemical entities (NCEs), new therapeutic biologics (NBs), new fixed-dose combinations (FDCs), new dosage forms of existing medicines, or "repurposed" medicines for new indications. We estimated the ratio of the number of approvals to the burden of each disease in Disability Adjusted Life Years (DALYs). Of 55 medicines approved over the study period, 11 were NCEs (eight medicines) or NBs (three medicines): three for tuberculosis; two each for Ebola, malaria, and sickle cell disease; and one each for human African trypanosomiasis and onchocerciasis. Eight of the 11 NCEs and NBs were approved after 2015. Forty-four of the approved medicines were repurposed drugs (12), FDCs (11), and new dosage forms (21). Of these, 23 were for tuberculosis, 11 for malaria, two each for sickle cell disease and leishmaniasis, and one each for six other diseases. No novel medicines were approved for 35 diseases. The number of approvals to DALY ratios in all disease areas studied was substantially lower than those that are typical for leading diseases in high-income countries. Therapeutic innovation for neglected diseases is severely limited, especially for new chemical or biologic entities, and unbalanced across disease areas. Given severe unmet needs including, in some cases, the threat of resistance to existing therapies, there is urgency to scale up R&D for novel medicines that address global health diseases.

6817

BUILDING CAPACITY FOR MATERNAL, NEWBORN AND CHILD HEALTH RESEARCH IN LOW-INCOME COUNTRY SETTINGS: A RESEARCH FELLOWSHIP EXPERIENCE IN ETHIOPIA

Kassahun Alemu Gelaye[1], Lisanu Taddesse[1], Clara Pons-Duran[2], Clara Pons-Duran[2], Bezawit Mesfin Hunegnaw[3], Robera Olana Fite[1], Abebe Belayneh Bekele[1], Frederick GB Goddard[4], Assaye K. Nigussie[5], Yifru Berhan[6], Delayehu Bekele[6], Theodros Getachew[7], Ebba Abate[8], Grace J. Chan[9]
[1]HeSET Maternal and Child Health Research Program, Addis Ababa, Ethiopia, [2]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA, Harvard School of Public Health, MA, United States, [3]Department of Pediatric and Child Health, Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, Addis Ababa, Ethiopia, [4]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA, Addis Ababa, MA, United States, [5]College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia, [6]Department of Obstetrics and Gynecology, Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, Addis Ababa, Ethiopia, [7]Health System and Reproductive Health Research Directorate, Ethiopian Public Health Institute, Addis Ababa, Ethiopia, Addis Ababa, Ethiopia, Addis

Ababa, Ethiopia, [8]Director General, Ethiopian Public Health Institute, Addis Ababa, Ethiopia, Addis Ababa, Ethiopia, [9]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA, Boston, MA, United States

In low- and middle-income countries, there is a need to build capacity for research to improve maternal, newborn and child health (MNCH). Collaborating with the Ministry of Health (MoH) and academic institutions, we co-designed the HaSET MNCH research fellowship program for academics and policymakers in Ethiopia. Based on interviews and focus group discussions on a landscape analysis of the MNCH research environment, we developed an innovative "learning by doing" model where fellows identified research questions, developed proposals, obtained IRB approvals, conducted research, analyzed data, disseminated their findings, and developed policy briefs. Post-doctoral fellows were paired with policymakers and health professionals at the MoH to foster translation of research findings to policy and programs. The HeSET fellowship curriculum was designed to include 10 modules covering topics from biostatistics to study operations and professional development. From March 2021 to July 2023, HaSET trained five post-doctoral fellows from local universities and four policymakers from the MoH and government research institutes to generate high-quality evidence to answer priority research questions and guide the implementation of national policies and programs. Leveraging existing data, the fellows completed 15 manuscripts and 11 policy briefs. Fellows presented their work at international and national conferences. The program established a functional research link between the Ministry of Health, regional health bureaus, local universities, and leveraged the expertise of a scientific advisory group for mentorship. This robust and comprehensive HaSET MNCH Research Fellowship cultivated a cohort of dedicated and effective public health professionals. Fellows conducted high-quality studies for informed policy decisions regarding MNCH interventions in Ethiopia. There is potential to scale the program to sustain successful capacity-building programs to build the next generation of leaders in research in low- and middle-income countries.

6818

EAST AND SOUTHERN AFRICAN CONSORTIUM FOR OUTBREAK EPIDEMIOLOGY TRAINING (ENTRANT)

Emily Webb[1], Nega Assefa[2], John Changalucha[3], Maryirene Ibeto[1], Joseph Jarvis[1], Achilles Kiwanuka[4], Madisa Mine[5], Julius Oyugi[6], Kwame Shanaube[7]

[1]London School of Hygiene and Tropical Medicine, London, United Kingdom, [2]Haramaya University, Haramaya, Ethiopia, [3]Mwanza Interventions Trials Unit, Mwanza, Tanzania, United Republic of, [4]MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda, [5]National Health Laboratories, Gaborone, Botswana, [6]University of Nairobi, Nairobi, Kenya, [7]Zambart, Lusaka, Zambia

East and Southern African countries are susceptible to disease outbreaks, and vulnerable to public health emergencies due to constrained health system resources. The East and Southern Africa Consortium for Outbreak Epidemiology Training (ENTRANT) programme was established with funding from EDCTP in collaboration with Africa CDC. The objective of ENTRANT is to provide epidemiological training and mentorship to early- to mid-career public health professionals working in the region. Through this we aim to promote the development of a critical mass of epidemiologists to work with National Public Health Institutes and Ministries of Health and thus strengthen public health and outbreak response capacity. ENTRANT is coordinated by a consortium of institutional partners relevant to outbreak response in the region, and supported by an independent Advisory Committee comprising experts in capacity strengthening for epidemiology in sub-Saharan Africa. A competitive application process was implemented to identify high-calibre public health professionals for entry into the programme. Fellows undertake MSc Epidemiology at London School of Hygiene and Tropical Medicine (LSHTM) followed by further focussed short course multidisciplinary training on the emergence, spread and response to pandemics. Fellows receive mentorship from LSHTM tutors and experienced epidemiologists in their home country, take part in regular transferable skills training and networking activities, and are supported to attend conferences. From a total of 324 applications, 15 public health professionals (eight female, seven male) from Botswana, Ethiopia, Kenya, Tanzania, Uganda and Zambia have been awarded Fellowships. To date, 13 have completed their MSc Epidemiology training, with the remaining Fellows due to complete in October 2024. Fellows who have completed formal training have gone on to work for Ministries of Health and public health research institutions. Fellows at all stages of the programme have formed a strong, mutually-supportive cohort through regular meetings and networking events.

6819

WHO ANC POLICY AND SKILLED BIRTH ATTENDANCE IN SUB-SAHARAN AFRICA

Michael Bride[1], **Bolanle Olapeju**[2]

[1]Johns Hopkins University Center for Communication Programs, Baltimore, MD, United States, [2]Uniformed Services University of the Health Sciences, Bethesda, MD, United States

Over half a million mothers are lost each year due to pregnancy-related complications. The World Health Organization (WHO) recommends that all pregnant women have a minimum of eight ANC contacts (WHO 2016 ANC policy) and delivery by an accredited health professional - such as a midwife, doctor or nurse. This study explores the association between skilled birth attendance at a prior pregnancy and the number of ANC contacts in the index pregnancy. A secondary analysis of data from 19 sub-Saharan African countries with available Demographic Health surveys from 2018 to date was performed. Key variables were skilled birth attendance (by a doctor, nurse, midwife and auxiliary nurse or midwife) during a participant's second most recent pregnancy and the number of ANC contacts in the most recently completed pregnancy in the past two years. Propensity score matching was used to explore the treatment effects of having a skilled birth attendance on the number of ANC contacts during pregnancy. 40,077 women had had at least two pregnancies in the five years preceding the survey. 60% of women had had a skilled delivery in their second most recent pregnancy which varied by county, with Ethiopia (37%) to Gabon (95%).The majority of these skilled providers (44%) were nurses. The mean number of ANC contacts in a woman's most recent pregnancy ranged from Mauritania (2.8) to Ghana (6.2) (mean 3.6). Having a skilled provider in their second most recent pregnancy had an average treatment effect of 1.20 (95% CI: 1.12-1.28), indicating a modest increase in number of ANC visits of their subsequent pregnancy compared to not having a skilled delivery, accounting for country, age, wealth, urbanization, and religion. This study highlights the influence of skilled delivery in current and subsequent pregnancies. Improving ANC contacts allows for an improved life course, providing more opportunities for health promotion, early detection of health complications, and many more benefits to the pregnant woman and unborn child. In countries with low percentages of skilled deliveries, improving access could increase ANC contacts and support more linkages to further health and wellbeing.

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ENHANCING THE QUALITY OF COMMUNITY HEALTH SERVICES IN MADAGASCAR: A MIXED METHODS EVALUATION OF A COMMUNITY HEALTH VOLUNTEERS (CHVS) PEER SUPERVISION MODEL IN FOUR REGIONS

Kanto Jude Ramanamahefa[1], **Samantha Herrera**[2], Tsinjo Fehizoro Razafindratsinana[1], Anna Bowen[3], Erica Berlin[4], Andry Rabemanantsoa[1], Hery Suzanette Gnetsa[5], Jose Clement Randrianarisoa[6], Jayne Webster[7], Jessie Hamon[7], Cara Smith Gueye[8]

[1]Population Services International, Antananarivo, Madagascar, [2]U.S. President's Malaria Initiative Insights, Washington, DC, United States, [3]U.S. President's Malaria Initiative, U.S. Centers for Disease Control and Prevention, Antananarivo, Madagascar, [4]Population Services International, Washington, DC, United States, [5]Community Health Service, Ministry of Public Health, Antananarivo, Madagascar, [6]National Malaria Control

Program, Antananarivo, Madagascar, [7]London School of Hygiene and Tropical Medicine, London, United Kingdom, [8]University of California, San Francisco Malaria Elimination Initiative, San Francisco, CA, United States

In 2019, Madagascar's Ministry of Public Health (MoPH) launched a national community health strategic plan, aiming to strengthen community health services through improved supervision of community health volunteers (CHVs). CHVs are traditionally supervised by health facility (HF) heads; however, insufficient facility staffing and high workloads have resulted in inadequate supervision. The MoPH is collaborating with the USAID ACCESS program to implement a new CHV supervision model that engages high-performing CHVs as peer supervisors in 13 regions; an evaluation of the model is expected to guide national scale-up and planning in other countries. We completed a mixed-methods study in 2023, conducting secondary data analysis to characterize the program and collecting primary data in four regions. In 16 health facility catchment areas, we conducted in-depth interviews (IDIs) with peer supervisors (n=16), CHVs (n=32), HF heads (n=16), and other stakeholders engaged in the peer supervision model rollout (n=41). IDI themes included how the model worked, the functionality of model components, and feasibility and acceptability. Qualitative data were coded using NVivo; a deductive approach was used for the thematic analysis. The new model was perceived to result in greater information sharing between CHVs and peer supervisors, better management of health providers' schedules, and improved quality of CHV services, including reporting. Aspects of the model not found to work well included the process of selecting peer supervisors, inadequate clinical supervision, high ratio of CHVs to peer supervisors, less time for peer supervisors to engage in income-generating activities, and lack of supervision tools and training for the HF heads. The new model shows promise; however, several aspects require reconsideration to improve the model's acceptability and feasibility, including reducing the number of CHVs per peer supervisor, bolstering clinical supervision, and providing adequate remuneration, training, and tools for CHVs, peer supervisors, and HF heads. Findings were shared with MoPH and ACCESS to inform national scale-up of the model.

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AI IN GLOBAL HEALTH: CHALLENGES AND OPPORTUNITIES

Naomi Waithira[1], Mavuto Mukaka[1], Evelyne Kestelyn[2], Keitcheya Chotthanawathit[1], Anne Osterreider[3], Trudie Lang[3], Phaik Yeong Cheah[1]

[1]MORU Tropical Health Network, Bangkok, Thailand, [2]Oxford Clinical Research Unit, Ho Chi Minh City, Vietnam, [3]University of Oxford, Oxford, United Kingdom

AI has enormous potential in healthcare, from aiding diagnosis to personalising medical care and predicting disease outbreaks. However, the accuracy of AI algorithms depends on the quality and diversity of the data used to train them. Concerns exist regarding the reliability and sufficiency of data from low-and-middle-income countries (LMICs) for training AI algorithms. There is a risk that a lack of contextually relevant data may result in incorrect algorithms or limited application of AI in LMICs. How, then, can we ensure that the benefits of technology are accessible to all? We present the results of a mixed-methods study exploring challenges and opportunities in using existing health data from LMICs. We conducted a cross-sectional study with 643 clinical researchers and 24 in-depth interviews with computational health scientists. The study reveals low data usage, especially for AI, mainly due to challenges with data findability. The study also highlights inequity in gains realised from data reuse. Career progression from data reuse was associated with affiliation with high-income and upper-middle-income countries (p=0.046, chi=8.0), while scientific progress through publications and collaborations was associated with gender (p=0.012, chi=10.9), with males more likely to benefit. Publicly publishing metadata of health datasets in machine and human-readable formats will enhance data discoverability without compromising data privacy. Intentional efforts to encourage and enable more analysts in LMICs, especially females, may reduce the equity gap. Capacity building in data management may improve the overall quality of prospectively collected data, while targeted efforts to curate existing data will increase the pool of data available for secondary use, including AI applications.

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CLINICODEMOGRAPHIC PROFILE AND SURVIVAL PROSPECTS OF WOMEN WITH PERIPARTUM CARDIOMYOPATHY IN TANZANIA: A PROSPECTIVE COHORT STUDY.

Pedro Kisali Pallangyo, Zabella Mkojera, Makrina Komba, Peter R. Kisenge

Jakaya Kikwete Cardiac Institute, Dar es Salaam, Tanzania, United Republic of

Background: Irrespective of a higher rate of complete recovery relative to other forms of systolic heart failure, peripartum cardiomyopathy (PPCM) remains the leading cause of non-obstetric feto-maternal morbidity and mortality worldwide. In view of the paucity of data, this present study aimed to shed light on the clinicodemographic characteristics and prognosis of PPCM in Tanzania. Methods: This prospective, multicenter PPCM study in Tanzania commenced in April 2016. Data was systematically collected at the very first contact and then upon three-, six-, and twelve-months visits. Clinical outcomes including complete recovery (LVEF>55%), persistent dysfunction, and death were recorded. Bivariate comparison and subsequent Cox proportional-hazards regression model were used to compare the women with respect to the primary end point. Results: We screened 1639 women and consecutively recruited 1210 who met the inclusion criteria. The mean age at diagnosis was 29.4 ± 6.7 years and in 31.2% women it was their first pregnancy. During a mean follow-up of 889 days, 23.6% of women had complete recovery, 48.2% had persistent LV systolic dysfunction, and 28.1% died. We observed thromboembolic events in 10.2% of women and infant mortality rate was 23.4%. Amongst 870 survivors (286 resolved, 584 persistent heart failure), 121 women (78 in the resolved group and 43 in the persistent heart failure) had subsequent deliveries. Recurrence was observed in 51.3%, resolution in 31.4%, and death in 8.3%. Following multivariate analysis in a cox regression model of 16 variables; Atrial fibrillation (HR 5.0, 95%CI 2.6-9.8, p<0.001), LVIDd ≥60 (HR 2.8, 95%CI 1.9-4.3, p<0.001), EF<30% (HR 1.7, 95%CI 1.1-2.5, p<0.001), TAPSE<14 (HR 7.4, 95%CI 5.1-11.1, p<0.001), and LV thrombus (HR 2.3, 95%CI 1.3-3.9, p<0.01) proved to be the predictors of mortality. Conclusions: In this largest cohort of African women with well-phenotyped PPCM, we observed myocardial recovery in just under a quarter of patients and maternal death in over a quarter of the enrolled women. Despite its relative rarity yet poor prognosis, PPCM remains a challenge to diagnose, prognosticate, and treat.

6823

BURDEN, DISTRIBUTION, TIMING AND CAUSES OF STILLBIRTH AND NEONATAL MORTALITIES IN A HEALTH AND DEMOGRAPHIC SURVEILLANCE SYSTEM (HDSS) IN KAREMO AND MANYATTA IN WESTERN KENYA, 2018-2023

George Aol Otieno[1], Richard O. Onyando[1], Godfrey M. Bigogo[1], Joyce Were[1], Beth A. Odhiambo[1], Stephen O. Munga[1], Beth T. Barr[2], Nehemia O. Abongo[1], Brian Genga[1], Jonathan A. Muir[1], Victor Akelo[3], Aggrey Igunza[1], Thomas Misore[1]

[1]kenya Medical Research Institute, Kisumu, Kenya, [2]nyanja Health Research Institute, Salima, Malawi, [3]liverpool School Of Tropical Medicine, Kisumu, Kenya

Sub-Saharan Africa has the highest stillbirth and neonatal mortality rates worldwide. We sought to estimate the burden, distribution, timing and causes of stillbirth and neonatal mortality using data from a Health and Demographic Surveillance System (HDSS) site operated by the Kenya Medical Research Institute and CHAMPS in western Kenya. Approximately 179,317 residents, in Karemo - Siaya County and Manyatta - Kisumu County are monitored every six months using a standardized questionnaire about events that happened since prior visit. All women of reproductive

age (12-49 years) are asked about their pregnancy status and outcome. Community health volunteers report deaths, births and pregnancies. Minimally invasive tissue sampling was conducted on stillbirth and neonatal deaths. Aseries of biopsies, blood and body fluids samples were analyzed and cause of death determined by medical experts. A total of 454 stillbirth and 606 neonatal deaths were reported of which 277 stillbirths and 268 neonates had cause of deaths determined. Between 2018 and 2023, stillbirth mortality rate (SMR) in Karemo was 18.0 and 23.6 and in Manyatta 12.4 and 28.1 deaths per 1000 births; Neonatal mortality rates (NMR) in Karemo was 23.1 and 23.2 and in Manyatta 13.9 and 22.6 deaths per 1000 livebirths. SMR among women aged 15-19 was 15.6, 20-24 (17.0), 30-34(20.0) 35-39 (24.8) and 45-49 (48.8) deaths per 1000 births. NMR among women aged 12-14, 15-19, 25-29, 30-34, 40-44 and 45-49 years was 32.8, 30.4. 20.2, 20.8, 31.0 and 54.1 deaths per 1000 livebirths respectively. Overall, 57% of the stillbirth deaths happened among fetuses over 38 weeks old; 63% of neonatal deaths happened on the delivery day. Leading cause of neonatal deaths were intrauterine hypoxia (33%), sepsis (20%) and respiratory distress syndrome (18%) while intrauterine hypoxia (88%) was leading cause of stillbirths. We observed an increase in neonatal and stillbirth mortality rates overtime. The highest mortality rates were observed among young women and those with advanced ages. Most deaths happened around time of delivery due to intrauterine hypoxia. There is need for improved obstetrical care for pregnant women in the study.

6824

VACCINATION COVERAGE AND TIMELINESS AMONG INFANTS IN ETHIOPIA

Clara Pons-Duran[1], Bezawit Mesfin Hunegnaw[2], Chalachew Bekele[2], Kassahun Alemu[1], Raffi Pontes[3], Fiseha Tadesse[4], Melkamu Ayalew[5], Abraham Alebie[2], Lisanu Taddesse[1], Delayehu Bekele[2], Sebastien Haneuse[3], Grace J. Chan[3]

[1]HaSET Maternal and Child Health Research Program, Addis Ababa, Ethiopia, [2]St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, [3]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [4]Debre Birhan Hospital, Debre Birhan, Ethiopia, [5]Federal Ministry of Health, Addis Ababa, Ethiopia

Vaccinations are key for preventing and controlling infectious diseases. However, in Ethiopia, a significant proportion of children remain unimmunized. This study aimed to describe the vaccination coverage among children in a rural site in Ethiopia, and to quantify the proportion of infants who were vaccinated on time according to the National vaccination schedule. We analyzed data of a longitudinal study conducted in Ethiopia, which includes a health and demographic surveillance system (HDSS) with house-to-house surveillance every 3 months. The study population were children born between 2018 and 2021, and enrolled in the HDSS. Vaccination data were collected through questionnaires administered as part of the routine surveillance. Data were abstracted from vaccination cards and caregivers reports. We used two analytical approaches to calculate the vaccination coverage of the full set of vaccines recommended in Ethiopia, the coverage of each specific recommended vaccine, and timeliness of vaccine administration. Data of 7,417 children were included in the analysis. The proportion of fully vaccinated children was between 25.8% (2018) and 30.6% (2021) using a longitudinal approach, and between 32.0% (2018) and 41.8% (2021) using a method that mimics a cross-sectional survey. Coverage of specific vaccines followed a similar pattern. Three quarters and 2 thirds of children who were measles vaccinated before 1 year of age received the vaccine within 4 weeks of vaccine eligibility using the longitudinal and the cross-sectional strategies, respectively. Four out of 10 received the third doses of oral poliovirus, pentavalent and pneumococcal vaccines, and the second dose of rotavirus vaccine within 4 weeks of vaccine eligibility. Vaccination rates in the study area were low. Less than half of infants received their vaccinations within 4 weeks of the recommended administration time. To ensure an accurate assessment of vaccine coverage and timeliness, it is recommended to implement strategies that leverage longitudinal data, reducing reliance on cross-sectional studies, and allowing for more precise monitoring of immunization efforts.

6825

UNDERSTANDING IMPACT OF DOMESTIC VIOLENCE ON PERINATAL DEATH IN RURAL BANGLADESH; FINDINGS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE, BANGLADESH

Mohammad Zahid Hossain[1], Afsana Afrin[1], Shahana Parveen[1], Daliya Yeasmin[1], Afruna Rahman[1], Shams El Arifeen[1], Emily Susan Gurley[2]

[1]Icddr,b, Dhaka, Bangladesh, [2]John Hopkins University, Baltimore, MD, United States

Domestic violence is a public health issue, different studies suggested that globally 15% to 71% of women experienced some form at some point in their lives. An estimated 40% to 70% of Bangladeshi married women experience domestic violence from their husbands, in-laws, and/or close relatives at least once during their lifetime. A countrywide sample-based study found that 3 out of 4 Bangladeshi women experienced domestic violence from their husbands especially who were less educated and poor. Various studies suggested that domestic violence during pregnancy can cause adverse pregnancy outcomes. The Child Health and Mortality Prevention Surveillance (CHAMPS) in Bangladesh is identifying the causes of stillbirths and death among children under five by employing minimally invasive tissue sampling (MITS) with clinical documents and verbal autopsies (VAs). We have reviewed VAs of 800 MITS cases, including narratives where mothers described the death events of their babies. A total of 12 mothers participating in the study (12/800; 1.5%) mentioned experiencing domestic violence during their pregnancies. Out of these 12 cases, 7 (58%) were stillbirths and 5 (42%) were early neonatal deaths. All MITS reports, clinical documents, and VAs were reviewed by an expert panel composed of epidemiologists, neonatologists, pediatricians, obstetricians, and pathologists to determine the cause of death. The panel considered domestic violence as a contributing maternal factor for perinatal death in 5 out of the 12 cases (5/12, 42%), all of which involved domestic violence close to the delivery date. Reporting of the violence was based on interviews with the mother at home, which could lead to underestimation of the problem due to fears of disclosing. Additional strategies could be used to identify women experiencing domestic violence during pregnancy. Engagement of field-level government health workers, and the introduction of social prescriptions by engaging support groups and community people can help these women in the future and connect them with appropriate authorities to prevent domestic violence and save lives.

6826

MASS AZITHROMYCIN DISTRIBUTION AND CAUSE-SPECIFIC MORTALITY AMONG CHILDREN AGED 1-59 MONTHS IN BURKINA FASO

Ali Sie[1], Mamadou Ouattara[1], Mamadou Bountogo[1], Boubacar Coulibaly[1], Valentin Boudo[1], Thierry Ouedraogo[1], Elisabeth Gebreegziabher[2], Huiyu Hu[2], Elodie Lebas[2], Benjamin F. Arnold[2], Thomas M. Lietman[2], **Catherine Oldenburg**[2]

[1]Centre de Recherche en Santé de Nouna, Nouna, Burkina Faso, [2]University of California, San Francisco, San Francisco, CA, United States

Mass azithromycin distribution has been shown to reduce all-cause child mortality in several settings in the Sahel, with an approximately 14-18% relative reduction in the risk of mortality in children living in communities receiving twice-annual mass azithromycin distribution compared to placebo. A previous trial in Niger found that mass azithromycin distribution to children aged 1-59 months reduced cause-specific mortality due to malaria, dysentery, meningitis, and pneumonia. However, this study was done in the absence of seasonal malaria chemoprevention (SMC), a mass drug administration strategy that involves distribution of sulfadoxine-pyramethamine and amodiaquine monthly to children aged 3-59 months during the high malaria transmission season. Here, we evaluated cause-specific mortality in a trial of mass azithromycin distribution compared to placebo in Burkina Faso, in a setting that was receiving SMC. The Child Health with Azithromycin Treatment (CHAT) trial randomized 341

communities in Nouna District, Burkina Faso to twice-yearly mass distribution of a single oral 20 mg/kg dose of azithromycin or matching placebo to children aged 1-59 months of age. Six rounds of distribution occurred over a 36-month period. An enumerative census was conducted during each twice-yearly distribution, during which vital status for all children in the community was collected. Verbal autopsy was performed to assess cause of death. Of 1,086 deaths recorded in the trial, verbal autopsy results were available for 919 (85%). The most common causes of death were infectious, including malaria (34%), diarrhea (24%), and pneumonia (9%). Children living in communities receiving azithromycin had significant reduction in malaria mortality (incidence rate ratio, IRR, 0.67, 95% confidence interval, CI, 0.50 to 0.90, P=0.008). Other infectious causes of mortality, including diarrhea and pneumonia, were lower in communities receiving azithromycin but were not statistically significantly different. Mass azithromycin distribution for child mortality has benefits in the context of SMC for reducing mortality, including for malaria mortality.

6827

CLUSTER VARIATION IN UNDER-FIVE MORTALITY IN A PROACTIVE CASE DETECTION INTERVENTION BY COMMUNITY HEALTH WORKERS IN MALI: ANALYSIS OF THE PROCCM TRIAL

Emily Treleaven[1], Amadou Beydi Cisse[2], Oumar Tolo[2], Noumoutie Sanogo[2], Kalo Dao[2], Djoume Diakite[2], Ari Johnson[3], Kassoum Kayentao[4]

[1]University of Michigan, Ann Arbor, MI, United States, [2]Muso, Bamako, Mali, [3]Muso, San Francisco, CA, United States, [4]Malaria Research & Training Center, Bamako, Mali

Community-based services delivered by community health workers (CHWs) have been shown to improve access to care for diarrhea, malaria, pneumonia, and malnutrition among children under five. Yet, evidence from national CHW programs has been mixed, in part from a lack of evidence on optimal delivery design, including how best to specify CHW workflows. In a three-year cluster-randomized trial, we tested the effectiveness of proactive case detection versus passive workflow by CHWs in rural Mali. Village clusters (N=137) were 1:1 randomized to receive daily case-finding home visits by CHWs or passive workflow (control), in which CHWs worked from a fixed post in the community. Using lifetime birth history data among women ages 15 to 49 at enrollment from annual surveys of all households in the study area at 12, 24, and 36 months, we analyzed cluster-level variance and predictors of U5M controlling for intervention arm, age, and child sex in mixed-effects regression models. We enrolled 31,587 children under five years of age over the trial (16,248 intervention, 15,339 control; 52,970 person-years of observation); 1,736 died during the trial period with no significant difference in under-five mortality (U5M) by study arm. We found substantial variation in crude death rates by cluster, ranging from 0.0 (8 clusters) to 142.3 deaths per 1,000 person-years (mean 32.5, SD 19.0). However, we observed greater within-cluster than between-cluster variance (ICC 0.039, SE 0.009). Distance to the nearest primary health center was not meaningfully associated with U5M in the intervention context, while CHW coverage indicators were associated with U5M. Children who lived in a cluster where < 50% of symptomatic children received care from a trained provider within 24 hours were twice as likely to die as children in clusters where > 75% of symptomatic children received timely care with a trained provider (OR 2.05, 95% CI 1.28, 3.29). Placing a trained, supervised, paid, and supplied CHW in each cluster can address distance-related barriers to care; empowering CHWs to identify and correctly treat symptomatic children in a timely manner can promote further reductions in U5M.

6828

COMBINATION OF A REDUCTASE INHIBITOR WITH PRIMAQUINE PREVENTS HEMOLYSIS OF G6PD DEFICIENT RBCS

Ariel M. Hay[1], Paul Buehler[2], Joseph Kao[2], Derek R. Lamb[2], Robert Commons[3], Eric A. Legenzov[2], Mitasha S. Palha[2], **James C. Zimring**[1]

[1]University of Virginia, Charlottesville, VA, United States, [2]University of Maryland, Baltimore, MD, United States, [3]Menzies School of Health Research, Darwin, Australia

The only two approved drugs that clear the hepatic hypnozoite phase of *P. vivax* (the 8-aminoquinolines (8-AQ) - primaquine and tafenoquine) can cause potentially lethal hemolysis in glucose-6-phosphate dehydrogenase deficient (G6PDd) patients due to drug metabolites that generate reactive oxygen species (ROS) in RBCs through redox cycling. Primaquine-5,6-orthoquinone (5,6-POQ) is a major hemolytic primaquine metabolite (PM). An enzymatic reductase in RBCs is required to drive redox cycling of PMs, but the specific enzyme(s) have never been identified. Using electron paramagnetic resonance (EPR) to measure superoxide, we report that treatment of intact murine RBCs with 5,6-POQ induced a robust increase in steady state superoxide levels (44 nM) compared to vehicle treated RBCs (5 nM), p =0.001. The addition of ES936, a selective inhibitor of the NAD(P)H:quinone oxidoreductase (NQO1), reduced levels of 5,6-POQ induced superoxide to 28 nM. Because most hemolysis is extravascular (consumption by macrophages), murine RBCs humanized to express the A- variant of human G6PD (hG6PD(A-)) were infused into mice and in vivo circulation was used as a metric of hemolysis. 5,6-POQ treatment of hG6PD(A-) RBCs resulted in a rapid clearance of 33% of RBCs with no clearance of control non-deficient RBCs. ES936 reversed 44% of 5,6-POQ induced hemolysis (p = 0.002). In addition to elucidating basic primaquine toxicology, these findings constitute a novel therapeutic approach with the potential to allow combination of an ES936-like inhibitor with primaquine or tafenoquine to achieve radical cure of *P. vivax* regardless of G6PD status. ES936 is predicted to not decrease the anti-relapse activity of 8-AQs for two reasons. First, ES936 does not inhibit cytochrome P450s, which drive redox cycling in hepatocytes but are not expressed in RBCs. Second, as an irreversible inhibitor, a short course of ES936 has been shown to only transiently inhibit reductases in hepatocytes (that can resynthesize the enzyme) but is predicted to provide permanent inhibition in RBCs, which cannot synthesize new proteins.

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RUXOLITINIB AS AN ADJUNCTIVE TREATMENT TO REDUCE INFLAMMATORY RESPONSES IN MALARIA: A RANDOMIZED PLACEBO CONTROLLED TRIAL IN VOLUNTEERS EXPERIMENTALLY INFECTED WITH *PLASMODIUM FALCIPARUM*

Bridget E. Barber[1], Rebecca Webster[1], Nischal Sahai[2], Indika Leelasena[2], Eniko Ujvary[2], Sue Mathison[2], Luzia Bukali[1], Damian Oyong[3], Fabian de Labastida Rivera[1], Jessica Engel[1], Dean W. Andrew[1], Megan S. Soon[1], Nicholas L. Dooley[3], Jessica R. Loughland[1], Jeremy Gower[1], Jenny Peters[1], Ria Woo[1], Adam Potter[1], Stacey Llewellyn[1], Fiona Amante[1], Teija Frame[1], Julianne Hamelink[1], Mayimuna Nalubega[1], Reena Mukhiya[3], James S. McCarthy[4], Christian Engwerda[1], Michelle J. Boyle[3]

[1]QIMR Berghofer Medical Research Institute, Brisbane, Australia, [2]University of Sunshine Coast, Brisbane, Australia, [3]Burnet Institute, Brisbane, Australia, [4]University of Melbourne, Melbourne, Australia

Case-fatality from severe malaria remains high despite the use of highly effective antiparasitic agents, due in part to the marked host inflammatory response to infection. Identification of agents that interrupt inflammatory pathways, without compromising anti-parasitic immune responses, may lead to novel adjunctive treatments for severe malaria. The JAK 1/2 inhibitor ruxolitinib exerts potent anti-inflammatory effects in *in vitro* models, and reduces inflammatory biomarkers when used

in the treatment of myeloproliferative disorders. Ruxolitinib also targets type-1 interferon mediated immunoregulatory pathways that impede development of antiparasitic immunity. We conducted a randomised placebo-controlled trial to evaluate the ability of ruxolitinib to reduce inflammatory responses and boost antimalarial immunity when administered alongside antimalarial treatment to volunteers experimentally infected with *Plasmodium falciparum*. Twenty participants were inoculated with blood-stage *P. falciparum*, and randomised on day 8 or 9 to receive artemether/lumefantrine in combination with either ruxolitinib (n=11) or placebo (n=9). All study drugs were given twice daily for 3 days. The primary endpoint was safety and tolerability. Ruxolitinib was safe and well tolerated, with a median of 4 (range 0 - 16) adverse events per participant in the ruxolitinib group compared to 7 (range 0 - 24) in the placebo group (p=0.25). Most adverse events were mild to moderate, and consistent with clinical symptoms of malaria. In the placebo group, the inflammatory marker CRP increased significantly following treatment. This increase was not seen in participants treated with ruxolitinib, with CRP levels on day 3 post-treatment significantly higher in the placebo vs ruxolitinib groups (p<0.01). Participants treated with ruxolitinib also had reduced post-treatment increases in ICAM-1 (p<0.001) and the liver enzyme alanine transaminase (p<0.001), and a reduced post-treatment fall in lymphocytes (p<0.001). Further studies evaluating the ability of ruxolitinib to reduce inflammatory responses and improve outcomes in clinical malaria are warranted.

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IMPROVING ANTIMALARIAL DRUG EFFICACY ASSESSMENT: COMPARATIVE ANALYSIS OF LENGTH POLYMORPHIC MARKERS AND CLASSIFICATION ALGORITHMS IN TWO PHASE II CLINICAL TRIALS

Daniela Montero Salas[1], Monica Golumbeanu[1], Sara L. Cantoreggi[1], Celine Risterucci[2], Cornelis Winnips[2], Christian Nsanzabana[1]

[1]Swiss Tropical and Public Health Institute, Allschwil, Switzerland, [2]Novartis Pharma, Basel, Switzerland

Development of new antimalarial drugs with new modes of action is crucial due to the emergence and spread of artemisinin partial resistance in Southeast Asia and Africa, and treatment failures after treatment with ACTs. Sensitive and robust methods for PCR-correction to distinguish recrudescences (treatment failures) from reinfections following new mosquito bites are essential to determine the accurate efficacy of a treatment in clinical trials. Since 2021, the WHO recommends genotyping the length polymorphic markers *msp1* and *msp2*, and replacing the marker *glurp* for one selected microsatellite due to biases that hinder the correct classification of recrudescences and reinfections. We reassessed the efficacy of two phase II clinical trials, including approximately 750 patients in total, by genotyping four combinations of length polymorphic markers, including *msp1* and *msp2*, and different microsatellites as the third marker (*PfPK2*, *Poly-α* and *TA40*), and compared them to *glurp*. We used three algorithms to classify recurrences into recrudescences or reinfections: the currently recommended WHO/MMV, the two out of three and the Bayesian algorithms. We compared twelve marker-algorithm combinations in total. We found that the use of *glurp* coupled with the WHO/MMV algorithm, used in the trials, indicated the least number of recrudescences across all methods tested, potentially underestimating treatment failure. We also found that the bin size used to classify two alleles as equal or different can influence the efficacy results and should be standardized in genotyping guidelines. The results observed in this study confirm, on the largest scale to our knowledge, results observed with *in silico* simulations, mixed laboratory strains or smaller-scale trials. The amount of samples included significantly increments the information available to determine a better recommendation for a sensitive and robust method, coupled to an appropriate algorithm of classification to determine treatment efficacy, which would translate in providing patients with a new effective treatment and bringing us closer to malaria elimination.

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FUNGAL DERIVED DEOXAPHOMINES TARGET *PLASMODIUM FALCIPARUM* SEGREGATION THROUGH INHIBITION OF PFACTIN1

Sarah Jiang[1], Jin Woo Lee[2], Jennifer Collins[3], Samuel Schaefer[1], Daisy Chen[1], Flore Nardella[3], Karen Wendt[4], Thilini Peramuna[4], Raphaella Paes[3], Greg Durst[5], Kirsten Hanson[6], Debopam Chakrabarti[3], Robert Cichewicz[4], Elizabeth Winzeler[1]

[1]UCSD, San Diego, CA, United States, [2]Duksung Women's University, Seoul, Korea, Republic of, [3]University of Central Florida, Orlando, FL, United States, [4]University of Oklahoma, Norman, OK, United States, [5]Lgenia Inc, Fortville, IN, United States, [6]University of Texas at San Antonio, San Antonio, TX, United States

Malaria remains a deadly disease that impacts millions every year. Resistance to all current frontline drugs has been observed, underscoring the urgent need for new therapeutic agents. Herein, we report the discovery of a natural product scaffold isolated from the fungi *Trichocladium asperum* with potent antiplasmodial activity. In total, six analogs were identified and have been dubbed methyldeoxaphomin NPDG A-F. The most potent compound, methyldeoxaphomin NPDG F displayed an EC_{50} of 550 nM in Dd2 and 290 nM in 3D7, with a selectivity index >60 over human HepG2 cells. This compound exhibited a gradual rate of killing, similar to atovaquone, with a lag phase of 24 h and a log (PRR) of 0.64. Morphologically, methyldoxaphomin NPDG F induced numerous abnormalities in merozoite segmentation during schizogony in both the blood and liver stages of *P. falciparum* and *P. berghei*, respectively. The *in vitro* evolution with NPDG F and whole genome sequencing revealed the probable drug target to be Pfactin1 (PF3D7_1246200). Of the 29 missense mutations found in the core genome of Dd2-Pol δ, 4 were observed in Pfactin1. A single nucleotide mutation, A136S, independently confers resistance in two of the three biological replicates. In the third biological replicate, SNPs A171V and I290L were found in 76% of the parasites with the remaining 24% bearing the mutations A171S and I290L. A molecular docking study with Pfactin1 found that methyldeoxaphomin NPDG F occupies the same binding pocket as cytochalasin D. The amino acids A171 and A136 line the binding cavity, while I290L was localized to the periphery. Resistance line parasites were found to be cross resistant to cytochalasin D (but not actin stabilizer Jasplakinolide), suggesting NPDG F displays a similar mode of action and interaction with PfActin1. Isobologram data also demonstrated that this compound exhibits an antagonistic effect with known inhibitors of actin polymerization, Latrunculin B and SMIFH2. Taken together, these findings support the inhibition of Pfactin1 polymerization as the likely mechanism of action of NPDG F, augmenting drug discovery efforts to target *Plasmodium* motor proteins.

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PLASMODIUM FALCIPARUM FIELD ISOLATES TO GUIDE CLINICALLY RELEVANT DOSE RATIOS FOR CABAMIQUINE: PYRONARIDINE COMBINATION USING TRANSLATIONAL MODELING

Mohamed MAIGA[1], Sebastian G. Wicha[2], Perrine Courlet[3], Abdoulaye Djimdé[1], Thomas Spangenberg[4], Laurent Dembélé[1], Claudia Demarta-Gatsi[4]

[1]Université des Sciences des Techniques et des Technologies de Bamako (USTTB), Bamako, Mali, [2]Universität Hamburg, Hamburg, Germany, [3]Merck Institute for Pharmacometrics, Ares Trading S.A., Lausanne, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany, [4]Global Health Institute of Merck, Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany

The emergence of drug resistance calls for the development of effective antimalarial combinations. However, the selection and combination of drug dose regimens involve complex considerations based on a totality of evidence approach, including pharmacokinetic (PK) and pharmacodynamic (PD) data, including potential interactions. We evaluated PD interactions between cabamiquine and pyronaridine, a combination currently in Phase 2 clinical trial. To do so, we used a real-world setting using immediate *ex vivo*

Plasmodium falciparum field isolates combined with translational modelling. The apparent parasite killing rate was simulated for cabamiquine and pyronaridine, alone and in combination to generate an interaction heat map. Concentration and time-dependent *in vitro* cidal activity of cabamiquine and pyronaridine alone as well as in combination were determined using *P. falciparum* field isolates and standard 48 hours SYBR Green assay-Mitotracker readout at different concentrations and time points. Potential PD interactions were quantified using non-linear mixed effects modelling describing the parasite growth and drug mediated-killing. These data are then fed into model to generate an interaction map that later is used to simulate meaningful clinical dose ratios.The parasite kinetics of field isolates was well described by the model. Whereas for cabamiquine, the regrowth observed in monotherapy arm suggesting adaptive resistance, was suppressed in combination when pyronaridine concentrations exceeded its EC50, highlighting the importance of the combination in controlling possible adaptive resistance to one of the two drugs. A stable killing rate was observed in cases where concentrations of pyronaridine or cabamiquine exceeded either EC50 after full adaptation. Finally, we were able to generate a range of EC50s for the two drugs, both as monotherapy and combination, that could then be translated into human doses.
This study innovatively used *P. falciparum* field isolates data, modeling and simulation techniques to assess cabamiquine and pyronaridine combination selection and reducing animal testing in pre-clinical studies.

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DIHYDROARTEMISININ-PIPERAQUINE PLUS SULFADOXINE-PYRIMETHAMINE FOR INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANT WOMEN: A DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

Abel Kakuru[1], Jimmy Kizza[1], Miriam Aguti[1], Harriet Adrama[1], John Ategeka[1], Peter Olwoch[1], Miriam Nakalembe[2], Joaniter Nankabirwa[1], Bishop Opira[1], Timothy Ssemukuye[1], Nida Ozarslan[3], Anju Ranjit[3], Erin Dela Cruz[3], Stephanie Gaw[3], Tamara D. Clark[3], Michelle E. Roh[3], Prasanna Jagannathan[4], Philip J. Rosenthal[3], Moses R. Kamya[2], Grant Dorsey[3]

[1]Infectious Diseases Research Collaboration, Kampala, Uganda, [2]Makerere University College of Health Sciences, Kampala, Uganda, [3]University of California, San Francisco, San Francisco, CA, United States, [4]Stanford University, San Francisco, CA, United States

The spread of antifolate resistance threatens the effectiveness of sulfadoxine-pyrimethamine (SP) for intermittent preventive treatment of malaria in pregnant women (IPTp) in Africa. Dihydroartemisinin-piperaquine (DP), an alternative to SP for IPTp, has shown superior antimalarial effects, but it does not reduce the risk of adverse birth outcomes compared to SP, suggesting that SP may have non-malaria benefits that impact on birth outcomes. Combining DP and SP could optimize the benefits of IPTp. We are conducting a double blinded randomized controlled trial comparing monthly IPTp with SP vs. DP vs. DP+SP (1:1:1) in HIV-uninfected pregnant women living in Busia district, Uganda, a high malaria transmission setting. From December 2020 to December 2023, we completed enrollment of 2757 women who were between 12-20 weeks of gestation. At enrollment, the prevalence of parasitemia was 38% by microscopy and 70% by PCR. Women are started on study drugs at 16 or 20 weeks of gestation and followed in a study clinic for all medical care. The primary outcome is the risk of a composite adverse birth outcome (spontaneous abortion, preterm delivery, low birth weight, small for gestational age, stillbirth, or neonatal death). Secondary outcomes included measures of malaria during pregnancy and at delivery and presence of reproductive tract infections (RTIs) at delivery. As of December 31, 2023, 199 women were prematurely withdrawn before delivery and 2101 had delivered. Malaria incidence during pregnancy was 1.19 and 0.18 episodes per person year before and after starting study drugs, respectively. Of the 2101 deliveries, 605 (28.8%) had a composite adverse birth outcome. The risk of placental malaria was 733/1723 (42.5%) by histopathology (presence of parasites or malaria pigment) and parasite DNA was detected in placental blood by PCR from 239/1918 (12.5%). At delivery, the risk of *Chlamydia trachomatis* was 107/1797 (6.0%), 47/1797 (2.6%) for *Neisseria gonorrhea*, 132/1989 (7.3%) for *Trichomonas vaginalis*, and 131/1343 (9.8%) for group B *Streptococcus*. We expect all women to deliver by August 2024. Unblinded results of the trial will be presented.

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EFFECT OF INTERMITTENT PREVENTIVE TREATMENT OF MALARIA IN PREGNANCY ON VAGINAL MICROBIOTA, HOST IMMUNE RESPONSE AND PREGNANCY OUTCOMES: A CASE-CONTROL STUDY FROM THE ASPIRE TRIAL IN ZAMBIA

Tanweer Beleil[1], Marwah Bagabas[1], Patricia Hunter[2], Sherrianne Ng[1], Jemima Hair[2], Gonçalo Correia[1], Yun S. Lee[1], Enesia B. Chaponda[3], Ephraim Chikwanda[4], Mike Chaponda[4], Nigel Klein[2], Lynne Sykes[1], Jane Bruce[5], Ludovica Ghilardi[5], Philippe Mayaud[5], Daniel Chandramohan[5], Phillip R. Bennett[1], R Matthew Chico[5], David A. MacIntyre[1]

[1]Imperial College London, London, United Kingdom, [2]University College London, London, United Kingdom, [3]University of Zambia, Lusaka, Zambia, [4]Tropical Diseases Research Centre, Ndola, Zambia, [5]London School of Hygiene & Tropical Medicine, London, United Kingdom

High prevalence of malaria and curable sexually transmitted and reproductive tract infections (STI/RTI) represent significant burden among pregnant women in East and Southern Africa. These are associated with adverse outcomes including preterm birth and low birthweight (LBW). The ASPIRE trial compared intermittent preventive treatment of malaria in pregnancy (IPTp) using sulfadoxine-pyrimethamine (SP) vs SP with metronidazole (MTZ) vs dihydroartemisinin-piperaquine (DP) with MTZ to reduce adverse pregnancy outcomes attributable to malaria and curable STIs/RTIs. Mechanisms by which these treatments may improve outcomes remain unclear. We aimed to investigate the effects of IPTp regimens on the vaginal microbiota, STI profiles and host immune response in term deliveries vs preterm and/or LBW. DNA was extracted from vaginal swabs collected from randomly selected sub-groups (SP n=99; SP+MTZ n=98; DP+MTZ n=94) at i) enrolment, prior to IPTp, ii) not less than one month after enrolment, before second IPTp dose, iii) prior to last IPTp dose before delivery. Microbiota were characterised using metataxonomic profiling. STIs were detected using quantitative PCR. Immune mediators were investigated using multiplexed Luminex assays. At enrolment, five vaginal microbiota community state types (CSTs) were identified i) *Lactobacillus iners* dominated (47.1%), ii) high-diversity compositions (36.4%), iii) *L. crispatus* (14.4%), *L. gasseri* (1.7%) and *L. jensenii* (0.3%). No change in vaginal microbiota composition was observed in women receiving three or more doses of SP or SP+MTZ. However, DP+MTZ was associated with reduced prevalence of high-diversity vaginal microbiota compositions and increased *L. iners* dominance (P<0.002). Integration of vaginal microbiota profiles with immune mediators, STI profiles, and clinical data is ongoing. Our data indicates that DP+MTZ is associated with reduced vaginal microbiota diversity, and may provide insight into how antenatal interventions alter microbe-host interactions associated with pregnancy outcome.

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SEROPREVALENCE OF *TAENIA SOLIUM* ANTIBODIES AND ASSOCIATED RISK FACTORS AMONG CHILDREN 0-14 YEARS IN NIGERIA

Jennifer Akamboe[1], Samuel A. Oyebanjo[2], Mary L. Kamb[1], Andrew Hill[1], Nishanth Parameswaran[1], Nnaemeka C. Iriemenam[3], Gretchen Cooley[1], Nwachukwu E. William[4], Nwando Mba[4], McPaul I. J. Okoye[3], Jeffrey W. Priest[5], Diana L. Martin[1], Paul Cantey[1], Chikwe Ihekweazu[4]

[1]Division of Parasitic Diseases and Malaria, U.S. Centers for Disease Control and Malaria, Atlanta, GA, United States, [2]Institute of Human Virology, Abuja, FCT, Nigeria, [3]Division of Global HIV & TB, U.S. Centers for Disease Control and Prevention, Abuja, FCT, Nigeria, [4]Nigeria Centre

for Disease Control and Prevention, Abuja, FCT, Nigeria, [5]Division of Foodborne, Waterborne and Environmental Diseases, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States

Children are vulnerable to *Taenia solium*, a parasitic tapeworm causing cysticercosis and taeniasis. Brain cysts may cause seizures. We sought to better understand risk factors for and prevalence of *T. solium* in Nigeria. We used data from a nationally representative, cross-sectional household survey estimating HIV incidence (2018) in which questionnaires and dried blood spots were collected from >31,000 children <15 years old. We determined the seroprevalence of *T. solium* IgG antibodies to rES33 (taeniasis) and T24H (cysticercosis) detected in a multiplex bead assay. We performed separate bivariate and multivariate logistic regression of weighted survey data for taeniasis and cysticercosis using household questionnaire and laboratory data. Positive antibodies against each antigen were detected in children from all states, with an overall antibody seroprevalence of 6.0% for T24H (range, 1.4%-19.3%) and 2.8% for rES33 (range, 0.5%-5.3%). Bivariate analyses found risk for each disease varied by state of residence and was significantly (P<0.05) associated with increasing age, rural (vs. urban) residence, association with pigs (vs. no free-roaming pigs), progressively lower socioeconomic status (vs. highest status), unimproved drinking water source, and lack of toilet facilities. In multivariate analyses, increasing age, rural residence, association with pigs, and lower socioeconomic status remained significant risks for cysticercosis. For taeniasis, the highest socioeconomic status had lower odds of infection compared to the lowest (aOR=0.40, 95% CI 0.22-0.75). Adjusting for all the other variables noted above, the individual impacts of safe water and improved toilets were not associated with decreased risk for each disease; but, regression results suggested a lower risk for cysticercosis when both safe factors were present. To our knowledge, this is the first nationally representative survey providing data on *T. solium* prevalence in Nigeria. The results support prioritizing control and public health strategies such as simultaneous access to improved water and safe toilet facilities to prevent brain cysts and epilepsy.

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PULMONARY CYSTIC ECHINOCOCCOSIS TREATMENT OUTCOMES AMONG 280 PATIENTS AT TWO TERTIARY CARE CENTERS IN CUSCO, PERU

Roberto Pineda-Reyes[1], Maria L. Morales[2], Karen Mozo[2], Maria A. Caravedo[3], Angel Gamarra[4], Ramiro Hermoza[4], Rocio Cuaresma[4], Miguel M. Cabada[3]

[1]Swiss Tropical and Public Health Institute, Allschwil, Switzerland, [2]Cusco Branch - Alexander von Humboldt Tropical Medicine Institute/Universidad Peruana Cayetano Heredia, Cusco, Peru, [3]Infectious Disease Division, University of Texas Medical Branch, Galveston, TX, United States, [4]Department of Surgery, Hospital Regional del Cusco, Cusco, Peru

The management of pulmonary cystic echinococcosis (pCE) is influenced by local practice and center volume. Treatment recommendations are largely based on expert opinion and small single-center case series. We reviewed medical records of patients discharged with a diagnosis of pCE from two referral centers in the Cusco Region of Peru between January 2009 and December 2019. Adverse hospitalizations outcomes were defined as discharge condition recorded as 'unchanged', 'worse', or 'dead'. Two hundred eighty cases with pCE were identified, 45% were younger than 18 years and 43% were female. A single lung cyst was diagnosed in 56% while 16% had 2 cysts, and 16% had ≥ 3 cysts. In 41% of cases the diameter of the largest cyst was ≥10 cm. Ten patients (4%) received pre-surgical albendazole (ABZ), 57 (20%) post-surgical ABZ, and 4 (1%) pre- and post-surgical ABZ. In 163 (58%) surgery was performed without documentation of ABZ prescription. Eight patients (3%) received ABZ with no surgery. The type of treatment prescribed was not documented in 29 patients (10%) and 9 (3%) received surgery and ABZ but the exact order of the interventions was unknown. Multivariate backwards logistic regression found pre-surgical respiratory insufficiency (OR=3.12, 95%CI 1.03-9.47) as predictor for adverse hospitalization outcomes. Subjects referred from a healthcare center (OR=0.21, 95%CI 0.1-0.5) and those hospitalized ≥1 month (OR=0.07, 95%CI 0.01-0.4) were less likely to have adverse hospitalization outcomes. Subjects with documentation of "infected cyst" (OR=11.39, 95%CI 1.2-108.2) and those having a concomitant liver cyst (OR=6.34, 95%CI 3.01-13.35) were more likely to have at least one readmission. No statistically significant differences were found for pre- or post-surgical ABZ and hospitalization outcome or readmission. Further studies analyzing the appropriate timing of antiparasitic therapy in patients with pCE are needed.

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TAENIA SOLIUM FATTY ACID BINDING PROTEIN 1 INDUCES SUPPRESSES TLR4 SIGNALING AND DOWNREGULATE IRE-1α IN A PPAR-G DEPENDENT MANNER

Amit Prasad, Suraj S. Rawat

Indian Institute of Technology Mandi, mandi, India

Neurocysticercosis is a major neurological threat, accounting for over 30% of cases in endemic areas. *Taenia solium*, the causative agent, and its other helminthic counterparts lack key components of the cellular machinery required for endogenous lipid biosynthesis. This deficiency enables the parasite to obtain all required lipids from its host organism. To facilitate effective lipid transport, the cestode parasite employs Fatty Acid Binding Proteins (FABPs), which bind to lipid ligands and allow lipid transport across membranes and into the cytosol. *T. solium* expresses an abundance of FABPs. Apart from transporting ligands, FABPs interacts with the host immune system, however the functional aspect of *T. solium* FABP is still unknown. Elucidating the functional outcome of FABP on host immune system will contribute to understand the detailed immunopathology of cysticercosis infection. TsFABP1 is one of the members of *T. solium* FABP family, which is secretory in nature, interacts with neighbouring cells, potentially modulating their functions. We expressed TsFABP1 in the pET23a vector, purified it with Ni-NTA affinity chromatography, and measured the molecular weight at 15 kDA. TsFABP1 purified form induced anti-inflammatory gene expression in THP-1-derived macrophages in a dose-dependent manner. TsFABP1 inhibits the CD14-TLR4 pathway by binding to CD14 at the LPS binding site, reducing ROS and cleaved IL-1β production. Interestingly macrophages readily internalize the cyanine5-labelled TsFABP1 and in the cytosol the protein may play significant role in immunomodulation. Here for the first time, we report that the TsFABP1 play role in PPAR-γ pathway, which was previously unknown. TsFABP1 suppresses IRE-1α in a PPAR-γ-dependent manner. In conclusion, TsFABP1 is an anti-inflammatory molecule that also downregulate the endoplasmic stress response associated molecule and apart from that TsFABP1 can be explored for therapeutic potential.

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HIGH PREVALENCE AND HOUSEHOLD CLUSTERING OF LIVER CYSTIC ECHINOCOCCOSIS IN A RURAL COMMUNITY IN THE CENTRAL ANDES OF PERU: A POPULATION - BASED SURVEY

Saul J. Santivanez[1], Percy Soto-Becerra[1], Raul Enriquez[1], Luis Tello[1], Oswaldo G.E. Espinoza-Hurtado[1], Andreas Neumayr[2], Hector H. Garcia[3]

[1]Universidad Continental, Huancayo, Peru, [2]Swiss Tropical and Public Health Institute, Basel, Switzerland, [3]Center for Global Health, Universidad Peruana Cayetano Heredia, Lima, Peru

Human cystic echinococcosis (CE), a zoonotic disease caused by the larval stage of the *Echinococcus granulosus* tapeworm, presents a significant public health challenge in the Peruvian central highlands. In this region, the disease's impact is profound, with some families reporting multiple infected individuals. The current study aimed to estimate the prevalence of CE in Corpacancha, a rural community in the Peruvian central highlands, utilizing abdominal ultrasound (US), electroimmuno transfer blot (EITB), and computed tomography (CT) scans for individuals with positive US or EITB results. Additionally, we explored household clustering of CE cases using the intraclass correlation coefficient (ICC) with 95% credibility intervals (CrI) estimated through Bayesian multilevel model, updating prevalence

data, and identifying risk determinants, particularly focusing on household clustering. The findings revealed a liver CE prevalence of 16.1% (95% CI: 11.1% - 22.7%) as detected by ultrasound and a seroprevalence of 24.1% (95% CI: 15.4% - 35.6%) using the EITB assay. Active liver CE was present in 11.9% (95% CI: 7.8% - 17.9%) of participants, predominantly in the CE1 stage, while inactive liver CE had a prevalence of 4.1% (95% CI: 2.3% - 7.4%). Lung involvement was identified in 30.6% (95% CI: 16.9% - 48.8%) of individuals undergoing CT evaluation. Our survey also indicated that approximately one quarter of households had at least one case of CE, with a third of these households reporting multiple cases. After adjusting by relevant predictors of liver CE and accounting by household as a random intercept, we found an ICC of 0.3334 (95% CrI 0.0025 to 0.7379). Overall, this study not only demonstrates hyperendemic levels of CE but also highlights significant household-level influences on disease prevalence, suggesting that intervention efforts may be more effective when targeted at the household level.

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DIAGNOSTIC PERFORMANCE OF A MULTIANTIGEN PRINT IMMUNOASSAY FOR ANTIBODY DETECTION IN HUMAN NEUROCYSTICERCOSIS

Luz M. Toribio Salazar[1], Carolina Guzman[1], Herbert Saavedra[2], Isidro Gonzales[1], Javier A. Bustos[1], Sukwan Handali[3], Hector Garcia[1]

[1]universidad Peruana Cayetano Heredia, Lima, Peru, [2]Instituto Nacional de Ciencias Neurologicas, Lima, Peru, [3]Division of Parasitic Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention USA, Atlanta, GA, United States

Neurocysticercosis (NCC) stands as the most prevalent helminthic infection affecting the human central nervous system. Although neuroimaging is required for definitive diagnosis, the gold standard for serology is the antibody detection using the enzyme-linked immunoelectrotransfer blot assay (EITB, Western blot), which uses seven highly antigenic lentil-lectin purified parasite glycoproteins. EITB is poorly accessible due to is technical complexity and the requirement of sophisticated equipment and parasitic material. We recently developed a 3-antigen-multiantigen print immunoassay (MAPIA) based on recombinant/synthetic antigens (rGP50, rT24H and sTs14), corresponding to the three principal EITB diagnostic families, that effectively address many of the aforementioned barriers. We expanded the initial evaluation of performance of this MAPIA assay using a well-defined set of serum samples from NCC patients confirmed by imaging, including 73 individuals with subarachnoid NCC, 73 with more than 5 parenchymal cysts, 62 with 3-5 parenchymal cysts, 98 with 1-2 parenchymal cysts and 80 healthy controls devoid of neurological disease. The assay overall sensitivity was 97.71% and specificity 97.5%. Subgroup analyses by type of NCC demonstrated a sensitivity of 100% for subarachnoid and parenchymal NCC with more than 5 cysts, slightly decreasing for the groups with 3-5 cysts (96.77%) and 1-2 cysts (94.9%). Equivalent results were obtained when comparing its performance with that of the reference EITB, reaching a sensitivity of 100% for subarachnoid and parenchymal NCC for more than 3 cysts and 95.92% for 1-2 cysts. Our 3-antigen MAPIA is comparable to EITB and emerges as a simpler, reproducible, and available alternative for antibody diagnosis in NCC.

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COMPARISON OF THE ANTIBODY DYNAMICS IN TWO MODELS OF EXPERIMENTAL PIG CYSTICERCOSIS USING A MULTIPLEX BEAD ASSAY

Luz M. Toribio Salazar[1], Sukwan Handali[2], Gianfranco Arroyo[1], Javier A. Bustos[1], Hector Garcia[1]

[1]universidad Peruana Cayetano Heredia, Lima, Peru, [2]Centers for Disease Control and Prevention, Atlanta, GA, Atlanta, GA, United States

Cysticercosis is a parasitic infection caused by *Taenia solium* that can invade the brain causing Neurocysticercosis (NCC). Controlled experimental infections of pigs allow to accurately determine timepoints during cysticercosis infection. Antibody responses have been characterized using the traditional lentil-lectin enzyme-linked immunoelectrotransfer blot (LLGP-EITB) assay; however, this qualitative technique presents technical challenges and depend on parasite material. We have developed a Multiplex Bead Assay (MBA) coupled to six recombinant/synthetic antigens used for diagnosis (rGP50,rT24H,sTs14,sTs18,sTsRS1,sTsRS2). To simultaneously quantify the dynamics of the antibody responses against mentioned antigens during infection, and to explore differences in antibody responses in two different experimental porcine cysticercosis models, one using oral infection with eggs and the other using intracarotid injection of activated oncospheres, we analyzed 60 archived serum samples from pigs orally (n=6) and intracarotid (n=6) infected, who developed viable cysticercosis and that were sampled at five time points post-infection (PI). Cyst establishment in brain tissue was predominant in the carotid model. Our 6-antigens MBA determine significantly higher antibody responses against sTs14 and sTs18 for both models ($p<0.01$) and differences against rGP50 and rT24H antibody levels, which were higher only in pig orally-infected. Antibody dynamics in both models described a similar pattern in which rT24H and rGP50 responses were detected from day 28 onwards with a gradual increase throughout the infection course, while smaller antigenic peptides showed a stronger response from day 35PI. Pigs orally infected exhibited a significant decrease in antibody response from day 57PI until necropsy, while this decrease occurred by day 70PI in pigs carotid infected. Although, antibody dynamic is consistent in both models, differences in antibody levels could be explained by the route of infection; natural route that parasite must go through to stablish as a cyst in oral infection could stimulate more antibodies against anchoring antigens (rGP50).

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CHARACTERIZATION OF THE ACUTE NEUROINFLAMMATORY RESPONSE INDUCED BY ANTIPARASITIC TREATMENT IN THE CAROTID PORCINE MODEL OF NEUROCYSTICERCOSIS

Gianfranco Arroyo[1], Lizzie Tello-Ccente[1], Rosa Diaz-Gongora[1], Yessenia Salas[1], Miguel A. Orrego-Solano[1], Javier A. Bustos[1], Manuela R Verastegui[1], Robert H Gilman[2], Hector H. Garcia[1]

[1]Universidad Peruana Cayetano Heredia, Lima, Peru, [2]Johns Hopkins University, Baltimore, MD, United States

Antiparasitic treatment (APT) in NCC causes cyst damage and activates the host's immune system, triggering early neuroinflammation. We evaluated the development of treatment-induced neuroinflammation in the experimental NCC pig model by intracarotid-oncosphere injection using histopathological, immunohistochemical, and molecular markers to provide evidence for the suitability of this model for studying neuroinflammation. Twelve NCC pigs by intracarotid-oncosphere injection were distributed as untreated (T1), treated with ABZ plus PZQ and sacrificed 48h (T2) and 120h (T3) after APT (n=4 pigs each). Before euthanasia, all pigs received intravenous Evans-Blue (EB) infusion to assess BBB disruption. EB-stained (blue) and non-stained (clear) cysts with adjacent tissue were stored in 10% formalin and paraffin-embedded; pericystic inflammation was assessed using histopathological scores (ISC, range: 0-400). Astrocytosis and microglia were assessed by IHQ using primary antibodies anti-GFAP and anti-IBA 1 and expressed as immunoreactive areas (percentages). Cysts with capsules were also assessed for gene-expression levels of cytokines (IFN-γ, TNF-α, IL6, IL10, and VGEF) by real time PCR. Almost all cysts from treated NCC pigs showed EB-disruption (94.3% [48h] and 100% [120h]) versus untreated pigs (50%, $P< 0.001$). EB-stained cysts showed increased ISCs 120h after APT (median: 400) versus 48h after APT and no-treatment (median: 283, and median: 275, $P<0.001$). Astrocyte and microglia immunoreactivity was higher in NCC pigs 120h after treatment versus 48h after treatment or untreated pigs ($P<0.05$). Increased expression levels of TNF-alpha, INF-gamma, IL-6, and VGEF were found in EB-stained cysts from NCC pigs 120h after APT compared to NCC pigs 48h after APT and untreated pigs ($P<0.005$); IL-10 levels increased 48h after treatment but decayed 120h after treatment ($P<0.005$). Acute pericystic neuroinflammation can be properly induced by 120h after treatment in the carotid model, thus providing a valuable tool to study neuroinflammation and evaluate pharmacological interventions to reduce pericystic neuroinflammation.

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A CRISPR-CAS13A ASSAY FOR DETECTION OF CIRCULATING CELL FREE RNA (CCFRNA) IN ACTIVE *WUCHERERIA BANCROFTI* INFECTION

Carlos F. Ng[1], Sasisekhar Bennuru[2], Amy Lyden[1], Andres A. Dextre[1], Zaina L. Moussa[1], María Díaz De León Derby[1], Thomas B. Nutman[2], Daniel A. Fletcher[1]

[1]University of California, Berkeley, Berkeley, CA, United States, [2]National Institutes of Health, Bethesda, MD, United States

Detecting parasitic circulating cell free nucleic acids (ccfDNA/ccfRNA) in plasma is a promising approach for sensitive and specific detection of active helminth infection including *Wuchereria bancrofti* (Wb). To identify potential Wb RNA targets, we performed Plasma-RNAseq using plasma from 10 Wb microfilaria-positive (mf-positive) individuals and 10 healthy blood bank individuals and used bioinformatic tools to ensure specificity. Six targets were identified that were specific to Wb and/or *Brugia malayi* (Bm), the causative agents of lymphatic filariasis, and not found in *Loa loa* (Ll) or *Onchocerca volvulus* (Ov), two closely related filarial parasites. Reverse transcriptase-PCR (RT-PCR) assays for each of these six targets were developed and tested on RNA from extracted daytime plasma from mf-positive patients with Wb and shown to be variably positive. To improve the sensitivity of the detection of ccfRNA in Wb infection and to develop a possible point-of-care (POC) assay concurrently, guide RNAs for the set of six ccfRNA targets were designed and used in a CRISPR-Cas13a (RNA-directed RNA nuclease) assay. We first tested these guide RNAs against synthetic target RNAs in the presence of reporter molecules that fluoresce after cleavage by activated Cas13a. By combining the most active guide RNAs into a pooled assay, results showed a limit of detection of approximately 1000 copies/µL using synthetic targets. The Cas13a assay requires no RNA purification, reverse transcription, or amplification and can be detected by a simple fluorescent reader. To demonstrate this, we added fluorescence illumination to a compact mobile phone-based digital microscope known as the NTDscope (aka LoaScope) and were able to detect an increasing fluorescence signal in the presence of RNA biomarkers compared to a control reaction without them. These data suggest that molecular testing for ccfRNA for Wb at the POC with an amplification-free Cas13a assay is feasible. The assay will be optimized prior to assessing the sensitivity and specificity using cryopreserved plasma samples from mf-positive Wb patients and Wb-uninfected controls.

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A BIOMARKER ASSAY TO DETECT PEOPLE WITH HIGH *LOA LOA* MICROFILARIA COUNTS

Sarah E. Greene[1], Yuefang Huang[1], Kerstin Fischer[1], Bruce A. Rosa[1], John Martin[1], Makedonka Mitreva[1], Samuel Wanji[2], Joseph Kamgno[3], Philip J. Budge[1], Gary J. Weil[1], Peter U. Fischer[1]

[1]Washington University in St Louis, Saint Louis, Mo, United States, [2]University of Buea, Buea, Cameroon, [3]University of Yaounde, Yaounde, Cameroon

Loiasis is a disease caused by infection with the nematode *Loa loa*. Some people with high *L. loa* microfilaria counts develop serious adverse drug reactions after treatment with ivermectin. This poses a significant challenge for lymphatic filariasis and onchocerciasis elimination programs in Central Africa where loiasis is endemic, as these programs rely on mass distribution of ivermectin. To address this problem, improved methods are needed to efficiently identify individuals with loiasis who are at increased risk of ivermectin-related adverse events. We have previously reported detection of the *L. loa* protein Ll-Bhp-1 in the sera of people with loiasis. Here, we describe use of this antigen as an infection biomarker that may be especially useful for identifying people with high *L. loa* infection burdens. We developed a prototype antigen capture ELISA that detected Ll-Bhp-1 in 74 of 116 (63.8%) loiasis patient sera. Antigen levels were significantly correlated with *L. loa* microfilarial counts. Assay sensitivity was excellent in samples from people with microfilarial counts that would put them at risk for serious adverse events (sensitivities of 94% and 100% in samples from people with ≥20,000 and ≥50,000 *L. loa* microfilaria per milliliter of blood, respectively). The assay is highly specific and did not detect Ll-Bhp-1 in any of 112 sera from people with other filarial infections or in 34 sera from non-endemic controls. Thus, this antigen assay appears to be highly sensitive for identifying people with high *L. loa* microfilarial counts who are at increased risk of serious adverse events after ivermectin. Optimization of this prototype assay and use of a rapid diagnostic platform could facilitate loiasis mapping and efforts to eliminate lymphatic filariasis and onchocerciasis in Central Africa.

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A RANDOMIZED DOUBLE-BLIND STUDY COMPARING THE EFFECT OF 3 ANNUAL OR FIVE 6-MONTHLY SINGLE DOSES OF MOXIDECTIN OR IVERMECTIN IN INDIVIDUALS ≥12 YEARS OLD WITH *ONCHOCERCA VOLVULUS* INFECTION IN ITURI PROVINCE, DEMOCRATIC REPUBLIC OF CONGO: EFFICACY AND SAFETY DATA 12 MONTHS AFTER THE FIRST TREATMENT

Tony O. Ukety[1], Michel Mandro-Ndahura[2], Pascal Adroba[1], Deogratias Ucima[1], Françoise Ngave[1], Kaki Kambale-Tsongo[1], Amos Nyathirombo[1], Innocent Mananu[1], Jack Zawadi[1], Gisèle Abeditho[1], Patrick Ubimo[1], Jules Upenjirwoth[1], Moïse Alidra[1], Joël Mande[1], Germain Abafule[1], Claude Uvon[1], Anuarite Raciu[1], Salomon Maki[1], Lyna Biwaga[1], Mathieu Njabu[1], Anouk Neven[3], Annette C. Kuesel[4], Moraye Bear[5], Beatriz Mosqueira[6], Mupenzi Mumbere[6], Melinda Lowe[6], Sally Kinrade[6]

[1]Centre de Recherche en Maladies Tropicales Ituri, Rethy, Congo, Democratic Republic of the, [2]Ituri Provincial Health Division, Bunia, Congo, Democratic Republic of the, [3]Luxembourg Institute of Health, Strassen, Luxembourg, [4]World Health Organization Special Programme for Research and Training in Tropical Diseases (TDR), Geneva, Switzerland, [5]Forsythe and Bear, LLC, Los Angeles County, CA, United States, [6]Medicines Development for Global Health, Southbank, Australia

Long-term community-directed treatment with ivermectin (IVM) has reduced onchocerciasis prevalence and may have eliminated onchocerciasis in some foci in Africa, but alternative strategies are needed for accelerating elimination across Africa. The US Food and Drug Administration approved moxidectin (MOX) 8 mg for treatment of individuals ≥12 years old with onchocerciasis based on Phase 2 and 3 study data showing that a single MOX dose reduced skin microfilariae levels (SmfL) better and for longer than a single 150 µg/kg IVM dose. MDGH is seeking regulatory approval for children 4 to 11 years old. A double-blind trial, initiated in the Ituri province of the Democratic Republic of Congo in May 2021, is comparing the safety and effect on SmfL in individuals ≥12 years old randomized in a ratio of 3:1:3:1 to three annual MOX doses, three annual IVM doses, five 6-monthly MOX doses or five 6-monthly IVM doses. The primary efficacy endpoint is the percentage of participants who received a single or two 6-monthly MOX doses and had undetectable (0) SmfL both 6 and 12 months after the first treatment. Safety endpoints are vital signs and the incidence and severity of adverse events (AEs) to 36 months and liver function to 12 months after the first treatment. Secondary efficacy analyses include SmfL 6, 12, 18, 24, 30 and 36 months after the first treatment. A total of 8925 people from 45 villages in the Logo and Nyarambe Health Zones were screened. Enrolment was completed in July 2023 with 323 participants with ≥10 mf/mg skin (based on 4 skin snips, mean 23.1 ± 20.8 mf/mg, range 10.0 to 175.4 mf/mg skin) randomized and treated. To-date, treatments have been well-tolerated. The majority of participants reported no AEs. The types of AEs were similar to those in the Phase 2 and 3 studies. AEs occurred primarily within the first 5 days after treatment. The severity of 96% of AEs was mild or moderate. Details of the study design, including the cost- and time-effective nested recruitment and screening strategy with a concurrent single dose safety study, participant population and results of the 12-month efficacy and safety analyses will be presented.

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MULTIPLEXING NOVEL BIOMARKERS TO AID POST-ELIMINATION SURVEILLANCE IN LYMPHATIC FILARIASIS

Rachel E. Pietrow[1], Belinda Jackson[2], Edward E. Mitre[2], Thomas B. Nutman[1], Sasisekhar Bennuru[1]

[1]Laboratory of Parasitic Diseases, NIAID, National Institutes of Health, Bethesda, MD, United States, [2]Microbiology and Immunology, School of Medicine, Uniformed Services University of Health Sciences, Bethesda, MD, United States

The success of mass drug administration (MDA) at reducing the prevalence of lymphatic filariasis (LF) in endemic areas has led to an increased need for diagnostic assays with high sensitivity and specificity. To be useful in post-elimination surveillance (PES) areas with low to zero prevalence, high test performance characteristics are required to enable the early detection of infection recrudescence without eliciting high numbers of false positive results. Antibodies to several *Wuchereria bancrofti* [*Wb*]- and *Brugia malayi* [*Bm*]-encoded antigens (e.g. Wb123, Bm33, BmR1) have been utilized to this end, but suffer either from sensitivity or specificity levels that fail to meet recently adopted target product profiles. Additional targets that could be used as confirmatory tests or in multiplexed assays could overcome these issues. From a screen of 12 targets (reported previously) we identified that immunoassays detecting IgG antibodies against Wb5 and Wb4 antigens were highly sensitive and specific for Wb and/or Bm infection and were associated with pre-patent (Wb5) or patent (Wb4) infection. Recombinant Wb4 and Wb5 proteins were generated for use in a variety of IgG4-based immunoassays. Screening of serum from *Brugia*-infected humans (n=19) revealed high prevalence of anti-Wb4 antibodies (14/19 positive) and minimal cross reactivity with other filarial infections. Using IgG4 based immunoassays at 100% specificity, Wb5 and Wb123 had individual sensitivities of 53.7% and 75.3%, respectively, while a combination resulted in 81.0% sensitivity in 381 samples (231 Wb-infected; 150 Wb-uninfected controls). Testing of prototype Wb5 IgG4-based lateral flow assays supports the finding that the addition of Wb5 to Wb123 increases sensitivity of LF detection. Moreover, kinetic studies of patients that were treated and followed longitudinally demonstrated a sharper decline in Wb5 titers compared to Wb123, suggesting the use of Wb5 as a marker of active infection. Ongoing studies to improve the detection of Wb4 and Wb5 paves the way for their use in combination with Wb123 (or other antigens) to increase the sensitivity of Ab-based assays for PES.

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FIELD EVALUATION IN GHANA OF A NEW OVND5 REAL-TIME PCR METHOD FOR DETECTION OF *ONCHOCERCA VOLVULUS* DNA IN POOLED *SIMULIUM DAMNOSUM S.L.* BLACKFLIES

Jessica Prince-Guerra[1], Gifty Boateng[2], Rexford Adade[2], Andrew Abbott[1], Joseph Opare[3], Odame Asiedu[3], Ellen J. Doku[3], Kofi Asemanyi-Mensah[3], Ben Masiira[4], Thomson Lakwo[4], Ernest Kenu[4], Moukaram Tertuliano[1], Stephen Lindstrom[1], Paul Cantey[1]

[1]US Centers for Disease Control and Prevention (CDC), Atlanta, GA, United States, [2]National Public Health and Reference Laboratory, Ghana Health Service, Accra, Ghana, [3]Neglected Tropical Diseases Program, Ghana Health Services, Accra, Ghana, [4]African Field Epidemiology Network, Kampala, Uganda

Onchocerciasis is a parasitic disease transmitted by blackflies and targeted by the World Health Organization (WHO) for elimination. WHO guidelines for stopping treatment (MDA) require screening pools of *Simulium* blackflies for the presence of *O. volvulus* using the O150 PCR-ELISA. A new qPCR assay using the ND5 region (OvND5) was found to be more sensitive and species-specific than O150 molecular methods. It is also faster, easier to perform, lower cost, and uses room-temperature stable reagents. However, the OvND5 qPCR method has not been evaluated in *Simulium* blackflies collected in endemic regions. As part of a larger study evaluating serological thresholds to stop MDA in Northern Ghana, DNA extracted from pools of heads from 22,772 *Simulium damnosum s.l.* blackflies, collected from 10 capture sites in 4 districts, were tested by OvND5 and O150 qPCR assays. A sample was considered positive if both OvND5 and O150 qPCRs were positive. Samples with discordant qPCR results were repeated at a higher (1/20) dilution of DNA. Of 233 pools analyzed, 3 were positive, each from a different site. Cycle threshold (Ct) values ranged from 29-34 (OvND5) and 24-27 (O150). The prevalence calculated using the Poolscreen software was 0.013% (95% CI 0.003-0.038%), which met WHO criteria for stopping MDA. There were 9 pools of blackflies with discordant qPCR results (O150+/OvND5-), 7 of which were from sites with a positive pool. All discordant samples had O150 Ct values > 36. Repeat testing of these samples with diluted DNA did not reveal inhibition; no OvND5 result became positive. It is possible that the high O150 qPCR Ct value represents a small amount of *O. volvulus* DNA that does not indicate an L3 larvae in the head or cross-reaction with another *Onchocerca* species. Further evaluation of the samples is ongoing including genetic sequence analysis to verify species identity, which would help better understand how to use this new method to inform stopping decisions. This evaluation of the OvND5 qPCR provided information on how this test will perform programmatically. Additional evaluations, including those ongoing in Tanzania, Benin, and Malawi, will be important.

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SAFETY AND EFFICACY OF A SINGLE DOSE OF 2 MG MOXIDECTIN IN *LOA LOA* INFECTED INDIVIDUALS: A DOUBLE-BLIND, RANDOMIZED IVERMECTIN-CONTROLLED TRIAL WITH ASCENDING MICROFILARIAL DENSITIES

Guy Wafeu[1], Tristan Lepage[2], **Jérémy T. Campillo**[3], Arnaud Efon-Ekangouo[1], Hugues C. Nana-Djeunga[1], Narcisse Nzune-Toche[1], André Domche[1], Laurentine Sumo[1], Guy-Roger Njitchouang[1], Martine A F Tsasse[1], Jean Bopda[1], Yves A. Balog[1], Yannick Niamsi-Emalio[1], Stève Mbickmen-Tchana[1], Gervais K. Talla[1], Yannick Sédrick N. Kana[1], Félicité Diane M. Messina[1], Sebastien D S Pion[4], Annette C. Kuesel[5], Michel Boussinesq[4], Cédric B. Chesnais[4]

[1]Higher Institute of Scientific and Medical Research, Yaoundé, Cameroon, [2]Montpellier University Hospital, Montpellier, France, [3]Inserm, Montpellier, France, [4]Institut de recherche pour le développement, Montpellier, France, [5]UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, Geneva, Switzerland

In 2018, the US FDA approved the macrocyclic lactone moxidectin (MOX) at 8 mg dosage for onchocerciasis treatment in individuals aged ≥12-year-old. Severe adverse reactions have occurred after ivermectin (IVM), also a macrocyclic lactone, in individuals with high *Loa loa* microfilaria density (MFD). This study compared the safety and efficacy of a 2 mg MOX dose and the standard 150 µg/kg IVM dose in individuals with low *L loa* MFD. A double-blind randomized, ivermectin-controlled, trial of a 2 mg moxidectin dose was conducted in Cameroon between May 2022 and May 2023. It enrolled 72 adult men with *L. loa* MFD between 5-1000 microfilaria/mL. Outcomes were occurrence of adverse events (AE) and *L. loa* MFD reduction rate during the first month off treatment. No serious or severe AEs occurred among the 36 MOX or the 36 IVM treated individuals. Forty-nine AEs occurred in the MOX arm vs 59 AEs in the IVM arm. Grade 2 AE incidence was higher among IVM than MOX treated participants (38.5% and 14.3%, respectively, p=0.043). Median MFD reduction rates were significantly higher after IVM than MOX at day 3 (D3) (70.2% vs 48.5%), D7 (76.4% vs 50.0%) and D30 (79.8% vs 48.1%). Efficacy results at D180 and D365 will be available in June 2024. A single 2 mg MOX dose is as safe as 150 µg/kg IVM in patients with low *L loa* MFD. Further studies with higher moxidectin doses and in patients with higher MFD are warranted.

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NEXT GENERATION OV16-BASED RAPID TESTS: FIELD DATA

Marco Biamonte[1], Sam Marton[1], Lauren Boone[1], Justin Nueve[1], Rhea Perez[1], Lily Sullins[1], Jean Saunders[2], Matthias Schwarz[2], Adina Gerson-Gurwitz[2], Sasisekhar Bennuru[3], Rachel Pietrow[3], Yaya Coulibaly[4], Patrick N. Kpanyen[5], Kerstin Fischer[6], Peter U. Fischer[6], Sarah Sullivan[7], Lee Hundley[7], Yvonne Ashong[8], Dziedzom K. de Souza[8]

[1]Big Eye Diagnostics, Inc., San Diego, CA, United States, [2]DDTD, San Diego, CA, United States, [3]NIAID, Bethesda, MD, United States, [4]ICER Mali, Université des Sciences, des Techniques et des Technologies de Bamako, Bamako, Mali, [5]National Public Health Institute of Liberia (NPHIL), Monrovia, Liberia, [6]Washington University School of Medicine, St Louis, MO, United States, [7]COR-NTD, Task Force for Global Health, Decatur, GA, United States, [8]Noguchi Memorial Institute for Medical Research, Accra, Ghana

Improved diagnostics are required to map onchocerciasis in low endemicity areas. In 2021 WHO issued a Target Product Profile (TPP) that calls for a sensitivity ≥ 60% and specificity ≥ 99.8%. To reach this stringent specificity requirement, we developed a prototype rapid diagnostic test that detects IgG4 antibodies to different recombinant *O. volvulus* proteins arranged as two different test lines. Both test lines must be visible to count the test positive. In the latest iteration, called “Biplex D”, the first test line (TL1) is made of Ov16 and the second test line (TL2) contains a mixture of OvOC3261 and Ov33.3. When evaluated in the laboratory against a panel of cryopreserved sera containing 86 microfilariae (Mf) positives and 234 other infections, the sensitivity of Biplex D was 79% (95%CI 69-86%) and its specificity 100% (99.95-100). An earlier test version, called “Biplex C” contains only OvOC3261 and no Ov33.3 at TL2. These two versions are being validated in the field using fingerstick blood. In Bong, Liberia, a preliminary dataset on 19 patients with onchocerciasis (all Mf and nodule positive before ivermectin 18 month ago) gave a sensitivity for Biplex D of 17/19 = 89% (69-97). Combining this with the specificity data obtained in the lab, we conclude that Biplex D meets the TPP sensitivity and specificity specifications, even at the lower bound of the 95% CI. The sensitivity of Biplex C was in Liberia 16/19 = 84% (62-94%), and in Nkwanta, Ghana 11/13 = 85% (57-97%). Combining the two data sets gives a mean sensitivity of 27/32 = 84 % (68-93%), above the 60% sensitivity threshold at the lower bound of the 95% CI. Antibody prevalence data were collected in Ghana with Biplex C. In Adaklu, which is not endemic for onchocerciasis and where no skin snip were Mf positive by microscopy, the seroprevalence in adult males was 3% (1.1-7.4), suggesting that at that level no MDA should be initiated. In adult males in Nkwanta, the Mf prevalence was 4% (1.9-7.9) and the seroprevalence 44% (37-51). Despite proven transmission, both the Mf prevalence and seroprevalence was 0% in children under the age of 10, suggesting that children would be an inadequate sentinel group post-MDA.

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IXOKALLIPIN, A NEW PLASMA KALLIKREIN INHIBITOR FROM *IXODES SCAPULARIS* BINDS TO THE CELL MEMBRANE AND IMPAIRS HEMOSTASIS AND THE SKIN WOUND HEALING

Markus Berger, Jan Kotal, **Lucas Tirloni**

National Institute of Allergy and Infectious Diseases, Hamilton, MT, United States

Besides its role in blood coagulation, plasma kallikrein (KLK) also induces keratinocyte migration accelerating wound healing process. Since ticks are blood pool feeders, we rise the hypothesis that KLK-kinin system components would have contact with keratinocytes from the skin and tick salivary proteins at the bite site. In this work we described for the first time an interesting molecule from *I. scapularis* saliva that binds to keratinocyte and endothelial cell membrane, blocking hemostasis and KLK-induced wound healing. We found a strong KLK inhibitory activity in *I. scapularis* saliva. This activity was purified, characterized and a new molecule from the serpin family, that was named ixokallipin, was identified. Ixokallipin inhibits the intrinsic pathway of blood coagulation targeting specifically KLK and factor XIIa. Ixokallipin inhibits the KLK generation on endothelial cell surface *in vitro* and the venous thrombosis *in vivo* without causing a significant bleeding effect. Ixokallipin binds to endothelial cell and keratinocyte surface mainly through phosphatidic acid. Keratinocyte surface supports high molecular weight kininogen-dependent plasma preKLK activation and production of active kallikrein. This event is modulated and completely blocked by ixokallipin. Ixokallipin inhibits keratinocyte migration by reducing cellular focal adhesions and membrane protrusions. The keratinocyte migration is dependent on PAR-1 but not PAR-2 activation. KLK cleaves PAR-1 at a non-canonical site generating a protective response associated with PKC-dependent calcium signaling which was down-regulated by ixokallipin. Looking in more details, ixokallipin inhibits kallikrein/PAR-1-dependent EGF/EGFR transactivation, down-regulating ERK1/2, AKT and paxillin activation, decreasing actin polymerization and consequently the cell migratory responses. Finally, using an *in vivo* model, we confirmed that ixokallipin causes a delay in the wound healing. Our results highlighted interesting new strategies used by the ticks to avoid host hemostasis and skin barriers at the same time.

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TSETSE-ENDOSYMBIONT METABOLIC COMPETITION FOR ACYL-CARNITINES REGULATES FLY FECUNDITY BY SUPPRESSING THE VIABILITY OF STORED SPERM

Brian L. Weiss, Erick Awuoche, Serap Aksoy

Yale School of Public Health, New Haven, CT, United States

Competition between insects and their endosymbiotic bacteria for environmentally limited nutrients can compromise the fitness of both organisms. Tsetse flies, the vectors of pathogenic African trypanosomes, harbor a host species and population-specific consortium of vertically transmitted endosymbiotic bacteria that range on the functional spectrum from mutualistic to parasitic. Tsetse’s indigenous microbiota can include a member of the genus *Spiroplasma*, and infection with this bacterium causes fecundity-reducing phenotypes in the fly that include a prolonged gonotrophic cycle and a reduction in the motility of stored spermatozoa post-copulation. Herein we demonstrate that *Spiroplasma* and tsetse spermatozoa utilize fly-derived acyl-carnitines, which in animals are a component of the carnitine shuttle that transports fatty acids across the mitochondrial matrix for use in energy production. The fat body of mated female flies increases acyl-carnitine production in response to infection with *Spiroplasma*. Additionally, their spermathecae (sperm storage organs), and likely the sperm within, up-regulate expression of *carnitine O-palmitoyltransferase-1*, which is indicative of increased carnitine shuttle activity and thus increased energy demand and energy production in this organ. These compensatory measures are insufficient to rescue the motility defect of spermatozoa stored in the spermathecae of *Spiroplasma* infected females and thus results in reduced fly fecundity. Our results provide insight into the mechanisms that facilitate the maintenance of bacterial endosymbioses, and how these relationships impact sperm motility and host fecundity. In the case of pest insects, a better understanding of the metabolic mechanisms that underlie these associations can lead to the development of novel control strategies.

6851

ANALYSIS OF THE SCABIES ASSOCIATED MICROBIOTA DEMONSTRATES A SHIFT TO OPPORTUNISTICALLY PATHOGENIC BACTERIA.

Sara Taylor[1], Martha Zakrzewski[1], Charlotte Bernigaud[2], Nuzhat Surve[3], Pallavi Surase[3], Deepani D. Fernando[1], Gourie P. Hule[4], Mohan G. Karmakar[4], Francoise Botterel[2], Olivier Chosidow[2], Katja Fischer[1]

[1]QIMR Berghofer MRI, Brisbane, Australia, [2]Dermatology Department, Assistance Publique des Hôpitaux de Paris (AP-HP), Hôpital Henri Mondor, Université Paris-Est, Créteil, France, Paris, France, [3]King Edward Memorial

Hospital Seth Gordhandas Sunderdas Medical College, Mumbai, India., Mumbai, India, [4]King Edward Memorial Hospital Seth Gordhandas Sunderdas Medical College, Mumbai, India, Mumbai, India

Scabies is a neglected tropical disease with a prevalence of 400 million cases annually. The disease is prevalent in tropical regions where there is an established link with secondary bacterial infections. The causative agent *Sarcoptes scabiei* is an obligate ectoparasitic mite that burrows into the superficial layers of the host skin. This action combined with a complex interaction between scabies mite excretory proteins and the host's immune system leave patients susceptible to secondary bacterial infections. It is these secondary complications that account for the disease burden that is estimated to be 0.21% disability-adjusted life years. Clinical research has shown a correlation between scabies infections and opportunistic pathogens. Despite this accepted correlation there is little molecular data to underpin this complex relationship. Our aim is to provide the fundamental molecular evidence of how scabies infections interfere with the host microbiome. We undertook a collaborative multi-national study that collected skin scrapings from scabies infected patients in India, France and Australia representing a diverse climate and socio-economic range. Microbial DNA was extracted and 16s full length rRNA and ITS[1-4] sequencing were performed using the PacBio sequel,utilising single molecule real-time technology to generate long read lengths. Using an established bioinformatics pipeline, a total of 22,678 amplicon sequence variant (ASVs) were identified from 751 samples. Community composition and microbial abundance was then analysed using the programing language R. Our data demonstrates that there is a significant increase in *Staphylococcus aureus* ($P<0.05$) in scabies infected lesions across all countries and in India and Australia there was a significant increase in *Streptococcus pyogenes* ($P<0.05$) in scabies infected lesions. We found no significant changes in the fungal microbiome and we found several commensal skin bacteria were significantly decreased. This study is the first to quantify the scabies associated microbiome at the molecular level, and address how it might differ globally.

6852

LEISHMANIA TRANSMISSION IS DISRUPTED IN SANDFLIES COLONIZED BY *DELFTIA TSURUHATENSIS* TC1 BACTERIA

Pedro Cecilio[1], Luana A. Rogerio[2], Tiago D. Serafim[2], Kristina Tang[2], Laura Willen[2], Eva Iniguez[2], Claudio Meneses[2], Luis F. Chaves[3], Yue Zhang[4], Wei Huang[5], Pablo Castaneda-Casado[6], Marcelo Jacobs-Lorena[5], Jesus G. Valenzuela[2], Janneth Rodrigues[6], Fabiano Oliveira[2]

[1]Vector Biology Section, LMVR, NIAID, NIH, Rockville, MD, United States, [2]Vector Molecular Biology Section, LMVR, NIAID, NIH, Rockville, MD, United States, [3]Department of Environmental and Occupational Health, School of Public Health-Bloomington, Indiana University, Bloomington, IN, United States, [4]Integrated Data Sciences Section (IDSS), Research Technologies Branch, NIAID, NIH, Bethesda, MD, United States, [5]Department of Molecular Microbiology and Immunology, Malaria Research Institute, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States, [6]Global Health Medicines R&D, GSK; Tres Cantos, Madrid, Spain

Most human pathogenic *Leishmania* species are zoonotic agents; therefore, sandfly-based control strategies are essential to prevent parasite circulation. Here, we used a *Delftia tsuruhatensis* strain that inhibits the development of *Plasmodium* in mosquitoes, but in the context of *Leishmania*-infected sandflies. Using GFP-expressing *D. tsuruhatensis* TC1, we show that this bacterium colonizes the midgut of *Phlebotomus duboscqi* sandflies. Such colonization impacts the development of *L. major* parasites in the vector, as per the significantly lower number of both total and infectious metacyclic parasites detected in the midguts of bacteria-fed *versus* control sandflies (90% reduction). This phenotype was consistently observed, regardless of the timing of bacterial feeding (from 1 week prior to infection to 8 days after infection), and was even stronger in sandflies given a second, uninfected, bloodmeal. Curiously, our data suggests this phenotype is likely an indirect effect of TC1 colonization, related with the induction of sandfly gut dysbiosis. These results have biological significance, since we observed that *Leishmania*-infected, bacteria-fed sandflies are less able to transmit *Leishmania major* parasites and cause disease in a mouse model of cutaneous leishmaniasis (parasites detected in 27% of animals bitten by bacteria-fed flies *versus* 100% of animals in the control group). Relevantly, modelling studies based on our results support the disruption of disease endemicity in the field. Altogether, these results highlight TC1 as a promising vector-based approach for the control of leishmaniasis in the field.

6853

BLOOD FEEDING ACTIVATES THE TERMINAL DIFFERENTIATION OF PRECURSOR CELLS IN TICK SALIVARY GLANDS

Sazzad Mahmood[1], Ana Beatriz Barletta Ferreira[2], Oladele Oluwayiose[3], Christine A. Schneider[4], Jacqueline Leung[4], Melina Garcia Guizzo[5], Stephen Lu[5], Lucas Christian Sousa-Paula[1], Markus Berger[1], Justin Lack[3], Carolina Barillas-Mury[2], Jose M. Ribeiro[5], Lucas Tirloni[1]

[1]Tick-Pathogen Transmission Unit, Laboratory of Bacteriology, National Institute of Allergy and Infectious Diseases, National Institute of Health, Hamilton, MT, United States, [2]Mosquito Immunity and Vector Competence Section, Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institute of Health, Rockville, MD, United States, [3]Collaborative Bioinformatics Research, National Institute of Allergy and Infectious Diseases, National Institute of Health, Bethesda, MD, United States, [4]Electron Microscopy Unit, Research Technologies Branch, National Institute of Allergy and Infectious Diseases, National Institute of Health, Hamilton, MT, United States, [5]Vector Biology Section, Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institute of Health, Rockville, MD, United States

Tick salivary glands secrete a complex saliva into their hosts to facilitate blood feeding and pathogen transmission. Thousands of transcripts coding for structural and secreted protein have been identified in tick salivary glands. The transcriptomic profile changes over time during feeding, indicating a switch in the sialome. Bulk RNA-seq of *Ixodes scapularis* salivary glands revealed temporal differences in the transcriptomic profile as blood feeding progresses, confirming the "sialome switching" takes place. To uncover the cellular mechanisms behind this phenomenon, we performed single cell RNA sequencing (scRNA-seq) of salivary glands. Salivary gland cells exhibited hypertrophy throughout the feeding process. Clustering analysis identified a total of ten different cellular clusters. Four clusters were observed in unfed ticks; and one of them expresses genes related to cell signaling, signal transduction, and transcription factors, including genes related to the non-canonical Wnt signaling pathway. This suggests that it may represent salivary gland cells in an undifferentiated stage. The abundance of these putative cells presents in unfed ticks decreased as blood feeding progresses, while new clusters appear which express canonical salivary genes. The identity and distribution of the cell clusters and their apparent differentiation were validated by RNA *in-situ* hybridization. Sialome switching appears as a result from cell differentiation rather than cell proliferation. Furthermore, the pJNK is activated during the transition from unfed to fed stage. Based on these findings, we propose that blood feeding activates terminal differentiation of tick salivary gland precursor cells into cells that express subsets of salivary genes in a dynamic process involving the non-canonical Wnt signaling pathway. These findings provide new insights on the dynamic transcriptional response of salivary glands required for successful blood feeding. Disrupting this process may offer potential strategies for controlling tick feeding and, consequently, tick-borne diseases.

6854

SEASONAL VARIATION IN TSETSE FLY APPARENT DENSITY AND TRYPANOSOMA SPP. INFECTION RATE AND OCCURRENCE OF DRUGRESISTANT TRYPANOSOMES IN LAMBWE, KENYA

Ivy S. Okello[1], Gillian Eastwood[2], Jahashi Nzalawahe[1], Eliakunda Mafie[1]

[1]Sokoine University of Agriculture, Morogoro, Tanzania, United Republic of, [2]Virginia Polytechnic Institute and State University, Blacksburg, VA, United States

Tsetse flies are major vectors of trypanosomes causing debilitating African animal trypanosomiasis. Emergence of drug resistant trypanosomes is a common problem in sub-Saharan Africa. This study aimed to identify tsetse flies' seasonal variation in apparent densities and their infection rates and occurrence of drug resistant trypanosomes. Tsetse flies were collected from Lambwe, Kenya in May and September 2021. Genomic DNA was extracted from them and *ITS1* gene amplified to detect *Trypanosoma* infection with subsequent species detection. Transporter genes *DMT*, *E6M6*, *TbAT/P2* and *TcoAde2* were targeted to detect polymorphisms associated with drug resistance using sequencing and comparison to drug sensitive species referenced in Genbank. A total of 498 tsetse flies and 29 non-tsetse flies were collected. Apparent density of flies was higher in wet season 6.2 fly per trap per density (FTD) than in dry season 2.3 FTD ($P = 0.001$). Male tsetse flies ($n = 311$) were numerous than females ($n = 187$) ($P = 0.001$). Non-tsetse flies included Tabanids and *Stomoxys* spp. *Trypanosoma* infection in tsetse was 5% (25/498) whereby *T. vivax* was 4% (11/25), *T. congolense* 36% (9/25) and *T. brucei* 20% (5/25) ($P = 0.186$ for species distribution) with infections being higher in females ($P = 0.019$) and during wet season ($P < 0.001$). Numerous polymorphisms and insertions associated with drug resistance were detected in *DMT* and *E6M6* genes in two *T. congolense* isolates while some isolates lacked these genes. *T. brucei* lacked *TbAT/P2* genes. *TcoAde2* in three *T. congolense* isolates were related to those in trypanosomes from cattle blood in our previous study, supporting tsetse fly involvement in transmission in the region. We report *Trypanosoma* associated with drug resistance in tsetse flies from Lambwe, Kenya. Female tsetse flies harbored more *Trypanosoma* infections than males. Tsetse transmission of trypanosomes is common in Lambwe. Risk of trypanosome infection seem higher in wet season when tsetse flies and *Trypanosoma* infections are more prevalent than in dry season. More efforts to control animal trypanosome vectors in the region are needed with particular focus on wet seasons.

6855

CHANGES IN CYTOFORM (CYTOSPECIES AND CYTOTYPE) COMPOSITION OF VECTORS OF ONCHOCERCIASIS IN NORTHERN CAMEROON AND ITS POSSIBLE IMPLICATIONS FOR DISEASE ELIMINATION

Franklin Ayisi[1], Dziedzom de Souza[2], Jamie Tallant[3], Eric Bertrand Fokam[4], Daniel Adjei Boakye[3]

[1]African Regional Postgraduate Programme in Insect Science (ARPPIS), University of Ghana, Accra, Ghana, [2]Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana, Accra, Ghana, [3]The End Fund/Reaching the Last Mile Fund (RLMF), New York, NY, United States, [4]Department of Animal Biology and Conservation, University of Buea, Buea, Cameroon

Onchocerciasis, caused by *Onchocerca volvulus*, is the second leading cause of infectious blindness worldwide. Members of the *Simulium damnosum* species complex are the major vectors in Africa, host to over 99% of the global disease burden. Attaining the WHO goal of transmission elimination (TE) requires regular surveys of vector cytoform composition (as part of monitoring and evaluation), since cytoform composition may change over time. This is especially important because cytoforms of the vectors differ in their vectorial efficiency, ecological distribution and biting pattern, and therefore influence disease epidemiology. Northern Cameroon (NC) is a savanna area with varying success towards TE. Cytoforms previously reported in NC are *S. damnosum* sensu stricto, *S. squamosum* cytotype A, *S. sirbanum* and *S. mengense*. There is paucity of recent information on the cytospecies/cytoform composition in NC, with data available only for few selected sites, and most available data date decades ago. We sampled larvae from rivers in three administrative regions that constitute NC. Larvae were identified by cytotaxonomy of polytene chromosomes. Five cytoforms were identified: *S. damnosum* s.s., *S. sirbanum*, *S. squamosum* cytotype C, *S. yahense* and a cytotype that we call *S. damnosum/sirbanum* because it could not be placed under either cytospecies. This is the first report of *S. yahense* in NC, a restricted species known only in forest areas. *S. yahense* is a very competent vector, more than all previously known vectors in NC. Also, this is the first report of *S. squamosum* C from NC. The *S. squamosum* cytotypes have been associated with differences in biting pattern. In addition, *S. damnosum* s.s. was observed to possess high frequency of inversion 2L-st/2b; this inversion was only previously reported in Ethiopia. Hence, there have been significant changes in cytoforms composition in NC. This change may be due to adaptation of species like *S. yahense* to dryer environments, and possibly due to climate change whose impact is tangible in NC with recorded increase in mean annual temperature. The observed changes in cytoform composition may impact the drive toward TE in NC.

6856

MATERNAL MICROCHIMERISM IS ASSOCIATED WITH AN ALTERED TRANSCRIPTIONAL PROFILE OF *PLASMODIUM FALCIPARUM*-SPECIFIC T CELLS IN MALIAN CORD BLOOD

Yonghou Jiang[1], John Houck[1], Marc Carlson[1], Almahamoudou Mahamar[2], Gaoussou Santara[2], Oumar Attaher[2], Robert Morrison[3], Sudhir Kumar[4], Blair Armistead[1], Irfan Zaidi[3], Stefan Kappe[5], Alassane Dicko[2], Patrick E. Duffy[3], Michal Fried[3], Marion Pepper[6], **Whitney E. Harrington**[5]

[1]Seattle Children's Research Institute, Seattle, WA, United States, [2]International Center for Excellence in Research, Bamako, Mali, [3]Laboratory of Malaria Immunology & Vaccinology, National Institute of Allergy and Infectious Disease, Bethesda, MD, United States, [4]Department of Biomedical Sciences, Iowa State University, Ames, IA, United States, [5]Seattle Children's Research Institute / University of Washington, Seattle, WA, United States, [6]University of Washington, Seattle, WA, United States

Plasmodium falciparum (Pf)-responsive T cells have previously been identified in cord blood from malaria-endemic settings, a phenomenon known as prenatal immune priming (PIP). We have found that maternal microchimerism (MMc) at delivery was associated with increased susceptibility to Pf infection in childhood, and we hypothesized that MMc modulates the quality of PIP. To investigate this hypothesis, we developed an approach to identify and characterize Pf-responsive T cells using single cell RNA sequencing (scRNAseq). Whole cord blood from Malian primigravidae living in a malaria endemic setting was first screened for MMc using qPCR assays targeting a maternal specific allele. Cord blood mononuclear cells (CBMC) from n=8 MMc+ and n=3 MMc- offspring were stimulated with purified Pf merozoite extract for 18 hours and CD3+ CD69+ cells were sorted by flow cytometry for scRNAseq using the 10X Genomics platform. Data from 31,792 T cells across 11 samples were normalized and aggregated for further analysis, including 19,882 CD4 T cells, 6,082 CD8 T cells, and 2,308 γδ T cells. To identify true antigen-specific vs. bystander activated T cells, we developed a T cell activation gene signature that included genes upregulated in the setting of T cell receptor (TCR) engagement (NR4A, IRF4, IL2RA, MIR155HG, CD40LG, TNFRSF4, and TNFRSF9). The gene signature identified 1,178 CD4 T cells, 184 CD8 T cells, and 375 γδ T cells with evidence of TCR engagement, suggesting antigen specificity. Within CD4 T cells, Pf-responsive vs. bystander cells had significantly increased expression of HLA-DR and HLA-DP genes, as well as IL1B, GZMB, IFI30, and CXCL8 (IL-8). Pf-responsive cells from MMc+ vs. MMc- cord bloods had significantly decreased expression of IL1B, GZMB, CXCL1, and CXCL2; and significantly increased expression of the immunoregulatory molecule CD52. Together, these data demonstrate the ability to identify Pf-responsive T cells in CBMC using modern, robust, single cell approaches and suggest the potential for differential function of these cells by MMc status.

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TRANSPLACENTAL TRANSFER OF FUNCTIONAL ANTIBODIES DIRECTED AGAINST *PLASMODIUM FALCIPARUM* BLOOD STAGE ANTIGENS

Djelili Biaou[1], Aziz Bouraïma[2], Ibrahim Sadissou[2], David Courtin[1], Andre Garcia[1], Florence Migot-Nabias[1], Achille Massougbodji[3], Michael Theisen[4], Sébastien Dechavanne[1], Celia Dechavanne[1]

[1]Affiliation 1: Université de Paris, Institut de Recherche pour le Développement (IRD), UMR 261 MERIT, Paris France. Affiliation 2: CERPAGE (Centre d'Etude et de Recherche sur les Pathologies Associées à la Grossesse et à l'Enfance), Cotonou, Benin, [2]CERPAGE (Centre d'Etude et de Recherche sur les Pathologies Associées à la Grossesse et à l'Enfance), Cotonou, Benin, [3]Institut de Recherche Clinique du Bénin (IRCB), Cotonou, Benin, [4]Centre for Medical Parasitology at Department of International Health, Immunology and Microbiology, University of Copenhagen and Department for Congenital Disorders, Statens Serum Institut, Copenhagen, Denmark

The transplacental transfer of maternal antibodies to the fetus is crucial in protecting neonates in early life. However, several studies have shown that infants born from mothers with *Plasmodium falciparum* Malaria infection at Delivery (MiD) present a high risk of infection and constitute a particularly vulnerable population. Many studies have investigated the efficacy of maternal antibodies transfer in MiD whereas the functionality of those antibodies remains to be assessed. The study was carried out in a rural region of southern Benin and neonates were followed-up from birth to 18 months of age. The functionality of immunoglobulin G (IgG) against 5 *Plasmodium falciparum* antigens was determined using a bead-based opsonic phagocytosis assay (BPA) and THP1 monocyte line with available maternal and cord serum (n=355). IgG, IgG1 and IgG3 specific to *Pf*-antigens were quantified from the same samples using ELISA. We observed that phagocytosis in the maternal compartment is strongly dependent on the concentration of antibodies specific to each antigen (AMA1 p=0.002; MSP1 p=0.014; MSP3 p=0.017; GLURP-R0 p<0.001 and GLURP-R2 p<0.001) whereas maternal hypergammaglobulinemia (total IgG greater than 16g.L^{-1}) was negatively associated with phagocytosis (AMA1 p=0.014, MSP3 p=0.013). Functional antibody transfer was positively associated with maternal antibody concentration (AMA1 p<0.001, MSP1 p=0.025, MSP3 p=0.043, GLURP-R0 p=0.013, GLURP-R2 p<0.001) and negatively associated with maternal exposure to malaria vector (AMA1 p= 0.07, MSP3 p= 0.008). Taken together, our data suggest that maternal specific antibodies are strongly secreted during MiD. They are functional until total IgG reaches a high concentration which will reduce the capability of specific IgG to induce phagocytosis. The transplacental transfer of functional antibodies is impaired when mothers are exposed to malaria vectors.

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ANTIBODY FC GLYCOSYLATION MODULATES NATURAL KILLER CELL-MEDIATED ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC) IN MALARIA-EXPOSED PREGNANT WOMEN

Savannah N. Lewis[1], Adam S. Kirosingh[1], Kattria van der Ploeg[1], Kathleen D. Press[1], Felistas Namirimu Nankya[2], Kenneth Musinguzi[2], Evelyn Nansubuga[2], Stephen Tukwasibwe[2], Mary Lopez-Perez[3], Moses R. Kamya[2], Philip Rosenthal[4], Grant Dorsey[4], Lars Hviid[3], Prasanna Jagannathan[1]

[1]Stanford University School of Medicine, Stanford, CA, United States, [2]Infectious Diseases Research Collaboration, Kampala, Uganda, [3]University of Copenhagen, Copenhagen, Denmark, [4]University of California, San Francisco, San Francisco, CA, United States

Antibody-dependent cellular cytotoxicity (ADCC) mediated by natural killer "NK" cells has been associated with clinical immunity to malaria in both children and adults in several endemic settings. However, it remains unclear whether NK cell-mediated ADCC is also protective against malaria in pregnancy. To study the NK cell response in malaria-exposed pregnant women, we leveraged peripheral blood mononuclear cell (PBMC) samples from the DPSP Clinical Trial (ID: NCT04336189), in which participants living in Busia District, Uganda were randomized to receive sulfadoxine-pyrimethamine, dihydroartemisinin piperaquine, or a combination of these drugs for intermittent preventive treatment of malaria in pregnancy. We first observed that primigravid donors had a higher risk of malaria-related complications than multigravid donors, suggesting that adaptive immune mechanisms may confer protection in this context. When we profiled the ability of NK cells to perform ADCC against erythrocytes infected with VAR2CSA-expressing *Plasmodium falciparum* (CS2), we observed that the magnitude of ADCC was significantly enhanced when infected erythrocytes were opsonized with pooled plasma from multigravid compared to primigravid donors. VAR2CSA-specific IgG titers were similar in both plasma pools. NK cell degranulation and cytokine production was similar between primigravida and multigravida PBMC donors, leading us to hypothesize that NK cell-extrinsic factors present in plasma underlie this observation. Previous serology work has shown that afucosylation of VAR2CSA-specific antibodies increases with gravidity, which enhances Fc-dependent effector responses. When we opsonized CS2-infected erythrocytes with pooled plasma with high and low Fc fucosylation of VAR2CSA-specific IgG, we found that lowly fucosylated plasma induced significantly more NK cell degranulation than highly fucosylated plasma in DPSP donors. We are currently working to identify phenotypic features of NK cells that respond to afucosylated VAR2CSA-specific IgG and to search for correlations between these phenotypes and birth outcomes within the DPSP study cohort.

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CHRONIC *PLASMODIUM* INFECTIONS CAUSE PERSISTENT CHANGES IN THE HOST IMMUNOLOGICAL LANDSCAPE

Saniya S. Sabnis[1], Celia L. Saney[1], Monica Cabrera-Mora[2], The MaHPIC Consortium --[2], Ignacio Sanz[2], F. Eun-Hyung Lee[2], Jessica C. Kissinger[1], Regina Joice-Cordy[3], Alberto Moreno[2], Tracey J. Lamb[4], Mary R. Galinski[2], Chester J. Joyner[1]

[1]University of Georgia, Athens, GA, United States, [2]Emory University, Atlanta, GA, United States, [3]Wake Forest University, Winston-Salem, NC, United States, [4]University of Utah, Salt Lake City, UT, United States

Chronic *Plasmodium falciparum* infections are the norm in endemic areas. While minimally symptomatic, these infections predispose individuals to secondary bacterial infections and reduce malaria vaccine efficacy. Thus, understanding how chronic infections alter the immunological landscape of infected individuals is needed. Here, we used samples collected from macaques infected with *P. coatneyi*, a model of *P. falciparum* malaria, to define host transcriptional changes and immunological responses that lead to the establishment of a chronic infection. Using whole blood RNA sequencing, we show that infections reach chronicity 50 to 80 days after inoculation with sporozoites. Based on transcriptional analysis of the host response, progression to chronicity is generally independent of parasitemia and, instead, related to time an infection has persisted. The transition from acute to chronic infections was defined by upregulation in gene signatures related to B cells and cytokine signaling and downregulation of interferon gamma signaling. Interestingly, Type I interferon signaling remained elevated from the acute to chronic phases. Inflammatory cytokine gene expression was upregulated during acute infection and decreased as the infection progressed to the chronic phase. However, some pro-inflammatory cytokines like TNFα remained elevated. Anti-inflammatory cytokines (e.g., IL-10) increased in the acute and returned to baseline when chronicity was reached. Flow cytometry analysis showed an increase in multiple B cell subsets, including CD21^{neg-} CD27^{neg-} B cells, and effector memory CD8^{+} T cells. Control of parasitemia was significantly correlated with the changes in B and T cell populations in addition to IgG and IgM against *P. coatneyi*, suggesting these responses are key for maintaining parasite control during chronic infections. In sum, this study defines the progression of a Plasmodium infection from acute to chronic and shows persistent derangements in the host immunological landscape that may influence malaria vaccine efficacy.

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BASELINE INNATE IMMUNE ACTIVATION AND INFLAMMATION IS CORRELATED WITH CONTROL OF SUBSEQUENT PARASITEMIA IN VERY YOUNG MALIAN CHILDREN

Prasida Holla[1], Jyoti Bhardwaj[2], Erik L. Gaskin[2], Safiatou Doumbo[3], Aissata Ongoiba[3], Philip L. Felgner[4], Christine S. Hopp[5], Xiaoling Xuei[6], Labeeb Hossain[7], Kassoum Kayentao[3], Boubacar Traore[3], Peter D. Crompton[8], Tuan M. Tran[9]

[1]Ryan White Center for Pediatric Infectious Diseases and Global Health, Indiana University School of Medicine, Indianapolis, IN, United States, [2]Division of Infectious Diseases, Department of medicine, Indiana University School of Medicine, Indianapolis, IN, United States, [3]Mali International Center of Excellence in Research, University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali, [4]Division of Infectious Diseases, School of Medicine, University of California, Irvine, Irvine, CA, United States, [5]Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, [6]Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN, United States, [7]Indiana University Bloomington, Bloomington, IN, United States, [8]Laboratory of Immunogenetics, National institute of Allergy and Infectious Diseases (NIAID), National institutes of health (NIH), North Bethesda, MD, United States, [9]Ryan White Center for Pediatric Infectious Diseases and Global Health & Division of Infectious Diseases, Department of medicine, Indiana University School of Medicine, Indianapolis, IN, United States

Reliable immune correlates of protection against *Plasmodium falciparum* (*Pf*) malaria remain elusive, in part because sustained protection from parasitemia through natural exposure is rarely observed. In a prospective cohort study of Malians living in an area of intense malaria transmission, we identified a subset of young children who remained aparasitemic during 7 months of biweekly active and passive surveillance. These children showed boosting of malaria-specific IgG during the season, suggesting evidence of malaria exposure despite remaining aparasitemic. To identify immune responses associated with apparent elite control of infection, we carried out CITE-seq of PBMCs from 7 pairs of age- and sex- matched aparasitemic and parasitemic children. We included *Pf* antigens MSP1- and AMA1- specific B cell tetramers in the CITE-seq cocktail and sequenced B cell receptors (BCRs) from these cells. To identify epigenetic changes that confer the aparasitemic phenotype, we performed scATAC-seq on cells from additional samples. Immune cell types from aparasitemic and parasitemic children exhibited markedly different transcriptional states and epigenetic landscapes. Notably, $CD14^+$ monocytes in aparasitemic children showed enrichment of inflammatory signatures including TNFα signaling via NF-κB along with differently accessible chromatin in the target genes of these pathways. We also identified 44 antigen-specific B cells, primarily from aparasitemic children, and cloned their BCRs into expression plasmids with the goal of producing *Pf*-specific monoclonal antibodies *in vitro* to assess their ability to control parasite growth and enhance the opsonophagocytosis capacity of monocytes.

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PVDBP GENE AMPLIFICATION PROTECTS *PLASMODIUM VIVAX* IN VIVO AGAINST HOST NATURALLY ACQUIRED ANTI-PVDBP IMMUNITY

Lea Baldor[1], Brice Feufack-Donfack[1], Dynang Seng[1], Sokleap Heng[1], Nichole D. Salinas[2], Niraj H. Tolia[2], Chetan E. Chitnis[3], Ivo Mueller[4], Christopher L. King[5], Eugenia Lo[6], Benoit Witkowski[7], Claude Flamand[1], Jean Popovici[1]

[1]Institut Pasteur Cambodge, Phnom Penh, Cambodia, [2]National Institute of Allergy and Infectious Diseases, Bethesda, MD, United States, [3]Institut Pasteur Paris, Paris, France, [4]The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, [5]Center for Global Health and Diseases, Cleveland, OH, United States, [6]Department of Microbiology and Immunology, Drexel University, Philadelphia, PA, United States, [7]Institut Pasteur Madagascar, Antananarivo, Madagascar

The key ligand involved in *Plasmodium vivax* (Pv) invasion is the Pv Duffy Binding Protein (PvDBP) binding to the Duffy. Anti-PvDBP human monoclonal antibodies (Abs) can inhibit the PvDBP-Duffy binding and neutralize invasion of reticulocytes by parasites. However, parasites with multiple copies of the PvDBP gene are protected *in vitro* against neutralization. Here, we aim to determine if this gene amplification also protects parasites *in vivo.* We hypothesize that: (i) multi-*pvdbp* copy parasites are more frequent in areas with a high Pv prevalence compared to low prevalence areas and (ii) individuals with naturally-acquired binding inhibitory anti-PvDBP Abs (Blabs) are predominantly infected over time by multi-copy parasites. To test these hypotheses, we analyzed samples from a longitudinal cohort of individuals living in nine villages in Eastern Cambodia with low (~5%) to high (~30%) prevalence. Using a PCR assay targeting the boundaries of the *pvdbp* duplication, we show a significant association between Pv prevalence and proportion of multicopy parasites (35% in low prevalence villages to 47% in high prevalence ones, p=0.0246). Then, using a flow cytometry assay, we determined the presence of naturally-acquired Blabs in the plasma of 657 participants of the cohort. The more inhibitory the Abs in the hosts' plasma, the higher the proportion of multicopy parasites: 87% (40/46) from individuals with highly inhibitory Abs (>90% inhibition) while 38% (167/436) from individuals without any Blabs ($p<0.0001$). Finally, we compared the gene copy number of parasites over the 21-month follow-up in the cohort participants according to the presence of Blabs at month 0. We show that the frequency of multicopy parasites was consistently higher in participants with highly inhibitory Abs compared to those without any Blabs for the entire follow-up. Overall, these results demonstrate that *pvdbp* duplication protects parasites *in vivo* against hosts' anti-PvDBP immunity. These results warrant further investigations to determine if immunization of individuals with a PvDBP vaccine could overcome this new immune evasion mechanism.

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IMMUNO-INFORMATIC APPROACH TO IDENTIFYING VARIANT-TRANSCENDENT NATURALLY-ACQUIRED PROTECTION AGAINST *PLASMODIUM FALCIPARUM*

Katherine Chew, Steve Taylor, Wendy O'Meara, Christine Markwalter

Duke University, Durham, NC, United States

Plasmodium falciparum antigenic diversity compromises the development of lasting immunity. Current available vaccines for malaria contain a single sequence of P. falciparum circumsporozoite protein (CSP), and protection following vaccination is variant-specific. Multi-variant vaccines may help to overcome antigenic diversity, but identifying a minimum set of variants that provide cross-protection against a broad range of CSP variants remains a challenge. We recently reported an epidemiologic signature of natural immunity to *P. falciparum* in which time to reinfection with parasites bearing homologous CSP T cell epitopes was delayed following symptomatic vs asymptomatic infections. We hypothesized that this delayed reinfection would extend to cross-protective 'epitope types' which are likely to be physiochemically similar. Thus, we applied 10 quantitative metrics of amino acid physiochemical properties (PCPs) to group CSP Th2R and Th3R epitope types via hierarchical clustering. Using *pfcsp* sequences (344 infections, 155 unique haplotypes) from a 14-month longitudinal cohort in Western Kenya, we evaluated PCP-based epitope clusters by assessing the phenotype of increased time to reinfection with parasites bearing physiochemically-similar epitopes after symptomatic vs asymptomatic infections. At Th2R, clustering epitope types by any of the PCP metrics reproduced the phenotype with >20 groups, but the Yampolsky and Stolzfus measure shows the phenotype in as few as 10 groups; no PCP metric displayed the phenotype with <10 groups. The Th3r epitope displayed the phenotype with 8 groups, but the PCP measures that meaningfully clustered epitypes were distinct from those identified for the Th2R locus. Overall, our study demonstrates that amino acid properties can identify immunologically-similar CSP epitopes that share recognition by naturally-acquired immune responses. This offers a path forward to exploiting parasite diversity and reducing the search space for variant-transcendent responses.

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OLYSET®PLUS CEILING NETS PROTECT AGAINST MALARIA: FINDINGS FROM A CLUSTER RANDOMIZED CONTROLLED TRIAL OF THE EFFECTIVENESS OF OLYSET®PLUS CEILING NET ON REDUCING MALARIA PREVALENCE AND INCIDENCE ON MFANGANO ISLAND, LAKE VICTORIA BASIN, KENYA

Wataru Kagaya[1], Chim Wai Chan[2], James Kongere[3], Bernard N. Kanoi[4], Mtakai Ngara[5], Protus Omondi[2], Laura Barbieri[2], Achyut KC[5], Gordon Okomo[6], Noboru Minakawa[1], Jesse Gitaka[4], Akira Kaneko[5]

[1]Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan, [2]Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan, [3]Cetre for Research in Tropical Medicine and Community Development, Nairobi, Kenya, [4]Directorate of Research and Innovation, Mount Kenya University, Thika, Kenya, [5]Karolinska Institutet, Stockholm, Sweden, [6]Ministry of Health, Homa Bay County, Homa Bay, Kenya

Novel vector control tools, such as Olyset®Plus ceiling net (2% permethrin+1% piperonyl butoxide), are needed to fight the malaria resurgence reported since 2016, especially in sub-Saharan Africa. We evaluated the protective effectiveness of adding Olyset®Plus ceiling net to existing control interventions on *Plasmodium falciparum* malaria prevalence and incidence. We conducted a two-arm, parallel group, superiority cluster randomized controlled trial with 10 clusters per arm during November 2021-May 2023 on Mfangano Island in western Kenya. Olyset®Plus ceiling nets were installed in eligible households in the intervention arm. The primary outcome, malaria prevalence in children (3-15 years old) at 12 months post-intervention, was measured during cross-sectional school surveys. The secondary outcome, cumulative malaria incidence in all age groups during a 12-month follow-up post-intervention, was tracked monthly for 12 months in a community cohort. Malaria infection was determined using malaria rapid diagnostic test (Paracheck-Pf® Orchid Biomedical Systems, India). Olyset®Plus ceiling nets were installed in 1006 houses (mean coverage: 93.4%). Eight hundred six eligible children were recruited in the control- and 831 in the intervention- arms to determine malaria prevalence. At 12 months post-intervention, malaria prevalence was 30.1% (95%CI: 27.1-33.3) in the control- and 16.4% (14.0-19.2) in the intervention- arms (prevalence ratio 0.55; 95% CI: 0.33-0.91, p = 0.056). Two hundred six eligible persons were recruited in the control- and 266 in the intervention-arms to determine malaria incidence. During the 12-month follow-up, malaria incidence was 0.11 per person-year (ppy) (0.07-0.15) in the control- and 0.05 (0.02-0.09) ppy (1.21-1.65) in the intervention- arms (incidence rate ratio 0.47; 95% CI: 0.24-0.95, p = 0.030). Olyset®Plus ceiling nets protected against malaria in addition to the effects of existing control interventions. Multi-county studies across different malaria transmission intensities are needed for wider adoption to complement existing vector control interventions.

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EFFECTIVENESS OF CHLORFENAPYR-PYRETHROID INSECTICIDE-TREATED NETS ON DECREASING MALARIA IN LIBERIA: AN OBSERVATIONAL ANALYSIS USING ROUTINE HEALTH FACILITY DATA, 2019-2023

Emily R. Hilton[1], D. Levi Hinneh[2], Chrispin Williams[3], Patrick Konwloh[2], Trokon Washington[2], Ibrahima Baber[4], Yemane Yihdego[5], Tuwuyor Belleh[4], Miriam Williams[5], Melissa Yoshimizu[6], Uwem Inyang[7], Sarah Burnett[8]

[1]PMI Evolve Project, PATH, Seattle, WA, United States, [2]National Malaria Control Program, Monrovia, Liberia, [3]National Malaria Control Program, Monrovia, Libya, [4]PMI Evolve Project, Abt Associates, Monrovia, Liberia, [5]PMI Evolve Project, Abt Associates, Rockville, MD, United States, [6]U.S. President's Malaria Initiative, U.S. Agency for International Development, Washington, DC, United States, [7]U.S. President's Malaria Initiative, U.S. Agency for International Development, Monrovia, Liberia, [8]PMI Evolve Project, PATH, Washington, DC, United States

Dual-active ingredient (AI) chlorfenapyr-pyrethroid insecticide-treated nets (ITNs) were distributed nationwide in Liberia in June 2021 to address growing pyrethroid resistance in malaria vector populations. This retrospective observational study evaluated the post-intervention impact of the new ITNs on epidemiological and entomological indicators of malaria compared to the pre-intervention baseline period when pyrethroid-only ITNs had been distributed. A negative binomial Bayesian mixed effects interrupted time series model was used to estimate the effect of dual AI ITN distribution on reported confirmed malaria cases from July 2019 to June 2023 in all 15 counties of Liberia and the number of cases averted by dual AI ITNs, controlling for month, community health worker reporting, non-malaria outpatient attendance, precipitation, and vegetation. Trends in vector human biting rate (HBR) and indoor resting density (IRD) measured during the high transmission season (March to June) one year before and after dual AI ITN distribution were descriptively analyzed. During the two years post-dual AI ITN distribution, an estimated 87.6 malaria cases per 1,000 population (95%CI=65.0 - 112.9) were averted with an estimated case incidence decrease of 41.0% (95%CI=43.9% - 38.4%) overall (from an estimated 239.9 [95%CI=236.6 - 243.4] cases per 1,000 during the baseline to an estimated 170.1 [95%CI=167.6 - 172.6] cases per 1,000). Case incidence reductions compared to baseline were greater in the first year post-distribution (mean=49.0%; 95%CI=52.4% - 45.6%) than in the second year (mean=33.9%; 95%CI=37.4 % - 30.7%). Indoor HBR of *An. funestus* s.l. and *An. gambiae* s.l. decreased in the year following dual AI distribution, although only *An. funestus* s.l. experienced a decrease in IRD during the same period. Dual AI chlorfenapyr-pyrethroid ITNs appeared to substantially reduce malaria case rates following nationwide mass distribution in 2021 and were associated with declining trends in malaria vector HBR.

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REDUCTION IN MALARIA CASES AFTER DEPLOYMENT OF IG2 NETS IN AN AREA WITH KNOWN PYRETHROID RESISTANCE AND MARKED OUTDOOR BITING - AN INTERRUPTED TIME SERIES ANALYSIS.

Samuel Kweku Oppong[1], Otubea Owusu-Akrofi[2], Christian Atta-Obeng[2], Wahjib Mohammed[2], Punam Amratia[3], Nana Yaw Peprah[2], Peter Gething[4], Keziah L. Malm[2]

[1]Curtin University, Bentley, Australia, [2]National Malaria Elimination Programme, Accra, Ghana, [3]Malaria Atlas Project, Dar esalam, Tanzania, United Republic of, [4]Malaria Atlas Project, Telethon Kids Institute, PERTH, Australia

In 2019, the first-ever stratification for subnational tailoring was conducted using data routine health facility data from 2015-2018. Results showed that the Western North region had one of the highest malaria burden in the country. Notwithstanding the high rate of outdoor biting, reported pyrethroid resistance in the region warranted the distribution of new generation ITNs in all the 9 districts in July 2021 to help reduce the cases. In this study we assessed the effect of IG2 nets on malaria cases between 2019 and 2023. Monthly health facility data on reported suspected, tested, confirmed, and presumed malaria cases were aggregated for each district from 2019 to 2023. We conducted a trend analysis and an interrupted time series analysis of the confirmed malaria cases for the period January 2019 to December 2023. The auto ARIMA function in R was used to choose the best model and adjust for seasonality and other dependency. A total of 1,235,126 confirmed malaria cases were reported between 2019 and 2023. Confirmed malaria cases decreased from 317,495 in 2019 to 182,856 in 2023. The baseline confirmed cases (intercept) from the regression model was 25,025 (95% CI = 22, 672, 27,737). The time coefficient showed a declining trend but was not statistically significant (-21.7; 95% CI = -150.1, 106.6). We observed an immediate, statistically significant decrease of 6,130 malaria cases (95% CI = -9,441, -2,820) after the intervention compared to the period before the intervention. Assessing the trend that would have been expected in absence of the intervention, the results

showed a non-significant sustained decrease of 107 (95% CI = -298, 84) in the monthly number of confirmed malaria cases during the intervention period. The ACF plot of the residuals showed the autocorrelations were not significant. This study shows that deployment of next generation ITN may have contributed significantly to the reduction in malaria incidence in Western North. The findings will support IG2 deployment decision making in the country to complement other malaria control interventions ultimately to reduce malaria burden in the country.

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EFFECT OF ATTRACTIVE TARGETED SUGAR BAITS (ATSBS) ON MALARIA INCIDENCE IN CHILDREN IN WESTERN KENYA: A CLUSTER-RANDOMIZED CONTROLLED TRIAL

Caroline Ogwang[1], Alice Kamau[2], Kizito Obiet[1], Brian Seda[1], Daniel McDermott[2], Julia M. Janssen[3], Wycliffe Odongo[3], Julie R. Gutman[3], Jonathan Schultz[4], Frank Aduwo[1], Mercy Chepkirui[1], Oliver Towett[1], Maia Lesosky[5], Martin Donnelly[2], Simon Kariuki[1], Aaron Samuels[4], Feiko ter Kuile[2], Sarah G. Staedke[2]

[1]Kenya Medical Research Institute, Centre for Global Health Research, Kisumu, Kenya, [2]Liverpool School of Tropical Medicine, Liverpool, Liverpool, United Kingdom, [3]Division of Parasitic Diseases and Malaria, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, United States, [4]Malaria Branch, National Center for Emerging and Zoonotic Infectious Diseases, US Centers for Disease Control and Prevention, Kisumu, Kenya, [5]Imperial College London, London, United Kingdom

Attractive Targeted Sugar Baits (ATSBs) are a novel malaria vector control tool designed to attract and kill mosquitoes outdoors. We conducted an open-label, cluster-randomised trial to evaluate the impact of ATSBs on clinical malaria incidence in Siaya County, western Kenya. Overall, 70 clusters (1-3 villages) were randomised 1:1 (35 per arm) to intervention (ATSBs) vs control (no ATSBs) using restricted randomisation. A 'fried egg' design was used for deployment of ATSBs (whole cluster) and evaluation of outcomes (core only), with a buffer zone of 600-1200m to limit contamination in the control arm. Two ATSB stations were hung on the outside walls all eligible structures and replaced every 6 months over 2 years. In total, 267,987 ATSBs were hung. All clusters received long-lasting insecticidal nets (LLINs) delivered by the Ministry of Health and supplemented by the study team, targeting a desired ratio of 1 net per every two people. From March 2022 to March 2024, three consecutive cohorts of children aged 1 to <15 years were enrolled and followed up sequentially over 2 years to assess the primary outcome of malaria incidence, aiming to accrue 1,260 person-years of follow-up time. Here, we present blinded results. Of 3,704 children screened, 217 declined, 525 were excluded, and 2,962 were enrolled into the cohorts, including 784 (26%) aged 1-4 years, and 2,178 (74%) aged 5 to <15 years. Cohort children completed 21,800 routine visits and 2,365 sick visits over the follow-up period. At 2,568 visits, children were tested for malaria by RDT; 1,766 (69%) were positive. Overall, 2,862 children were included in the endpoint analysis; 104 were excluded due to loss to follow-up (n=56), lack of at-risk person-time (n=31), and other (n=17). In total, 1,939 malaria cases over 1,435 person-years were captured, (1.35 malaria episodes per person-year). Complete unblinded results will be presented.

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SAFETY < EFFICACY OF INTERMITTENT PRESUMPTIVE TREATMENT IN PREGNANCY WITH SULFADOXINE-PYRIMETHAMINE USING RAPID DIAGNOSTIC TEST SCREENING < TREATMENT WITH DIHYDROARTEMSININ-PIPERAQUINE AT FIRST ANTENATAL CARE VISIT PRELIMINARY RESULTS

Jean-Bertin Bukasa Kabuya[1], Matthew Ippolito[2], Christine Manyando[1]

[1]Tropical Diseases Research Centre, Ndola, Zambia, [2]Johns Hopkins University, Baltimore, MD, United States

Intermittent presumptive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is a life-saving intervention for African pregnant women and their offspring, but increasing parasite resistance to SP has challenged its effectiveness. Alternative strategies are therefore being tested in clinical trials throughout Africa that include the incorporation of artemisinin-based combination therapy as an alternative to SP. We conducted a randomized controlled trial to assess the safety and efficacy of an IPTp approach that incorporates screening with RDT and treatment with dihydroartemisinin-piperaquine (DP) at the first antenatal care (ANC) visit. Asymptomatic pregnant women were randomized to IPTp-SP or hybrid IPTp-SP plus screening and treatment (IPTp-SP+). In the IPTp-SP+ arm, mothers testing positive by RDT were treated with DP at the first ANC visit, while those who screened negative received SP. In the control arm, IPTp-SP was administered per current guidelines. All received SP on days 35 and 63 and were followed biweekly up to day 63 then monthly until delivery. 393 pregnant women were recruited. Our results showed that the intervention was associated with 41% reduced odds of clinical malaria during pregnancy (OR = 0.59, 95% CI 0.38-0.92, P=0.019), adjusted for age, net use, indoor residual spraying, and gravidity. We found no significant difference in hemoglobin on day 63 (Hb 10.9±1.6 vs 11.1±1.4 g/dL, P=0.22), hemoglobin at delivery (Hb 10.9±1.6 vs 10.9±1.6 g/dL, P=0.77), congenital malaria (6% vs 3%, P=0.24), birth weight (3.0 ±0.4 vs 2.9±4.9 kg, P=0.092) or the prevalence of stillbirth (1% vs 3%, P=0.16) in the control compared to the intervention arm, respectively. The odds of low birth weight (LBW; OR 2.56, 95%CI 1.17 - 5.61, P=0.019) were higher in the IPTp-SP+ arm. However, no significant difference in LBW was detected between first-visit SP and DP in an IPTp-SP+ within-group analysis (61% vs 39%, P=0.94). IPTp-SP+ reduced the odds of malaria in pregnancy compared to the current standard of care and was shown to be safe and well-tolerated.

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THE IMPACT OF SEASONAL MALARIA CHEMOPREVENTION ON THE EDUCATIONAL OUTCOMES OF SCHOOL-AGED CHILDREN IN SUB-SAHARAN AFRICA

Mohammed Ndiaye[1], Donal Bisanzio[2], Amber Gove[2], Lauren Cohee[3], Richard Reithinger[2]

[1]University of Maryland, College Park, MD, United States, [2]RTI International, Washington, DC, United States, [3]Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Early childhood is a time of substantial growth and cognitive development—it is also the time when children are most at risk of malaria-related morbidity. Severe malaria, especially cerebral malaria, is associated with increased individual-level risk of adverse neurocognitive and behavioral outcomes. However, the population-level impact of repeated events of uncomplicated malaria on cognitive development and early learning is not known. Seasonal malaria chemoprevention (SMC) has led to substantial reductions in the burden of malaria in young children. To address this knowledge gap, we conducted a literature review to establish a foundational understanding of the nexus between health and educational outcomes, as well as define a set of harmonized malariometric, educational and other indicator data studies investigating the link between malaria and education should collect. This groundwork facilitated the use of ecological analyses to measure the impact of SMC on cognitive function and early learning. We identified countries (Gambia, Guinea, Senegal) in which cognitive and/or educational

assessments took place before/after SMC introduction and/or in areas with and without SMC. We used generalized additive mixed models (GAMMs) to investigate the relationship between SMC implementation and education indicators, and show that educational indicators have significantly improved in regions where SMC has been implemented over several years. Findings broaden our understanding of the potential educational and economic impacts of malaria prevention and may support further multi-sectoral investments in malaria control.

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URGENCY OF PHARMACEUTICAL SECTOR REFORM TO ACHIEVE UNIVERSAL HEALTH COVERAGE IN NEPAL

Pradip Lamsal, Krishna P Adhikary

Helping Hands Community Hospital, Kathmandu, Nepal

The Constitution of Nepal 2015 has established health as a fundamental right of the citizens. Both the National Health Sector Strategy and the National Health Policy were developed to realize the constitutional aspirations and are anchored to Nepal's commitment to Universal Health Coverage. The government cannot provide financial risk protection without equitable access to pharmaceuticals. Quality assured medicine are needed to expand health coverage and services. To fulfill the government's promise to improve public health, key policy reforms are required to unleash this potential. To discuss critical issues of Nepal's pharmaceutical sector, including the regulatory environment and domestic manufacturing, a high-level multispectral policy dialogue was organized in November 2021, and a series of intensive focus group discussions were carried out to encapsulate a vision for Nepal's pharmaceutical sector, outline the building blocks for pharmaceutical sector reform, and propose key reform priorities. The paper aims to provide a holistic view of the reform agenda and is mainly intended for the consumption of policymakers, development partners, and stakeholders directly or indirectly associated with Nepal's pharmaceutical sector. To unleash the full potential of Nepal's pharmaceutical sector, several critical challenges need to be addressed. The main buckets of issues and challenges are self-reliance, regulation, quality assurance, institutional restructuring, innovation, and strategic positioning of the pharmaceutical sector. The building blocks of the pharmaceutical sector fall under seven domains: policy coherence and harmonization, regulatory stewardship, local manufacturing promotion, institutional governance, pharmaceutical services, and technology and innovation. As Nepal transitions to federalism, the government shoulders the mandate of safeguarding the health of the citizens by espousing the principles of equality, prosperity, and social justice, the question "What should be the new vision for the pharmaceutical sector?" needs to be answered from the perspective of both consumers and providers.

6870

UNDERSTANDING COVID-19 VACCINE HESITANCY AMONG KEY STAKEHOLDERS IN A CONFLICT AFFECTED AREA OF CAMEROON, A FOCUS GROUP DISCUSSION APPROACH

Henry Fomukong Nzozone[1], Ngwingnchi Belove Asaah[2], Joyce Amambo Nzozone[1], Oben Pamela epse Besong[3]

[1]konye Health District, Regional Delegation Of Public Health, Southwest, Cameroon, [2]panafrican Institude Of Development, West Africa, Southwest, Cameroon, [3]regional Coordination Unit Epi, Regional Delegation Of Public Health, Southwest, Cameroon

The COVID-19 vaccine hesitancy issue is a significant challenge in Africa, influenced by historical, cultural, and socio-political factors. Health workers play a crucial role in shaping public perceptions of vaccines, and understanding their perspectives is essential for informed decision-making. Focus group discussions (FGDs) can help uncover these factors and provide insights into regional variations, enabling targeted interventions in urban and rural areas. This qualitative survey explored perceptions and attitudes towards COVID-19 vaccination in the Kumba community, South West Cameroon. Ten focus groups representing diverse demographics were involved. Recorded Discussions lasted less than 60mins on 24 themes. The recordings were uploaded into Nvivo version 12, coded and transcribed during narration. Results revealed a lack of understanding about vaccines' preventive nature, with 68% initially welcoming the vaccine with fear due to social media misinformation. Seventy-three percent of participants, including health workers, had not been vaccinated, citing fear and misinformation. Despite acknowledging their ethical responsibility, 42.1% negatively influenced others' vaccination decisions. Only 37.5% believed measures against COVID-19 in Cameroon were effective. Unvaccinated participants stressed the need for clarification and rural outreach. Recommendations include culturally tailored communication, community engagement, health education, equitable vaccine distribution, and continuous research to address vaccine hesitancy. Addressing vaccine hesitancy in Cameroon demands a multifaceted approach. The findings underscore the urgency of combating misinformation on social media and involve health workers actively in vaccination campaigns. Continuous research and evaluation will guide adaptive strategies, ensuring a comprehensive and inclusive response to COVID-19 vaccination challenges in Cameroon

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THE INFLUENCING FACTORS OF QUALITY OF LIFE AMONG INDIVIDUALS RESIDING IN RURAL AND URBAN AREAS OF THAILAND DURING THE COVID-19 PANDEMIC

Wiriya Mahikul, Wisut Lamlertthon, Kanchana Ngaosuwan, Kornphaka Phatthanagumphol, Pisinee Narayam, Nattakitta Mektripop

Chulabhorn Royal Academy, Lak Si, Thailand

The COVID-19 pandemic has profoundly impacted individuals' quality of life worldwide. This cross-sectional study was designed to explore the factors influencing the quality of life among residents in rural (Ban Luang district, Nan province) and urban (Lak Si, Bangkok) areas of Thailand during the pandemic. Participants were selected using a stratified sampling method. Quality of life was assessed using the WHOQOL-BREF-THAI questionnaire. Descriptive statistical methods and logistic regression analysis were applied to analyze the collected data. Of the 867 survey participants, 420 individuals were from rural areas and 447 were from urban areas. The mean age of participants was 35.6 ± 10.2 years in rural areas and 38.2 ± 9.8 years in urban areas. In urban areas, a majority of participants were women, married, and had lower education levels (71.1%, 50.3%, 58.8%, respectively). The overall quality of life (QOL) score was 98.2 (SD = 10.8) in rural areas and 98.5 (SD = 14.5) in urban areas. In urban areas, living in a nuclear family was associated with approximately 3.3 times higher QOL compared to living in an extended family (AOR = 3.31, 95% CI [1.75-6.27]). Additionally, using social media was associated with approximately 3.3 times higher QOL compared to not using social media (AOR = 2.06, 95% CI [1.03-4.10]). In rural areas, having an average household monthly income over 10,000 THB was associated with approximately 3.7 times higher QOL compared to lower income levels (AOR = 3.68, 95% CI [1.39-9.72]). Similarly, drinking alcohol in rural areas was associated with approximately 2.1 times higher QOL compared to not drinking (AOR = 2.12, 95% CI [1.36-3.31]).This study emphasizes the differences in QOL and related factors between rural and urban areas of Thailand during the COVID-19 pandemic. To enhance QOL, it is important to address specific challenges unique to each setting, such as those living in extended families and the use of social media in urban areas, as well as among individuals in rural areas with lower income levels. Our findings can inform the development of public health policies aimed at improving QOL in these specific settings.

6872

MEASURING CLIENT EXPERIENCE OF CARE FOR PERENNIAL MALARIA CHEMOPREVENTION IN BENIN

Cyprien Zinsou[1], Paul Bouanchaud[2], Isidore Kikissagbe[1], Ghyslain Guedegbe[1], Maya Schane[3], Charlotte Eddis[3]

[1]ABMS, Cotonou, Benin, [2]PSI, Washington, DC, United States, [3]PSI, Abidjan, Côte D'Ivoire

The right to dignified, respectful health care is enshrined by WHO. Client experience in the health system is an important driver of health service attendance and treatment adherence. There is a lack of measurement of client experience of care in malaria chemoprevention and malaria service provision more broadly. The Plus Project (funded by Unitaid, implemented by ABMS/PSI) provides Perennial Malaria Chemoprevention (PMC) to children under 2 years in selected districts of Benin. This study aims to develop and test measures for client experience of care with respect to PMC in children in Benin and goes beyond measures of client satisfaction to centre clients' voices in defining the metrics. We conducted in-depth interviews (IDI) (N=30) to establish key domains of client experience and priorities among caregivers of children under 2 in the three project zones in Benin who have received PMC. We used these data to develop survey questions which were then piloted and improved through cognitive interviews (N=30) with the target population. Once finalised. the questions were fielded in a quantitative client exit survey (N=308). Data collection was between December 2023 and March 2024. IDIs revealed the importance of caregivers' interactions with health providers, including greetings, health center cleanliness and security, perceptions of fairness in service provision, quality of explanations from providers, and quality of products. Of the 22 questionnaire items developed from IDIs, six were significantly reformulated through cognitive interviewing. Quantitative data reveal mothers attending PMC with their child had a mean age of 27.5 years and over 55% had no formal education. We found overall good client experience across all domains, with variability by geographic zone and respondent demographics. The person-centered, iterative approach to questionnaire development enabled us to readjust the collection tools so that they are adapted to socio-cultural realities and participants' lived experiences and priorities. We demonstrate how client experience may be captured for PMC and can lead to actionable recommendations to improve service provision.

6873

THE WHO VACCINE INNOVATION FRAMEWORK: COUNTRY STAKEHOLDER DELIBERATIONS TO ASSESS THE PROGRAMMATIC NEED AND USE CASE FOR INNOVATIVE VACCINE PRODUCTS

Anna-Lea Kahn, Dijana Spasenoska

World Health Organization, Geneva, Switzerland

Insufficient understanding of country needs and preferences cam lead to development of vaccines and vaccine technologies that do not meet country requirements. This results in uncertainty in market demand and poor country uptake. To strengthen country-level engagement in product development for immunization, the World Health Organization (WHO) has developed the Vaccine Innovation Framework, with an objective to assess country needs and preferences. The Framework is conceived as a four-step inclusive process which fosters deliberation and communication between stakeholders from diverse levels and disciplines across national immunization systems. It aims to evaluate vaccine product innovations that facilitate vaccine storage, delivery or handling, or improve acceptability. Multi-stakeholder discussions occur in a workshop setting, enabling participants to compare current practices with novel innovations and express their opinion on perceived value and acceptability in the context of country-level immunization challenges and priorities. This allows for the identification of criteria and evidence needed for decision-making processes. To date, the Vaccine Innovation Framework has been used by the WHO as a platform for engagement with relevant country stakeholders from 14 countries in the African, Southeast Asian and American Regions. It has been adapted for three innovations: Microarray Patches (MAPs), thermostable vaccines and oral cholera vaccine capsules. In this presentation, we provide an overview of how this Framework generates evidence, promotes equity, informs research agendas, optimizes product development and implementation, and has the potential for still broader applicability.

6874

EQUALITY IN AJTMH PUBLICATIONS FROM 1952 TO 2024: WHAT CAN WE LEARN TO MAKE GLOBAL HEALTH RESEARCH PUBLISHING MORE EQUITABLE? PROTOCOL FOR A BIBLIOMETRIC ANALYSIS

Nabila F. Youssouf[1], Rebecca L. Luckett[1], Sara Schwanke Khilji[1], Pooja Gala[2]

[1]Botswana Harvard Health Partnership, Gaborone, Botswana, [2]New York University, New York City, NY, United States

The long overdue focus on decolonising global health has prompted various institutions to assess existing inequities in global health research partnership and resulting publications. Recent reviews have demonstrated inequities in published global health research between researchers from high-income countries and low- and middle-income countries in terms of authorship, gender and academic affiliations, among others. Reflecting the American Society of Tropical Medicine and Hygiene's aim to advance health equity globally, we propose to conduct a bibliometric analysis of the American Journal of Tropical Medicine and Hygiene (AJTMH) publications between 1952 and 2024. Specifically, we propose to assess the following: -Author order-Author affiliation(s), classified using World Bank country income classifications-Author gender, when available-Funding source-Study type-Study topic-Region of publication-Year of publication.Funding sources will be recorded primarily to identify main stakeholders for further dissemination of our findings. Data will be analysed using Student's t-tests and Chi-square, followed by logistic regression. Results from this review will 1) inform a widening participation strategy launched by the ASTMH in 2022, to reflect the current make-up of global health researchers worldwide and 2) strengthen the record of AJTMH as an innovative publication with not only its finger on the pulse of change, but also actively seeking to equalise the field of global health reporting. Finally, the authors will propose further direct collaboration with the AJTMH and its affiliates to update guidelines and prepare authorship guidelines describing the Journal's commitment to inclusivity, equality and fairness.

6875

FINANCING LANDSCAPE FOR KEY POPULATIONS HIV/AIDS IN UGANDA: MARCH 2022

Arnold Taremwa[1], Charlotte Muheki[2], Felix Rutaro[3]

[1]Ministry Of Health, Kampala, Uganda, [2]Healthnet Consult, Kampala, Uganda, [3]HealthNet Consult, Kampala, Uganda

Uganda, a low-income country with a growing population of 45.74 million, faces challenges in healthcare financing. Amidst economic fluctuations and the COVID-19 pandemic, Uganda's health sector struggles with inadequate funding, especially for key populations affected by HIV/AIDS. HIV prevalence remains high at 6.2%, necessitating targeted interventions. This study examines Uganda's health financing and its implications for key populations affected by HIV/AIDS. It reviews government expenditure, donor contributions, and out-of-pocket spending. The study also assesses funding trends for HIV/AIDS response, particularly for key populations. Uganda's health expenditure constitutes 9.5% of the GDP, with public, private, and donor contributions. Notably, donor funding comprises 42% of total health financing. HIV/AIDS intervention expenditures peaked in 2016/17 and then declined. While the government's domestic public expenditure on the HIV/AIDS response increased significantly, it remains below recommended levels. Key populations, disproportionately affected by HIV/AIDS, receive less than 1% of HIV prevention funding, with sex workers receiving the majority. Uganda's health sector faces financial challenges, with HIV/AIDS interventions for key populations requiring urgent attention. Donor reliance raises sustainability concerns, and declining

funding threatens progress. Sustainable financing strategies, innovative resource allocation, and increased government commitment are crucial for addressing HIV/AIDS in key populations. Without addressing these financial gaps, achieving the 90-90-90 goals and mitigating the HIV epidemic's impact will remain challenging.

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EXPLORING ROLES, POWER DYNAMICS, AND CULTURAL SIGNIFICANCE OF ELDERS' AUTHORITY DURING DEATH IN RURAL SOUTH AFRICA

Zokwane L. Mondlane[1], Laura-Lynne Brandt[1], Gift Mathebula[1], Sara Jewett[2], Kathleen Kahn[1], Jessica Price[1], Ryan G. Wagner[1]

[1]MRC/Wits Rural Health and Health Transition Unit, Agincourt, University of the Witwatersrand, Bushbuckridge, South Africa, [2]University of the Witwatersrand, Health & Society Division, School of Public Health, Johannesburg, South Africa

In rural South African villages, the authority of elders during the process of death holds profound significance. An elder typically refers to an older person who holds a position of respect and authority within their community or family. They are valued for their wisdom, experience, and role in preserving cultural traditions and values. Elders may certify deaths, guide mourning, organize funerals, and transmit cultural knowledge surrounding death. We thematically analysed 20 in-depth interviews of community members who experienced a death in the past 2 years within the Agincourt Health and socio-Demographic Surveillance System site and 6 focus group discussions from different stakeholders to investigate the role of elders in managing the challenges of death rituals in distinct cultural contexts. Determinants sustaining the elder's authority included age, gender, and familial hierarchy. In some families, elders believe in miraculous resurrections and wait 2-6 hours to confirm the death before notification. Additionally, reflecting cultural values, infants are typically buried by elderly women at sunset. These practices underscore the deep-rooted cultural significance and reverence for rituals surrounding death within these communities. Elders' knowledge of traditional customs is often unfamiliar to younger generations and their absence results in incomplete traditional customs, with subsequent misfortunes that befall families often attributed to not following burial rituals. Elders hold considerable authority within the family structure, giving them influence over decision-making processes, including whether to participate in Minimally Invasive Tissue Sampling in research studies. Our work underscores the role of elders in rural communities as primary decision-makers in death rituals. We emphasize their authority and contributions in shaping communal responses to death, offering valuable cultural insights and wisdom. Recognizing elders' significance in future studies is crucial for understanding traditional customs and coping mechanisms related to death.

6877

CENTRING LIVED EXPERIENCE WITHIN HEALTH SYSTEMS REFORM CO-PRODUCED APPROACHES AMONG PEOPLE AFFECTED BY SKIN NEGLECTED TROPICAL DISEASES IN LIBERIA

Emmanuel Zaizay[1], **Hannah Berrian**[2], Laura Dean[3], Shahreen Chowdhury[3], India Hotopf[3], Wede Tate[2], Jerry Kollie[2], Colleen Parker[4], John Solunta Smith Jr.[2], Karsor Kollie[4], Zeela Zaizay[5], Tia Akpan[6], Rosalind McCollum[3], Sally Theobald[3]

[1], Monrovia, Liberia, [2]UL-PIRE Africa Center, Monrovia, Liberia, [3]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [4]Ministry of Health, Monrovia, Liberia, [5]Actions Transforming Lives (ACT), Monrovia, Liberia, [6]American Leprosy Missions (ALM), Greenville, SC, United States*

Persons affected by skin Neglected Tropical Diseases (NTDs), are one example of a vulnerable population who often experience stigma and discrimination due to supernatural beliefs aboutcausation. Discrimination often leads to barriers accessing timely, quality health services,limiting participation and within their community contributing to worsening physical andmental morbidities. Involving persons affected by skin NTDs in health systems and policyreform is essential, yet there is limited evidence surrounding best practices for equitable co-production. Persons affected by skin NTDs, together with academic researchers, presentlearnings from co-produced research study (REDRESS) in Liberia guided by Gaventa's powercube analysis, which aimed to focus on our lived experience and perspectives to support thedevelopment of more person-centred care. We carried out in-depth interviews with Ministry of Health at county and national levels (17),persons affected (12), paired in-depth interviews (3) and ripple effect mapping with co-researchers (2) to reflect on the value of their participation and the impact of co-production onhealth systems reform for persons affected.When underlying power dynamics are considered, with co-produced activities shaped toencourage engagement e.g. using world café small group discussions to prompt contributionsfrom all, these approaches bring value for both the individuals and the wider community andhealth system. Involving persons affected to shape the proposal, and as co-researchers broughtstronger advocacy and awareness raising within community, national and global levelsgenerating awareness of the needs and priorities of persons affected, with stronger relationshipsand ability to engage with policy actors. Persons affected placed greater trust in those withshared lived experience strengthening referral pathways.Using co-produced research approaches promotes inclusion and belonging for persons affectedwithin decision-spaces, contributing to greater capacity and advocacy roles by those directlyinvolved as co-researchers, as well as more inclusive health services.

6878

EMPOWERING EARLY-CAREER WOMEN IN BIOSCIENCES: A PILOT MENTORSHIP INITIATIVE AT NNAMDI AZIKIWE UNIVERSITY, NIGERIA

Ogechukwu Benedicta Aribodor[1], Eneyi E. Kpokiri[2]

[1]Department of Zoology, Nnamdi Azikiwe University, Awka, Nigeria, [2]Department of Clinical Research, Faculty of Infectious and Tropical Diseases London School of Hygiene and Tropical Medicine, London, United Kingdom

Female early-career academics often face gender biases and stereotypes that hinder their professional growth. This pilot mentorship program aims to equip women with the skills for effective leadership, drawing inspiration from the WHO TDR Health Research Mentorship in low- and middle-income countries (HERMES) Practical Guide for institutionalizing health research mentorship. The absence of a formal mentorship program at the University since its inception in 1991 underscores the significance of this initiative, which seeks to institutionalize mentorship, and enhance diversity, inclusivity, and excellence within the biosciences faculty. To address this gap, a needs assessment survey was conducted in March 2024 to identify the challenges and needs of early-career women in biosciences, recruiting participants through the university networks using an online platform. All 19 participants were women aged 25-44 years, with 85% having 1-10 years of academic experience. Most (90%) were married, with 65% having children aged 3 months to 10 years. Challenges included balancing family and career, lack of mentorship, and financial support. All participants expressed the need for mentorship programs, implicit bias training, and family-friendly policies for academic career support. Of the participants, 36.8% (7/19) had prior mentorship experience, while 63.2% (12/19) had not. Among those with prior experience, 42.9% (3/7) reported mixed experiences or challenges, and 28.6% cited a lack of follow-up or short program duration. Respondents suggested promoting gender equity initiatives, providing mentorship and sponsorship programs, creating inclusive and supportive environments, offering professional and leadership development opportunities, encouraging work-life balance, effective time management skills, celebrating achievements and visibility, addressing implicit bias and stereotypes, and supporting networking and collaboration. The findings underscore the critical role of tailored support in advancing early-career women's careers in biosciences, emphasizing the importance of mentorship and inclusive policies.

6879

NAVIGATING HEALTHCARE HURDLES IN LORETO: EVALUATING BARRIERS TO ACCESS

Maribel Paredes Olortegui[1], Karin F. Perez Garcia[1], Mario Güimack Fajardo[1], Loida F. Zegarra Paredes[1], Francesa Schiaffino[2], Josh M. Colston[3], Pablo Peñataro Yori[3], Patricia Pavlinac[4], Margaret N. Kosek[3]

[1]Asosciacion Benefica Prisma, Iquitos, Peru, [2]Universidad Peruana Cayetano Heredia, Lima, Peru, [3]University of Virginia, Charlottesville, VA, United States, [4]University of Washington, Seattle, WA, United States

Covering nearly one-third of Peru's territory, Loreto faces a complex healthcare landscape with significant challenges that hinder healthcare-seeking behavior. Barriers to healthcare seeking are generally attributed to the lack of healthcare facilities and, consequently, long travel time to the facility, as well as limited economic resources. However, it is yet to be determined if discrimination in healthcare settings is perceived as a barrier in Loreto. This study was implemented as a sub-study of The Enterics for Global Health study and utilized an already validated survey to measure discrimination in health establishments. Its aim was to determine if discrimination was a barrier to seeking care among children with acute diarrheal illness and to determine if structural deficiencies were prevalent among health posts, including the presence of health care providers, treatment options, and basic services, such as potable water and electricity. The survey was deployed in the area of influence of 5 health care centers in Iquitos, Loreto, and the availability of services was evaluated using spot checks by health care workers once a week. Between June and December 2023, 2183 participants completed the questionnaire. Of these, 67.9% (1483/2183) attended a health post in the last year, of which 8.3% (82/977) had a child under 5 with diarrhea. 38.3% (836/2183) of participants indicated they felt mistreated or discriminated against in a health center. Additionally, each healthcare center was surveyed on 190 days on average. It was identified that services, including electricity and water, were generally available in all 5 health centers, yet piped water was only available in one. Healthcare personnel worked on over 90% of the days in which spot checks were performed. Diarrhea treatment options, including antibiotics, were available in over 90% of days surveyed. However, zinc was not available on 37% of days and ORS in 18% of days surveyed.

6880

ADDRESSING STRUCTURAL BARRIERS AND HUMAN RIGHTS IN MALARIA SERVICES IN UGANDA AND KENYA

Joseph J. Amon[1], Megan McLemore[1], Alistair Shaw[2], Alexandrina Iovita[2]

[1]Drexel University, Philadelphia, PA, United States, [2]Global Fund Against HIV, TB and Malaria, Geneva, Switzerland

The Global Fund's Breaking Down Barriers (BDB) initiative provides support in Uganda and Kenya for the scale-up of evidence-based programs to remove equity-, rights-, and gender-related barriers to malaria services, with the aim to increase the effectiveness of Global Fund grants and ensure that health services reach those most affected. An evaluation of these efforts was conducted in both countries in 2023, and findings were compared with an earlier 2017 baseline assessment which found in both countries few or no formalized programs to address these barriers. By 2023, both countries had created programs seeking to better understand and strengthen availability and accessibility of services. For example, Malaria Matchbox assessments identified populations most at risk, as well as those underserved by existing interventions. Both countries integrated human rights and gender into their national strategies, and in policy and program implementation. Community leadership - through, for example, community dialogues - led to increased resources closer to communities, allowing for timely identification of challenges and locally driven solutions to drive a more effective malaria response. The evaluation also found that there has been a renewed focus within both countries on understanding gender norms and their influence on the effectiveness of malaria programming, and increased collaboration across health sectors, for example in mapping vulnerable populations and implementing some malaria activities. Nonetheless, significant challenges remain. Many malaria stakeholders lack the training, staff and technology for integrating human rights principles and approaches into service delivery. A dearth of disaggregated data by age, gender and other factors related to risk and vulnerability impedes the ability to effectively tailor approaches to subnational levels, and remove structural barriers that exist. Advocacy to reduce law and policy-related barriers to malaria services remained in early stages. Local capacity for effective monitoring and evaluation related to malaria and human rights programs needs to be strengthened.

6881

ADVANCING GENDER EQUALITY WILL STRENGTHEN INTERVENTIONS FOCUSED ON ENDING THE MALARIA EPIDEMIC

Alistair Shaw[1], Emilomo Ogbe[1], Thea Willis[1], Tara Talvacchia[2], Kirsten Gagnaire[2]

[1]The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland, [2]Kati Collective, Vashon, WA, United States

Gender equality is increasingly recognized as a crucial element in the fight against malaria. Drawing from evidence-based approaches and experiences gleaned from Malaria Matchbox assessments conducted in over 20 countries receiving Global Fund funding, and other interventions, three programmatic entry points for advancing gender equality have demonstrated to be contributory to the malaria response. Firstly, women's economic empowerment ensures women's participation in markets, control over resources, access to decent work, and agency in decision-making processes. Evidence suggests that integrating activities to enhance women's economic agency accelerates the malaria response, resulting in greater net use within households and improved health seeking behaviors. Second, ANC promotes healthy behaviors such as the use of insecticide-treated bed nets and intermittent preventive treatment of malaria during pregnancy. However, barriers such as poverty, mobility constraints, and power dynamics within households impede women's access to and utilization of ANC services. Strengthening access to and utilization of ANC services not only improves maternal and child health, but also provides opportunities to reach more people with malaria prevention commodities and services. Furthermore, addressing gender disparities within the malaria health workforce is imperative. Women are disproportionately represented in lower-paid roles and face discrimination and exploitation. Women are often inadequately compensated and lack opportunities for professional advancement. Achieving gender equality within the health workforce is essential for ensuring equitable access to malaria care and improving program effectiveness. Strategies aimed at challenging gender inequalities and norms enhance the effectiveness of investments and contribute to long-term program outcomes. In 2024, the Global Fund has newly committed at least US $2 million to specifically advance gender equality and thereby accelerate progress towards ending the malaria epidemic.

6882

LEVERAGING GLOBAL FUND INVESTMENTS: PROTECTING THE RIGHT TO HEALTH AND LIMITING FINANCIAL HARDSHIP

Alistair Shaw, Michelle Remme, Alexandrina Iovita

The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland

Financial barriers to healthcare, rooted in economic disparities, structural inequalities and health system financing models, can significantly impede accessibility to essential health services. These barriers manifest in many forms including out-of-pocket expenditure, lack of adequate health insurance coverage, costs of additional medicines, transportation costs to reach a clinic or care provider, lost income, informal payments, and intra-household decision making on family finances. For many individuals and families, particularly those living in low-income communities or rural areas, these financial barriers can be prohibitive, keeping people away

from essential health services, causing financial hardship, and deepening poverty. Addressing financial barriers to healthcare is more than an issue of affordability, it is a fundamental imperative for ensuring equitable access and for protecting the right to health for all. Global Fund resources have been instrumental in driving change in this area. It has supported health financing and insurance schemes to prevent catastrophic financial impact as a result of severe malaria; strengthened community-based service delivery models to reduce transport costs incurred by patients; subsidized malaria commodities to ensure they are provided at no cost to users; enabled the use of non-malaria medications for integrated community case management of childhood illness, reducing indirect costs to families that may have prevented them seeking care; and supported ongoing monitoring of financial barriers through community-led monitoring (CLM). By working to reduce financial barriers to health services, and prioritizing high risk and underserved populations, the Global Fund partnership has accelerated progress towards malaria elimination and realizing a world free of the burden of malaria with better, equitable health for all.

6883

CITIZENS AS INFLUENCERS OF HEALTH SERVICE AVAILABILITY AND NOT AS CONSUMERS ONLY

Alex Mukembo, Alex Mukembo

World Vision International, Kampala, Uganda

Advocacy for health services is critical for availability of health services in resource limited settings. Availability of health services influences utilization and ultimately the health status of the community. While advocacy for health service has been recognized as a major tool to influence service, often advocates focuses on service providers or duty bearers with limited engagement of service citizens in influencing availability of health services. It is oftentimes led by external, leaving the citizens as consumers of services and not influencers. World Vision adopted Citizen Voice and Action advocacy approach which is a social accountability methodology that empowers communities to monitor the performance of local governments in providing essential services like health care at the local level. It empowers citizen to monitor actual availability, quality and quantity of health services in their community against the government standards and use the identified gaps to engage and influence through dialogues. Communities were first sensitized on the health facilities (HFs) monitoring standards and relevant health policies, like patient charters. This was followed by gatherings at HFs, involving about 50 community members, grouped according to sex and age. During the gathering, communities scored availability, quantity and quality of services against government standards. Based on identified gaps, dialogues were created between the citizens, health workers and duty bearers to close the identified gaps. This resulted in actions to closing the identified gaps. Implementation of actions was monitored by the CVA for 18 months. Improvement in staffing in HFs, from 54% to 72%, and recruitment of more critical staffs. The district allocated 500 million in additional funding for infrastructure development. Absenteeism among health workers reduced, while blood transfusion services were operationalized at Nankoma H/CIV. Citizens are critical influencers of service availability, when considered as being more than consumers.

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

Tippa Wongstitwilairoong[1], Darunee Buddhari[2], John Mark Velasco[3], Diones Paula Corazon[3], Alera Maria Theresa[4], Sanjaya Kumar Shrestha[5], Tipawan Kangvanrattana[1], Kathryn McGuckin Wuertz[1], Aaron Farmer[1]

[1]WRAIR-Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand, [2]Kamphaeng Phet/AFRIMS Virology Research Unit, Kamphaeng Phet, Thailand, [3]Philippines/AFRIMS Virology Research Unit, Manila, Philippines, [4]Philippines/AFRIMS Virology Research Unit, Cebu, Philippines, [5]Walter Reed/AFRIMS Research Unit, Kathmadu, Nepal

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

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SYNDEMIC MODELLING: A NOVEL MATHEMATICAL MODELLING FRAMEWORK FOR SIMULATING MULTIPLE PATHOGENS DYNAMICS IN CONTEXT

Caroline Franco[1], Lisa J. White[2], Sheetal Silal[3]

[1]University of Aberdeen, Aberdeen, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]University of Cape Town, Cape Town, South Africa

Mathematical models have historically been used to understand and predict disease transmission dynamics, slowly evolving along with our understanding of the underlying biology of disease spread. Knowledge of disease dynamics and interactions can be combined with socio-economic considerations to produce models robust enough to simulate and compare control strategies, thus becoming useful tools to inform health policy making. It is still a challenge, however, to produce robust mathematical models that can concomitantly address the dynamics and interactions among multiple etiological agents. Models for multiple strains or species of pathogens are challenging due to the number of equations required to accurately account for the inter-species interactions, which increases exponentially with the number of species, making numerical and structural identifiability increasingly improbable.We have developed a mathematical approximation which allows the dimension of the resulting model to increase linearly with the number of species (instead of exponentially). For a two-species SIRS model, we have shown through mathematical analysis that this approximation is appropriate for species with low levels of interaction. We have recently been working on generalising this framework through further analysis and numerical simulations, and exploring less analytically tractable examples of multi-species malaria and multi-pathogen epidemics (e.g. COVID-19 and flu syndemics). Our overarching aim is to use the proposed framework to develop better context-informed models with policy-making impact at local, national and international levels.

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MALARIA IN THE REPUBLIC OF GUINEA: COSTS ASSOCIATED WITH THE CARE PATHWAY FROM THE PATIENT'S PERSPECTIVE, 2022 - 2023

Elhadj Marouf Diallo[1], Fatoumata Bintou Traore[1], Alice Langlet[2], Marie Blanquet[2], Bienvenu Salim Camara[3], Alioune Camara[4], Laurent Gerbaud[2]

[1]African Center of Excellence for the Prevention and Control of Communicable Diseases, Faculty of Health Sciences and Techniques, University of Conakry, Dixinn, Conakry, Guinea, [2]CHU Clermont-Ferrand, UFR Medicine & Paramedical Professions, University Clermont Auvergne, CNRS, Sigma Clermont Institute Pascal, Clermont-Ferrand, France, [3]Centre National de Recherche et de Formation en Santé Rurale de Maferinyah Guinée (CNRFSR), Maferenya, Forecariah, Guinea, [4]National Malaria Control Program, Dixinn, Conakry, Guinea

Access to safe, affordable healthcare is crucial for reducing health disparities. In Guinea, malaria is a major public health issue with significant economic consequences. In 2010, the country introduced free healthcare services for malaria to control the endemic disease. This paper analyzes the costs (out-of-pocket expenses) associated with the care of malaria patients in the Republic of Guinea. An economic analysis of the costs of managing malaria in Guinea was conducted using data from a cross-sectional survey on the determinants of malaria prevention. Data were collected between December 2022 and March 2023 in health facilities and at the community level. The Time-Driven Activity Based Costing approach and micro-costing were used to evaluate the costs associated with care-seeking, management, and related costs. The study enrolled a total of 3,300 patients from 60 healthcare facilities, predominantly in urban areas (65%), with one-third being children under 5 years of age (mean age 27 months). Most patients were accompanied by their mothers, had no formal education, came from households led by husbands, and had a median monthly income of $115.95. Around 41% were seeking care for the first time. The costs of seeking care varied based on the type of malaria, with $3.48 for uncomplicated cases and $13.45 for severe cases. The median direct care costs in healthcare facilities for uncomplicated malaria were $7.30, and $30.84 for severe cases. Overall costs associated with malaria varied by type and age group, with median costs borne by patients estimated at $17.57 for uncomplicated malaria and $44.87 for severe cases. Delay in seeking care accounted for 19% of the costs incurred by malaria patients in Guinea ($p < 0.001$). Despite the implementation of free malaria prevention services, patients continue to experience costs and income loss. An approach based on selective free access and affordable flat-rate costs could ensure the financial sustainability of healthcare facilities and reduce out-of-pocket expenses for patients.

6887

EXPLORING THE MIGRATION PATTERNS AND POPULATION HEALTH OUTCOMES IN URBAN AFRICA: A CASE OF NAIROBI CITY

Evans Omondi, Samuel Iddi, Steve Cygu, Abdhalah Ziraba, Damazo Kadengye, Agnes Kiragga

African Population and Health Research Center, Nairobi, Kenya

Understanding the dynamics of transitions between different residency states is essential for informing effective population management strategies. Our aim is to characterize the trajectories of residency events within the Nairobi Urban Health and Demographic Surveillance System (NUHDSS), encompassing key residency events. Thus, we intend to unravel patterns and trends that can guide the development of targeted policies and interventions to address the evolving needs of the population. We proposed a continuous time homogeneous multi-state Markov model for the NUHDSS longitudinal residency data collected from 223,350 individuals in Korogocho and Viwandani slums in Nairobi. The model is used to effectively capture and model residency events; births, deaths, in-migrations, and out-migrations that directly impact the population dynamics including population growth, and population decline. However, exit and entry are included in the descriptive analysis to offer some insights into the magnitude and patterns of internal population movements over time. From the findings the hazard ratio (HR) of 0.7684 suggests that adjusting for the effects of gender, ethnicity, area of birth and age, the transition of individuals in Viwandani from birth to death is associated with a 23.16% lower than those in Korogocho. Same results are seen for the individuals in Viwandani for the transitions from enumeration to death, and in-migration to death. Our findings provide unique insights into the frequency of events, their transition rates, and the impact of gender, slum area, age, ethnicity, and area of birth. These results have implications for preventive health interventions and planning for appropriate levels of residential care. Moreover, modelling the residency events helps in understanding the expected burden of the migration and population growth.

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WHATSAPP MESSAGING AND USE OF MALARIA SERVICE GUIDES AND FEVER MANAGEMENT TOOLS IN CROSS RIVER STATE, NIGERIA

Oluwatobiloba Akerele[1], Uchenna Nwokenna[2], IniAbasi Nglass[2], Aniefiok Akpasa[3], Etieno Etuk[1], Victor Bassey[1], Udeh Phillip[1], Damola Abikoye[1], Olayemi Abimbola[2], Rudi Thetard[4], Arja Huestis[4], Thomas Hall[4], Dorathy Iwasam[3], Grace Nwankwo[5], Erkwagh Dagba[6], Veronica Momoh[6], Jules Mihigo[6], Chukwu Okoronkwo[7], Nnenna Ogbulafor[7], Godwin Ntadom[7]

[1]Management Sciences for Health, Cross River, Nigeria, [2]Management Sciences for Health, Abuja, Nigeria, [3]Cross River State Malaria Elimination Programme, Cross River, Nigeria, [4]Management Sciences for Health, Arlington, VA, United States, [5] United States Agency for International Development, United States President's Malaria Initiative, Abuja, Nigeria, [6]United States Agency for International Development, United States President's Malaria Initiative, Abuja, Nigeria, [7]National Malaria Elimination Programme, Abuja, Nigeria

Appropriate and timely fever management are crucial to prevent severe malaria (Agunbiade et al, 2022). The U.S. President's Malaria Initiative for States project (PMI-S) aimed to improve fever case management in 165 health facilities (HFs) in Cross River State using Behavioral Economics Prototypes (BEPs), a set of tools and processes designed to guides appropriate fever management. In March 2023, BEP monitoring teams observed that the tools were not adequately used or accessible on request. PMI-S addressed this poor BEPs use by sharing them across four relevant WhatsApp groups with 32, 66, 43 and 36 participants. The BEPs were disseminated twice a week from July to September 2023: (1) "Is it malaria?" An interactive group discussion guide, (2) Whole Site Counseling Tool, (3) Performance-Tracking Poster, (4) Malaria Testing and Treatment Tally Form, (5) Fever Evaluation Tool, and (6) Pediatric Evaluation Form. Netnographic and conversation analyses were conducted on the WhatsApp platforms where the BEPs were shared. This revealed that more than 50% of participants downloaded the tools over a three-month period (July to September 2023). Conversational analysis of the WhatsApp response thread showed that sharing BEPs enabled discussion on their application, including challenges. District Health Information System data analyzed found that malaria test positivity rate (TPR) reduced across 165 HFs from an average of 64% from July to September 2022 to 58% with BEP implementation in the same period in 2023. TPR reductions rely on improved testing, which may have been aided by the shared BEPs being made immediately available on WhatsApp. Additional studies could further explore the utility of sharing BEPs through mobile messaging platforms, the uptake of tools, and the resulting changes in key malaria case management indicators.

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COMPARATIVE ANALYSIS: USING A HYBRID ICF VERIFICATION TOOL IN A 28,000-PARTICIPANT CLINICAL TRIAL AT COMMUNITY LEVEL IN MOZAMBIQUE AND KENYA

Eldo Aly Elobolobo[1], Lisa Collins[2], Leslie Sam[2], Jamal Salim[3], Paula Ruiz-Castillo[2], Mary Mael[2], Isaac Ringera[3], Mercie Kariuki[3], Shadrack Karisa[3], Vegovito Vegove[4], Patricia Bellot[2], Isaiah Omondi[3], Carlos Chaccour[2], Regina Rabinovich[2], Marta Maia[3]

[1]Databrew, Manica, Mozambique, [2]Isglobal, Barcelona, Spain, [3]Kenya Medical Research Institute - KEMRI, Kwale, Kenya, [4]Centro de Investigação em Saúde de Manhiça - CISM, Manhiça, Mozambique

Clinical trials in low- and middle-income countries (LMICs) face unique challenges when adapting traditional methodologies to comply with Good Clinical Practice (GCP) standards and ensuring participant safety. The BOHEMIA trial in Mozambique and Kenya assessed the impact of mass ivermectin distribution on malaria transmission, enrolling over 58,000 participants. Handling 50,000+ paper-based informed consent forms (ICFs) per country was risky and inefficient. In Mozambique, paper reliance and manual tracking led to potential compliance issues with ICH E6 (R2) standards due to cumbersome systems and disconnection from the main database. Conversely, the Kenyan team implemented a hybrid approach, integrating paper ICFs with an electronic registry, enhancing real-time management, data security, and stakeholder collaboration. This system streamlined verification, query resolution, and archiving, also enabling prompt identification and correction of missing ICFs, ensuring data integrity. The digital tool developed in Kenya outperformed traditional methods, improving transparency, efficiency, and safety in participant management. Its potential integration with machine learning and AI, and compatibility with existing electronic data capture systems (EDC), exemplifies innovative approaches in clinical trial methodologies, particularly suitable for LMIC settings where resources are limited. The BOHEMIA study's success demonstrates the effectiveness of this approach in overcoming traditional research barriers.

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NETWORKING OF MEDICAL LABORATORY DATA IN MADAGASCAR

Omega Raobela[1], Tovonahary Rakotomanga[1], Freddy Lokossa[2], Sandy M. Ralisata[2], Andry Patrick Raoiliarison[2], Daniella Randriamanana[2], Sandratra Harizaka Rakotoarisoa[2], Davida Natolotra Razafindratsaravahy[2], Tolotriniaina Eric Rafanomezantsoa[2]

[1]Madagascar Ministry of Health, Antananarivo, Madagascar, [2]Population Services International Madagascar, Antananarivo, Madagascar

The Ministry of Health (MOH) in Madagascar, through the Directorate of Pharmacies, Laboratories and Traditional Medicine (DPLMT), the Malagasy Medical Analysis Laboratory (LA2M) and the Directorate of Studies, Planning and Information System in Health (DEPSI) is strengthening its data reporting system of medical analysis laboratories, through the digitalization of an electronic laboratory register. To date, each health program has its own laboratory reporting system, making compilation and monitoring difficult for an integrated approach to communicable disease control. This strengthening of the electronic reporting system meets the MOH's digitalization objective for the surveillance of malaria, tuberculosis, HIV and COVID. 19.73 (37%) of the 198 analysis laboratories in Madagascar with internet connection have benefited from training and provision of electronic tablets for this electronic register. Laboratories were selected to represent the 12 TB and HIV priority districts, those with the highest malaria risk level and those in pre-elimination, alongside public and private facilities. Among the 73 laboratories supported for this intervention between October 2023 and January 2024, 77% (56/73) reported data electronically, including 47% (34/73) on diagnosed malaria cases diagnosed, 52% (38/73) on detected tuberculosis cases, 47 % (34/73) for HIV testing and 3% (2/73) for COVID19 cases. The 23% of laboratories not reporting was due to the poor-quality connectivity, non-daily data entry, the absence of post-training monitoring for the period, and a reported lack of willingness for some. Future supportive supervision by regional laboratory managers will aim to resolve these obstacles. Laboratory data, training curricula and modules are currently available in the Ministry of Health's DHIS2 server, under the responsibility of DEPSI.

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PHYSICIANS' PERSPECTIVES OF INFORMAL HEALTH PRACTITIONERS IN BANGLADESH AND POTENTIAL FOR ENGAGEMENT

Zahid Hasan Khan[1], Olivia R. Hanson[2], **Sarah A. Dallas**[2], Mohammad Ashraful Amin[1], Ishtiakul Islam Khan[1], Debashish Biswas[1], Md. Taufiqul Islam[1], Eric J. Nelson[3], Firdausi Qadri[1], Melissa H. Watt[2], Daniel Leung[2], Ashraful Islam Khan[1]

[1]icddr,b, Dhaka, Bangladesh, [2]University of Utah, Salt Lake City, UT, United States, [3]University of Florida, Gainesville, FL, United States

The healthcare landscape of rural Bangladesh faces various complex challenges, including limited resources and a shortage of qualified healthcare professionals. Informal healthcare providers, locally termed village doctors, fill this void and provide the majority of primary care, especially in remote villages and hard-to-reach areas. In many parts of Bangladesh, patients who present to formal healthcare facilities have first been to see a village doctor for assessment and treatment. This study aimed to qualitatively explore the perspectives of formally trained physicians on the role of village doctors in Bangladesh's healthcare system. This study was conducted in the Sitakunda Upazila subdistrict of Southeast Bangladesh. We recruited twelve formally trained physicians through a purposive sampling technique. Individual in-depth interviews were conducted by an ethnographic research team in Bangladesh. Interviews were transcribed and thematically coded to examine both positive and negative opinions of village doctors. The interviews unveiled three prominent themes highlighting the perceived positive contributions of village doctors: 1) provision of essential services and resources in isolated areas, 2) enhanced accessibility and familiarity with the community, and 3) active involvement in public health education. Additionally, the interviews revealed five themes related to physician's perspectives of the negative impacts of village doctors in the healthcare system: 1) insufficient education and training, 2) use of inappropriate treatments, 3) inappropriate referral practices, 4) the misuse and overuse of antibiotics, and 5) prioritization of financial gain. This study sheds light on the complex relationship between formal and informal healthcare providers in the larger healthcare system and emphasizes both the contributions and impedance of village doctors to rural healthcare settings. Coordination between formal and informal healthcare providers is necessary to meet the needs of rural patients in Bangladesh.

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MODELING THE IMPACT OF CORE AND SUPPLEMENTARY TOOLS ON PYRETHROID RESISTANCE AND MALARIA TRANSMISSION DYNAMICS

Hamenyimana Emanuel Gervas

Ifakara Health Institute, Morogoro, Tanzania, United Republic of

Significant investments in malaria vector control during the previous 20 years have led to a 40% decrease in the number of clinical cases of malaria and the anticipated prevention of 663 million cases in sub-Saharan Africa. Vector control methods such as indoor residual spraying (IRS), larval source management (LSM), insecticide-treated nets (ITNs) have been credited with these results. The unexpected increase in malaria incidence and prevalence in Africa is concerning, even if there has been a decrease in malaria cases and fatalities as a result of ITNs and IRS deployments. A number of factors have led to the decline in these achievements, including changes in the behavior of the malaria vector species and, most importantly, insecticide resistance in the malaria vectors. The most dependable instruments in Tanzania for controlling malaria vectors, IRS and ITNs, are seriously threatened by the outbreak of insecticide resistance. For example, by 2020,

more than 80% of sentinel sites had pyrethroid resistance, up from 0% in 2004. Therefore, a new mathematical model for the dynamics of malaria transmission has been developed and thoroughly examined in this study in order to assess the effects of ITNs, IRS, and Attractive Sugar Baits (ATSB) on pyrethroid resistance in the context of Tanzania. This model takes into account the susceptible and resistant *Anopheles gambiae s.l.* and *An. funestus* species and the fact that the effectiveness of vector control measures deteriorates with time. Once more, the model takes into account the varying resistance levels of the resistant *An. funestus* and *An. gambiae s.l.* species. Using secondary data from previously published studies and datasets, a number of simulations using the Python programming language are being run to assess the effects of combining various forms of ITNs with IRS and ATSB. The preliminary findings demonstrate the substantial impact of supplementing ITNs with IRS and ATSB. Additionally, the study plans to evaluate the impact of these vector control methods on the allele frequencies of the mosquito species using the Epidemiological Modeling Software (EMOD).

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THE EFFICACY OF MOBILE SERIOUS GAMES (SWAZIYOLO) IN INCREASING HIV RISK PERCEPTION IN ESWATINI: A RANDOMIZED CONTROL TRIAL.

Bhekumusa Lukhele[1], Mac Delay[1], Fortunate Shabalala[2], Mfundi Motsa[3], Alexander Kay[4], Christina El-saedi[5], Bongani Masango[3], Gregory Pavela[1], Katia Bruxvoort[1]

[1]University of Alabama at Birmingham, Birmingham, AL, United States, [2]University of Eswatini, Mbabane, Eswatini, [3]Ministry of Health, Mbabane, Eswatini, [4]Baylor College of Medicine, Houston, TX, United States, [5]City of San Antonio Metropolitan Health District, San Antonio, TX, United States

Eswatini has one of the highest HIV prevalence rates globally (24.8% among people ≥15 years of age). Unprotected heterosexual transmission accounts for more than 90% of new HIV infections in the country. Mobile phone technology is growing rapidly, offering opportunities for technology-driven interventions for HIV prevention. Our team developed SwaziYolo, a smartphone, interactive, educational story game that places the player in the role of a young adult looking for love in Eswatini's capital city. We conducted the Serious Games HIV Prevention Trial (SGPrev-Trial), a 4-week, 2-arm, 1:1 randomized controlled trial of SwaziYolo among people 18-25 years of age in Eswatini. The main outcome was HIV risk perception scores (10-item index and a subscale 8-item index), assessed using intention-to-treat and per-protocol difference-in-difference (DID) analysis. Secondary analyses examined differences in reported sexual behavior and serious game acceptability. Of 380 people who agreed to participate in this study, 130 in the control arm and 127 in the intervention arm completed follow-up. Among the 79.5% (101/127) of intervention arm participants who completed at least one game (per-protocol analysis) we observed an increase in the 10-item HIV risk perception index compared to control arm participants (DID mean score of 1.63, p-value 0.048) and a borderline increase for the 8-item HIV risk perception index (DID mean of 1.37, p-value 0.060). In intention to treat analysis, there were no significant differences between arms in both the 10-item and 8-item indices. Nearly all (96.1%) participants strongly agreed or agreed that they would recommend SwaziYolo to their peers. The high retention rate observed in this study demonstrates the feasibility of online technology-based interventions for HIV prevention in Eswatini. Our preliminary results suggest that serious game interventions can be effective at increasing HIV risk perception. Future research will explore how to optimize SwaziYolo to promote and sustain HIV prevention among young people in Eswatini and adapt the intervention to other settings.

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DIGITIZATION OF COMMUNITY HEALTH IN BURKINA FASO: CONSIDERING THE PERSPECTIVES OF COMMUNITY WORKERS THROUGH USER ACCEPTABILITY TESTING

Alain Kabore[1], Assetta Bara /Compaore[1], Fatou Fall[2], Bry Sylla[3], Adama Yameogo[1], William Ouango[3], Jean Serge Dimitri Ouattara[3]

[1]PATH, Ouagadougou, Burkina Faso, [2]PATH, Dakar, Senegal, [3]Ministry of health and public hygiene, Ouagadougou, Burkina Faso

Malaria remains a major public health burden in Burkina Faso. With an incidence of 525.4 per 1000 inhabitants (2022), it is the leading cause of morbidity and mortality. The government of Burkina Faso implemented a 2019-2023 community health strategy, with digitization of service delivery as a priority intervention. The aim was to set up a digital solution to provide decision support to community health workers to improve the quality of services, the quality of data and the performance of these players. One of the fundamental principles of digitization is the end-user-centered approach. To comply with this principle, Digital Square at PATH with funding from the US Presidential Malaria Initiative, provided technical support to the Ministry of Health to conduct a training of 58 community health workers and 15 supervisors, followed by user acceptance tests in the Boromo health district. The training consisted in showing the participants how to use the Android mobile phone and the decision-support application developed on Commcare platform. An evaluation using interview and observation gathered feedback and suggestions from the participants. Although a good satisfaction (70%) about application accessibility, user-friendliness and stability, concerns about the applications were raised by 35% of participants, including data not being transmitted via SMS, certain modules not being displayed, discrepancies between the content of the modules and actual actions in the field, and the need for the supervisor to have controlled access to the CHW's telephone. In addition, concerns were raised about the system in general, particularly the security of the devices in the hands of CHWs, maintenance/updating, renewal, and the availability of an energy source for recharging at the community level. Overall, the UATs make it possible to check that applications and devices are working in real time on the ground, to assess the ability of stakeholders to use them, and to gather concerns and worries, with a view to improving the system so that it meets the expectations of the first users as well as the goals of community health digital transformation.

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EXPLORING PERSPECTIVES ON THE SCANNABLE MATERNAL & CHILD HEALTH HANDBOOK IN SIAYA, KENYA: A QUALITATIVE ASSESSMENT OF HEALTHCARE PROVIDERS & ANC CLIENTS

Fredrick omiti[1], Wycliffe Odongo[2], Mevis Omollo[1], Kizito Obiet[1], Brian Seda[1], , Victoria , Seffren[2], Jonathan Schultz[3], Simon Kariuki[1], Feiko terKuile[4], Gutman Julie R[2]

[1]Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya, [2]Malaria Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, United States, [3]4Malaria Branch, Division of Parasitic Diseases and Malaria, US Centers for Disease Control and Prevention, kisumu, Kenya, [4]3Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

A scannable version of the Kenyan Ministry of Health (MOH) Maternal and Child Health (MCH) handbook was piloted to assess impact on data quality and utility in Siaya, western Kenya. Acceptance by healthcare providers and antenatal care (ANC) attendees is crucial for successful implementation and adoption of such a tool. We conducted a qualitative assessment to explore the perspectives of healthcare providers and ANC clients on implementation and associated challenges. From the pilot, 36 ANC clients were purposively identified and split into 3 focus groups by number of contact visits: a) 2-3, b) 4-5, and c) 6-8. Additionally, 10 key informant interviews (KIIs) were conducted individually with 8 service providers and 2 county health officials. Interviews were transcribed, coded, and thematically analyzed in NVivo v.12. The results showed that the scannable handbook's resemblance to

the standard handbook made it familiar and user friendly, with its revised structure and flow simplifying data entry. Digitization of individual data from the handbook facilitates tracking ANC services individual women received across multiple facilities. Results also suggested that the books' design, size, material quality, spiral binding and hard cover provided extra protection, making it durable, aesthetically pleasing, easier to handle and minimized chances of misplacement or loss. Possible barriers identified included scanning (photographing) difficulties to abstract data with some providers finding it time-consuming. ANC clients faced difficulties at non-pilot facilities with providers unfamiliar with the handbook emphasizing the need for sufficient sensitization and training before implementation. The scannable MCH handbook is widely accepted in Siaya county due to several advantages including its user-friendliness, durability, and the ability to digitally abstract data and track ANC clients across multiple health facilities. Addressing the challenges such as scanning, training, and orientation are crucial to improving negative experiences before potentially scaling up.

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EXPLORING EXPERTS' PERSPECTIVES ON THE ADOPTION AND USE OF MULTIPLEX BEAD ASSAYS FOR INTEGRATED SEROSURVEILLANCE IN LOW- AND MIDDLE-INCOME COUNTRIES

Alex C. Kong, Andrea C. Carcelen, William J. Moss

Johns Hopkins Bloomberg School of Public Health International Vaccine Access Center, Baltimore, MD, United States

Serological surveillance ('serosurveillance') enables health systems and researchers to estimate a community's level of exposure or immunity to various pathogens and guide the implementation and monitoring of public health interventions. The use of multiplex bead immunoassays (MBAs) can streamline this approach by allowing for the simultaneous detection of several antibodies to different antigens and pathogens in a single reaction. However, this technology has not been universally adopted, particularly in low- and middle-income countries (LMICs). To understand experts' perceptions on the value of MBAs for integrated serosurveillance, and challenges to adoption and scale-up in LMICs, we conducted 20 semi-structured interviews with key informants working in LMICs and high-income countries (HICs) who were familiar with MBAs. These experts came from academia, funding agencies, implementing organizations, and the private sector. We recorded and transcribed the interviews and used inductive and deductive coding to support thematic analysis of the data. Although MBAs can serve as powerful tools for integrated serosurveillance and have demonstrated value in several settings, not all countries are well-positioned to adopt this technology. Some prioritize other investments, including those which could support the use of these assays in the future, like improvements to maintain stable electricity supplies and controlled laboratory environments. The immense amount of data that MBAs produce can be a double-edged sword as analytical bottlenecks can impede the use of data to guide public health responses. Amid these challenges, the LMICs which have been best prepared to adopt and scale the use of this technology are often those which possess comparably strong laboratory networks. Many of these countries have longstanding relationships with laboratories in HICs. Commercialization and standardization of some assays could support the adoption and expansion of this technology to other LMICs, but maintaining a country's ability to decide what they monitor is critical for establishing buy-in.

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DETECTION OF RECURRENT MALARIA BY IMPROVING THE ACCURACY OF UNIQUE PATIENT IDENTIFICATION WITH BIOMETRICS IN PAPUA, INDONESIA

Liony Fransisca[1], Reynold Rizal Ubra[2], Enny Kenangalem[1], Benedikt Ley[3], Ric N. Price[3], Nicholas M. Douglas[3], Jeanne Rini Poespoprodjo[1]

[1]Papuan Community Health and Development Foundation, Timika, Indonesia, [2]Mimika Regency Health Office, Timika, Indonesia, [3]Menzies School of Health Research, Charles Darwin University, Darwin, Australia

Detection of malaria recurrence requires unique identification of patients through multiple presentations to a health facility. This can be challenging in resource-limited settings. The impact of adding fingerprint identification to an existing physical "malaria card" identification system was assessed at two remote clinics in Papua, Indonesia. A three-stage approach was taken with one clinic serving as a control. In Stage 1 (3 months), standard patient identification practices using the malaria card system for malaria patients were observed at both clinics. In Stage 2 (6 months), fingerprint scanning using the Flexcode 4500™ system was added to standard patient identification procedures for suspected malaria patients at the intervention clinic. In Stage 3 (6 months) fingerprint scanning continued at the intervention clinic but with the addition of linkage to prior fingerprint registrations. At the intervention clinic, the proportion of malaria patients carrying a malaria card rose from 24.3% (467/1,925) in Stage 1 to 44.0% (3,566/8,103) in Stage 3 ($p<0.001$), compared to a more modest increase from 18.2% (397/2,187) to 25.1% (1,019/4,067, $p<0.001$) at the control clinic. Detection of duplicate (1 number assigned to multiple patients) or multiple (1 patient assigned multiple numbers) malaria card numbers increased from 0.3% (6/1,925) in Stage 1 to 4.1% (246/5,939) in Stage 2 with no corresponding increase at the control clinic. The proportion of repeat visit increased from 42.4% (816/1,925) in Stage 1 using standard patient identification practices, to 44.0% (2,612/5,939) in Stage 2 and 56.0% (4,556/8,103) in Stage 3 after adding fingerprinting to the patient verification process. In Stage 3, 99.8% of patients attending the intervention clinic could be definitively linked to a unique malaria card identification number versus 88.9% at the control clinic. Very few patients refused fingerprinting. The use of biometric fingerprinting was well-accepted and was associated with improved patient identification through multiple presentations to a healthcare facility.

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THE ROLE OF DIGITIZATION IN IMPROVING DATA QUALITY FOR ITN DISTRIBUTION CAMPAIGNS IN MALI

Boubacar Sidiki Maiga[1], Alassane Bangoura[1], Jean Yves Mukamba[2], Chrestien Yameni[3], Fatoumata Keita[1]

[1]Catholic Relief Services - CRS, Bamako, Mali, [2]Catholic Relief Services - CRS, Congo, Congo, Democratic Republic of the, [3]Catholic Relief Services - CRS, Dakar, Senegal

From 2011 to 2020, Mali made efforts to provide universal coverage of Insecticide-Treated Nets (ITN) through campaigns. The campaigns covered all regions an average of three times, except for the northern regions, which were not covered as much. However, these campaigns faced challenges such as poor data quality, complex stock management, uncovered areas, and long wait times for beneficiaries. NMCP is partnering with other organizations to digitize data for ITN distribution campaigns. The aim is to improve data quality and support evidence-based decisions. This study aims to compare the benefits of digitization using two different approaches. The ITN campaign was conducted in 29 health districts using digital means, while 17 health districts used non-digitized methods. All villages in the health areas were mapped and integrated into DHIS2 to allow for comprehensive analysis of ITN campaign data at all levels of the health system, including the distribution sites. ITN enumerators and distributors collected data at the community level using smartphones and unique QR code coupons in digitized areas. Non-digitized areas used paper collection and an Excel file as the database. However, data collection in non-digital

zones was slow and often riddled with errors. Digitization has highlighted the many challenges posed by traditional distribution methods. It also enabled us to identify non-covered areas and ensure household traceability for better decision-making. According to the report, out of the planned 10,878,186 ITNs, 10,673,108 ITNs have been distributed at an impressive rate of 99.26% for the 46 districts. This distribution rate represents 98.8% for the 29 digitized districts and 99.2% for the 17 non-digitized districts. Regarding household and population coverage rates, 2,067,913 households were served out of 2,106,140, meaning a household coverage rate of 98.17%. Additionally, 21,285,182 people were covered out of 22,048,413, resulting in a coverage rate of 97%. 638. In short, digitization optimizes net distribution and combined with recommended practices, effectively reinforces malaria prevention.

6899

SUCCESSFUL TASK SHIFTING: CROSS-SECTIONAL STUDY OF AN EMERGENCY OBSTETRIC CARE PROGRAM IN AN LMIC SETTING

Rita Thapa[1], **Abigail Knoble**[2], Suresh Tamang[1], Bal Sundar Chansi Shrestha[1], Arpana Kalaunee[1], Indra Rai[1], Bikash Shrestha[1], Pravin Paudel[1], Archana Amatya[1], Ruma Rajbhandari[2]

[1]Nick Simons Institute, Kathmandu, Nepal, [2]Mass General Birgham, Boston, MA, United States

Direct obstetric causes of maternal mortality still account for approximately 86% of all global maternal deaths, the majority of which are preventable. In Nepal, 12% of all deaths for women of reproductive age are due to preventable obstetric complications. However, the distribution of human resources (HR) and availability of healthcare workers capable of providing CSs in LMICs is a significant limiting factor to reducing MMR. To address this disparity the Advanced Skilled Birth Attendant (ASBA) task-shifting initiative was developed to train medical officers to perform Cesarean sections (CSs) to manage obstetric emergencies. Until now, there has been limited study of the program's efficacy. A survey targeting all 234 ASBA graduates resulted in 93 usable surveys. Additionally, 7 rural CEONC government hospitals with posted ASBAs were selected for 13 in-depth interviews and 6 focus group discussions with Operation Theater (OT) staff. Results were then triangulated. Immediately after the training, 92.7% of ASBA graduates reported performing CSs at their hospital with the majority (65.6%) continuing to perform CSs today. Of the ASBAs not performing CSs, 51.7% could be explained by the lack of a functional operating theater, underscoring the need for a holistic approach to clinical service provision. ASBAs were significantly more likely to be performing CSs if a family physician or another ASBA was present at their current hospital ($p < 0.001$; $p < 0.001$). Their work was perceived to increase the use of services by the community, facilitate a positive working environment, improve healthcare access, reduce referrals, and reduce the burden of CSs on any one staff member. Staff were motivated to provide CSs when they otherwise might not have been able to and perceived the hospital to be in better standing with the community. The ASBA program is a successful task-shifting initiative that reduces human resource shortages, expands the provision of CSs, and improves the working conditions in rural hospitals within the LMIC setting. The program should be continued to further increase access to CSs in rural hospitals with a functioning operating theater.

6900

COMMUNITY-BASED PARTICIPATORY INTERVENTION TO FIGHT DENGUE FEVER IN CÔTE D'IVOIRE

Véronique Koffi[1], Julien Zahouli[2], Carelle Brika[1], Larissa Angoua[3], Claver Adjobi[4], Pélagie Aboa[2], Sarah Ruel-Bergeron[5], Laura Vavassory[6], Giovanfrancesco Ferrari[7], Pie Müller[7]

[1]Centre Suisse de Recherches Scientifiques- Côte d'Ivoire, Abidjan, Côte D'Ivoire, [2]Centre d'Entomologie Médicale et Vétérinaire de l'Université Alassane Ouattara, Bouaké, Côte D'Ivoire, [3]univerty Felix Houphouet Boigny, Abidjan, Côte D'Ivoire, [4]Université Félix Houphouet-Boigny, Abidjan, Côte D'Ivoire, [5]ARCHIVE Global, Washington, WA, United States, [6]Swiss Tropical Institute of Tropical and Public Health Institute, Allschwill, Switzerland, [7]Swiss Tropical Institute of Tropical and Public Health Institute, Basel, Switzerland

Dengue fever is the most widespread mosquito-borne viral infection. Abidjan has a population of nearly 6 million, and Aedes breeding sites are ubiquitous. Given that people's knowledge, attitudes, practices and beliefs play an important role in the resurgence of mosquitoes, it is therefore important to carry out a community-based participatory intervention to sustain mosquito control actions, as mosquito control is essential for effective dengue prevention. Measure the population's knowledge, attitudes, practices and beliefs (KAPB) related to dengue fever in the Cocody-Bingerville health district. Probability sampling was used and a questionnaire survey was carried out among heads of households or their representatives in 40 clusters, with 11 households visited per cluster. Individual interviews were also conducted with community leaders. A participatory photovoice approach, as already implemented in the context of malaria vector control (Makungu et al., 2017) was used. The results showed that communities are not aware of dengue fever. Only 40% know about it. Those who have heard of it have little information about the disease. Admittedly, the populations do not strictly refute the thesis of the existence of a link between dengue fever and dengue fever. For an effective fight against dengue, we need to improve the population's knowledge of this emerging disease in our country.

6901

METHODOLOGICAL INSIGHTS FROM REFLEXIVE VIDEO ETHNOGRAPHY: A CASE STUDY OF LEPROSY PATIENTS IN MALAYSIA

Norana Abdul Rahman[1], Vaikunthan Rajaratnam[2]

[1]Athena Institute, Vrije University, Amsterdam, Netherlands, [2]Khoo Teck Puat Hospital, Yishun, Singapore, Singapore

This methodological review presents reflexive video ethnography (RVE) as a novel approach to exploring health-related social phenomena, illustrated through a case study of six leprosy patients in Malaysia. The study's core methodology integrates video ethnography with reflexive practices to capture and analyse the complex experiences of individuals affected by leprosy, living both within a leprosarium and in community settings. Our approach is distinguished by its emphasis on the participatory analysis of video data, facilitating deep engagement with the lived realities of participants. The research process was structured around three principal phases: extensive video documentation of participants' daily interactions and environments, reflexive review sessions involving researchers and participants, and a thematic analysis rooted in reflexive discussions. Ethical considerations were paramount, guiding the informed consent process and ensuring the confidentiality and dignity of all participants. This reflexive process enabled a contextual understanding of leprosy's social, emotional, and physical impacts, revealing insights into patient resilience, community integration, and the stigma associated with the disease. Our findings demonstrate the efficacy of RVE in uncovering the depth and breadth of patient experiences, emphasizing the methodology's capacity to elicit rich, participatory insights beyond traditional qualitative research methods. The case study of leprosy patients in Malaysia is a compelling example of RVE's potential to contribute to health sciences research, offering a comprehensive framework for researchers seeking to adopt a similar approach. This review argues for adopting RVE in the health sciences to enhance our understanding of patient experiences and inform the development of more empathetic and effective health interventions. By detailing the methodological execution and outcomes of our study, we aim to contribute to the broader discourse on qualitative research methodologies, advocating for reflexivity as a catalyst for methodological innovation and deeper social understanding.

6902

REASONS FOR NON-PARTICIPATION IN AZITHROMYCIN MASS DRUG ADMINISTRATION TO REDUCE MORTALITY AMONG CHILDREN 1-11 MONTHS OLD IN NIGER: A CROSS-SECTIONAL COVERAGE EVALUATION SURVEY

Carolyn Brandt[1], Ahmed M. Arzika[2], Ramatou Maliki[2], Alio Karamba[2], Nasser Galo[2], Naser Harouna[2], Diallo Beidi[2], Elodie Lebas[1], Brittany Peterson[1], Benjamin F. Arnold[1], Thomas M. Lietman[1], Kieran S. O'Brien[1]

[1]Francis I. Proctor Foundation, University of California, San Francisco, San Francisco, CA, United States, [2]Centre de Recherche et Interventions en Santé Publique, Birni N'Gaoure, Niger

The World Health Organization recommends biannual azithromycin mass drug administration (MDA) among infants aged 1-11 months to reduce mortality, following promising results of trials in Africa. However, with less resources than trials, coverage may decline during programmatic delivery, with the children missed likely at a higher risk of mortality. We aimed to understand reasons for participation and non-participation, how the intervention was received, and adverse events following azithromycin MDA in Niger by utilizing a coverage evaluation survey. In August 2023, trained community health workers delivered oral azithromycin MDA to children 1-11 months of age across 2,028 communities (42 integrated health centers [CSI]) in Tahoua, as a part of the AVENIR trial. Within 4 weeks of receiving the MDA, a separate data collection team conducted the survey. Separate mixed effects logistic regression models were used to analyze community-, household-, and child-level predictors associated with non-participation in azithromycin MDA, with random effects for community to account for clustering. A total of 3,848 households across 57 communities (7 randomly selected CSIs) were surveyed. Among children who were eligible for the distribution, 69% (n=721) received treatment based on caregiver self-report, compared to 92% community-health worker reported coverage. When asked why the treatment was not taken, the most frequently stated reasons were; not being in the age range (26.4%), someone not coming to the house (26.1%), absence (23.9%), and not receiving enough information (14.3%). In unadjusted models, factors that increased the odds of a child receiving treatment included being older (OR: 1.41, 95% CI: 1.33-1.49, p<0.0001) and receiving information about the program before (OR: 33.06, 95% CI: 21.82-50.07, p<0.0001, REF=did not receive information or do not know). Adverse events were reported among 6.5% of children who received treatment, and fever was the most reported symptom. Strengthening community preparation activities and understanding why younger children were less likely to be included may help to increase treatment coverage.

6903

TRENDS IN ANTENATAL CARE (ANC) CONTACTS AND EXCLUSIVE BREASTFEEDING IN SUB-SAHARAN AFRICA

Bolanle Olapeju[1], Michael Bride[2]

[1]Uniformed Services University of the Health Sciences, Bethesda, MD, United States, [2]Johns Hopkins University Center for Communication Programs, Baltimore, MD, United States

Exclusive breastfeeding is the safest and healthiest option for the first six months of life recommended by the World Health Organization (WHO), particularly in low resource settings. It is associated with reduced risk of malaria, diarrhea and other tropical health outcomes. The WHO 2016 ANC policy recommends at least eight (8+) ANC contacts during pregnancy and frequent antenatal care (ANC) contacts is correlated with exclusive breastfeeding. This study explores trends in breastfeeding practices in sub-Saharan Africa since the roll-out of the WHO 2016 ANC policy. A secondary analysis of data from 19 countries with available Demographic Health surveys from 2018 to date was performed. Key variables include exclusive breastfeeding, early initiation (within one hour of birth) of breastfeeding and number of ANC contacts (0-3, 4-7, 8+) in the most recent pregnancy in the two years prior to the survey. Exclusive breastfeeding ranged from 19% in Gabon to 81% in Rwanda (median=53%) while early initiation of breastfeeding ranged from 32% in Senegal to 85% in Rwanda (median=60%). Minimal women had 8+ ANC contacts, ranging from 0.3% in Rwanda to 39% in Ghana (median= 4%). The overall number of ANC contacts was positively associated with exclusive (AOR: 1.06, 95% CI: 1.05-1.08) and early initiation (AOR: 1.02, 95% CI: 1.01-1.03) of breastfeeding. However, women with 8+ ANC contacts were not more likely to exclusively or quickly initiate breastfeeding compared to women with 4-7 contacts. Study findings highlight the abysmally low rates of eight or more ANC contacts amidst a backdrop of suboptimal breastfeeding rates across sub-Saharan Africa. Findings also suggest a limited utility of eight compared to four ANC contacts and the WHO 2016 ANC policy in the context of exclusive and early breastfeeding. Behavior change efforts to improve the quantity of ANC contacts and complementary health service delivery interventions to improve the quality of ANC contacts are sorely needed and should remain a priority for sub-national and global stakeholders.

6904

ASSOCIATIONS BETWEEN IMMUNE STATUS AND CHILD DEVELOPMENT IN RURAL BANGLADESH

Sophia T. Tan[1], Andrew N. Mertens[2], Md. Ziaur Rahman[3], Fahmida Tofail Tofail[4], Helen O. Pitchik[2], Da Kyung Jung[2], Caitlin Hemlock[5], Benjamin F. Arnold[6], Lisa Hester[7], Mohammed Rabiul Karim[4], Sunny Shahriar[4], Shahjahan Ali[8], Abul K. Shoab[4], Md. Saheen Hossen[4], Palash Mutsuddi[4], Syeda L. Famida[4], Salma Akther[4], Mahbubur Rahman[4], Leanne Unicomb[4], Patricia Kariger[2], Alan E. Hubbard[2], Christine P. Stewart[9], John M. Colford Jr.[2], Stephen P. Luby[1], Firdaus S. Dhabhar[10], Lia C. H. Fernald[2], Audrie Lin[3]

[1]Division of Infectious Diseases and Geographic Medicine, Stanford University, Palo Alto, CA, United States, [2]School of Public Health, University of California, Berkeley, Berkeley, CA, United States, [3]Department of Microbiology and Environmental Toxicology, University of California, Santa Cruz, Santa Cruz, CA, United States, [4]International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [5]School of Public Health, University of Washington, Seattle, WA, United States, [6]Francis I. Proctor Foundation, University of California, San Francisco, San Francisco, CA, United States, [7]Department of Medicine, University of Maryland, Baltimore, MD, United States, [8]Colorado School of Public Health, University of Colorado, Denver, CO, United States, [9]Institute for Global Nutrition, University of California, Davis, Davis, CA, United States, [10]University of Miami, Miami, FL, United States

A healthy immune system will mount controlled inflammatory responses to physiological stressors. High levels of inflammation are known to disrupt memory and learning, which has detrimental implications for child development. Here, we conducted observational analyses on the association between immune status, including markers of protective, regulatory, and pathological responses, and development in the first two years of life among participants in the WASH Benefits trial. We used Cox proportional hazard models to assess differences in the rate of attainment of motor milestones at the 75th and 25th percentiles of exposure. We used generalized additive models to assess the relationships between immune markers and scaled development measures and reported the mean difference in predicted outcomes. We found that children with a larger concentration of Th1 cytokines relative to Th2 cytokines at 14 months were more likely to be crawling [Hazard ratio (HR) 1.15 95% CI (1.02, 1.29)] and standing alone [HR 1.19 (1.03, 1.39)] by 14 months. An increased ratio of Th1/Th2 was also predictive of improved development at 28 months, though these results were marginally significant. Previously, we reported on a high prevalence of intracellular pathogens at 14 months and evidence of chronic gut inflammation in the study population; elevated levels of Th1 cytokines, which respond to intracellular pathogens, may therefore reflect a robust protective immune response to the environment. In contrast, C-reactive protein (CRP) and alpha-1-acid glycoprotein (AGP), markers of systemic inflammation, were negatively associated with early development. CRP at 14 months was negatively associated with the number of motor milestones achieved by 14 months [-0.26 (-0.5, -0.02)]. AGP at 28 months was negatively associated with EASQ communication scores [-0.24 (-0.44, -0.04)] and the CDI expressive language score [-0.34 (-0.57, -0.11)] at 28 months. Our results suggest that in early life, regulated protective immune

responses may be key for healthy development, but development may be impaired by systemic inflammation and unregulated pathological immune response.

6905

CONTRIBUTION OF VACCINE PREVENTABLE DISEASES TO CHILD MORTALITY IN AFRICA AND ASIA - CHILD HEALTH AND MORTALITY PREVENTIONS SURVEILLANCE (CHAMPS)

Rosauro Varo[1], Ikechukwu U. Ogbuanu[2], Elisio Xerinda[3], Marcelino Garrine[3], Jaime Fanjul[1], Sara Ajanovic[1], David Torres-Fernández[1], Kyu Han Lee[4], Dianna Blau[4], Cynthia Whitney[4], Inácio Mandomando[3], Quique Bassat[1], Portia Mutevedzi[4]

[1]Barcelona Institute for Global Health, Barcelona, Spain, [2]Crown Agents in Sierra Leone, Freetown, Sierra Leone, [3]Manhiça Health Research Center, Manhiça, Mozambique, [4]Emory Global Health Institute, Emory University, Atlanta, GA, United States

Despite significant reductions in child mortality, children under five years of age remain disproportionately at-risk in Africa and Southern Asia. This is mainly attributed to uneven immunization, with over 30 million infections and 500,000 deaths annually estimated as due to vaccine-preventable diseases (VPD). We aimed to describe deaths attributed to VPDs using data from the Child Health And Mortality Prevention Surveillance network (CHAMPS). Cause of death determination was carried out through minimally invasive tissue sampling for microbiological and histopathological assessments, and determination of the chain of events leading to death using an expert panel at each CHAMPS site. During the study period, 6119 deaths had a COD determined through a DeCoDe panel on time for the analysis. Not considering stillbirths and neonates, 1459 deaths were counted: VPD deaths were responsible for 617 (42.28%) of deaths, of which 267 (18.3%) were included in the EPI schedules (*VPD-EPI* deaths: diphtheria, hepatitis B, Haemophilus influenzae type B infection (Hib), measles, whooping cough or pertussis, pneumococcal disease (PND), poliomyelitis, rotavirus diarrhea (Rota), rubella, tetanus or tuberculosis); and 350 (23.9%) were not (*VPD-non-EPI* deaths). Considering VPD-EPI deaths, the main etiology in was PND, being present in around 4 out 5 of deaths; followed by Rota (10%) and Tuberculosis (6.7%). Malaria accounted for vast majority of *VPD-non-EPI* deaths (90.6%). The second leading cause was Influenza and there were also cases reported of cholera, meningococcal meningitis, COVID-19, and rabies. A number of deaths presented with more than one VPD, and both, *VPD-EPI* and *VPD-non-EPI*, also presented with other pathologies in the casual chain. Malnutrition was especially important but also infectious diseases like HIV, LRTIs, malaria and sepsis. Updating the documented role of VPD's through postmortem sampling information on the subject is a strong and reliable tool to monitor vaccine delivery and uptake and surveillance of VPD remains crucial to improve vaccination programs and reduce child mortality due to VPDs.

6906

ENHANCING DATA AVAILABILITY AND QUALITY WITH AN EASY-TO-USE TOOL DURING THE LOGISTICS MANAGEMENT INFORMATION SYSTEM REFORM IN MADAGASCAR, 2022-2023

Maherison Jaona Andrianaivoravelona

PSI - Madagascar/ Impact, Antananarivo, Madagascar

The logistics management information system (LMIS) in Madagascar faced significant challenges for years, including low reporting rates, poor data quality, and lack of data visualization. To address these issues, the Ministry of Public Health (MOPH) decided to replace the offline national LMIS software (CHANNEL) with the online and open-source system, OpenLMIS, but this has been extensively delayed. During the wait, a reliable data tool was needed to maintain data quality and reporting. In October 2022, the PMI-funded Improving Market Partnerships and Access to Commodities Together (IMPACT) program supported the MoPH to develop e-LMIS (an Excel-based web, easy-to-use tool) and deploy it in all 115 districts beginning in January 2023. IMPACT conducted quarterly supportive supervision visits and routine data quality assessments (RDQA) at district pharmacies with reports from January to December 2022 for CHANNEL and January to December 2023 for e-LMIS. RDQA data were used to evaluate changes in quality of data on malaria commodities during the transition from CHANNEL to e-LMIS, comparing results from the 78 supported pharmacies in 2022 and 2023; we focused on completeness, timeliness, and accuracy. For malaria commodities, of 936 reports expected each year, 847 (90%) were submitted in 2022 and 907 (97%) in 2023 ($p<0.001$). In the same period, the on-time reporting rate increased from 579 (68%) of the 847 reports received in 2022 to 807 (89%) of 907 reports received in 2023 ($p<0.001$). Accuracy scores for three malaria products (rapid diagnostic tests and artemisinin-based combination therapy [1- to 5-year-old formulation and adult formulation] were 80% in 2022 and 96% in 2023.The use of e-LMIS tool was helpful and will continue to be used while awaiting deployment of Open-LMIS to generate quality data for commodity quantification, supply planning, and optimize availability of malaria commodities where and when needed.

6907

INTEGRATED DISEASE SURVEILLANCE AND RESPONSE SYSTEM: NEED FOR LABORATORY CONFIRMATION OF CASES IN BONO REGION, GHANA

Samara Ansata Mohammed[1], Kofi Amoh Kodie[1], Prince Quarshie[1], Jane Addae Kyereme[1], Bernice Konadu[1], George Asare Tarbi[1], Emmanuel Bachan[1], Joshua Asare[1], Daniel Konka[2], Dennis Adu-Gyasi[3]

[1]Ghana Health Service, Sunyani, Ghana, [2]Ghana Health Service - Sunyani West Municipality, Sunyani West, Ghana, [3]Kintampo Health Research Centre and University of Energy and Natural Resources, Kintampo North, Ghana

The Bono Regional Health Directorate with focus on one health, uses the various programs in the surveillance systems adopted by Ghana to identify and contain disease outbreaks and pandemics. Laboratory confirmation of identified cases is key in control and preventive measures in IDSR. We undertook a review of the IDSR records in the Bono Region to assess laboratory infrastructure necessary for commonly identified pathogens. This review of IDSR data from 2015-2024 in the Bono Region of Ghana considers weekly IDSR summaries from the District Health Information Management System (DHIMS2). The summaries include cases of diseases, recorded deaths from the diseases and the number of the cases that are confirmed by the laboratory, collated from the respective health system units and uploaded by public health officers. The data was organized and analyzed basically with Microsoft Excel version 2020. Permission for use of the data was sought from the Regional Director of Health Service. The diseases that were highlighted in the surveillance with laboratory confirmation were acute watery diarrhoea, cholera, COVID-19, diarrhoea by shigella, Measles, Meningococcal meningitis, Rabies, and Yellow Fever. With the exception of Rabies that had 100% of identified cases being confirmed by the laboratory in 2018, and Cholera with 90% in 2015, none of the cases identified for all the diseases had more than 25% laboratory confirmation. Even though Meningococcal meningitis consistently had some of the identified cases confirmed by the laboratory from 2015 to 2024, it was only in 2024 that a highest of 21% of the cases recorded was confirmed in the Bono Region. Considering COVID-19, less than 20% of the cases were confirmed by the laboratory.Laboratory confirmation of diseases earmarked for surveillance is low in the Bono Region of Ghana. Availability and access to laboratory facilities play critical role in laboratory confirmation. Adequate logistics and laboratory consumables hinder the ability of the health systems to confirm identified cases. Laboratory facilities are required foundations for effective IDSR implementation.

6908

RECURRENT ADMISSIONS AND MORTALITY RATE IN CHILDREN LESS THAN TWO YEARS OLD IN RURAL GAMBIAN SETTING

Abdoullah Nyassi, Isaac Osei, Yekini A. Olatunji, Golam Sarwar, Grant Mackenzie

Medical Research Council Unit The Gambia at London School of Hygiene & Tropical Medicine, Fajara, Gambia

Diseases resulting from hospital admission contribute to a significant clinical and economic burden globally. Some of these are reported to be recurring. Recurrent hospital admissions may have negative developmental effects, particularly in chronically ill children. The cost of hospitalization for serious medical problems can be up to 60 times higher than that of a mild or moderate condition managed by primary care services. In the Gambia, the direct cost of inpatient admission is $9.19, and indirect costs are $4.07 per visit. There have been no studies that looked at longitudinal data to provide more insight into readmission and death in a rural sub-Saharan environment. This calls for action to better understand and, therefore, contribute to the design of interventions to reduce recurrent admissions in young infants. We assessed the proportion of children less than 2 years of age readmitted, predictors associated with readmission, and the incidence of mortality in health facilities within the Basse Health and Demographic Surveillance System (BHDSS). A retrospective analysis of admitted patients that are less than 2 years of age with medical problems as the principal diagnosis at health facilities in BHDSS between January 2011 and December 2017 was performed. We calculated risk-standardized mortality rates at the first admission, risk-standardized readmission rates, and in-hospital mortality at 30 days, 90 days, and 2 years of readmission by using a multivariate mixed model. We included 4773 patients admitted with medical problems. The mean age was 7.6±5.5 months, and 56.9% were male. A total of 588 (12.3%) experienced at least a single episode of readmission. The number of readmissions for 30 days, 90 days, and 2 years is 103 (17.5%), 170 (28.9%), and 15 (53.6%). In-hospital mortality during the readmission episode was 128 (2.7%) throughout the years of follow-up. Readmissions are a significant contributor to the burden on the healthcare system, and early detection of patients who are at risk can help launch efficient interventions that lower costs and boost the standard of care.

6909

UTILIZING GEOSPATIAL DATA FOR TARGETED ADVOCACY TO ENHANCE MINIMALLY INVASIVE TISSUE SAMPLING (MITS) COLLECTION FOR CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS) IN PAKISTAN

Hannah Melchinger[1], Sameer Belgaumi[1], Nazia Ahsan[2], Raheel Allana[2], Fauzia Malik[1], Saad B. Omer[1], Momin Kazi[2]

[1]Peter O'Donnell Jr. School of Public Health, UT Southwestern, Dallas, TX, United States, [2]Aga Khan University, Karachi, Pakistan

The Child Health and Mortality Prevention Surveillance (CHAMPS) project is focused on understanding and preventing child mortality through comprehensive data collection, including post-mortem minimally invasive tissue sampling (MITS). However, MITS can be challenging to perform in resource-constrained settings with limited community engagement. Geographic Information Systems (GIS) offers the opportunity to improve MITS collection by informing targeted CHAMPS advocacy, which can increase the number of death alerts received from the community and improve awareness and acceptability of MITS within the catchment area. In Pakistan CHAMPS, we started by collecting and cleaning data on child mortality rates, healthcare facilities, and MITS collection sites. We then analyzed this data using GIS techniques to identify hotspots of child mortality: these areas were then targeted for increased MITS collection and optimized resource allocation. The integration of geospatial data is crucial to creating an accurate picture of community needs: we combined population demographics, healthcare accessibility, and environmental factors onto one database. Preliminary findings from GIS data revealed a direct correlation between increased advocacy efforts and an increased number of death alerts, thereby improving potential effectiveness of MITS. Furthermore, targeting areas of high mortality with decreased MITS consent allowed us to make our advocacy and MITS efforts more effective overall. By mapping areas with lower advocacy coverage, we identified gaps in community engagement and targeted these areas with intensified advocacy campaigns to improve child mortality surveillance. GIS-driven targeted advocacy has revolutionized MITS collection in Pakistan, bridging gaps in community engagement and maximizing study impact. This innovative approach highlights the power of data-driven strategies to enhance public health interventions.

6910

PERCEPTIONS TO AND DECISION-MAKING DYNAMICS OF ANTENATAL CARE DURING PREGNANCY: A QUALITATIVE EXPLORATION IN RURAL BANGLADESH

Shahana Parveen[1], Dalia Yeasmin[1], Farhana Hasnat Khan[1], Syead Tamim Mahmud[1], Faruqe Hussain[1], Shams El Arifeen[1], Mohammad Zahid Hossain[1], Emily S. Gurley[2]

[1]icddr,b, Dhaka, Bangladesh, [2]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States

Antenatal care (ANC) visits can identify pregnancy complications and promote optimal birth outcomes. The Child Health and Mortality Prevention Surveillance project in Bangladesh, uses minimally invasive tissue sampling (MITS) to determine the cause of death for stillbirths and deaths of children aged <5 years. Among the deaths enrolled in MITS, 94% were perinatal deaths and perinatal asphyxia was the leading cause of these deaths. In the catchment area rural Baliakandi, 90% of women received at least one ANC, but care was often sought late and from non-qualified providers. We explored the pregnant women's ANC perceptions and practices, aiming to design a culturally credible intervention to increase the uptake of timely and quality ANC. We interviewed 41 women between May and October 2022, who experienced a child loss and a subsequent pregnancy with a birth outcome to understand if any changes in ANC practices between their first and second pregnancy. Women perceived pregnancy is a normal physiological phenomenon in a woman's life and 46% believed that ANC is only required if they experienced a complication. Thirty-seven percent said that they should visit a qualified physician for an ultrasonogram between 5-7 months of the pregnancy to identify the sex, health condition and position of the fetus, so their family could plan for a home delivery if no complications were found. Fifty-three percent of women did not receive any ANC during the pregnancy where the child died, but did receive one to three ANC during the subsequent pregnancy; they stated that the child loss increased their interest in ANC. However, only 7% of these women met the guideline for at least 4 ANC visits in their subsequent pregnancy and were unaware about possible danger signs. Unfortunately, 23% of the women experienced a miscarriage or early neonatal death during their subsequently pregnancy. The existing practices of not seeking timely and quality ANC suggested the gap between perceived risks during pregnancy and required action points. Counseling women and families for quality ANC, outcome of the danger signs and ensuring quality care could promote care seeking during pregnancy.

6911

HOW SUPPLY CHAIN SHAPES LABORATORY PERFORMANCE IN SEROSURVEILLANCE BEFORE, DURING, AFTER COVID-19

Shahjahan Ali[1], Ibrahim Swaray[2], Wilhelmina Strasheim[3], Daniel Mumba[4], Oscar Kai[5], May Chu[1]

[1]Colorado School of Public Health, Aurora, CO, United States, [2]Centre for Global Health Research, Toronto, ON, Canada, [3]National Institute for Communicable Diseases, Johannesburg, South Africa, [4]Malawi Liverpool Wellcome Programme, Blantyre, Malawi, [5]Kenya Medical Research Institute, Kilifi, Kenya

The importance of the supply chain (SC) in effectively supporting laboratory-based serosurveillance is often overlooked. We identified the

SC pain points before, during, and after the COVID-19 pandemic to extract lessons learned for Sierra Leone, Kenya, Malawi, South Africa and beyond. SC bottlenecks contributed to months- and even year-long delays in receiving deliveries resulting in low efficiency/higher costs and impacted evidence-based decisions. We used a mixed-methods approach, reviewed 52 papers (published 2006-2023), conducted 12 interviews and surveyed 8 key SC principals: researchers/staff, manufacturers, and SC professionals. Transcribed data were coded using inductive and emergent coding methods then analyzed by narrative synthesis and thematic analytic processes. Sites (75%), before COVID-19, dealt with delayed and incomplete shipments and deliveries, did not have procurement planning/ forecasting capabilities, lacked SC resource allocation, lacked inventory management systems and transportation logistics. During COVID-19, all SCs were severely disrupted: non-alignment of customs procedures and regulations between countries, disrupted shipping and inconsistent cold-chain handling instructions added to the challenges suppliers and users had to navigate. After COVID-19 customs-related issues improved for half of the sites with differing issues that will require both general and context-specific solutions. Many researchers tell us that they find "off-book" SC alternatives to ease their pain points. We will discuss the potential solutions tailored to fix infrastructural and systematic needs: adopting model regulations, personnel SC training, inventory management, one-stop serosurveillance bundles and fostering collaboration among stakeholders. During and post-COVID-19, the SC for genomics has paved a way for solutions by bundling purchases and improved logistics processes that have not been reflected for serosurveillance activities. These efforts should be better coordinated and funded. Innovations in product design and one-stop bundle packaging could ameliorate key barriers.

6912

ASSESSING THE QUALITY OF CARE PROVIDED TO WOMEN ATTENDING ANTENATAL CLINIC IN SIAYA COUNTY WESTERN KENYA

Kizito O. Obiet[1], Wycliffe Odongo[2], Fredrick Omiti[1], Brian Seda[1], Victoria Seffren[2], Feiko O. ter Kuile[3], Sarah G. Staedke[4], Jonathan Schultz Schultz[5], Simon Kariuki[1], Julie Gutman[2]

[1]Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya, [2]Malaria Branch, Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, United States, [3]Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [4]Department of Vector Biology, Liverpool School of Tropical Medicine, Kisumu, Kenya, [5]4Malaria Branch, Division of Parasitic Diseases and Malaria, US Centers for Disease Control and Prevention, Kisumu, Kenya

In Kenya, up to 52% of women do not reach the minimum 8 antenatal care (ANC) visits recommended by the Ministry of Health (MOH). While ANC plays a crucial role in the well-being of both mother and child from pregnancy through postpartum, the quality of care (QoC) can vary significantly across healthcare settings, impacting maternal and neonatal outcomes. To evaluate this, we assessed the QoC of ANC in Siaya County, western Kenya. Women aged 13-49 attending any ANC visit from Aug-Oct 2023 in 7 health facilities (HF); level 2 (n=4), 3 (n=2), and 5 (n=1) participating in a scannable maternal and child health (MCH) handbook feasibility pilot were included. Each woman was issued a scannable handbook and followed for six months. If women were enrolled after the first ANC visit, data from previous visits were copied into the scannable book. Data on services, including physical examination, ANC profile, ultrasound, and intermittent preventive treatment (IPTp) of malaria, were electronically abstracted. QoC was evaluated using 19 MOH recommended services, 11 of which were scored per pregnancy (once), while 8 were scored at every routine ANC visit; scores >75% were considered high quality, 50-74% moderate, <50% low. 567 women participated in the pilot. Most underwent both physical exam and ANC profile tests 97%(n=549), but fewer received deworming (36%) or ultrasound (12%) at any visit. The average QoC score per the national guideline was 71.9% (SD=7.6). Most women received moderate (64%) or high (34%) quality care. Primigravida women (aOR=0.6, 95%CI=-0.9-0,01, p=0.03) and those attending HF level 3 or higher (vs level 2) (aOR=0.5, 95%CI=-1.1-0.3, p=0.002) were less likely to receive higher QoC. While the average QoC score was moderate, indicating a reasonable adherence to MOH guidelines, there is need to ensure the highest standard of care for all women. The relationship between gravidity and HF level and QoC suggests the need for targeted efforts to improve ANC service quality. Using a scannable handbook to track women longitudinally across facilities provides a robust framework for assessing and potentially improving ANC quality over time.

6913

COMMUNITY-BASED ASSESSMENT OF SOCIAL BEHAVIOR AND INTERACTION PATTERNS USING WEARABLE PROXIMITY SENSORS AND CONTACT DIARIES IN PAKISTAN: A QUALITATIVE STUDY

Noureen Ahmed[1], Hannah Melchinger[1], Nazia Ahsan[2], Raheel Allana[2], Tehreem Maqsood[2], Najeeb ur Rehman[2], Benjamin A. Lopman[3], Saad B. Omer[1], Fauzia A. Malik[1], Abdul Momin Kazi[2]

[1]Peter O'Donnell Jr. School of Public Health at UT Southwestern Medical Center, Dallas, TX, United States, [2]Aga Khan University, Karachi, Pakistan, [3]Rollins School of Public Health, Emory University, Atlanta, GA, United States

In Pakistan, cultural norms, and community dynamics - including complex social hierarchies, traditional practices, and close-knit family structures - play a crucial role in shaping contact behaviors. Moreover, there are significant differences in contact behaviors between urban and rural areas due to varying lifestyles, population densities, and access to resources. Exploring a community's structure through innovative and direct methods can provide valuable insights. We completed a qualitative study in Karachi, Pakistan, to understand the social dynamics in urban vs. rural areas and assess the feasibility and acceptability of tracking community social interactions through contact diaries and proximity sensors. We conducted 24 focus group discussions (12 rural/ 12 urban) and 36 cognitive interviews (17 rural/ 19 urban) and analyzed data using thematic analysis. In analysis, key themes emerged, including gender preference, pre-appointment permission, and privacy concerns related to the documentation of daily interactions. Both urban and rural participants considered contact diaries to be important tools for interaction documentation, while rural participants emphasized the need to record interactions within extended families due to shared living spaces, the urban participants highlighted the need to document diverse interactions with individuals both within and outside of the household. The community overall identified the proximity sensors as new and unfamiliar. The urban participants were particularly concerned about privacy when wearing the sensors, while rural participants were concerned about wearability. Potential solutions brainstormed with the community included using Ajrak (Sindhi block-print fabric) pouches for rural wearers, blue pouches for urban adults, and T-shirts with concealed pockets for urban children. These results gave valuable insight into how cultural factors impact the acceptability of contact tracking tools. These findings laid the groundwork for successful implementation of a social behavior study in both rural and urban settings of low- and middle-income countries.

6914

ENGAGING PRIVATE PROVIDERS FOR ROUTINE IMMUNIZATION (RI) -INTEGRATED HEALTH SERVICES IN URBAN SLUMS OF HIGH-RISK UNION COUNCILS IN KARACHI, PAKISTAN

Zahid A. Memon[1], Shifa Habib[1], Ammarah Ali[1], Ahsanullah Bhurgri[2], Shehla Zaidi[3]

[1]Aga Khan University, Karachi, Pakistan, [2]Technical Focal Person, Karachi, Pakistan, [3]University College of London, London, United Kingdom

Fully Immunized Children coverage is low (39%-48%) in Karachi's high risk urban areas due to sparse government health infrastructure and lack of engagement of private sector in providing preventive health services. An implementation research project to integrate RI and nutrition counseling, screening, and management through private sector health care providers

in collaboration with the Expanded Program of Immunization, Department of Health, Sindh, and the Aga Khan University is underway in 8 high risk urban areas of Karachi. Through private provider engagement model, RI-integrated health service corners have been established at 18 private clinics enrolled on criteria including registration with the health care commission, lack of public health facility in the geographical proximity, adequate maternal deliveries or child OPD volumes and agreement for no charging policy for immunization. The child friendly corners have been supplemented with two vaccinators and one female counselor to provide vaccination, nutrition screening, and counseling (nutrition, breastfeeding, balanced diet, and WASH) services at no service charge. The project uses an innovative social mobilization and digital communication approach for community awareness and engagement, ensuring active participation through social gatherings planned in collaboration with local community influencers. We present retrospective data collected from the Sindh Electronic Immunization Registry for percentage coverage against quarterly 0-11 month vaccination target for 2023 at the 18 private immunization centers. Continuous improvement in vaccination coverage was seen, exceeding targets in Q4 of 2023. The coverage of Penta-1 improved from 74% in Q1 to 108% in Q4 of 2023. Similarly, Penta-2 increased from 64% to 98% , Penta-3 went from 70% to 105%, while IPV-1 rose from 74% to 104%. The MR-1 increased from 47% to 83% in the Q4 of 2023. BCG's trend was similar, increasing from 56% to 86% in Q4 of 2023. Private sector involvement is crucial for addressing immunization gaps and the inequities developed due to inaccessibility to government health infrastructure and services.

6915

UNDERSTANDING COMMUNITY PERSPECTIVES AND DECISION MAKING TO INFORM CHILD MORTALITY SURVEILLANCE AND MINIMALLY INVASIVE TISSUE SAMPLING (MITS) STRATEGIES IN KARACHI PAKISTAN: ESTABLISHING A NEW SITE

Nazia Ahsan[1], Shaheen Sarfraz Sarfraz[1], Sameer Mohiuddin Belgaumi[2], Hannah Melchinger[3], Saima Jamal[1], Sania Ali[1], Saad Bin Omer[3], A Momin Kazi[1], Fauzia A. Malik[3]

[1]Aga Khan University, Karachi, Pakistan, [2]UT South western, Dallas, TX, United States, [3]UT Southwestern, Dallas, TX, United States

Under-five child mortality is of major concern in Pakistan.[1] The CHAMPS Network collects data globally to understand these deaths using minimally invasive tissue sampling (MITS). A CHAMPS site in Karachi, Pakistan, presents the opportunity to understand regional causes of child mortality, but MITS in this setting can be challenging without a culturally nuanced approach. To assess CHAMPS implementation feasibility, we conducted a five-month-long qualitative investigation with community leaders and members. This included eight focus group discussions, 43 in-depth interviews in three low-income peri-urban communities with diverse categories of stakeholders. Major themes were derived from coded data to identify patterns and were analyzed using thematic analysis framework. We examined study acceptability, practicality, and ease of implementation. Most perspectives aligned with study goals: primary motivators of acceptance included understanding cause of death and a desire to prevent future deaths. Grief counseling was supported as an additional incentive for participation. Challenges to acceptability included worry about MITS invasiveness and discomfort a child's spirit might feel during MITS; belief that death is predetermined, and therefore cause of death is irrelevant; and social pressure during consent. Logistical challenges included the narrow window between death and ritual bathing/shrouding during which samples can be collected. Considering this, we implemented key strategies to improve study feasibility. These include strong community and religious advocacy to increase awareness and reduce stigma of participation; a robust network of key informants to encourage early death alerts for timely MITS sample collection; using a MITS van to assist families with rituals after conducting post-mortem sampling; and strengthening relationships between staff and community through transparency, targeted advocacy, and communication in local languages. These strategies have helped improve community acceptance, enhance community-based mortality surveillance, and successfully implement MITS in Pakistan.

6916

HEALTHCARE SEEKING BEHAVIOR AND DISEASE PERCEPTION ASSOCIATED WITH CHOLERA AND DIARRHEAL ILLNESSES AMONG POPULATIONS IN CHOLERA ENDEMIC REGIONS IN NAMPULA PROVINCE, MOZAMBIQUE

Yeonji Jeon[1], Liliana Dengo Baloi[2], Saemna Park[1], Sofião Manjor[2], Hyoryoung Lee[1], Ju Yeon Park[1], Geun Hyeog Jang[1], Young Ae You[1], Deok Ryun Kim[1], Nelmo Manjate[2], Aurea Tovele[2], Madalena Zacarias[3], Jamilo Chabane[3], Américo Barata[3], Julia Lynch[1], José Paulo Langa[2], Se Eun Park[1]

[1]International Vaccine Institute, Seoul, Korea, Republic of, [2]National Institute of Health, Maputo, Mozambique, [3]Provincial Delegation, National Institute of Health, Nampula, Mozambique

Healthcare seeking behavior and knowledge on cholera and diarrheal diseases in local populations influence disease control and prevention strategies. During November 10-19, 2023, we conducted a cross-sectional household survey in Nampula province, one of the most cholera affected regions in Mozambique. Households were selected using a two-stage cluster random sampling in cholera endemic and high priority hotspots in Nampula city and Meconta and Monapo districts of the province. A total of 838 households participated in the survey using tablet-based data collection and Electronic Data Capturing (EDC) system (REDCap). Age-group stratified healthcare seeking behavior associated with cholera and diarrheal diseases are being analyzed, which will support tailored community engagement for cholera control and serve as an adjustment factor in cholera incidence estimation. Accessibility to healthcare facilities by local populations is investigated by looking into various types of healthcare options near household, mode of transportation, travel distance, travel time, and travel cost to visit healthcare facilities. Socio-economic and demographic factors such as wealth and education level of household heads and history of symptoms related to acute watery diarrhea are analyzed to explore the potential association with healthcare seeking behavior for cholera and diarrheal diseases. Vaccination history of household members in each surveyed household and the community perception towards the oral cholera vaccine are being analyzed. These analyses will be ready for presentation at the upcoming ASTMH conference. Our study findings will fill the basic knowledge gap on the population-level risk factors associated with cholera, contributing to formulating more practical and appropriate community interventions to better control and prevention the disease in areas affected by periodic and persistent cholera epidemics.

6917

PROGNOSTIC PREDICTION MODELS FOR ADVERSE BIRTH OUTCOMES: A SYSTEMATIC REVIEW

Achenef Asmamaw Muche[1], Yifru B. Mitke[2], Likelesh L. Baruda[3], Clara Pons-Duran[4], Bezawit M. Hunegnaw[2], Kassahun A. Gelaye[1], Alemayehu W. Yalew[5], Sebastien Haneuse[4], Lisanu Taddesse[6], Delayehu Bekele[2], Grace J. Chan[4]

[1]University of Gondar, Gondar, Ethiopia, [2]Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia, [3], Federal Ministry of Health, Addis Ababa, Ethiopia, [4]Harvard T.H. Chan School of Public Health, Boston, MA, United States, [5]Addis Ababa University, Addis Ababa, Ethiopia, [6]HaSET Maternal and Child Health Research Program, Addis Ababa, Ethiopia

Despite progress in reducing maternal and child mortality globally, adverse birth outcomes have been observed to be disproportionately high in low- and middle-income countries (LMICs). Developing and validating a prediction model for adverse birth outcomes allows for early risk detection and prevention strategies. This systematic review aimed to assess the performance of existing prediction models for adverse birth outcomes and provide a comprehensive summary report of their findings. We used the Population, Index prediction model, Comparator, Outcome, Timing, and Setting (PICOTS) approach to retrieve studies PubMed/MEDLINE, Scopus, CINAHL, Web of Science, AJOL, EMBASE, and the Cochrane library.

We searched for grey literature using WorldCat, Google, and/or Google Scholar. Data were extracted using the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS), and analyzed for risk using the Prediction model Risk of Bias Assessment Tool (PROBAST). We descriptively reported results in tables and graphs**.** We included 115 prediction models: composite adverse birth outcomes (6), low birth weight (17), small for gestational age (23), preterm birth (71), and stillbirth (9). Maternal clinical and medical characteristics were the most widely used prognostic factors for preterm and low birth weight prediction, while uterine artery pulsatility index was used for stillbirth and small for gestational age prediction. The discrimination performance of preterm birth prediction ranged from an area under the curve of 0.51 to 0.83. Only 6% of the models reported model calibration. Current adverse birth outcome prediction models have poor to very good discrimination performance, but most did not report calibration performance. Inconsistent prognostic factors were included for each adverse birth outcome prediction. Prediction models with consistent prognostic factors that warrant external validation should be accessible to practitioners.

6918

UNDERLYING CONDITIONS AND CONTRIBUTORS OF PERINATAL ASPHYXIA AMONG STILLBIRTHS AND EARLY NEONATAL DEATHS ENROLLED IN THE CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS), WESTERN KENYA, 2017 TO 2022

Joyce Akinyi Were[1], Richard Omore[1], Aggrey Igunza[1], Dickson Gethi[1], Harun Owuor[1], Kephas Otieno[1], Edwin Kiplagat[1], Fredrick Onduru[1], Broline Asuma Sagini[1], Beth Tippett Barr[1], Victor Akelo[2]
[1]Kenya Medical Research Institute, Kisumu, Kenya, [2]Liverpool School Of Tropical Medicine, London, United Kingdom

Perinatal asphyxia (PA) describes neonatal encephalopathy resulting from severe oxygen deprivation during childbirth, largely due to pre-existing maternal or fetal conditions and events around labor and delivery. We describe conditions and contributors of PA among stillbirths and early neonatal deaths enrolled in the Kenya Child Health and Mortality Prevention Surveillance (CHAMPS). CHAMPS investigates causes of death (CoD) in children under-five years (U5) in defined catchment areas in 9 countries in Sub-Saharan Africa and South Asia. CoDs are determined by an expert panel using data from post-mortem minimally invasive tissue specimen testing, child and maternal clinical records, and verbal autopsy. Designated immediate, intervening, and underlying conditions are considered to be in the causal chain (CA) leading to death. Between 2017 and 2022, CHAMPS-Kenya enrolled 911 U5 deaths, of which 27.9%(254) were stillbirths and 25.0%(228) early neonates. Two thirds (64.1%) of the stillbirth and <7-day decedents had PA in the CA; 304 (63.1%) as underlying CoD and 5(1.0%) as immediate CoD. Nearly all deaths (296,95.8%) occurred in a health facility. The 5 cases with PA as immediate CoD all had other underlying conditions that likely increased the risk of asphyxia. Underlying maternal conditions were identified in most asphyxia deaths (264,85.4%), including hypertension (61,23.1%), HIV (57,21.6%), antepartum hemorrhage (39,14.8%), multiple pregnancy (27,10.2%), chorioamnionitis (27,9.5%), anemia (21,8.0%) and malaria (14,5.3%). Nearly all deaths (302,97.7%) were determined to be preventable and recommended public health actions to the deaths included improvement in obstetric care and management (34.6%), infection prevention and control (31.3%), maternal health education (21.1%) and emergency transportation (17.8%). HIV disease, hypertensive disorders and antepartum hemorrhage accounted for >65% of all maternal conditions underlying PA. A high index of clinical suspicion with appropriate antenatal and labor management should be encouraged to aid in diagnosis and management of high-risk pregnancies likely to result in PA

6919

SOCIO-DEMOGRAPHIC AND OBSTETRIC RISK FACTORS ASSOCIATED WITH LATE INITIATION OF ANTENATAL CARE (ANC) IN RURAL BANGLADESH: FINDINGS FROM THE CHAMPS PROJECT

Taukir Tanjim[1], Shovo Debnath[1], Emily S. Gurley[2], Kazi Munisul Islam[1], Rajib Biswas[1], Maria Rahman Mim[1], Qazi Sadeq-ur Rahman[1], Md. Abdus Salam[1], Md. Atique Iqbal Chowdhury[1], Sanwarul Bari[1], Shams El Arifeen[1], Mohammad Zahid Hossain[1]
[1]International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [2]Johns Hopkins University, Baltimore, MD, United States

Antenatal care (ANC) is important for ensuring optimal pregnancy outcomes by detecting and managing pregnancy complications. Late initiation of ANC, defined as receiving the first ANC visit after 12 weeks of gestation, can have major adverse impacts on maternal and child health. To improve timely ANC utilization in rural Bangladesh, we aimed to identify the socio-demographic and obstetric risk factors associated with delayed ANC initiation. Child Health and Mortality Prevention Surveillance (CHAMPS) has been conducting pregnancy surveillance in Baliakandi, a rural sub-district of Bangladesh, monitoring each pregnancy, including antenatal care utilization. A cross-sectional study was conducted among women from Baliakandi who were pregnant in 2022 and received at least one ANC visit. The association between socio-demographic and obstetric characteristics and late ANC initiation was analyzed using multivariate logistic regression. Out of 7085 pregnancy events, in 2317 pregnancies, mothers did not take any ANC. A total of 4768 pregnancies with ≥1 ANC were recorded; ANC was delayed in 44% (n=2081) of these cases. Women who received delayed ANC were younger in age compared to women who sought ANC on time (37% were aged ≤20 years, compared to 34.5%). In our study population, 81% of the mothers had educational attainment only up to 10 years. Women who sought care on time were more educated than those who initiated ANC late (24% vs 13% with more than 10 years of education). In multivariate logistic regression, age ≤20 years (adjusted odd ratio [aOR]: 1.79, 95% CI: 1.36-2.36), maternal education ≤10 years (aOR: 1.40, 95% CI: 1.13-1.73), and spousal education ≤10 years (aOR: 1.41, 95% CI: 1.17-1.71) were significantly associated with delayed ANC initiation. With each living child, the risk of late initiation of ANC was increased (aOR: 1.40, 95% CI: 1.26-1.55). Whereas a history of miscarriage (aOR: 0.75, 95% CI: 0.63-0.90) showed higher chances of timely ANC. Our study suggests that younger women with lower levels of education tend to receive their first ANC later. Interventions designed to target this group may help minimize the gap.

6920

IMPACT OF TWO-DOSE ORAL CHOLERA VACCINE IN CHOLERA ENDEMIC AND HIGH PRIORITY HOTSPOT IN CUAMBA DISTRICT IN CONTEXT OF THE 2023 CHOLERA OUTBREAK IN MOZAMBIQUE: FIVE YEARS AFTER A PREEMPTIVE MASS VACCINATION CAMPAIGN

José Paulo Langa[1], Cynthia Semá Baltazar[1], Liliana Dengo Baloi[1], José Alberto Manuel[2], Ramos B. J. Mboane[2], Sadate Assane[2], Alide Omar[3], Mariana Manso[3], Jucunú J. Elias Chitio[1], Naira Luiz Kanje[4], Saemna Park[4], Yeonji Jeon[4], Julia Lynch[4], **Se Eun Park**[4]
[1]National Institute of Health, Maputo, Mozambique, [2]Provincial Health Directorate, Niassa, Mozambique, [3]District Health Directorate, Cuamba, Mozambique, [4]International Vaccine Institute, Seoul, Korea, Republic of

Cholera remains a major public health concern in Mozambique with outbreaks occurring almost every year since 1989 with a marked seasonal pattern. Mozambique has experienced several large cholera outbreaks over the past four decades with more than 35,000 cases reported between 2022 and 2023 alone, the largest in last 20 years. The Northern and Central regions, particularly Nampula, Niassa, and Zambezia Provinces have been disproportionately affected, compared to the South region. Cholera outbreaks occurred across multiple districts in Niassa province in 2023 with 3,500 cholera cases (clinically suspected with a sub-set of patients positive

with rapid diagnostics test and culture confirmed with *V. cholerae)* and case fatality rate (CFR) of 0.71% (25/3500). Here we describe the impact of a two-dose OCV mass vaccination campaign we had conducted in Cuamba district located in Niassa province in 2018 (two-dose coverage of 60.4% (±3.4%)); in context of the recent cholera outbreaks in Niassa province. Routine epidemiological data from the local government were analyzed. During the cholera outbreaks in 2022-2023, 69% (11/16) of all districts in Niassa province were affected. Cuamba district was unaffected (no cases reported) and the remaining four districts minimally affected. The most affected districts were Lichinga (1,719 cases, 8 deaths, 4.4 attack rate (AR), 0.47% CFR), followed by Lago (652 cases, 7 deaths, 9.5% AR, 1.07% CFR) and lake region of Mecanhelas bordering Cuamba District (392 cases, 3.95 AR, 0.26% CFR, mainly fishermen aged 20-29 years) districts. These areas and Cuamba district are considered traditional cholera hot zones in Niassa province but had no history of OCV vaccination in the past five years, except for Cuamba. Two of the five unaffected or minimally affected districts also border Cuamba district, which were Mandimba (11 cases, 0.1% AR, no deaths) and Metarica (no cases) districts. Our findings suggest a preventive OCV use in cholera endemic and high priority hotspots with at least 60.4% coverage rate demonstrated the direct and indirect protection against cholera outbreaks at five years post-vaccination timepoint.

6921

ASSESSMENT OF HEALTHCARE WORKERS AND COMMUNITIES BEHAVIORS TOWARDS ANTIBIOTICS IN YIRIMADIO, MALI

Lazare Coulibaly[1], Demoutiery J. Sanou[1], Mamadou M. Teketé[1], Antoine Dara[1], Ibrahim Cissé[2], Bintou Diarra[1], Boi koné[1], Lassina Timbiné[1], Abdoulaye A. Djimdé[1]

[1]PDNA, Bamako, Mali, [2]Yirimadio health Center, Bamako, Mali

Antibiotic resistance is becoming a public health problem worldwide. A systematic analysis estimated 4.95 million deaths associated with bacterial AMR in 2019. A study in Mali has observed 93.8% and 92.6% of *E. coli* resistance to some of the antibiotics widely used in Mali, amoxicillin and cotrimoxazole, respectively. To better understand this problem there is a need for scientific information at the community and healthcare personnel levels regarding antibiotics. This study aims to assess the knowledge, attitude, and practices of antibiotics use and prescriptions in the Yirimadio health district in Mali. The population aged more than 18 years and health workers of Yirimadio health district was surveyed between 07 to 13 September 2023 and the survey was carried out in 11 sectors of the Yirimadio health area. Community permission was obtained from sector heads and interviewers were trained to collect data from the population, health workers, and focus groups. A total of 300 people were quantitatively surveyed, 100 health workers were interviewed and 6 in-depth interviews were carried out. Of those surveyed, 61% were women and 82% were aged between 24 and 65 years. In the general population, 57% declared that they had heard about antibiotics, 84% said they obtained antibiotics without a prescription, and 75% confirmed that they self-medicated with antibiotics. In our study, 61% of health workers surveyed were women, 81% prescribed antibiotics without requesting a bacteriological test, 83% prescribed without antibiogram testing. Moreover, 47% of health workers advised antibiotics without a prescription, 31% advised by phone, and 22% advised using social media. This study revealed that, in addition to the general population, some health workers need more training, awareness-raising, advice, and education on the optimal use of antibiotics.

6922

HAPPY FEET: UNDERSTANDING THE PREVALENCE OF PODOCONIOSIS AND ASSOCIATED RISK FACTORS IN SODO ZURIA AND OFFA DISTRICTS, SOUTHERN ETHIOPIA.

Tedila Habte Memera[1], Hannah Margaret Edwards[2], Esey Gabore[1], Helen Hawkings[2]

[1]Malaria Conssortium, Hawassa, Ethiopia, [2]Malaria Conssortium, London, United Kingdom

Podoconiosis is non-infectious lymphedema caused by barefoot exposure to irritant volcanic red clay soil. An estimated one-third of the 4 million global cases are reported in Ethiopia. However, reliable data on prevalence and risk factors associated with the disease are scarce. We investigated the prevalence and risk factors of podoconiosis in two districts of southern Ethiopia to provide evidence for policy and control programme planning. A mixed methods study was conducted in Sodo Zuria and Offa districts. Cross-sectional surveys were conducted with household heads in 968 households, including 116 household members with podoconiosis. In addition, four focus group discussions (FGDs) were carried out, two with community members with the disease and two without. Each FGD included eight female or male participants, totalling 32 community members (16 female and 16 male). Our results show the prevalence of podoconiosis among in the study districts was 3.95% with prevalence twice as high in women (5%) than men (2.5%). Although knowledge of podoconiosis and the prevention methods was high among community members, 29.7% were observed without shoes and 50% reported regularly walking to work barefoot. In addition, the mean age for first shoe-wearing among participants was 13.44 (± 9.4) years. Furthermore, among participants with podoconiosis, only 32% had clean and intact feet, and 71% reported seeking treatment for swelling from health facilities. FGD participants reported financial limitations and cultural barriers as reasons for not wearing shoes. FGD participants also reported men have greater access to shoes, are more likely to be able to afford shoes and spend more time outside which may be reasons for higher rates of shoe wearing among men. This study found a high prevalence of podoconiosis in Sodo Zuria and Offa districts in Ethiopia. Women were most affected by the disease and were reported to have lower access to shoes. To improve access to shoes and other preventative measures and encourage treatment-seeking behaviour we are implementing contextualized social behaviour change and healthcare interventions in these communities.

6923

ALL-CAUSE MORTALITY ATTRIBUTABLE TO THE COVID-19 PANDEMIC IN THE CONTEXT OF URBAN POVERTY: INSIGHTS FROM A COHORT IN PAU DA LIMA IN BRAZIL

Homegnon Antonin Ferreol Bah[1], Ana Paula Medeiros Pereira[2], Juan Pablo Aguilar Ticona[1], Nivison Nery Jr[1], Mariam O. Fofana[3], Murilo Enrique Dorion Nieto[3], Renato Victoriano[4], Cristiane Wanderley Cardoso[2], Federico Costa[1], Mitermayer G. Reis[4], Derek A. T. Cummings[5], Albert I. Ko[3]

[1]Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, Brazil, [2]Centro de Informações Estratégicas em Vigilância em Saúde do município de Salvador, Salvador, Brazil, [3]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, United States, [4]Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Ministério da Saúde, Salvador, Brazil, [5]Department of Biostatistics, University of Florida, Gainesville, FL, United States

There is limited evidence on the direct and indirect health burdens of the COVID-19 pandemic on the vulnerable populations. The aim of this study was to identify the causes of mortality in a cohort of residents of an urban informal settlement in the city of Salvador, Brazil and estimate excess mortality attributable to COVID-19 in comparison to trends before (2017-2019) and after (2020-2023) the pandemic. We extracted information on the primary causes of death (ICD-10 codes) from the Brazilian Mortality Information System (SIM) to identify for individuals ≥5 years old who participated in the cohort from 2016 to 2023. We computed the P-score (percentage difference between reported and expected number of deaths)

to estimate pandemic-related excess mortality. Among 4538 cohort participants, we identified 124 deaths from 2016 to 2023. We estimated the expected number of deaths to be 13 based on mortality date from 2017-2019. The reported number of deaths was 17 (P-score 31%) in the first two years of the pandemic period, rose to 27 (P-score 108%) in 2022, and was 20 (P-score 54%) in 2023. Men who died during the pandemic were younger than women (40 vs. 55 years; p<0.001). Among men, the most frequent cause of deaths were external causes (EC, 44%), such as accidents and assault, and non-communicable diseases (NCD, 40%). In contrast, the most frequent case of death among women were NCDs (68%). Overall, infectious diseases, including COVID-19, accounted for 10% of deaths throughout the study period. Compared to the pre-pandemic period, the proportion of deaths attributable to infectious diseases and EC increased by 1.6- and 1.9-fold, respectively, during the pandemic. In this vulnerable and marginalized urban population, the COVD-19 pandemic was associated with increased mortality due to NCD and EC in addition to infectious causes, suggesting that the pandemic was associated with a significant indirect burden with respect to mortality. This finding highlights the critical importance of structural interventions to address the social determinants of health during periods of major social and economic disruption that occurred during the pandemic.

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IMPACT OF LADY HEALTH WORKER VISITS IN THE PRENATAL AND POSTNATAL PERIOD ON THE UPTAKE OF CONTINUUM OF CARE INTERVENTIONS AND MORTALITY IN PAKISTAN

Shah Muhammad[1], zahid Ali Memon[1], Abeer Mian[1], arjumand Rizvi[1], Sajid Bashir Soofi[1], Simon Cousens[2], Zulfiqar A. Bhutta[1]
[1]Aga Khan University, Karachi, Pakistan, [2]London School of Hygiene & Tropical Medicine, London, United Kingdom

In Pakistan, Lady Health Workers (LHWs) play a crucial role in bridging the gap between communities and healthcare facilities since the inception of the LHW initiative in 1994. However, the quality of care offered, and their impact on population level coverage of key maternal, newborn, and child health (MNCH) interventions, as well as mortality are not yet fully understood. We used household survey data from eight districts across Pakistan with each household having at least one woman of reproductive age (WRA) with a child under the age of five. The study aimed to quantify the uptake of MNCH interventions by examining the association between a woman's interactions with LHWs, measured by coverage of antenatal and postnatal visits, and MNCH intervention coverage and mortality. We classified interaction with LHWs into three groups: no contact, contact during the antenatal period or the postnatal period, and contact during both the antenatal and postnatal periods. Logistic regression, accounting for survey design, determined the odd ratios of receiving each intervention at each LHW contact level. After adjusting for apriori confounders, it was found that compared to households who had received no LHW visits, there was a statistically significant difference in key interventions across the continuum of care including antenatal care visits, skilled birth attendance, postnatal checkups for mother and newborn. Similarly, among households that had reported receiving antenatal or postnatal visits by LHW, or both, there was significant improvement seen in childhood health interventions such as BCG vaccinations, care-seeking for diarrhea and full immunization (p-value<0.001). No statistically significant differences were observed in neonatal, post neonatal, or under-5 mortality in LHW-covered areas. This study provides evidence for the impact of LHW contact towards improving maternal and child health. Thus, the work of LHWs remains critical to empowering communities, specifically within the rural context of Pakistan.

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ETIOLOGY OF POSTPARTUM SEPSIS AMONG RECENTLY DELIVERED WOMEN IN PAKISTAN

Shabina Ariff
Aga Khan University, Karachi, Pakistan

ETIOLOGY OF POSTPARTUM SEPSIS AMONG RECENTLY DELIVERED WOMEN IN PAKISTAN Type: Abstract SubmissionShabina Ariff1, Uswa Jiwani2, Tooba Jawed Khan2, Muhammad Jawwad1, Sajid Soofi1*1The Aga Khan University Hospital, Pediatrics & Child Health, Karachi, Pakistan, 2The Aga Khan University, Centre of Excellence in Women and Child Health, Karachi, Pakistan*

Untreated postpartum-endometritis escalates to postpartum-sepsis, with a 17% fatality rate. This study aimed to provide the first population-level data on the epidemiology and microbiology of endometritis in Pakistan. A prospective-observational-cohort-study was conducted in Matiari and peri-urban areas of Karachi. Surveillance-system instituted in the study areas was utilized to recruit women within-14 days of delivery. Participants were followed on postpartum-days 0, 2, 6, 13, 20, 27, 34, 41, 48, and 59 by trained Community-Health-Workers (CHWs) after obtaining informed-consent. All women with physician-confirmed sepsis were referred for endometrial sample collection and treated according to WHO-recommendations. CHWs suspected sepsis in 1762(14.1%) of the 12509 eligible and consenting women. Physicians assessed 1451(82.34%) of the suspected sepsis cases and 1919 healthy women. CHWs identified sepsis with a sensitivity and specificity of 86% and 72%, respectively. Altogether, 466(52.1%) of the 894 women with physician-confirmed sepsis provided endometrial cultures. The most common pathogens were*; E. coli* (40.5%), *G. vaginalis*(15.3%), *S. pyogenes*(11.5%), and *S. aureus* (9.2%). Of the 10 most common pathogens, 67.6% were sensitive to combined clindamycin and gentamycin, 53.2% were sensitive to imipenem, 35.6% were sensitive to combined amoxicillin-clavulanic acid and metronidazole, and 19.4% were sensitive to combined ampicillin and metronidazole. Pakistan's high postpartum sepsis rates necessitate treatment guidelines based on common pathogen susceptibility, preventive strategies are imperative to improve the outcomes of postpartum women and reduce maternal mortality in Pakistan.

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RETROSPECTIVE ANALYSIS OF CHOLERA/ACUTE WATERY DIARRHEA (AWD) OUTBREAKS IN ETHIOPIA FROM 2001 TO 2023: INCIDENCE, CASE FATALITY RATE (CFR), AND SEASONAL AND MULTI-YEAR EPIDEMIC PATTERNS

Yeshambel Worku Demlie[1], **Abel Gedefaw**[2], Yeonji Jeon[2], Dejene Hailu[2], Tomas Getahun[3], Ondari D. Mogeni[2], David Mukasa[2], Geun Hyeog Jang[2], Gi Deok Pak[2], Deok Ryun Kim[2], Edlawit Mesfin Getachew[3], Biruk Yeshitela[3], Samuyel Ayele Abebe[3], Moti Edosa[1], Mesfin Wossen[1], Mekonnen Teferi[3], Se Eun Park[2]
[1]Ethiopia Public Health Institute, Addis Ababa, Ethiopia, [2]International Vaccine Institute, Seoul, Korea, Republic of, [3]Armauer Hansen Research Institute, Addis Ababa, Ethiopia

Ethiopian government has developed the multi-sectoral cholera elimination plan with an aim of reducing cholera incidence and case fatality rate (CFR). To better understand and monitor the progress of this plan, a comprehensive review of national cholera epidemiology was needed. Reported data on cholera/acute watery diarrhea (AWD) cases in the recent 20 years were extracted from Ethiopian Public Health Institute and World Health Organization databases. Descriptive statistics, Pearson's chi-square, and logistic regression analyses were conducted. From January 2001 to November 2023, total 215,205 cholera/AWD cases, 2,355 deaths with a cumulative CFR of 1.094% (95% CI: 1.092-1.095) and a mean annual incidence rate of 8.9 (95% CI: 6.5-11.3) per 100,000 population were reported. Cholera outbreaks peaked in 2006-7, 2009 and 2016-2017 with over 20,000 cholera/AWD cases per year; followed by the 2020 outbreak (over 15,000 cases). In 2023, nearly 30,000 cases were reported. During

2015-2023, around 54.0% (53,990/99,945) of cases were those aged 15-44 years. In 2019-2022, cholera outbreaks largely hit the southern and eastern regions. Cholera CFR has increased in recent years; highest CFR (3.13%; 95% CI: 2.1-4.5%) in 2022. During the cholera outbreak years, cases sharply increased in major rainy season (June-August). Regional distribution of cholera CFR showed a significant variation during 2015-2023; B/Gumz region (5.2% CFR) with the highest CFR, followed by Sidama (2.3%) region. Cholera cases and attack rates peaked during the El Niño years, indicating the potential impact of climate change on the magnitude of cholera outbreaks. Cholera/AWD patients in older adults (45 years and above), severe dehydration, peak outbreak season, patients treated at outpatient level were associated with higher risk of deaths. Upsurge of cholera cases and deaths in 2023 signals a critical need for reactive and preemptive cholera vaccinations in cholera hotspots. Continued systematic cholera surveillance, early case detection and adequate case management are critical for reducing deaths and controlling cholera transmissions in communities.

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THE TROPICAL MEDICINE IN THE GULF OF MEXICO (TROP-G) NETWORK AS A MODEL TO BRIDGE RESEARCH GAPS, FACILITATE COLLABORATION, AND EMPOWER THE NEXT GENERATION OF NTD SCIENTISTS

Claudia Herrera[1], **Leroy Versteeg**[2], Priscila Silva Farani[3], Antoine Amblard-Rambert[4], Norman Beatty[5], Maria Elena Botazzi[2], Pierre Buekens[6], Eric Dumonteil[1], Angel Ramos-Ligonio[7], Peter Hotez[2], Rachel Clear[1], Bridget Knudson[1], Etienne Waleckx[8], Idalia Paredes Sotelo[9]

[1]Department of Tropical Medicine and Infectious Disease, Tulane University,, New Orleans, LA, United States, [2]Texas Children's Hospital Center for Vaccine Development, Baylor College of Medicine; Texas Children's Hospital Center for Vaccine Development, Baylor College of Medicine, Houston, Texas, USA, Houston, TX, United States, [3]Department of Biological Sciences, Border Biomedical Research Center, The University of Texas at El Paso, El Paso, TX, United States, [4]Universidad Atonoma de Yucatan, Merida, Mexico, [5]Division of Infectious Diseases and Global Medicine, Department of Medicine, University of Florida College of Medicine, Gainesville, FL, United States, [6]Department of Epidemiology, Tulane University,, New Orleans, LA, United States, [7]LADISER Inmunología y Biología Molecular, Facultad de Ciencias Químicas, Universidad Veracruzana, Orizaba, Mexico, [8]Laboratorio de Parasitología, Centro de Investigaciones Regionales Dr. Hideyo Noguchi, Universidad Autónoma de Yucatan, Merida, Mexico, [9]Department of Chemical and Biological Sciences, University of Sonora, Hermosillo, Mexico

Neglected Tropical Diseases (NTDs) affect people primarily in low- and middle-income regions. The Gulf of Mexico region has been identified as a vulnerable and "hot zone" for emerging NTDs. Amidst these challenges, researchers in global health and NTDs navigate a path full of obstacles, such as scarcity of funding opportunities, limited access to critical samples or data, and lack of public support due to a low priority of global health on the political agenda. To address these challenges, the Tropical Medicine in the Gulf of Mexico (Trop-G) collaborating network (https://trop-g.org/) was established. Trop-G brings together doctoral candidates, postdoctoral scholars, and academics to collaborate on NTD research in the Gulf of Mexico region. The Trop-G goals include A) providing networking opportunities and events to build professional relationships, B) promoting interdisciplinary collaboration between people from diverse backgrounds, C) sharing knowledge by hosting regular discussions and presentations, and D) raising awareness on NTDs by engaging with the academic community and planning public outreach strategies. As part of its activities, Trop-G leads a 'Journal Club' to promote teamwork and networking, increasing awareness of NTDs. Trop-G Journal emerged through collaboration with Universidad Veracruzana, Universidad Autonoma de Yucatan, Baylor College of Medicine, and Tulane University. Today, our community counts 18 PhD students, 2 Postdocs, and eight researchers, with three additional institutions—the University of Florida, the University of Texas at El Paso, John Hopkins University, Universidad Autonoma de Nuevo Leon, and Universidad de Sonora. We have discussed 16 papers, showcased seven research project presentations, and hosted three guest talks. By organizing biweekly gatherings and showcasing the work through seminars and conferences, Trop-G fosters a dynamic forum for discussion and discovery and significantly boosts the visibility of NTDs research. This increased visibility can potentially lead to more opportunities for resources to be allocated toward NTDs research and improved public support.

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VACCINATION EXPERIENCE IMPACTS ON VACCINE CONFIDENCE AND FUTURE VACCINE BEHAVIORS IN KENYA, NIGERIA, AND SOUTH AFRICA

Alee Lockman[1], Tim Callaghan[2], Christine Blackburn[1], **Brian Colwell**[1]

[1]Texas A&M School of Public Health, College Station, TX, United States, [2]Boston University School of Public Health, Boston, MA, United States

We conducted large surveys as part of a larger project examining vaccination attitudes in three African countries (Kenya, N=1,545, Nigeria, N=1,557, and South Africa, N=1,588). We examined COVID-19 vaccination experiences & impressions in each country and the spillover of COVID-19 vaccine experiences on confidence in the safety, efficacy & importance of all vaccines approved for use in each country. We also asked about likelihood of self- and child vaccination in the future resulting from COVID-19 vaccine perception spillover. Majorities in all 3 countries indicated that, because of positive experiences with COVID-19 immunizations, they were more confident in the safety of other vaccines (72% in Kenya, 58.9% in Nigeria & 48.6% in South Africa), more confident of vaccine effectiveness (64.3% in Kenya, 55.9% in Nigeria & 49.2% in South Africa), & increased their beliefs that vaccines are important (71.7% in Kenya, 55.6% in Nigeria, 53.8% in South Africa). Other evidence of positive spillover was reflected in an increased likelihood of respondents indicating that they were more likely to vaccinate themselves & their children in the future because of positive experiences with the COVID-19 vaccination process. Among Kenyans, 71.5% were more likely to vaccinate themselves and 78.5% were more likely to vaccinate their children, 60,1% of Nigerians were more likely to get vaccinated in the future, and 64.6% were more likely to vaccinate their children. Fewer South Africans were more likely to vaccinate themselves (60.1%) and 64.6% were more likely to vaccinate their children in the future. In all 3 countries, about 25% of respondents expressed less confidence in vaccine safety and effectiveness after the COVID-19 vaccination process. Multivariate modeling found varying drivers of spillover effects in each country, but misinformation and confidence in government were stable predictors. Personal experiences with the COVID-19 vaccination process appear to be key drivers of generalized vaccination perceptions and predict self- and child vaccination in the future. The discussion will focus on improving vaccine acceptance among varying populations.

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INTESTINAL INFLAMMATION AND ENTERIC PATHOGENS CARRIAGE IN POST COVID-19 PATIENTS

Cinthia Copeticona-Callejas, Lucia Isabel Mendieta Elena, Sonia Guadalupe Jiménez Pacohuanca, Volga Ana Iñiguez Rojas

Instituto de Biologia Molecular y Biotecnologia, La Paz, Bolivia, Plurinational State of

The COVID-19 pandemic has affected millions of people. As a result of the SARS-CoV-2 infection, a broad array of sequelae have been observed, affecting one or multiple organs, including gastrointestinal inflammation. In developing countries, intestinal inflammation triggered by SARSCOV2 infection should be considered in the context of chronic or recurring infections by enteric pathogens. The main objective of this study was to evaluate the presence of intestinal inflammation and enteropathogenic carriage in post-COVID-19 patients. To this end, a total of 201 fecal samples were collected from post-COVID-19 patients (1-24 years of age) in the period of at least 2-4 weeks following their recovery from the disease. Intestinal inflammation was evaluated by the quantification of fecal calprotectin using an ELISA kit (ORG 580 kit). 14 enteric pathogens were

analyzed by real-time PCR. Pathogens included viruses (rotavirus, norovirus GI and GII, astrovirus, sapovirus, and adenovirus), bacteria (*Salmonella*, *Shigella*, ETEC (estA, eltB) and EPEC (eae, bfpA), *Clostridium difficile* (tcdA, tcdB), *Helicobacter pylori*, and *Campylobacter*), and parasites (*Giardia lamblia* and *Entamoeba histolytica*).In general, levels of calprotectin varied broadly from 6.1 ug/g to 2257.4 ug/g. 94% of the study population displayed levels above the normal range (50 ug/g), and 54% displayed high levels of calprotectin (>200 ug/g), suggesting inflammation. Regarding enteric pathogen infections, 21% carried at least one of the tested pathogens. The most frequently found pathogens were EPEC (34%), ETEC (20%), and *Shigella* (17%). No association was found between COVID-19 severity and inflammation. Overall calprotectin levels correlated positively with a higher number of pathogens (ANOVA, P = 0.012). The data obtained throughout this study indicates that pathogenic bacterial infections and inflammation are common in the study population.

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LESSONS FROM COVID-19 VACCINATION IMPLEMENTATION IN 52 AFRICAN COUNTRIES: IMPLICATIONS FOR FUTURE PANDEMIC PREPAREDNESS

Muhammed Olanrewaju Afolabi[1], Oghenebrume Wariri[2], Christinah Mukandavire[1], Yauba Saidu[3], Emmanuel A. Okpo[4], Olalekan Uthman[5], Beate Kampmann[1]

[1]London School of Hygiene & Tropical Medicine, London, United Kingdom, [2]MRC Unit The Gambia at the London School of Hygiene & Tropical Medicine,, Banjul, Gambia, [3]Clinton Health Access Initiative, Yaounde, Cameroon, [4]UK Health Security Agency, Newcastle, United Kingdom, [5]University of Warwick Medical School, Coventry, United Kingdom

Driven by the global imperatives to end the COVID-19 pandemic, the WHO set a goal in 2021 to fully vaccinate 70% of the global population by mid-2022. We projected the COVID-19 vaccination trajectory in 52 African countries and compared the projected to the 'actual' or 'observed' coverage as of December 2022. We also estimated the required vaccination speed needed to have attained the WHO 70% coverage target by December 2022. We obtained publicly available, country-reported daily COVID-19 vaccination data, covering the initial 9 months following the deployment of vaccines. We used a deterministic compartmental Susceptible-Exposed-Infectious-Recovered-type model and fit the model to the number of COVID-19 cases and vaccination coverage in each African country using a Markov chain Monte Carlo approach within a Bayesian framework. Only nine of the 52 African countries were on track to achieve full COVID-19 vaccination coverage rates ranging from 72% to 97% by the end of December 2022, based on their progress after 9 months of vaccine deployment. Of the 52 countries, 26 (50%) achieved 'actual' or 'observed' vaccination coverage rates within ±10 percentage points of their projected vaccination coverage. Among the countries projected to achieve <30% by December 2022, nine of them achieved a higher observed coverage than the projected coverage, ranging from 12.3 percentage points in South Sudan to 35.7 percentage points above the projected coverage in Tanzania. Among the 52 countries, 83% (43 out of 52) needed to at least double their vaccination trajectory after 9 months of deployment to reach the 70% target by December 2022. Our findings can guide countries in planning strategies for future global health emergencies and learning from each other, especially those that exceeded expectations and made significant progress towards the WHO's 2022 COVID-19 vaccination target despite projected poor coverage rates.

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UNIQUE AND ADAPTIVE PANDEMIC PREPAREDNESS IN LMIC HEALTH SYSTEM- AN INTEGRATED SURVEILLANCE POTENTIAL OF A RAPID TB AND COVID-19 DIAGNOSTIC IN BANGLADESH

Farzana Zaman[1], Muhammad Asaduzzaman[2]

[1]Directorate General of Health Services (DGHS), Dhaka, Bangladesh, [2]University of Oslo, Oslo, Norway

The COVID-19 pandemic with continuous emergence of its new variants largely affected the aviation system and international travel. Quarantine and proper testing of incoming travelers were considered as the most important preventive strategy. However, many unprecedented challenges were observed at the resource poor settings such as inadequate airport quarantine facilities, lack of highly sensitive but rapid testing and cost-effective management system. In this current study, we present a cost-effective and timely alternative diagnostic and quarantine facility for the incoming impoverished travelers in Bangladesh during the pandemic. We conducted a cross-sectional serosurvey from December 15, 2020 to November 30, 2021 for inbound travelers to Bangladesh. These impoverished travelers (unable to afford hotel quarantine) were quarantined in Hajj camp (a government facility near the airport reserved for muslim pilgrims) with full coverage of food and lodging at subsidized cost and free testing by GeneXpert, which is capable of Nucleic Acid Amplification Test (NAAT) for both COVID-19 and Tuberculosis (TB). Among 1328 participants, SARS-COV-2 positive patients were 106 (7.98%), out of which 72 were male. The highest infection rate was observed in travelers from Singapore (n=16/71, 22.53%) followed by USA and Malaysia. The result processing time was only 1 hour for the NAAT and 1222 participants (92%) were able to travel to their destinations on the same day. The positive cases were kept in quarantine for further assessment. Majority of the participants (95%) were satisfied with the service and processing time. This study is a scalable example of implementation research in resource poor settings which supports the equitable access to COVID-19 diagnostics for disadvantaged group and emergency preparedness for similar pandemics. Due to high sensitivity and specificity, NAAT is also recommended by WHO for diagnosis of acute COVID-19 cases. Our research also emphasizes on the potential to equip hard to reach laboratory facilities by GeneXpert for both TB and COVID-19 diagnostics specially where the double burden exists.

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RAPID RESPONSE MOBILE SUITCASE LABORATORY AS A TOOL FOR COMBATING INFECTIOUS DISEASE OUTBREAKS

Paula Emily Schweizer[1], Rea Maja Kobialka[1], Arianna Ceruti[1], Prakash Ghosh[1], Martin Faye[2], Oumar Faye[2], Andy Mahine Diouf[2], Soa Fy Andriamandimby[3], Dinesh Mondal[4], Sarah Schurig[1], Manfred Weidmann[5], Julius Boniface Okuni[6], Kamal H Eltom[7], Sheila Makiala-Mandanda[8], Mitali Chatterjee[9], Michael Frimpong[10], Ndongo Dia[2], George Olusegun Ademowo[11], Mohamed A. Shalaby[12], Uwe Truyen[1], Ahmed Abd El Wahed[1]

[1]Institute of Animal Hygiene and Veterinary Public Health, Leipzig University, Leipzig, Germany, [2]Virology Department, Institut Pasteur de Dakar, Dakar, Senegal, [3]Virology Unit, Institut Pasteur de Madagascar, Madagascar, Madagascar, [4]Nutrition Research Division, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, [5]Institute of Microbiology and Virology, Medizinische Hochschule Brandenburg Theodor Fontane, Neuruppin, Germany, [6]College of Veterinary Medicine, Animal Resources and Biosecurity, Makerere University, Kampala, Uganda, [7]Department of Animal Health and Safety of Animal Products, Institute for Studies and Promotion of Animal Exports, University of Khartoum, Khartoum, Sudan, [8]Department of Virology at the Institut National de Recherche Biomédicale (INRB); Faculty of Medicine, University of Kinshasa, Kinshasa, Congo, Democratic Republic of the, [9]Department of Pharmacology, Institute of Postgraduate Medical Education and Research, Kolkata, India, [10]Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, [11]Institute for Advanced Medical Research and Training

(IAMRAT), College of Medicine, University of Ibadan, Ibadan, Nigeria, [12]Department of Virology, Faculty of Veterinary Medicine, Cairo University, Cairo, Egypt

In times of emerging pathogens, point-of-need diagnostics represent the first line of defense. In the last two decades, there have been six pandemics and numerous outbreaks of infectious diseases worldwide. Especially in low- and middle-income countries, healthcare facilities are inadequate to manage and control outbreaks. The Mobile Suitcase Lab (MSL) provides a highly functional minimalist work unit that enables capacity development in remote settings in addition to the ease of delivery and deployment. The molecular methods used in the MSL are isothermal amplification (recombinase-aided amplification or recombinase polymerase amplification assay), rapid real-time PCR, and nanopore sequencing. Nucleic acid extraction can be performed within 15 min using simple and rapid reverse purification extraction methods. The MSL operates with a glove box for working with highly contagious pathogens. All reagents needed are cold chain independent and stable at ambient temperature of tropical areas. Independent power supply is achieved via solar power batteries. Members of the research group have released the first mobile Next Generation Sequencing protocol, where all necessary steps can be performed in a suitcase lab, enabling truly mobile use of this technology including offline data basecalling and analysis.The MSL team is working as an international consortium, consisting of 38 members from 17 countries, including public health, academic and governmental institutions. The MSL has been deployed to outbreaks of Ebola, SARS-CoV-2, Dengue, Zika, Avian Influenza and Marburg. As participants in the WHO's simulation exercise programme for Rapid Response Mobile Laboratories, the team contributed to the establishment of Minimum Operational Standards and the improvement of interoperability with other response forces. The MSL Consortium enables disease outbreak investigation and pathogen detection directly at the point-of-need, while strengthening international collaboration and local capacity building.

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ADAPTING RAPID LABORATORY BIORISK SELF-ASSESSMENTS TO BETTER INCORPORATE CYBER-BIOSECURITY RISKS

Ming Yang Ong[1], Emilie Ryan-Castillo[1], Lauren Miller[1], Brian Samuelson[1], Claire Standley[1], Kaitlin Sandhaus[2], Kevin Omondi[3], Tura Galgado[3]

[1]Georgetown University Center for Health Science and Security, Washington D.C., DC, United States, [2]Global Implementation Solutions, Chicago, IL, United States, [3]Global Implementation Solutions, Nairobi, Kenya

Recent technological advances have highlighted the global catastrophic biological threat that generative AI could pose. A key building block of this threat is the ease of access to sensitive genetic and diagnostic material stemming from laboratories working with high-consequence pathogens. It is vitally important to secure critical high-containment laboratories and biorepositories from physical and digital biosecurity threats that could contribute to heightening AI and biotechnology risks. Since 2017, the Georgetown University Center for Global Health Science and Security has engaged with laboratory systems to identify gaps and strengthen biosecurity and biosafety capacities using the Laboratory Self-Assessment Tool (S-LAT). In light of rising cyber-biosecurity threats, we have developed an adaptation of the S-LAT including components specifically targeted at identifying and mitigating gaps in cyber-biosecurity capacities. The cyber-biosecurity component focuses on building biosecurity capacities across synthetic biology, toxicology, and genomic research communities, especially those deploying biotechnologies. It also establishes measures for biological and genomic data security, including capacities supporting oversight, enforcement, and/or reporting mechanisms. This presentation will examine the process of developing and incorporating the cyber-biosecurity component of the S-LAT, and provide an update on key considerations in mitigating the cyber-biosecurity threat of high-consequence pathogens from a laboratory perspective.

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AGRICULTURAL WORKERS IN GUATEMALA WITH CHRONIC KIDNEY DISEASE ARE AT HIGHER RISK OF ACUTE RESPIRATORY ILLNESS: FINDINGS FROM THE AGRICULTURAL WORKERS AND RESPIRATORY ILLNESS IMPACT (AGRI) STUDY

Molly M. Lamb[1], Diva M. Calvimontes[2], Neudy Rojop[2], Kareen Arias[2], Jenae Stutzman[3], Wanda Mejia[2], Melissa Gomez[2], Chelsea Iwamoto[4], Ian D. Plumb[4], Julio del Cid-Villatoro[2], Claudia Paiz[2], Lyndsay Krisher[5], Jose C. Monzon[6], Guillermo A. Bolanos[2], Ashley Fowlkes[4], Emily Zielinski-Gutierrez[6], Eduardo Azziz-Baumgartner[4], Lee S. Newman[5], Edwin J. Asturias[3], Daniel Olson[3]

[1]Colorado School of Public Health, AURORA, CO, United States, [2]Fundacion para la Salud Integral de los Guatemaltecos, Retalhuleu, Guatemala, [3]University of Colorado School of Medicine, Aurora, CO, United States, [4]Center for Disease Control and Prevention, Atlanta, GA, United States, [5]Colorado School of Public Health, Aurora, CO, United States, [6]Center for Disease Control and Prevention, Guatemala City, Guatemala

Chronic kidney disease (CKD) of unknown origin (CKDu) is a major public health concern in Central American agricultural workers. While CKD is a risk factor for severe COVID-19 and influenza, it is unknown if populations at risk for CKDu, which are typically younger with fewer comorbidities, are also at risk. During 2020-2022, we annually estimated glomerular filtration rate (eGFR) using serum creatinine among banana farm workers in southwest Guatemala enrolled in a longitudinal cohort (AGRI) study. Influenza-like illness (ILI) was defined as ≥ 1 day of cough, fever, or dyspnea reported on weekly symptom surveys. Workers with ILI completed a questionnaire (flu-iiQ), which produced severity scores for 'systemic' and 'respiratory' symptoms, and impact on 'daily activities,' 'emotions,' and 'other people.' We defined moderate and mild renal impairment as eGFR <60 mL/min/1.73m^2 at one measurement, and 60 to < 90 mL/min/1.73m^2 at two measurements, respectively. We assessed the association between renal impairment and ILI using multivariable regression models adjusted for sex, chronic disease, and job type. During 2020-2022, we screened 2,149 workers (2023 data pending); median age was 28.7 years (interquartile range 23.9 – 35.4) and 82% were male. Overall, 77 (3.6%) had moderate and 234 (10.9%) had mild renal impairment. Of the 352 ILI episodes reported, 17 (4.8%) and 32 (9.1%) were among workers with moderate and mild impairment, respectively. Compared to workers without renal impairment, workers with moderate impairment had marginally higher ILI risk (relative risk = 1.43, 95% CI: 0.94-2.16, p = 0.09), while those with mild impairment had marginally lower ILI risk (RR = 0.76, 95% CI: 0.55-1.04, p = 0.09). The flu-iiQ 'Impact on Others' severity score was higher as renal impairment increased (β= 0.15, p = 0.02); other flu-iiQ scores were similar. These preliminary results from farm workers at high risk for CKDu suggest moderate renal impairment may impact the risk and severity of symptomatic respiratory infections. These findings may help public health authorities to prioritize disproportionately affected populations for vaccination campaigns.

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PERFORMANCE OF MALARIA ELIMINATION ACTIVITIES IN SEKE DISTRICT, MASHONALAND EAST PROVINCE, ZIMBABWE, 2023

Julius Shamuyarira

Zimbabwe Assistance Program in Malaria II, Abt Global, Harare, Zimbabwe

Seke district in Zimbabwe became an elimination district in 2022 after achieving an annual parasite incidence <5 cases/1,000 population per year for three consecutive years; a favorable assessment of operational and financial feasibility; and sustainability of the 1-3-7 strategy to report confirmed cases within one day, case investigation within three days, and foci investigation and response within seven days. We conducted a descriptive analysis of malaria surveillance data from Seke District for 2023. Of the 2,409 reported suspected cases passively identified at health facilities, 2,388 (99%) were tested using a malaria rapid diagnostic test or microscopy; of which, 169 (7.1%) tested positive. Through reactive case

detection, 590 household contacts were tested, and 15 (2.5%) tested positive; among whom, 12 (80%) were symptomatic. All 184 confirmed cases (passive and reactive) received appropriate malaria treatment, and 167 (91%) received additional gametocytocidal therapy as single low-dose primaquine. Overall, 172 (94%) cases were uncomplicated, while 11 (6%) were severe cases requiring hospitalization. Among confirmed cases, 60 (33%) were students, 20 (11%) vendors, 14 (8%) farmworkers, and 14 (8%) children <5 years. 88 (48%) of cases sought treatment within 48 hours. Among the 96 cases who sought treatment after 48 hours, 31% were students, 10% vendors, 8% children < 5 years, 8% unemployed, and 41% were other occupations. Overall, 178 (97%) cases were classified as imported; of these, 132 (74%) had a history of travel from malaria high-burden districts, and 11 (6%) from low-burden districts in-country, and 35 (20%) from international locations, mostly from Mozambique (26). All 184 confirmed cases were notified within one day, 156 (85%) of these were investigated within three days, while 12 cases were lost to follow-up, and 16 cases had missing data. No foci investigations were conducted. Case notification and investigation performance was high. Increased capacity for foci investigation and response is needed. Targeted messaging for travelers and students might promote malaria preventive and early care-seeking behaviors.

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UTILIZATION OF PREPOSITIONED RESEARCH LABORATORY CAPABILITIES TO SUPPORT SUDAN VIRUS DISEASE RESPONSE IN UGANDA

Willy Kayondo[1], Prossy Naluyima[1], Melissa Gregory[2], Godfrey Pimundu[3], Paul Blair[2], Sharon Atukunda[1], Lydia Tumubeere[1], Brenda Kusiima[1], Paul Ngobi[1], Maurice Kasule Ndawula[1], Michael Luzinda[4], Sarah Namuyanja[4], Stephen Okello[1], Abdullah Wailagala[4], Peter Mutebi[1], Helen Badu[2], Peter Waitt[4], Betty Mwesigwa[1], Vamsi Vasireddy[5], Isaac Ssewanyana[6], Mohammed Lamorde[4], Danielle Clark[2], Susan Nabadda[6], Hannah Kibuuka[1]

[1]Makere University Walter Reed Project, Kampala, Uganda, [2]Austere environments Consortium for Enhanced Sepsis Outcomes, Bethesda, MD, United States, [3]National Health Laboratory & Diagnostics Services, Ministry of Health, Butabika, Uganda, [4]Infectious Diseases Institute, Kampala, Uganda, [5]Walter Reed Army Institute of Research, Silver Spring, MD, United States, [6]National Health Laboratory & Diagnostics Services, Ministry of Health,, Butabika, Uganda

Uganda is prone to outbreaks of high-consequence pathogens including 7 Ebola outbreaks to date. Prepositioning laboratory capability for early detection and effective response is essential for limiting disease spread. The Joint Mobile Emerging Infectious Disease Intervention Clinical Capability (JMEDICC) was established with funding from U.S. Department of Defense and maintained by a partnership across Makerere University Walter Reed Project, the Infectious Diseases Institute and the Austere environments Consortium for Enhanced Sepsis Outcomes. The purpose was to ready a local team to conduct clinical research of medical countermeasures in a filovirus outbreak setting. Laboratory capability development included strategic instrument acquisition allowing for operation inside rapid containment kits, staff competence in Infection Prevention and Control, as well as maintenance of skills through drills/simulation exercises. The Ministry of Health (MoH) leveraged JMEDICC capabilities during the 2022 Sudan virus disease outbreak to offer clinical laboratory testing (biochemistry, hematology and serology) to patients in three Ebola Treatment Units (ETU) for the first time in Uganda. The data generated was crucial for patient care. Prepositioned research capacity and capability enabled safe rapid deployment of mobile clinical laboratories. JMEDICC-MoH collaboration further illustrated the benefits of partnerships to combat global health threats.

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A SURVIVOR CASE OF NEONATAL TETANUS: CASE DESCRIPTION AND SURVEILLANCE SYSTEM EVALUATION IN THE URBAN HEALTH DISTRICT OF EBOLOWA, CAMEROON, MARCH 2023

Ngotty Essebe Ruth-Aimée[1], Signe Banjamin[2], Atouba Benjamin[3], Anya Priscilla[4], Mendjime Patricia[5]

[1]Cameroon Field Epidemiology Training Program, Ministry of Public Health, Regional Delagation for the West, Bafoussam, Cameroon, [2]Ministry of Public Health, Regional Delegation for the South, Ebolowa, Cameroon, [3]Ministry of Public Health, Regional Delagation for the South, Ebolowa, Cameroon, [4]Department for the Control of Disease Epidemics and Pandemics; Cameroon Field Epidemiology Training Program, Yaounde, Cameroon, [5]Department for the Control of Disease Epidemics and Pandemics; Cameroon Field Epidemiology Training Program,, Yaounde, Cameroon

Neonatal tetanus (NNT) is a vaccine preventable disease with high lethality rate (80-100%). Cameroon was declared "Maternal and NNT free" in 2012. Elimination strategy of NNT include high vaccination coverage in tetanus toxoid vaccin (≥2 doses) [TT2+] among Women of child bearing age (WCBA) and high-quality surveillance of NNT. On March 9th 2023, the Ebolowa Health District (EHD) was notified of a suspected living NNT case. We aim to investigate to identify exposure factors. A cross-sectional descriptive study was conducted from March 17-26, 2023 in EHD. The case's family was interviewed for case description. Vaccine coverage (VC) and knowledge on NNT evaluation were conducted in the neighbourhood. Health-care workers were interviewed to assess Surveillance system (SS) attributes according to the *2001 CDC guidelines*. Excel (97.2003) software was used for data analysis. Means and proportions were calculated, results presented in tables and figures. The case, female, was born on the floor at home (February 28th, 2023) from a non-vaccinated mother. Umbilical cord was tied with sewing thread and cut using bamboo pestle. The baby presented incessant crying, difficulties breastfeeding, seizures, neck stiffness and spasms 7 days later. Globally 201 neighbours were interviewed. Only 37(18.4%) knew of NNT and 15(7.5%) were aware of its transmission mode. Among the 201 neighbours, WCBA were 85(42%). VC of TT2+ was 21% (18/85) for those WCBA, and 58(68.2%) of them were zero dose for TT2+. A total of 39 health-care workers were interviewed for NNT-SS evaluation, with 16(41%) having at list 3 years' professional experience. The SS was not flexible (51.28%). Completeness (99%), promptness (95%) and usefulness (100%) were satisfactory. Simplicity (70.57%) and acceptability (73.99%) were moderately satisfactory. The EHD recorded the first NNT survivor case in the country. Exposure factors were non aseptic delivery and zero dose mother. VC and knowledge on NNT were very low in the neighbourhood. Utility, completeness and promptness of the NNT-SS were satisfactory. We recommended sensitization, intensive vaccination and training of health-care workers.

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THE IMPACT OF COVID-19 POLICY CHANGES ON RT ESTIMATION IN WEST VIRGINIA, JANUARY 22, 2020-DECEMBER 31, 2020

Abigail A. Buesseler[1], Xinyi Hua[1], Dorcas Adom[1], Shobhan Das[1], Wendy Kutten[1], Olawumi O. Olatunde[1], Olivia Sheppard[1], Jhy-Charm Soo[1], Jing Kersey[1], Kin On Kwok[2], Gerardo Chowell[3], **Isaac Chun-Hai Fung**[1]

[1]Georgia Southern University, Statesboro, GA, United States, [2]Chinese University of Hong Kong, Hong Kong, Hong Kong, [3]Georgia State University, Atlanta, GA, United States

Substate-level analysis enables us to better understand geographical variation in COVID-19 transmission and facilitate improvement of prevention efforts with greater granularity. This study analyzes daily cases in West Virginia (data from Johns Hopkins data repository) to estimate the time-varying reproduction number, R_t, in 9 regions across the state. We used the R package EpiEstim to estimate R_t with 7-day-sliding-windows and with non-overlapping-time-windows between 5 policy changes and used

Poisson regression to estimate the incidence rate ratio (IRR) between those 9 regions and West Virginia. Statewide R_t fluctuated throughout the year, with the highest in March 2020 (close to 2) and the lowest R_t (<1) seen in June 2020. The Stay-at-Home Order, Face Mask Mandate, and Virtual Learning Resumes saw 38.7% (95% confidence interval [CI]: 21.9%-57.5%), 10.6% (3.2%-18.9%), and 9.4% (3.2%-15.4%) corresponding decreases in R_t statewide, and varying decreases across the 9 regions. The Eastern region saw no significant R_t changes for all five policy changes. Using the state as the reference group, all regions except Metro-Charleston found significant differences in IRRs. The Northern region had the smallest IRR in 2020 at 0.32 (0.32-0.33), and the Wood-Jackson region had the highest IRR of 1.90 (1.87-1.94). R_t estimates between policy changes showed that policies that isolated people, such as the Stay-at-Home Order and Virtual Learning Resumes, effectively reduced transmission across the state. Geographical variation in case burden is reflected in regions that consistently had IRR >1 or <1 compared to the statewide incidence rate.

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ASSESSING IMMUNIZATION COVERAGE AND POLIO VACCINATION STATUS AMONG CHILDREN AGED 12-23 MONTHS. FINDINGS FROM A CROSS-SECTIONAL SURVEY IN HIGH-RISK UNION COUNCILS OF PAKISTAN

Imtiaz Hussain, Muhammad Umer, Ahmad Khan, Sajid B. Soofi
Aga Khan University, Pakistan, Karachi, Pakistan

The current polio epidemiology in Pakistan poses a unique challenge for global eradication as the country is affected by ongoing endemic poliovirus transmission. Across the country, union councils (UCs) that serve as core reservoirs for poliovirus with continuous incidences of polio cases are categorized as super-high-risk union councils (SHRUCs). A cross-sectional survey was conducted in 2023 in 39 SHRUCs over 7 districts using a two-stage stratified cluster sampling technique. 8,011 children aged 12-23 months were covered. A structured questionnaire was used for data collection. Data were analyzed using STATA version 17. Based on both vaccination records and recall, 60% of children were fully-, 34% were partially-, and 6% were non-vaccinated in the SHRUC districts. Among the SHRUC districts, Peshawar in Khyber Pakhtunkhwa (KP) had the highest percentage of fully vaccinated children (83%), followed by SHRUC districts in Sindh (with more than 50%), while the least proportion of fully vaccinated children was found in SHRUC districts of Balochistan. Vaccination cards were available for more than 70% of children in the SHRUC districts of KP and Sindh, and for more than half in the SHRUC districts of Balochistan, except for Killa Abdullah. Results for polio vacancies show that 72.9% of children from the SHRUC districts were vaccinated with at least three doses of OPV and one dose of IPV, while 92.4% were vaccinated with any OPV doses or IPV and 7.6% of children did not receive any polio vaccines. The dropout rate between dose pairs (Penta1 vs Penta3, OPV1 vs OPV3, PCV1 vs PCV3, MCV1 vs MCV2, BCG vs MCV1, and Penta1 vs MCV1) was higher than the WHO-recommended cutoff point of 10% for all vaccine doses in the SHRUC districts except for district Peshawar. To enhance and sustain immunization coverage in the SHRUCs, a multifaceted approach is imperative. This may involve targeted community engagement to dispel misconceptions, enhance vaccine acceptance, and strengthen healthcare systems through training and reliable supply chains.

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THE ACCEPTABILITY OF MINIMALLY INVASIVE TISSUE SAMPLING FOR CAUSE OF DEATH DETERMINATION IN RURAL SOUTH AFRICA: A QUALITATIVE ANALYSIS.

Laura-Lynne Brandt, Jessica Price, Zokwane L. Modlane, Gift Mathebula, Sara Jewett, Kathleen Kahn, Ryan G. Wagner
The University of the Witwatersrand, Johannesburg, South Africa

Minimally invasive tissue sampling (MITS) is increasingly being used to strengthen cause of death data in resource-limited settings. However, information on the acceptability of MITS for community deaths across all ages is scarce, as most studies have focused on child and facility deaths. This qualitative study describes factors influencing the acceptability of MITS for community deaths in a rural South African community and reviews the utility of the theoretical framework for acceptability (TFA). We conducted thematic analysis of 20 in-depth interviews with community members from the Agincourt Health and socio-Demographic Surveillance System site who experienced a death in the last 24 months, and 6 focus group discussions with religious leaders, mortuary workers, healthcare workers, traditional healers, and community members. Most community members had positive attitudes towards MITS as they felt knowing cause of death would provide closure, help prevent further deaths and reduce witchcraft accusations. The participants' belief systems did not forbid participation in MITS, but local traditions dictate that infants and traditional healers be buried within one day of death, which might limit participation of these groups. Rumours of organ-trafficking during autopsies made some participants wary of the MITS. However, MITS was considered more acceptable than standard autopsies as it does not involve the removal of organs from the body. Engaging with local traditional leaders and community members, as well as community education about MITS was considered crucial to improving uptake and building trust. Fieldworkers must empathize with grieving families to facilitate consent, minimize the psychological burden of participating in MITS activities and assist with the grieving process. Our findings were largely in line with the TFA; however, the framework failed to account for trust between providers and participants. Given that this trust influenced the acceptability of our intervention, we propose the modification of the TFA to account for this factor.

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REACHING THE UNREACHABLE CHILDREN FOR ESSENTIAL VACCINATIONS AN OUTREACH APPROACH THROUGH HEALTH CAMP IMPLEMENTATION

Muhammad Umer, Imtiaz Hussain, Ahmad Khan, Sajid Soofi
The Aga Khan University, Karachi, Pakistan

Despite the robust polio eradication efforts, Pakistan remains a polio-endemic nation. To address the persistent poliovirus transmission, the National Emergency Centre for Polio Eradication has initiated integrated health camps in Polio Super High-Risk Union Councils (SHRUCs) as a part of targeted Supplementary Immunization Activities (SIAs) in collaboration with Aga Khan University, Pakistan. The health camps are meant to deliver basic maternal, child health and essential immunization services. This study presents the coverage of priority children for essential vaccinations from the health camps. High-risk union councils are the primary targets of immunization initiatives during SIAs. To reach out to the underserved children who were either missed or inaccessible during the polio campaigns, health camps are systematically organized on a rotational basis post-campaign. Provincial and District EOCs and the Polio Program offices assist in identifying suitable locations for these health camps. Between July 2021 and September 2023, a total of 2,739 health camps were organized in 41 districts with coverage extending to 201 union councils across all four provinces on a rotational basis. During these camps, 80,780 priority children under the age of five received essential vaccinations. Among them, 28,349 were children who had not received any prior doses, and another 28,349 children were those who had been missed or were unavailable during previous immunization campaigns. Within these health camps, 44,934 children who had consistently been missed by previous immunization campaigns were reached, and 11,396 children who had previously refused vaccination were covered. Additionally, the camps provided essential vaccinations to 273,978 more children. The health camp model, as an outreach strategy, is a highly effective approach for delivering vaccination services to underprivileged populations and enhancing immunization to curb the circulation of the polio virus in the country.

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EARLY DETECTION OF CHOLERA OUTBREAKS IN URBAN AND RURAL AREAS OF NAMPULA PROVINCE IN MOZAMBIQUE: PRELIMINARY INTERIM RESULTS OF ENHANCED ACUTE DIARRHEAL DISEASE SURVEILLANCE IN CHOLERA ENDEMIC SETTINGS

Liliana Dengo Baloi[1], José Paulo Langa[1], Cynthia Semá Baltazar[1], Jucunú J. Elias Chitio[1], Imelda Miambo[1], Sofião Manjor[1], Nelmo Manjate[1], Simões Mala[1], Naira Luiz Kanje[1], Aurea Tovele[1], Américo Barata[2], Atija Marcelino[2], Madalena Zacarias[2], Jamilo Chabane[2], Ondari D. Mogeni[3], Saemna Park[3], David Mukasa[3], Geun Hyeog Jang[3], Hyoryoung Lee[3], Young Ae You[3], Deok Ryun Kim[3], Yeonji Jeon[3], Ju Yeon Park[3], Julia Lynch[3], Se Eun Park[3]

[1]National Institute of Health, Maputo, Mozambique, [2]Provincial Delegation, National Institute of Health, Nampula, Mozambique, [3]International Vaccine Institute, Seoul, Korea, Republic of

World Health Organization warned in 2023 that one billion people in 43 countries are at risk of cholera with children under five particularly vulnerable. Mozambique is one of the cholera high-risk countries. Coastal areas of North and Central regions, including Nampula province, are periodically affected by cyclones and floodings. This, coupled with poor water, sanitation, hygiene, and weak healthcare systems, leads to frequent cholera outbreaks. A prospective cholera and diarrheal disease surveillance has been set-up in five sentinel healthcare facilities in Nampula city, Monapo and Meconta Districts of Nampula province. Patients with acute diarrheal symptoms were eligible for enrolment. Clinical data and rectal swab samples were collected for cholera rapid diagnostics test (RDT) and laboratory confirmation. Our preliminary interim analysis shows the following findings while surveillance and data cleaning are ongoing. From September 2022 to January 2024, total 904 eligible patients were enrolled, of which 33.5% (183/547) were RDT positive for cholera. 44.6% (332/745) were culture positive for *V. cholerae* and 55.8% (416/745) positive for non-cholera isolates out of total culture positive isolates. Most cholera cases (counted by either RDT or culture positive) were enrolled at Cholera Treatment Center (64.8%; 289/446) and detected among patients in 15+ years age-group (86.8%; 387/446). Most enrolled patients were from Nampula city (88.3%; 798/904), though outbreaks were detected in both urban and rural areas. Overall crude incidence of cholera was 24.9/100,000 person-years (PY); highest in 15+ years (40.8/100,000 PY). Crude incidence of non-cholera diarrheal disease was 25.6/100,000 PY; highest in 15+ years (44.0/100,000 PY). 83.2% (371/446) of cholera patients were hospitalized for treatment; 75.8% (347/458) of non-cholera diarrheal patients hospitalized. Enhanced and sustained surveillance capacity is critical in early detection of cholera outbreaks and case management. Timely planning and pre-positing of cholera RDT and laboratory diagnostics supplies on sites closer to the cholera high-risk areas are critical.

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ANALYSIS AND OPTIMIZATION OF LABORATORY NETWORKS FOR LASSA AND YELLOW FEVER IN NIGERIA: A COMPREHENSIVE APPROACH

Nsonghomanyi Fritz Roland Fonkeng[1], Marie Brunetti[1], Manuela Rehr[1], Onyebuchi Okoro[2], Toluwanimi Adewole[1], Devy Emperador[1], Emmanuel Agogo[1], Heidi Albert[1], Afolabi Akinpelu[3], Babatunde Olajumoke[3]

[1]FIND, Geneva, Switzerland, [2]African Field Epidemiology Network, Abuja, Nigeria, [3]NCDC, Abuja, Nigeria

Nigeria faces significant public health challenges posed by epidemic-prone diseases; the National Centre for Disease Control and Prevention (NCDC) has been actively expanding surveillance and diagnostic networks to enhance outbreak detection and response. However, accessibility to testing remains a key challenge. A descriptive and optimization analysis of the Lassa (LF) and Yellow fever (YF) diagnostic networks and associated sample transport systems were conducted to inform NCDC's policy and future strategic planning. The analysis provided valuable insights into the laboratory network and sample referral systems for both outbreak diseases, focusing on turnaround times for sample transport and laboratory procedures during previous outbreaks. Additionally, the study provided valuable insights for designing an optimized diagnostic network capable of promptly detecting and responding to outbreaks. The DNO analysis revealed that while the average transport time for LF samples met NCDC targets at 0.8 days, YF samples experienced a significantly longer transport time of 10.1 days, primarily due to delays during transportation from sample collection to sample hub. This disparity suggests differing specimen management practices at the local government area or health facility level. Implementing mitigative measures such as allowing cross-border transport or expanding hubs could alleviate long distances between health facilities and hubs, potentially reducing transport time. However, addressing variations in specimen management for YF samples would be crucial for optimizing overall transport efficiency. More studies and research are required to include all priority diseases which requires strengthened data systems and sample collection to provide a comprehensive report. DNO has the potential to offer a systematic and evidence-based approach to enhancing laboratory networks for epidemic-prone diseases.

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HEALTH SYSTEM STRENGTHENING THROUGH DATA QUALITY IMPROVEMENTS: A COMPARATIVE ANALYSIS OF HEALTH FACILITY DATA QUALITY PERFORMANCE FROM INITIAL ASSESSMENTS TO SUBSEQUENT VISITS

Aderonke Omokhapue[1], Gloria Sillo[2], Comfort Kingsley-Randa[3], Chinwe Nweze[4], Olayemi Abimbola[1], Justice Adaji[1], IniAbasi Nglass[1], Uchenna Nwokenna[1], Abanyi Liambee [5], Peter Ejim[6], Pam Danjuma[7], Kabiru Bungudu[8], Arja Huestis[9], Rudi Thetard[9], Thomas Hall[9], Grace Nwankwo[10], Erkwagh Dagba[10], Veronica Momoh[10], Jules Mihigo[10], Chukwu Okoronkwo[11], Nnenna Ogbulafor[11], Godwin Ntadom[11]

[1]United States President's Malaria Initiative for States, Management Sciences for Health , Abuja, Nigeria, [2]United States President's Malaria Initiative for States, Management Sciences for Health, Benue, Nigeria, [3]United States President's Malaria Initiative for States, Management Sciences for Health , Nasarawa, Nigeria, [4]United States President's Malaria Initiative for States, Management Sciences for Health , Cross River, Nigeria, [5]State Malaria Elimination Program, Ministry of Health, Benue, Nigeria, [6]State Malaria Elimination Program, Ministry of Health, Nasarawa, Nigeria, [7]State Malaria Elimination Program, Ministry of Health, Plateau, Nigeria, [8]State Malaria Elimination Program, Ministry of Health, Zamfara, Nigeria, [9]Management Sciences for Health, Arlington, VA, United States, [10]United States Agency for International Development, United States President's Malaria Initiative, Abuja, Nigeria, [11]National Malaria Elimination Programme, Abuja, Nigeria

Data quality assessments (DQAs) are crucial for ensuring reliable health information and effective healthcare management, aiding stakeholders to understand system strengths and weaknesses. Teams at state and local government levels were trained on malaria DQA processes and conducted routine assessments using the national malaria DQA checklist. The checklist was scripted on KoboCollect, and a PowerBi dashboard was developed to monitor health facility performance. The assessments focused on data availability, consistency, and validity. This study analyzes DQA trends over three years (2021-2023) across four Nigerian states—Benue, Nasarawa, Plateau, and Zamfara. A total of 2,239 HFs were visited, of which 480 (21%) and 70 (3%) received a second and third visit respectively. This aligns with the national DQA guideline that stipulates a minimum of 10% of visited HFs should be revisited. Data availability declined from 84% during the first visit to 82% in health facilities visited for a second time, then increased to 91% among those visited for a third time. The average consistency scores across the first, second, and third visits are 54%, 50%, and 55%, respectively, with a marginal increase observed across the second and the third visit. Consistency scores have been linked to transcription errors from client cards to OPD registers and non-use of client cards due to cost barriers for clients. The validity scores across the first, second, and third visits are 91%, 93%, and 96%, respectively, showing an increasing trend with the highest average score observed in the third visit. Implementation

of improvement plans and maintaining a steady supply of the National Health Management Information System Registers in the HFs are important requirements for data quality. Continuous training to dedicated DQA teams should be adopted to further improve the availability, validity, and particularly the consistency of data to ensure that decision-making, resource allocation, and program adaptation are based on reliable information.

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ETIOLOGY OF INFECTIOUS DIARRHEA IN MADAGASCAR: FINDINGS FROM THE COMMUNITY-BASED SURVEILLANCE SYSTEM FROM 2019 TO 2023

Iony Manitra Razanajatovo[1], Laurence Randrianasolo[1], Odile Lalainasoa Rivolala[1], Aina Harimanana[1], Ulrich Raveloson[1], Nirina Nantenaina Ranoelison[1], Léa Randriamampionona[2], Vaoary Razafimbia[2], Antso Hasina Raherinandrasana[3], Dany Bakoly Ranoaritiana Ranoaritiana[4], Manuella Christophère Vololoniaina[5], Soa Fy Andriamandimby[1], Philippe Dussart[1], Rindra Vatosoa Randremanana[1], Tania Crucitti[1], Jean-Michel Heraud[6], Vincent Lacoste[1]

[1]institut Pasteur De Madagascar, Antananarivo, Madagascar, [2]who, Madagascar, Antananarivo, Madagascar, [3]public Health Department Of The Faculty Of Medicine Of Antananarivo, Antananarivo, Madagascar, [4]ministry Of Public Health -Direction De la Veille Sanitaire, De La Surveillance Epidémiologique Et Riposte, Antananarivo, Madagascar, [5]ministry Of Public Health - Direction De la Veille Sanitaire, De La Surveillanceepidémiologique Et Riposte, Antananarivo, Madagascar, [6]who, Geneva, Antananarivo, Madagascar

Diarrhea remains the highest cause of morbidity and mortality among children under five years-old in South Asia and sub-Saharan Africa. Therefore, systematic collection and analysis of data on the etiologies of diarrhea in community settings are needed to prioritize interventions. Our work describes the first laboratory-based surveillance conducted in children under five years, contributing to enrich data on diarrheal etiology in community settings in Madagascar. A pediatric diarrhea surveillance network was carried out from 2019 to 2023 on 21 sentinel surveillance sites of Madagascar. Five children under five-year-old presenting > 3 loose stools in a 24-h period were enrolled weekly. Stool specimens were collected and analyzed by quantitative PCR for a panel of 4 viruses, 4 bacteria and 3 protozoa. Prevalence and seasonal patterns of diarrhea were determined. From 2019 to 2023, the surveillance system captured 1951 diarrhea cases. The median age was 1,3-years old. Of the 1951 stools tested, 1562 (80%) were positive for at least one pathogen. Among positives, 845 (43.3%) were infected with viruses, 1198 (76.7%) with bacteria, 280 (14.3%) with parasites and 947 (60.6%) had co-infections. Enteropathogenic bacteria *Escherichia coli* was detected in 855 (43.8%) stools followed by *Shigella* spp. in 496 (25.4%), *Campylobacter* spp. in 283 (14.7%). Rotavirus was the most prevalent virus detected in 533 (27.7%) stools, adenovirus in 205 (10.5%), astrovirus in 180 (9.2%) and norovirus GII in 101 (5.2%). *Giardia intestinalis* was the most prevalent parasite detected in 202 (10.4%) stools whereas *C. parvum* and *E. histolytica* were infrequent (3.7% and 0.9% respectively). We observed a seasonal pattern where diarrhea occurred during the hot-rainy and the dry-cold seasons. Detection of diarrhea reached its lowest during the inter-season of March and September. This work has, for the first time, described the etiologies of pediatric diarrhea in Madagascar and a sketch of their seasonal circulation. The data highlight the importance of strengthening laboratory capacity for rapid detection and for implementation of diarrhea control and prevention.

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IMPACTS OF BAD OBSTETRIC HISTORY ON ANTENATAL CARE UPTAKE IN SUBSEQUENT PREGNANCIES: INSIGHTS FROM CHILD HEALTH AND MORTALITY PREVENTION SURVEILLANCE (CHAMPS), BANGLADESH

Maria Rahman Mim[1], Rajib Biswas[1], Shovo Debnath[1], Taukir Tanjim[1], Emily S. Gurley[2], Kazi Munisul Islam[1], Qazi Sadeq-ur Rahman[1], Md. Abdus Salam[1], Md. Atique Iqbal Chowdhury[1], Sanwarul Bari[1], Shams El Arifeen[1], Mohammad Zahid Hossain[1]

[1]International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh, [2]John Hopkins University, Baltimore, MD, United States

Women who suffer adverse pregnancy outcomes require extra care in subsequent pregnancies to ensure healthy outcomes for mother and baby. To understand whether adverse pregnancy outcomes influence subsequent health-seeking behavior, particularly antenatal care (ANC), we conducted an observational study using the Child Health and Mortality Prevention Surveillance (CHAMPS) data. It includes detailed pregnancy data with ANC histories from all pregnant women in Baliakandi, a rural subdistrict of Bangladesh. We defined a bad obstetric history if a mother had a history of either stillbirth, neonatal death, a child with a congenital anomaly, or ≥2 consecutive miscarriages. Mothers with a bad obstetric history and at least two pregnancy outcomes between January 2018 and January 2024 were included in this analysis. We compared ANC utilization between the pregnancy associated with the bad obstetric outcome and the subsequent pregnancy. A total of 137 mothers were included. In the first pregnancy, 35% received no ANC, increasing to 43% in subsequent pregnancy. However, no difference was found between the first and subsequent pregnancy in the proportion who received the first ANC visit within 12 weeks of pregnancy (31% vs 36%). In spite of an adverse outcome, 43% received ANC from qualified doctors in the first pregnancy, and this decreased to 39% in subsequent pregnancy. Additionally, the proportion completing 4 ANC visits decreased from 17% to 10%. Only 7% mothers in 1st pregnancy and 4% mothers in the 2nd pregnancy took ≥4 ANC from qualified doctors. However, the mean number of ANC visits in the first and subsequent pregnancy remained almost similar (2.4 ± 1.9 vs 2.0 ± 1.3). We have found that mothers with bad obstetric history had less ANC uptake compared to their subsequent pregnancies from qualified health care providers. In addition, few mothers took the recommended 4 ANC visits, which is alarming. Different sociodemographic factors may be responsible for this. However, future research should be directed toward identifying the challenges and developing interventions to encourage mothers to utilize government health facilities to ensure quality ANC.

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DENGUE PREPAREDNESS. FRAMEWORK FOR INNOVATIVE TOOLS AND STRATEGIES FOR SURVEILLANCE AND RESPONSE IN OIL AND GAS COMPANY

Joyce Ighedosa, Susan Ngunjiri, Candace McAlester, Patricia Sviech, Yolanda Hill, Gabriel Shi Ze Chia

ExxonMobil Corporation, Spring, TX, United States

The World Health Organization (WHO) in 2023 reported half of the world's population is at risk of dengue, estimating 100-400 million infections each year. *Aedes aegypti*, one of the main vectors for dengue, has an indoor and outdoor day biting pattern. ExxonMobil (EM) has a global workforce with some resident workers and travelers in remote high-risk areas. EM surveillance and evidence-based driven decision led to the development of a global Dengue Control Program, which includes health risk assessments, increased awareness, bite prevention, prompt diagnosis and treatment. Additional strategy includes pre-travel preparation, preventive measures to minimize disease risk, serious illness events, health costs, and business disruption. A retrospective review of case trends and program implementation allows a multidisciplinary approach of a sustainable dengue control program. Regular clinician training on vector-borne diseases such as dengue fever with ongoing review of suitability and availability of dengue vaccines in high-risk areas to ensure current knowledge for appropriate

guidance to travelers. Optimized pre-travel preparation using an innovative tableau travel health dashboard that shows country specific health risks and travel requirements. GeoSentinel Surveillance Network studies in travelers have found dengue as the leading cause of febrile illness among ill travelers returning from Southeast Asia, Latin America, and the Caribbean. Increased emphasis on awareness has shown a steady use of preventive materials. Global business locations are evaluated by required facility specifications, environmental management, and surveillance to ensure program compliance. The Company pretravel preparation ensures 100% identification of risk locations and documentation of risk reviews in the travel health dashboard for clinicians and employees. Dengue disease burden has expanded globally. A robust surveillance and technology embedded in company dengue control program provides guidance and sustainable mitigation tools to reduce serious illness event and support evidence-based priorities in traveler health.

6948

ADVANCING MALARIA CARE THROUGH VARIED INTERVENTIONS: IMPROVING MALARIA RAPID DIAGNOSTIC TEST (RDT) USE IN FOUR NIGERIAN STATES - BENUE, NASARAWA, PLATEAU, AND ZAMFARA

Comfort Kingsley-Randa[1], Attahir Abubakar[2], Olayemi Abimbola[3], Aderonke Omokhapue[3], Methodius Okouzi[1], Arja Huestis[4], Justice Adaji[3], IniAbasi Nglass[3], Uchenna Nwokenna[3], Rudi Thetard[4], Thomas Hall[4], Grace Nwankwo[5], Erkwagh Dagba[5], Veronica Momoh[5], Jules Mihigo[5], Chukwu Okoronkwo[6], Nnenna Ogbulafor[6], Godwin Ntadom[6]

[1]United States President's Malaria Initiative for States, Management Sciences for Health, Nasarawa, Nigeria, [2]United States President's Malaria Initiative for States, Management Sciences for Health, Plateau, Nigeria, [3]United States President's Malaria Initiative for States, Management Sciences for Health, Abuja, Nigeria, [4]Management Sciences for Health, Arlington, VA, United States, [5]United States Agency for International Development, United States President's Malaria Initiative, Abuja, Nigeria, [6]National Malaria Elimination Programme, Abuja, Nigeria

Inaccurate malaria diagnosis and treatment increase disease burden and drive potential drug resistance. In 2020, 180,394 (18%) fever cases were clinically diagnosed as malaria by assessing symptoms without a confirmatory parasitological test in four States: Benue, Nasarawa, Plateau and Zamfara. WHO recommends Rapid Diagnostic Tests (RDTs) for malaria diagnosis before treatment in areas with limited access to malaria microscopy due to their simplicity and rapid results. The U.S. President's Malaria Initiative for States (PMI-S) aims to improve malaria case management (MCM) by increasing RDT use through various interventions (training, guidelines, RDT availability and supervision). Data from health facilities' (HFs) mentoring visits at baseline (December 2020) and regular follow-up supervisory visits from August 2022 to December 2023 were analyzed. Through collaboration with the supply chain implementing partner, RDT availability increased from 45 to 512 HFs, and RDT use increased from 152 healthcare workers (HCWs) in 73 HFs to 1008 HCWs in 616 HFs. PMI-S increased the availability of MCM job aids, standard operating procedures (SOPs) and revised national guidelines from 30 HFs to 491 HFs. PMI-S advocated for and supported regular supervisory visits by trained government staff to 614 HFs. The increased use of RDTs reflects better adherence to national guidelines, which call for parasitological confirmation of malaria, and reduced clinical diagnoses, which dropped to 2% in December 2023. The availability of jobs aids, the enhanced competence in utilizing RDTs, and the continuous supervisory visits resulted in better diagnosis, and, therefore, appropriate treatment for confirmed cases.

6949

OPTIMIZING THE END OF CYCLE (EOC) REPORTING FOR SEASONAL MALARIA CHEMOPREVENTION (SMC) CAMPAIGN IN ZAMFARA STATE, NIGERIA

Dlakwa Shiwan[1], Abdulmajid Idris Safana[1], Abba Abdullahi Sagagi[1], Yusuf Na Allah Jega[1], Munira Isma'il Mustapha[1], Sherifah Ibrahim[1], Muhammad Murtala[1], Comfort Kingsley-Randa[2], Olayemi Abimbola[3], Aderonke Omokhapue[3], Arja Huestis[4], Justice Adaji[3], IniAbasi Nglass[3], Uchenna Nwokenna[3], Rudi Thetard[4], Thomas Hall[4], Aliyu Sani[5], Kabiru Mohammed Bungudu[5], Rufai Ahmad Anka[5], Grace Nwankwo[6], Erkwagh Dagba[6], Veronica Momoh[6], Jules Mihigo[6], Chukwu Okoronkwo[7], Nnenna Ogbulafor[7], Godwin Ntadom[7]

[1]United States President's Malaria Initiative for States, Management Sciences for Health, Zamfara, Nigeria, [2]United States President's Malaria Initiative for States, Management Sciences for Health, Nasarawa, Nigeria, [3]United States President's Malaria Initiative for States, Management Sciences for Health, Abuja, Nigeria, [4]Management Sciences for Health, Arlington, VA, United States, [5]State Malaria Elimination Program, Ministry of Health, Zamfara, Nigeria, [6]United States Agency for International Development, United States President's Malaria Initiative, Abuja, Nigeria, [7]National Malaria Elimination Programme, Abuja, Nigeria

Zamfara state has been implementing seasonal malaria chemoprevention (SMC) campaigns amidst security challenges which makes reporting and follow ups to facilities with data quality issues difficult, affecting the timeliness of reporting SMC data. The SMC campaign in 2023 included end of cycle (EOC) meetings, occurring 2 days after completion of each cycle of the mass drug administration (MDA). This study aims to assess the effectiveness of introducing a data aggregator system in the EOC meeting to aggregate data across 599 HFs in 14 Local Government Areas (LGAs) of Zamfara State. The Android-based tool enabled LGA data officers to validate SMC MDA data during the EOC meeting, using logical checks. The true figures were confirmed from the primary source document (tally sheet) and corrected. Validated entries were securely transmitted to the central server then exported to the backend view where the data is managed and processed. The system conducted secondary deduplication and data cleaning using unique identifiers. The non-duplicate entries were sorted and displayed on each LGA visualization accessible through a secure web interface. The system generated state and LGA aggregate preliminary reports tables and charts of children reached and treated. Compared to the 2022 cycle 1 baseline of 7% data quality issues requiring retrospective correction, all four 2023 SMC cycles achieved 0% data quality issues upon EOC submission. Reporting timeliness improved from 7 working days (2022) to just 2 days (2023) after each SMC MDA cycle. The EOC meeting approach improved data quality by creating a dedicated time and space close to the end of each SMC cycle, to validate, consolidate, and correct erroneous data discovered during data validation at the EOC meeting. Additionally, the use of an Android tool for the data validation enabled faster correction at the point of validation and reliability of SMC data, reduced security risk and travel to facility costs for correction of data and eliminated human errors typical of paper-based tools. This further exemplifies the potential for automated, real-time EOC reporting and validating tools.

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IMPLEMENTATION OF AN APPROACH TO INTEGRATE COMMUNITY HEALTH INTERVENTIONS INTO COORDINATION, MONITORING AND EVALUATION AT THE HEALTH DISTRICT LEVEL IN CÔTE D'IVOIRE

Monné Thérèse Bomin Epse Bleu[1], Melly Aissatou Traore[2], Jean Louis Assa[2], Mamadou Silue[2], Ervé Marius Onané[2], Mea Antoine Tanoh[1], Collette Yah Epse Kokrasset[1], Patricia L. Yepassis-Zembrou[3], Pascal Zinzindohoue[4], Blaise Blaise Kouadio[4]

[1]Côte d'Ivoire National Malaria Control Program, Abidjan, Côte D'Ivoire, [2]Population Services International Côte d'Ivoire, Abidjan, Côte D'Ivoire,

[3]U.S. President's Malaria Initiative, Centers for Disease Control and Prevention, Abidjan, Côte d'Ivoire, [4]U.S. President's Malaria Initiative, U.S. Agency for International Development, Abidjan, Côte D'Ivoire

In Côte d'Ivoire, the coordination and monitoring of community activities is mainly carried out by civil society organizations (CSOs) under contract with international NGOs. The end of these contracts usually leads to partial or total cessation of activities, and access of populations to basic health care. Since 2021, the PMI Stop Djekoidjo project has initiated an approach aimed at increasing local ownership of the coordination, monitoring and evaluation of community health worker (CHW) activities in 29 health districts. The process encompassed 1) development and validation of an operational document, 2) identifying a Community Activities Coordinator (CAC) in each district, 3) training CACs on their job description and entry of data into DHIS2, 4) support for the supervision of CHWs), and 5) organization of coordination meetings with CACs. From January 2021 to December 2023, CHWs recorded data on fever case management for children under five years of age living in communities beyond five km from a health center. Data from all CHWs in the health area were then compiled into a report and forwarded to the health district and entered DHIS2 by the CAC. Data completeness is the percentage of expected CHWs reports submitted in DHIS2.1,600 CHWs were operational during the 2021 to 2023 period. The completeness of data entered DHIS2 increased from 75.3% to 98.6% between 2021 and 2023. The number of fever cases recorded by these CHWs increased by 57.6%, from 76,269 in 2021 to 120,206 in 2023. In addition, the proportion of fever cases tested by rapid diagnostic test increased from 73% in 2021 to 89% in 2023, and positive cases treated with artemisinin-combination therapy increased from 91% in 2021 to 98% in 2023. Despite the withdrawal of CSOs, there has been a gradual increase in the volume of CHW activities between 2021 and 2023. The completeness of data and management of fever cases improved after the introduction of CACs. Thus, the approach appears to be an efficient strategy for consideration in the context of resource scarcity and sustainability of services to the communities.

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PROJECTING *IXODES SCAPULARIS* DENSITIES OF INFECTED NYMPHS (DIN), IN EASTERN UNITED STATES, 1997-2022

Madiha Shafquat[1], Julie Davis[2], James H. Stark[1], Patrick H. Kelly[3]

[1]Vaccines and Antivirals Medical Affairs, Pfizer US Commercial Division, Cambridge, MA, United States, [2]Life Sciences, Clarivate Analytics, Chandler, AZ, United States, [3]Vaccines and Antivirals Medical Affairs, Pfizer US Commercial Division, New York, NY, United States

Ixodes scapularis is the primary vector of *Borrelia burgdorferi* sensu lato (*Bbsl*), the causative agent of Lyme disease (LD) in the United States. Risk for LD can be partly quantified by the densities of infected *I. scapularis* nymphs (DIN), a metric of the ecological hazard across areas. We predicted DIN across parts of the Eastern US using meta-analytic models trained on published data. Two systematic literature searches were conducted in PubMed to identify studies published between 1 Jan 2000 and 23 Aug 2023 that measured density of nymphs (DON) and prevalence of *Bbsl* infection in nymphs (NIP) in the 25 states and DC categorized as high-incidence (>10 LD cases/100,000 population) or neighboring high-incidence jurisdictions in 2022 CDC surveillance data. Studies that reported county-level DIN per unit area and NIP were included. Separate multivariate, linear mixed effects models were fit for DON and NIP. Significant ($p<0.05$) model covariates included latitude and longitude, proportion of wild-urban interface, proportion of forested area, white-tailed deer density, presence of *I. scapularis,* LD incidence, and geographic division (US Census). Best fitting models were chosen via Akaike information criterion and used to predict DON and NIP across all counties in the 25 states and DC. Predicted DIN was calculated as the product of predicted DON and predicted NIP. The literature review yielded n = 934 DON observations (26 studies) and n = 845 NIP observations (57 studies). Most observations for both DON and NIP were in the Northeast and reported by two multi-year, multi-county studies. Observations for DON had wider geographic coverage (96% of jurisdictions) than observations for NIP (81% of jurisdictions). DON was predicted to be highest in parts of NY, NJ, PA, and WI and moderately high in the Mid-Atlantic and East North Central. NIP was predicted to be highest in the Northeast and parts of MN, MI, and WI. DIN was thus highest in the Mid-Atlantic. This study demonstrates the utility of existing published data on *I. scapularis* populations that can be used to inform ecological hazard of LD, but also highlights the spatial and temporal limitations of these data.

6952

A SIMPLE AND SENSITIVE COLORIMETRIC NUCLEIC ACID TEST FOR *BABESIA MICROTI* SURVEILLANCE IN WHOLE BLOOD AND TICK VECTORS

Zhiru Li, Katell Kunin, Elodie Sévère, Andy Alhassan, Nathan Tanner, Amit Sinha, Clotilde Carlow

New England Biolabs, Ipswich, MA, United States

Human babesiosis is a disease of increasing public health importance resulting from infection of red blood cells by protozoan parasites of the genus *Babesia*. The parasite is primarily transmitted to humans by *Ixodes* ticks and can also be transmitted through contaminated blood transfusion. We have developed a simple and sensitive RT-LAMP assay with colorimetric readout for the detection of *Babesia microti* targeting the 18S rRNA gene. The assay simultaneously detects both RNA and DNA and shows higher sensitivity than published qPCR assay. The assay showed no cross-amplification with DNAs from *Homo sapiens*, *Ixodes scapularis*, *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, or *Plasmodium falciparum*. The visual colorimetric detection of this isothermal LAMP assay eliminates the need for sophisticated equipment. In addition, its high tolerance to inhibitors enabled us to develop a direct blood protocol without the need for nucleic acid extraction. Using this assay, we also conducted surveillance of 332 *I. scapularis* collected at Ipswich in Massachusetts (USA), and New Hampshire (USA) for *B. microti*, in parallel with LAMP-assays detecting *B. burgdorferi* and *A. phagocytophilum.* We found 18% (27 of 152) of Ipswich and 7% (13 of 180) of New Hampshire ticks positive for *B. microti*. Our results demonstrate that this simple colorimetric nucleic acid test is suitable for *Babesia microti* surveillance in whole blood and tick vectors.

6953

DISENTANGLING THE RELATIONSHIP BETWEEN THE DEER TICK MICROBIOME AND TICK-BORNE PATHOGENS

Sofia Roitman, Zhiru Li, Elodie Sévère, Cécile Hugel, Daniel Bergeron, Clotilde KS Carlow, **Amit Sinha**

New England Biolabs Inc., Ipswich, MA, United States

Tick-borne diseases are a growing threat to public health worldwide, further exacerbated by their range expansions. Aside from known pathogens, ticks also carry a wide variety of other infectious and non-infectious organisms. We aimed to catalog the full spectrum of bacteria present in deer ticks (*Ixodes scapularis*) and the effect of biotic factors such as tick sex, geographic region, and presence of known pathogens on microbiome composition. We sequenced the V4 region of the bacterial 16S rRNA gene from about 300 individual *I. scapularis* ticks from Massachusetts and New Hampshire. A total of 1.63 billion reads were obtained from runs on a Illumina NovaSeq instrument, providing a median depth of 5.6 million reads per sample. Microbiome analysis using the QIIME2 pipeline and Deblur algorithm identified a total of 24,070 bacterial Amplicon Sequence Variants (ASVs) across all samples. A rarefaction curve analysis determined that a minimum sample read count of approximately 125,000 is needed to capture the full spectrum of bacterial diversity in over 90% of our tick samples. Beta diversity analyses and significance testing across all samples indicate that the sex of the tick, geographical region, and *Borrelia burgdorferi* (Lyme disease) infection status are key drivers of tick bacterial microbiome composition. We observed previously unreported correlations between the presence of *Borrelia* and certain microbiome members, including bacteria with pathogenic potential, such as *Mycobacterium* and *Roseomonas*. The microbiome members found to be highly associated with *Borrelia* warrant further study to determine their role in disease.

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COINFECTION OF *ANAPLASMA PHAGOCYTOPHILUM* AND *BORRELIA BURGDORFERI* IN NON-HUMAN PRIMATES. IMPACT ON IMMUNE RESPONSE AND DISEASE SEVERITY

Folasade Adekanmbi, Monica Embers

Tulane University National Primate Center, Covington, LA, United States

Anaplasma phagocytophilum (Ap) and *Borrelia burgdorferi* (Bb), the agents of Human Granulocytic Anaplasmosis (HGA) and Lyme disease, respectively, are transmitted by *Ixodes scapularis* ticks. Coinfection has been reported in humans and animals. Ap preferentially infects the neutrophils, which are critical for clearing Bb infection. Severe Combined Immune Deficient (SCID) mice have higher Bb tissue load and pathology and are susceptible to Ap infection, which persists for several months. Nonhuman primates (NHPs) are the most relevant animal models for translational diagnostic and therapeutic intervention due to their susceptibility to both pathogens and reproduction of human disease. Our overarching goal is to study the effect of coinfection in NHPs, but we first investigated concurrent Ap/Bb infections and transmission to uninfected mice. We infected immunocompetent mice with Bb culture and Ap-Infected HL60 (human promyelocytic leukemia) cells via syringe inoculation and confirmed infection of larval ticks. Transmission of both pathogens to uninfected mice through those ticks, post-molt into nymphs, was subsequently demonstrated. We evaluated coinfection using conventional PCR by targeting the *Msp2* gene in Ap, blood smear, immunofluorescence (IFA), and cell culture for Bb. Bb was detected in the ears, heart, skeletal muscle, tibiotarsal joints, spleen, and bladder, while Ap was detected in the blood, liver, and spleen of coinfected and Ap-infected mice. We will propagate Ap in SCID mice and capillary-feed the infected blood to nymphs to generate infected ticks as well. We will use infected ticks to assess coinfection in NHPs by determining pathogen burden in blood and tissues utilizing qPCR, IFA and blood smear. Gross and histopathology, immune responses using flow cytometry, serum cytokine profiles and antibody responses will be assessed. Based on previous studies, we hypothesize that the coinfected NHPs will have a higher bacterial burden, significantly reduced immune response, and more severe tissue pathology than the single-pathogen-infected groups.

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HEMOPLASMA AND PIROPLASM SPECIES IN WHITE-EARED OPOSSUMS (*DIDELPHIS ALBIVENTRIS*) FROM ALAGOAS, NORTHEASTERN BRAZIL - PRELIMINARY DATA

Ana CS Silva[1], **Jessica Miller**[2], Epitácio C. Farias Junior[3], Ana CP Azevedo[4], Jonatas C. Almeida[5], Joao L. Garcia[1], Thiago F. Martins[6], Marcelo B. Labruna[6], Thallitha SWJ Vieira[2], Rafael Vieira[2]

[1]Universidade Estadual de Londrina, Londrina, Brazil, [2]The University of North Carolina at Charlotte, Charlotte, NC, United States, [3]Universidade Federal de Alagoas, Viçosa, Brazil, [4]Centro de Triagem de Animais Silvestres, Maceió, Brazil, [5]Universidade Federal de Alagoas, Maceió, Brazil, [6]Universidade de São Paulo, São Paulo, Brazil

The presence of marsupials in domestic environments is relevant for public health purposes, with species of hemotropic *Mycoplasma* (hemoplasmas, HM) and piroplasms known to infect domestic and wild animals, including *Didelphis*. This study aimed to molecularly characterize HM and piroplasm species in white-eared opossums (*Didelphis albiventris*) from transitional areas between the Atlantic Forest and Caatinga biomes in the State of Alagoas, northeastern Brazil. DNA was extracted from EDTA-blood samples from 30 (19 males and 11 females) white-eared opossums using a commercial kit. DNA samples were initially screened by a SYBR Green Universal Real-Time PCR (qPCR) targeting the 16S rRNA gene of HM. Samples were also screened by a nested-PCR (nPCR) assay targeting a fragment of the 18S rRNA gene of piroplasms. Four out of 30 (13.33%, 95% CI 5.31-29.62%) animals tested positive for HM and piroplasms, with one animal was co-infected by both agents. Hemoplasma-positive samples were subjected to conventional PCR assays targeting a fragment of the 16S rRNA (~900 bp) and 23S rRNA (800 bp) genes, followed by Sanger sequencing. Sequencing of both the 16S and 23S rRNA genes revealed that the animals were infected by '*Candidatus* Mycoplasma haemoalbiventris'. Piroplasm 18S rRNA gene sequences showed 100% identity with *Babesia* sp. from *D. albiventris* from Brasília, central-western Brazil (MW290046). Phylogenetic analyses using Bayesian inference revealed the detected *Babesia* sp. formed a polytomy with piroplasm sequences detected in marsupials from Brazil, reinforcing the existence of the piroplasmid clade "South American Marsupialia". Our future steps involve sequencing other gene fragments (*cox-1*, *cox-3*, and *hsp70*) to confirm our preliminary findings. This is the first of *Babesia* sp. in white-eared opossums from Northeastern Brazil.

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POTENTIALLY NOVEL *EHRLICHIA* SP. IN WHITE-EARED OPOSSUMS (*DIDELPHIS ALBIVENTRIS*) FROM ALAGOAS, NORTHEASTERN BRAZIL-PRELIMINARY DATA

Ana CS Silva[1], **Jessica Miller**[2], Epitácio C. Farias Junior[3], Ana CP Azevedo[4], Jonatas C. Almeida[3], João L. Garcia[1], Thiago F. Martins[5], Marcelo B. Labruna[5], Thállitha SWJ Vieira[2], Rafael Vieira[2]

[1]Universidade Estadual de Londrina, Londrina, Brazil, [2]The University of North Carolina at Charlotte, Charlotte, NC, United States, [3]Universidade Federal de Alagoas, Viçosa, Brazil, [4]Centro de Triagem de Animais Silvestres, Maceió, Brazil, [5]Universidade de São Paulo, São Paulo, Brazil

The genus *Didelphis*, comprising synanthropic marsupials, is known to host various vector-borne agents, including tick-borne bacteria. Here, we detected a potentially novel *Ehrlichia* spp. in white-eared opossums (*D. albiventris*) in transitional areas of the Atlantic Forest and Caatinga biomes in Alagoas, northeastern Brazil. DNA was extracted using a commercial kit from EDTA-blood samples from 30 (19 males and 11 females) white-eared opossums. DNA samples were initially screened by a nested-PCR (nPCR) assay targeting a fragment of the *dsb* gene of *Ehrlichia* sp. A total of 24/30 (80%; 95% CI: 62.69 - 90.49%) white-eared opossums tested positive for *Ehrlichia* spp. by the *dsb*-nPCR assay. After that, *Ehrlichia*-positive samples were subjected to a PCR targeting a fragment (~844 bp) of the *groEL* gene of *Ehrlichia*, followed by Sanger sequencing. Seven DNA samples were sequenced. *Ehrlichia groEL* gene sequences obtained herein showed 93.77% identity with *Ehrlichia* sp. from *Ornithodoros capensis* of birds from Japan (LC649942). Phylogenetic analyses using Bayesian inference revealed the detected *Ehrlichia* grouped in a single clade, suggesting the white-eared opossums were infected by a putative new *Ehrlichia* sp. species. A total of six/30 white-eared opossums were infested by larvae of *Ornithodoros mimon* ticks at the time of sampling. We report a potentially novel *Ehrlichia* species in white-eared opossums from Alagoas, northeastern Brazil. Our future steps involve sequencing other gene fragments (16S rRNA, *dsb*, *sodB,* and *gltA*) to confirm our preliminary findings.

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HUMAN HEALTH DISPARITIES IN MITE-BORNE ILLNESSES

James H. H. Diaz

LSU Health, New Orleans, LA, United States

Mites transmit bacterial infections, such as scrub typhus and rickettsialpox, and cause chronic infestations, such as crusted and nodular scabies. Secondary infections cause impetigo, rheumatic fever, and glomerulonephritis. Mite-borne allergens cause asthma and anaphylaxis. Some populations are disproportionately affected by mite-borne illnesses. Several Internet search engines were queried to identify the most significant population-level risk factors for mite-borne illnesses. There are several human health disparities in mite-borne illnesses characterized by either reduced host immunocompetency or excessive mite exposures. Immunocompetency levels wane with advancing age, viral infections, especially HIV and HTLV-1, cancer and chemotherapy, corticosteroid and transplant antirejection therapy. Excessive mite exposure levels occur in crowded venues including shelters for refugees, evacuees, and the homeless, chronic care institutions, sexually transmitted disease clinics,

animal shelters and veterinary clinics, and food and fruit-processing workplaces. Some populations may be uniquely predisposed to crusted scabies and secondary infections including patients with Down syndrome, other cognitive disabilities, Australian Aborigines, and the indigenous inhabitants of the Fijian, Samoan, and Solomon islands in the South Pacific. Others may be exposed to animal scabies or plant, insect, and foodborne mite infestations in their workplaces. Targeted interventions to control and prevent mite-borne illnesses should be directed at these neglected populations and excessive exposure groups worldwide.

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A NEW MULTIPLEX SEROLOGIC ASSAY FOR DETECTION OF *BARTONELLA* SPECIES IN IRAQ DEPLOYED MILITARY WORKING DOGS

Fernanda Fortes de Araujo[1], Jennifer Safko[1], Jessica Bolton[2], Heather Richardson[3], Le Jiang[4], Sarah Jenkins[4], Edward Breitschwerdt[5], Elke BergmannLeitner[2], Naomi Aronson[1]

[1]Uniformed Services University, Bethesda, MD, United States, [2]Walter Reed Army Institute of Research, Silver Spring, MD, United States, [3]DoD Food Analysis and Diagnostic Laboratory, San Antonio, TX, United States, [4]Naval Medical Research Command, Silver Spring, MD, United States, [5]North Carolina State University, Raleigh, NC, United States

Bartonella species seroprevalence was 47.4% in feral dogs in Iraq; blood collected by the U.S. Army Zoonotic Disease Surveillance Program in 2008-9. *Candidatus* Bartonella merieuxii *(C*bm*)* DNA, an uncultured *Bartonella* species, was amplified from 37% of Iraq feral dogs` blood. The objectives of this surveillance study were 1) to define the prevalence of bartonellosis in military working dogs (MWDs) that had deployed to Iraq, 2) to report the species profile. Medical records and paired sera/whole blood samples were obtained from pre and post Iraq deployment for 104 MWDs. Conventional diagnostic testing for *Bartonella* species was performed including Indirect Immunofluorescence Assay (IFA) for *B. bovis, B. henselae, B. koehlerae* and *B. vinsonii berkhoffii* with ≥ 1:64 considered seroreactive. *Bartonella* genus *rpoB* gene qPCR assay was conducted using whole blood DNA, with amplicon sequences compared to GenBank by BLAST analysis. Fifty paired sera were evaluated by Mesoscale/MSD V-PLEX™ platform using a new 10-plex assay with a total of 20 peptides representing B cell linear epitopes predicted by the Bepipred algorithm (Immune Epitope Database iedb.org). The studied population (n=104 MWDs) showed no significant clinical differences in those testing positively for *Bartonella* acquired in Iraq except for a decrease in white blood cells, *p=0.032*. Twelve dogs (12%) were IFA seroreactive for any *Bartonella* spp. including four dogs (4%) IFA seroreactive to the *C*Bm surrogate (*B. bovis)* with titers 1:128 or 1:1024. *Bartonella* genus-specific qPCR assay identified Iraq-related infection of one (1%) MWD with sequencing of *rpoB* gene determined to be *C*Bm with 99.9% sequence homology. In the new Mesoscale assay 15 MWDs (30%) showed statistical differences between pre and post deployment sera (p<0.001), suggesting seroconversion during deployment (luminescence signal post/pre >2). In conclusion, MWDs acquired novel *Bartonella* spp. infections during deployment in Iraq and our newly developed MSD assay can serve as a new diagnostic tool providing an alternative high-throughput assay.

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SEVERE TICK-BORNE DISEASE IN NORTH CAROLINA, A TEN-YEAR REVIEW OF HOSPITALIZED CASES

Diana L. Zychowski, Ross Boyce

University of North Carolina, Chapel Hill, NC, United States

Tick-borne diseases such as spotted fever group rickettsiosis (SFGR) and ehrlichiosis are a growing public health concern in the United States. Clinical manifestations are non-specific and include fever, arthralgia, diarrhea, headache, and rash. Delays in treatment are strongly associated with morbidity and death. Yet other demographic and clinical risk factors associated with severe disease remain poorly described. Utilizing a retrospective cross-sectional design, we performed a 10-year review of ehrlichiosis and SFGR cases admitted to the University of North Carolina health system from 2014 to 2024 to identify factors associated with severe disease. A total of 242 admissions from 239 unique individuals with a diagnosis of ehrlichiosis (N=30), SFGR (N=204), or both (N=8) were included in this study. The median age was 55 years (IQR 37-67), with most participants identifying as white (186, 76.9%), non-Hispanic (221, 91.3%), and male (161, 66.5%). Over 88% (N=214) of cases occurred between April and October. Twenty-two percent (N=55) had some form of immunocompromise including asplenia, bone marrow or solid organ transplant, cancer, chronic dialysis, neutropenia, or human immunodeficiency virus. Nearly 15% (N=35) were admitted to the ICU, with 27/35 (77%) having SFGR. Approximately 10% (N=24) required mechanical ventilation. The average number of days from admission to doxycycline administration was 2.2, though the use of doxycycline was not significantly higher among patients requiring ICU care (OR 0.8, 95% CI: 0.3-1.9). Risk factors for ICU admission included underlying pre-existing cardiovascular disease (OR 4.4, 95% CI: 2.1-9.2), diabetes mellitus (OR 2.1, 95% CI: 1.0-4.4), and male sex (OR 2.7, 95% CI: 1.1-6.9). However, older age (e.g. >65 years) and immunocompromised status were not statistically associated with ICU care. Our results show that diabetes and cardiovascular disease may be risk factors for severe
ehrlichiosis or SFGR and there should be a low threshold to administer doxycycline in these high-risk groups when consistent symptoms, laboratory abnormalities and/or exposures are present.

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MINIMUM FEEDING TIME REQUIRED FOR *HAEMAPHYSALIS LONGICORNIS* TO TRANSMIT SEVERE FEVER WITH THROMBOCYTOPENIA SYNDROME VIRUS

Bailey J. Hettinger, Eliane Esteves, Clemence Obellianne, Ahmed Garba, Meghan E. Hermance

University of South Alabama Frederick P. Whiddon College of Medicine, Mobile, AL, United States

Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV) is an emerging tick-borne bandavirus that can cause disease in humans with a 6-30% mortality rate. The major tick vector of SFTSV is *Haemaphysalis longicornis*, which is native to eastern Asia but recently emerged in the United States. Emerging viruses and invasive tick species highlight the importance of understanding how a virus such as SFTSV associates with and is transmitted by its tick vector. A notable factor in this tick-pathogen association is the minimum tick attachment time required for the tick to successfully transmit a pathogen during feeding. This transmission time is understood for some bacteria but for many tick-borne viruses, including SFTSV, this tick-to-host transmission time is unknown. The objective of this study is to define the minimum feeding time required for *H. longicornis* nymphs to transmit SFTSV to a vertebrate host. Nymphs were infected with SFTSV by transovarial transmission to generate a population of infected ticks to be used in the tick-to-host transmission time experiments. In a pilot study, mice were each infested with 8 - 10 putatively infected nymphs that were allowed to feed for 5 hours. At the 5 hour post-attachment (h.p.a.) timepoint, nymphs were manually removed from mice and screened via q-RT-PCR for SFTSV RNA. Samples of mouse blood and skin biopsies (proximal and distal to the tick feeding site) were also collected at 5 h.p.a. and screened for viral RNA. SFTSV RNA was detected in the proximal skin biopsies from several mice. These preliminary results suggest that after feeding for 5 hours, SFTSV-infected *H. longicornis* nymphs were able to transmit SFTSV to mice; however, detection of infectious virus in the vertebrate host still needs to be assessed. Follow-up studies will assess tick feeding timepoints less than 5 hours. Methods to pre-screen putatively infected nymphs for SFTSV before they are included in the transmission experiment are also being optimized. In upcoming tick-to-host transmission time experiments, this optimized model system will be used to define the minimum feeding time required for *H. longicornis* nymphs to transmit SFTSV to a host.

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INVESTIGATION INTO THE BACTERIOME OF TICKS COLLECTED FROM NINE KENYAN COUNTIES.

Bryson B. Kimemia[1], Lillian Musila[1], Solomon K. Langat[2], Erick Odoyo[1], Stephanie Cinkovich[3], Samoel A. Khamadi[2], Jaree Johnson[4], Elly H. Ojwang[5], Timothy E. Egbo[5], Eric C. Garges[5], Fredrick L. Eyase[1]

[1]Walter Reed Army Institute of Research-Africa (WRAIR-Africa)/Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [2]Centre for Virus Research, Kenya Medical Research Institute (KEMRI), Nairobi, Kenya, [3]United States Armed Forces Health Surveillance Division, Global Emerging Infections Surveillance Branch, Silver Springs, MD, United States, [4]United States Armed Forces Pest Management Board, Silver Springs, MD, United States, [5]Walter Reed Army Institute of Research-Africa (WRAIR-Africa), Kisumu, Kenya

Vector surveillance has become a very important component in public health preparedness. Continuous and rigorous screening of vectors such as ticks allows for up-to-date pathogen situational awareness. This study sought to enhance the knowledge of bacterial pathogens circulating in ticks from Kenya by sampling and screening ticks from nine counties representing major regions in the Country. These are representative of the North-eastern, Coastal, Western, and the Rift Valley region. These were selected to represent a wide variety of climatic and socio-economic zones thus generating a clearer picture of the situation in the country. 16S rRNA metagenomic sequencing on the MinION (Oxford Nanopore Technologies) platform was used to screen the ticks. Bioinformatics analysis involved base-calling, adapter trimming and demultiplexing using Dorado, quality trimming and filtering using Trimmomatic, deduplication, chimaera filtering and OTU clustering using QIIME2-VSearch. Taxonomic classification of the representative sequences was done using a Bayes classifier that was trained on 16S rRNA sequence data from the SILVA 138 database. 1,562 ticks were collected, surface sterilized and pooled into 251 pools with an average of 6 ticks per pool. The ticks collected belonged to 3 genera and 14 species. 237 bacterial species were identified in the ticks and of these, 78 species were identified as pathogens and opportunistic pathogens. The top 5 pathogens with the highest Minimum Infectivity Rate (M.I.R) were *Staphylococcus pseudintermedius* (6.91%), *Staphylococcus aureus* (6.85%), *Rickettsia africae* (3.65%), *Coxiella burnetii* (3.59%) and *Rickettsia japonica* (3.20%). The diverse nature of bacteria identified both pathogens and non-pathogens is proof that ticks are complex arthropod vectors that offer a rich source of emerging and re-emerging infectious diseases. Further investigation needs to be done to determine which of these pathogens are viable and subsequently transmissible. This study greatly contributes to public health awareness within the country.

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HOUSEHOLD INSECTICIDE USE AND REAT FLEA RESISTANCE IN MADAGASCAR: IMPLICATIONS FOR PUBLIC HEALTH

Adélaïde Miarinjara[1], Annick Onimalala Raveloson[2], Mireille Harimalala[3], Beza Ramasindrazana[3], Diego Ayala[3], Thomas Gillespie[1]

[1]Emory University, Atlanta, GA, United States, [2]Institut Pasteur de Madagascar. Ecole doctorale Sciences de la Vie et de l'Environnement, Université d'Antananarivo, Antananarivo, Madagascar, [3]Institut Pasteur de Madagascar, Antananarivo, Madagascar

In Madagascar where bubonic plague, a flea-borne disease, is endemic, there is a gap in knowledge regarding household pest control that may impact health and insecticide resistance in vectors. In this study, we investigated 254 households distributed in seven villages within three districts in plague-endemic areas of Madagascar to understand the pattern of insecticide use in homes and to assess rat flea (*Xenopsylla cheopis*) susceptibility to insecticides. Here we present the results from household surveys and insecticide bioassays. We found that insecticide was the most common means for domestic pest control for 91.66 % of respondents, primarily targeting the house flea (80.11%). Most applied liquid formulations (78.41%),and 62.50% used insecticides without dilution. Bedrooms (90.90%) and floors (89.78%) were primarily treated. Only 46.02% of respondents were satisfied with the treatment results. Products were bought from outdoor market vendors (38.64%) or agricultural stores (31.25%). Retailer advice (55.68%) and neighbors' opinions (21.02%) guided insecticide selection. Retailers provided most (84.65%) information on insecticide usage. Yet, 39.54% of respondents could not recall the commercial name of the insecticide used, given that only 26.13% bought labeled products. Laboratory insecticide bioassay revealed widespread resistance to DDT (mortality rate, MR: 0 - 7.50%) and deltamethrin (MR: 0 - 42.50%) among rat fleas from these villages. Flea populations were tolerant (MR: 82.8 - 95.10%) and susceptible (MR: 97.60 -100%) to fenitrothion, with only fleas from one village showing resistance (MR: 45%). The significant reliance on insecticide to control household pests and limited product knowledge pose a risk for health and may contribute to the development of resistance in non-target insects such as the plague vector, *X. cheopis.* Our findings suggest that interventions focused on retailers (i.e., education, incentives) would equip households with accurate pesticide knowledge. Addressing these challenges is imperative for safeguarding public health and mitigating insecticide resistance.

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*COXIELLA BURNETII*I N RUMINANTSAND DONKEYS *(EQUUS ASINUS)* FROM SOMALIA

Aamir M. Osman[1], Caroline T. Secato[2], Igor S. Silito[3], Ahmed A. Hassan-Kadle[4], Mohamed A. Shair[4], Abdalla M. Ibrahim[5], Maria CA Serpa[3], Marcos R. André[2], Thallitha SWJ Vieira[6], Marcelo B. Labruna[3], Rosangela Z. Machado[2], **Rafael FC Vieira**[6]

[1]Universidade Federal do Paraná, Curitiba, Brazil, [2]Universidade Estadual Paulista, Jaboticabal, Brazil, [3]Universidade de São Paulo, São Paulo, Brazil, [4]Abrar University, Mogadishu, Somalia, [5]Abrar University, Mogadishu, Brazil, [6]The University of North Carolina at Charlotte, Charlotte, NC, United States

Coxiella burnetii, a zoonotic obligate intracellular bacterium that causes Q fever in humans and coxiellosis in ruminants, may pose significant economic losses and health risks. Understanding its epidemiology is paramount for implementing effective control measures. Our study investigated the presence of *C. burnetii* in ruminants and donkeys in Somalia using serological and molecular techniques. Serum samples from 402 animals (190 goats, 133 cattle, 49 sheep, and 30 donkeys) in the Benadir and Lower Shabelle Regions of Somalia underwent testing using the Indirect Fluorescent Antibody Test (IFAT) against *C. burnetii* strain At12. IgG titers for each *C. burnetii* antigen were determined by diluting the samples in two-fold increments with phosphate-buffered saline (PBS), starting at a 1:64 dilution. DNA was extracted from EDTA-blood samples (199 goat, 131 cattle, and 45 sheep) and screened using a qPCR assay based on the repetitive element IS1111 for *C. burnetii.* A total of 53**/**402 (13.2%) animals (endpoint titer: 64 – 8.192) showed antibodies reactive to *C. burnetii.* Donkeys exhibited seroreactivity 6/30 (20%) (endpoint titer: 64 – 512), goats 40/190 (21.1%) (endpoint titer: 64 – 2.048), and sheep 7/49 (14.3%) (endpoint titer: 64 – 8.192), while cattle showed negative results. Two goats tested qPCR-positive for *C. burnetti*. All other animals tested qPCR-negative. This study confirms the presence of anti-*C. burnetii* antibodies in Somali livestock (goats, sheep, and donkeys). Our data highlighting its potential impact on animal and public health through zoonotic transmission. Further investigation into the epidemiology of *C. burnetii* in Somalia and the development of targeted control measures are needed.

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SEROPREVALENCE OF *RICKETTSIA* SPP. IN CATTLE, SHEEP, GOATS AND DONKEYS (*EQUUS ASINUS*) FROM SOMALIA

Aamir M. Osman[1], Igor S. Silito[2], Ahmed A. Hassan-Kadle[3], Mohamed A. Shair[3], Abdalla M. Ibrahim[3], Maria CA Serpa[2], Thallitha SWJ Vieira[4], Marcelo B. Labruna[2], **Rafael Vieira**[4]

[1]Universidade Federal do Paraná, Curitiba, Brazil, [2]Universidade de São Paulo, São Paulo, Brazil, [3]Abrar University, Mogadishu, Somalia, [4]The University of North Carolina at Charlotte, Charlotte, NC, United States

Rickettsia spp. are gram-negative obligate intracellular bacteria, with *Rickettsia africae* being transmitted by *Amblyomma* ticks and posing a zoonotic risk, notably causing African tick bite fever (ATBF). Livestock and donkeys (*Equus asinus*) play vital roles in Somalia's economy, facing tick-borne disease risks. Our study investigates rickettsial exposure in livestock and donkeys across two bioclimatic regions in the country. A cross-sectional study collected 402 (190 goats, 133 cattle, 49 sheep, and 30 donkeys) serum samples from Benadir and Lower Shabelle regions of Somalia. Immunofluorescence assays (IFA) were conducted using crude antigens of *R. africae* and *R. rhipicephali*. Sera were diluted in two-fold increments with phosphate-buffered saline (PBS) starting at a 1:64 dilution, and endpoint IgG titers for each *Rickettsia* antigen were determined. A total of 212/402 (52.7%) (endpoint titer: 64–2.048) samples were seropositive for *Rickettsia* spp. *R. africae* was predominant in 20.9% of cases, while *R. rhipicephali* was detected in 9.9%. Co-reactivity was observed in 21.9 percent of the samples. Cattle showed the highest seroreactivity at 90.2%, primarily with *R. africae* (50.4%), followed by goats at 27.4%, primarily with *R. rhipicephali* (18.9%), and sheep at 28.6%, mainly with *R. africae* (18.4%). Donkeys showed 83.3% seroreactivity, mainly to *R. africae* (23.3%). Co-reactivity was prevalent across species. Cattle, donkeys, and sheep were more likely to be seroreactive to *Rickettsia* spp. than goats (OR: 24.5, 13.2, and 1.1, respectively). This study reveals the first serological evidence of *Rickettsia* sp. in Somali ruminants and donkeys, emphasizing the importance of investigating tick-borne diseases within the One Health framework.

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ELUCIDATING THE TICK MICROBIAL PROFILE IN DISTINCT ECOLOGICAL REGIONS OF EAST AFRICA

Victor O. Anyango[1], Aool W. Opiyo[1], Lukindu, M[2], Paula Lado[3], Cohnstaedt, L. W[3], Hensley L. E[3], Corey Brelsfoard[1], Maria G. Onyango[1]

[1]Texas Tech University, Lubbock, TX, United States, [2]Uganda Virus Research Institute, Entebbe, Uganda, [3]National Bio and Agro-Defense Facility-USDA, Manhattan, KS, United States

In Africa, where pastoralism is pivotal in the economy, the interaction between ticks and humans may be more significant than initially perceived. Pastoralism contributes to the stability of many African economies, accounting for a significant portion of the Gross Domestic Product (GDP) in countries where it is practiced. These regions are crucial economic hubs and are home to a significant portion of the country's livestock and wildlife. One of the key challenges and threats faced by these pastoralist communities is the increasing risk of animal and zoonotic diseases. This risk poses a significant danger to both the livelihoods of pastoralists as well as their health. To identify habitats with increased transmission of tick pathogens in East Africa, we sampled ticks in six districts of Uganda and four Kenyan counties in high-intense pastoralist farming regions with distinct ecology. We carried out an Illumina sequencing of tick singletons in the 16S V3-V4 hypervariable rRNA region. The microbial abundance and diversity were assessed. Our findings identified diverse microbes of significant public health concern circulating in ticks collected from the East African region. These microbes were not geographically clustered in unique regions but were identified across the different ecological regions. Our findings demonstrate a high incidence of tick-borne pathogens in the East African pastoralist zones. The factors driving tick-borne pathogen transmission in different habitats of East Africa are not well understood. There is a need to better define these factors to prevent tick-borne pathogen epidemics in Africa and global spillover.

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EFFICACY OF TWO DOSES OF IVERMECTIN TABLET IN TREATMENT OF SCABIES IN COMPARISON TO ONCE APPLICATION OF 5% PERMETHRIN LOTION- A RANDOMIZED CONTROLLED TRIAL

Priyamadhaba Behera, Debkumar Pal, Chandra Sekhar Sirka, Binod Kumar Patro

All India Institute of Medical Sciences, Bhubaneswar, Bhubaneswar, India

Scabies may cause community outbreaks without early diagnosis and appropriate treatment. Oral ivermectin offsets some challenges associated with topical permethrin 5% application for treating scabies. We aimed to evaluate the efficacy of two doses of oral ivermectin [200 microgram/kg] on day one and day seven compared to 5% [weight/volume] once whole-body application of permethrin lotion in treating scabies. We recruited one hundred participants with mild or moderate scabies and randomized into ivermectin and permethrin arms using computer-generated sequences. Participants and their contacts in the ivermectin arm received two doses of ivermectin [200 micrograms per kg] on days one and seven. The participants and their contacts in the permethrin arm received treatment with 5% [w/v] permethrin application over the whole body. The participants were followed up after four to six weeks of the intervention to determine the cure rate. Institutional ethics approval was obatined from Institutional Ethics Committee of All India Institute of Medical Sciences, Bhubaneswar [IEC reference number: T/IM-NF/CM&FM/21/149]. The trial was registered in ctri.nic.in (CTRI/2022/03/040762) prospectively. We got a similar cure rate (100%) in both arms for the patients after one dose of whole-body application of permethrin or two appropriate doses of ivermectin among mild to moderate cases of scabies. The cost was lower in the ivermectin arm than in the permethrin arm. The cure rate of scabies with one local application of 5% permethrin lotion and two doses of oral ivermectin tablets is similar. Ivermectin has an added advantage regarding lower cost and convenience in its usage.

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CORRECT KNOWLEDGE, ATTITUDES, AND CONFIDENCE FOR APPROACHING RICKETTSIOSIS IN A SAMPLE OF MEDICAL STUDENTS IN CLINICAL SCIENCES FROM ENDEMIC AND NON-ENDEMIC REGIONS OF MEXICO

Karla Dzul-Rosado[1], Luis R. Alvarez-Martin[2], Yuliana V Priego Escamilla[2], Kyra Argaez-Ojeda[2], Juan J. Arias-Leon[3], Fernando Puerto-Manzano[4], **Osvaldo Huchim**[5], Baldomero Sanchez-Barragan[6], Luis Emilio Ramon-Garcia[1], Hamid A. Cervantes-Marin[5], Nina Mendez-Dominguez[2]

[1]Centro de Investigaciones Regionales Dr. Hideyo Noguchi. Universidad Autónoma de Yucatan, MERIDA, Mexico, [2]Hospital Regional de Alta Especialidad de la Peninsula de Yucatan, MERIDA, Mexico, [3]Facultad de Medicina. Universidad Autónoma de Yucatan, MERIDA, Mexico, [4]Hospital Regional de Alta Especialidad de la Península de Yucatan IMSS-BIENESTAR, MERIDA, Mexico, [5]Universidad Anahuac, MERIDA, Mexico, [6]Universidad Juarez Autonoma de Tabasco, MERIDA, Mexico

Medical diagnosis is commonly guided by clinical and epidemiological evidence and experience. Anamnesis is fundamental to identifying causes and risks for Rickettsiosis. Ticks, mosquitoes, and other vectors may coexist in undeserved regions, and they may relate to unspecific signs and symptoms. Medical education programs vary across Mexico Objective: We aimed at evaluating differences in knowledge about preventing and diagnosing rickettsiosis, personal experience when assisting patients with probable diagnosis and the confidence they self-identify for accurately establishing a diagnosis of rickettsiosis among medical students from endemic and non-endemic regions. In this cross-sectional study, 144 medical students from seven universities. Were invited to participate by responding a 30-item questionnaire. Sample size was obtained for

two-proportion comparison with 95% confidence, p<0.05, considering a difference of 25% between endemic or non-endemic regions. From 144 participants, 50% male, aged 24.2 years, 46.5 were from non-endemic regions, while 53.4% from endemic regions. Students from endemic regions had more knowledge about the vector, transmission, prevention, and risks for rickettsial infections (64% more); 85% of non-endemic region identified differential diagnoses, compared to 100% residing in endemic regions. In regression analysis, those from endemic regions were more likely to correctly consider rickettsiosis (OR:1.34) in differential diagnosis, to revise specific protocols and guidelines (OR:2.74), were more confident of their diagnostic capacity (OR:1.49), more prone to consider themselves as well trained (20.77) and to indicate appropriately the clinical tests (OR:1.34). Rickettsiosis diagnosis is part of general physicians every day's activities. Knowledge is fundamental for medical students from endemic and non-endemic regions of Mexico, even when experience with rickettsioses may depend on the epidemiology of the region.

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EXPLORING TICK VECTOR DYNAMICS IN CRIMEAN-CONGO HEMORRHAGIC FEVER OUTBREAK ZONES OF EAST AFRICA

Winnifred Opio Aool[1], Victor O. Anyango[1], Martin Lukindu[2], Paula Lado[3], Cohnstaedt, W. Lee[4], Lisa Hensley[4], Corey Brelsfoard[1], Maria G. Onyango[1]

[1]Texas Tech University, Lubbock, Tx, United States, [2]Uganda Virus Research Institute, Entebbe, Uganda, [3]National Bio And Agro-Defense Facility-USDA, Manhattan, KS, United States, [4]National Bio and Agro-Defense Facility-USDA, Manhatan, KS, United States

Crimean-Congo hemorrhagic fever virus (CCHFV), a member of the Nairoviridae family and Orthonairovirus genus, is a tick borne, negative-sense RNA virus that causes Crimean-Congo hemorrhagic fever (CCHF). This disease, characterized by a severe course, has a case fatality rate of 30% or more. The primary vector for CCHFV is recognized as *Hyalomma marginatum*, and its presence has been closely linked to outbreaks of human disease. In East Africa, Uganda has faced several CCHF outbreaks since 2013, while Western Kenya documented just one case in October 2000. Interestingly, Central and Western Uganda, where most CCHFV cases occurred previously, show very low environmental suitability for *Hyalomma* species. To deepen our understanding of tick species distribution in CCHF high-risk zones across East Africa and the prevalence of CCHFV infection, we conducted field surveys in six districts in Uganda's high-risk regions and four counties in Kenya's intensive pastoralist farming areas. The findings revealed significant variations in tick species diversity and distribution between and within Kenya and Uganda, with minimal overlap. Surprisingly, no *Hyalomma* species were found in Central Uganda's CCHF high-risk zone, whereas the arid North of Kenya was predominantly (over 60%) populated by this species. In Uganda, *Rhipicephalus appendiculatus* emerged as the most prevalent tick species, constituting 62% of the total collection. We successfully isolated CCHFV from pools of *Rh. appendiculatus* collected from Uganda's CCHF high-risk region. These results suggest that CCHF epidemiology in Uganda may be regionally specific and that *Hyalomma* species might not be the primary vector driving CCHFV transmission in all areas. The absence of the main host species in Uganda's high-risk region may indicate a regional variation in CCHFV's host. These findings provide significant implications for tick and CCHFV control strategies in East Africa.

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A DETAILED CHARACTERIZATION OF *RICKETTSIA BELLII* ECOLOGY AND HOST INTERACTIONS

Jaylon Vaughn, Samniqueka Halsey, Deborah Anderson

University of Missouri, Columbia, MO, United States

Vector-borne diseases are a group of ailments transmitted through an arthropod host. One genus of bacteria that falls into this group is *Rickettsia. Rickettsia* are obligate intracellular bacteria that are transmitted to vertebrate hosts through different vectors, specifically ticks, fleas, and human lice. These bacteria present a wide range of phenotypes with some being of medical importance, such as *R. felis,* and others being nonvirulent, such as *R. bellii.* These nonvirulent species often serve as endosymbionts within ticks, bringing on a positive impact on feeding and reproduction. As vector-borne diseases continue to become a growing concern, methods of control are of the utmost urgency. Eliminating vital endosymbiotic species in the tick microbiome has been a discussed method to reduce current tick population size and reproductive capability. *R. bellii* is common throughout the Americas within ticks of multiple genera in their microbiome but its role in tick physiology and immune response to pathogenic *Rickettsia* are not known. The prevalence of other rickettsial agents and the downstream effects of removing them from ticks has been examined yet *R. bellii* has been neglected. Although they share similar genomes, this need of *R. bellii* characterization has not been met. Our long-term goal is to establish the importance of *R. bellii* in influencing the transmission of pathogenic *Rickettsia*. In this study, we examine the presence of *R. bellii* and other endosymbionts within field caught ticks, commenting on their infection rate in ticks. Preliminary data with field-caught *A. amblyomma* ticks in Central Missouri has identified high prevalence of endosymbiont *Rickettisa*, where it appears to dominate the ticks' microbiome. Towards understanding how this may impact the host response, we are characterizing transcriptional and cellular responses to *R. bellii* in vitro. Laboratory studies have highlighted an increase of cytotoxic activity over time, reaching 50% by day 4 post infection. This work will bridge missing gaps in the literature surrounding *R. bellii* while illuminating the role of endosymbiotic bacteria vector-borne diseases control.

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TWO HIGHLY SELECTED MUTATIONS IN THE TANDEMLY DUPLICATED CYP6P4A AND CYP6P4B GENES DRIVE PYRETHROID INSECTICIDE RESISTANCE AND CAUSE LOSS OF INSECTICIDE-TREATED BED NET EFFICACY AGAINST THE MAJOR MALARIA VECTOR *ANOPHELES FUNESTUS* IN WEST AFRICA

Nelly Manuela Tchatchoua Tatchou-Nebangwa[1], Leon M.J. Mugenzi[2], Abdullahi Muhammad[3], Derrick N. Nebangwa[4], Mersimine F.M. Kouamo[5], Carlos S.D. Tagne[6], Theofelix A. Tekoh[1], Magellan Tchouakui[5], Stephen M. Ghogomu[1], Sulaiman S. Ibrahim[7], Charles S. Wondji[3]

[1]University of Buea, Buea, Cameroon, [2]Syngenta Crop Protection, Switzerland, Switzerland, [3]Liverpool School of Tropical Medicine, Liverpool, United Kingdom, [4]Kings's College London, London, United Kingdom, [5]Centre for Research in Infectious Diseases, Yaounde, Cameroon, [6]University of Bamenda, Bamenda, Cameroon, [7]Bayero University, Kano, Nigeria

Insecticide-based vector control tools have been crucial in reducing malaria. However, the emergence of insecticide resistance (IR) in malaria vectors is seriously hampering their effectiveness. To address this challenge, National Malaria Control Programs (NMCPs) must apply evidence-based resistance management strategies along with the WHO recommendations for routine genetic monitoring of IR. As such, our study investigated how two genes, *Cytochrome 6P4a* and *Cytochrome 6P4b,* contribute to IR in the major malaria vector *Anopheles funestus*. We used population genetics, molecular biology, *in vitro* insecticide depletion assays, and generation of transgenic Drosophila flies exposed to insecticides to establish the impact of mutations and overexpression of the genes on the resistance phenotype. We further designed two field-deployable diagnostic tools to detect and monitor IR. Our population genetics studies unveiled the striking selection of two mutant gene variants in Ghana between 2014 and 2021. These mutants exhibited a 3-fold greater capacity to deplete pyrethroid insecticides compared to the wild types. Also, overexpression of the mutant alleles in the transgenic flies resulted in significantly higher insecticide resistance compared to the wild-type flies (mortality <50% vs. >80%, respectively), confirming the role of *6P4a* and *6P4b* in causing IR. In addition, using our designed diagnostic tools, a strong association was established between carrying the mutant alleles and the inefficacy of bed nets, where mosquitoes

carrying the mutant alleles resisted exposure to insecticide-treated bed nets like OLYSET® and DURANET® than non-mutants, -hence increased mosquito life-span which leads to higher malaria transmission rates. We also confirmed that the mutations are predominantly found in the West African region. Overall, our study established that *CYP6P4a* and *CYP6P4*b confer highly escalated insecticide resistance in the major malaria vector *An. funestus* and provides two field-applicable resistance diagnostic tools with significant implications for NMCP implementation of vector control strategies in Africa.

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INSECTICIDE RESISTANCE STATUS AND HIGH *KDR* FREQUENCY IN *AEDES AEGYPTI* IN A DENGUE ENDEMIC CITY OF HONDURAS

Denis Gustavo Escobar[1], Cindy Reyes-Perdomo[1], Luis Galo[1], Oscar Urrutia[2], Lucrecia Vizcaino[3], Audrey Lenhart[3], Gustavo Fontecha[1]

[1]Instituto de Investigaciones en Microbiología-Universidad Nacional Autónoma de Honduras, Tegucigalpa, Honduras, [2]Secretaria de Salud Honduras, Tegucigalpa, Honduras, [3]Entomology Branch, Division of Parasitic Diseases and Malaria, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States

Several arboviruses are transmitted to humans through bites from infected *Ae. aegypti*, and insecticide-based interventions are the main strategy for outbreak control. In Honduras, cyclic arbovirus epidemics have led to the intensive use of pyrethroids, leading to the emergence of insecticide resistance. So far, limited data are available about the participation of resistance mechanisms in *Ae. aegypti* in Honduras. Here, we aimed to conduct a phenotypic assessment of insecticide resistance and detect *kdr* alleles in *Ae. aegypti* from the Central District of Honduras. Between May-June 2023, *Ae. aegypti* larvae were collected in 4 localities: Loarque (LO), La Concordia (LC), Rio Abajo (RA) and Altos de Villa Vieja (AV) and reared until F1 as adults for bioassays. Susceptibility bioassays were carried out using the diagnostic doses of deltamethrin, permethrin, malathion and bendiocarb. AS-PCR was employed to detect *kdr* alleles at the 1534 and 1016 positions in mosquitoes randomly selected from each population and phenotype, and allele frequencies were calculated. A total of 1,592 *Ae. aegypti* were bioassayed. Mortality rates for deltamethrin ranged between 86 and 100%, with LC population showing the lowest mortality. For permethrin, the mortality ranged between 1 and 48%, with LC exhibiting the lowest mortality and RA the highest. Similarly, all populations showed malathion resistance, with mortalities between 24 and 74%. All populations were susceptible to bendiocarb. Screening of 275 individuals revealed the presence of *kdr* genotypes at both loci. The allele frequencies for F1534C and V1016I were 1.0 and 0.89, respectively. It is noteworthy that the frequency of the V1016I mutation showed variability between locations. Only the phenotypically resistant mosquitoes to deltamethrin and permethrin, from LC and LO, showed a frequency of 1.0 for the mutant genotype, while the others ranged from 0.48 to 0.97. These findings reveal resistance in *Ae. aegypti* to the pyrethroids used for vector control in Honduras, and resistance to malathion. Additionally, *kdr* alleles were present at high frequencies and were associated with phenotypic resistance.

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RELATIONSHIPS BETWEEN BIOLOGICAL AGE, DISTANCE FROM AQUATIC HABITATS, AND PYRETHROID RESISTANCE STATUS OF *ANOPHELES FUNESTUS* MOSQUITOES IN SOUTH-EASTERN TANZANIA

Polius G. Polius

Ifakara Health Institute, Morogoro, Tanzania, United Republic of

Malaria transmission can be highly heterogeneous between and within localities and is influenced by factors such as the survival and biting frequencies of *Anopheles* mosquitoes. This study investigated the relationships between the biological age, distance from aquatic habitats, and pyrethroid resistance status of *Anopheles funestus* mosquitoes, which currently dominate malaria transmission in south-east Tanzania. Female *An. funestus* were collected in houses located 50-100 m, 150-200 m, or over 200 m from the nearest known aquatic habitats. The mosquitoes were exposed to 1×, 5× and 10× the diagnostic doses of pyrethroid (deltamethrin or permethrin), or the synergist, piperonyl butoxide (PBO) followed by the pyrethroids, then monitored for 24 h-mortality. Ovaries of exposed and non-exposed mosquitoes were dissected to assess parity as a proxy for biological age. Adults emerging from larval collections in the same villages were tested against the same insecticides at 3-5, 8-11, or 17-20 days old. Mosquitoes collected nearest to the aquatic habitats (50-100 m) had the lowest mortalities compared to other distances, with a maximum of 51% mortality at 10× permethrin. For the age-synchronized mosquitoes collected as larvae, the insecticide-induced mortality assessed at both the diagnostic and multiplicative doses (1×, 5×, and 10×) increased with mosquito age. The highest mortalities at 1× doses were observed among the oldest mosquitoes (17-20 days). Pre-exposure to PBO increased the potency of both pyrethroids. The proportion of parous females was highest among mosquitoes collected furthest from the habitats. Older An. funestus near the center of the village are more susceptible to pyrethroids than those at the edge of the village. Pyrethroid-based interventions may remain at least moderately effective despite widespread pyrethroid-resistance, by killing the older, less-resistant, and potentially-infective mosquitoes.

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HOUSEHOLD RISK FACTORS ASSOCIATED WITH INCREASED MOSQUITO DENSITIES AND INSECTICIDE RESISTANCE PROFILES OF MAIN MALARIA VECTORS IN KWALE COUNTY, COASTAL KENYA

Miguel G. Okoko[1], Caroline W. Kiuru[2], Jonathan M. Karisa[3], Rehema G. Gona[1], Tobias T. Odongo[1], Bruno O. Otieno[1], Festus Y. Yaa[1], Faiz M. Shee[4], Caroline K. Wanjiku[3], Joseph Mwangangi[5], Carlos C. Chaccour[2], Marta F. Maia[6]

[1]Kenya Medical Research Institute- Center for Vector Disease Control, Kwale, Kenya, [2]Barcelona Institute of Global Health Spain, Barcelona, Spain, [3]KEMRI Wellcome- Trust Research Programme Kilifi, Kenya, Kilifi, Kenya, [4]Pwani University, Kilifi, Kenya, [5]Kenya Medical Research Institute-Center for Geographical Medicine Research, Kilifi, Kenya, [6]University of Oxford, Center for Global Health and Tropical Medicine, Oxford, UK, UK, United Kingdom

The spread of insecticide resistance threatens the efficacy of current malaria control programs which rely heavily on insecticide-based vector control interventions. The aim of this study was to determine the insecticide resistance profiles of the main malaria vector species complex in coastal Kenya (Kwale county) and explore household risk factors leading to increased densities of mosquitoes. Adult mosquitoes and larval sampling were performed in the same sites, collected larvae were reared to F1 for susceptibility tests using WHO tube assay kits. A synergist assay with piperonyl butoxide (PBO 4%) was performed to investigate the possible involvement of metabolic resistance mechanisms. GLMM (negative binomial regression models) were used to identify factors influencing the indoor density of different vector species complex.Approximately 8302 mosquitoes were collected, composed of *An. funestus s.l.* (70%), *An. gambiae s.l.* (17%) and other Anophelines (13%). The presence of ITNs in households significantly reduced *An. funestus s.l.* count by 65% (IRR = 0.35, 95% CI 0.13-0.97, P<0.044). Moreover, palm leaves roof type (IRR = 4.46, 95% CI 2.30-8.64, P<0.001) and mud walls (IRR = 6.74, 95% CI 2.81-16.17, P<0.001) significantly increased *An. funestus s.l.* We did not find statistically significant association between indoors densities of *An. gambiae s.l.* and different house characteristics. *An. gambiae s.l.* exhibited resistance to deltamethrin and permethrin, but was susceptible to DDT, pirimiphos-methyl, and bendiocarb. *An. funestus s.l.* also demonstrated resistance to deltamethrin while DDT remained susceptible. The reversal of resistance was observed during the synergistic assay with PBO in both *An. funestus s.l.* and *An. gambiae s.l*. Resistance to pyrethroids is widespread and likely to involve metabolic mechanisms of resistance. Despite resistance, net usage continues to be associated with fewer indoor mosquitoes.

Household structural characteristics strongly influenced indoors densities of malaria vectors, further confirming the association between built environment and potential exposure to malaria.

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

Arthur SOVI[1], Constantin J. Adoha[1], Boulais Yovogan[1], Chad L. Cross[2], Dominic P. Dee[3], Alphonse K. Konkon[1], Aboubakar Sidick[1], Manfred Accrombessi[1], Minassou J. Ahouandjinou[1], Razaki Ossè[1], Edouard Dangbénon[1], Linda Towakinou[1], Clément Agbangla[4], Germain G. Padonou[1], Thomas Churcher[3], Corine Ngufor[5], Jackie Cook[6], Natacha Protopopoff[5], Martin C. Akogbéto[1], Louisa A. Messenger[7]

[1]Centre de Recherche Entomologique de Cotonou, Cotonou, Benin, [2]Department of Epidemiology and Biostatistics, School of Public Health, University of Nevada, Las Vegas, NV, United States, [3]Medical Research Council (MRC) Centre for Global Infectious Disease Analysis, Department of Infectious Disease Epidemiology, Imperial College London, London, United Kingdom, [4]Faculté des Sciences et Techniques, Université d'Abomey-Calavi, Abomey-Calavi, Benin, [5]Faculty of Infectious and Tropical Diseases, Department of Disease Control, London School of Hygiene and Tropical Medicine, London, United Kingdom, [6]MRC International Statistics and Epidemiology Group, London School of Hygiene and Tropical Medicine, London, United Kingdom, [7]Department of Environmental and Occupational Health, School of Public Health, University of Nevada, Las Vegas, NV, United States

To delay the evolution and spread of resistance and alleviate reversals in malaria control gains, long-lasting insecticidal nets (LLINs) incorporating new active ingredients (A.I.s), with distinct modes of action, are urgently needed. Through a three-year, three-arm cluster-randomised controlled trial (cRCT), we assessed the longitudinal impact of dual-A.I. LLINs (chlorfenapyr-PY and pyriproxyfen-PY LLINs) on insecticide resistance, compared to pyrethroid-LLINs (PY-LLINs). Longitudinal phenotypic and genotypic insecticide resistance profiles were measured among 19,292 *An. gambiae* s.l. collected over 39 months (3 months of baseline, followed by three years, post-intervention), using insecticide resistance bioassays and quantitative real-time reverse transcription PCR of metabolic resistance genes, respectively. In all three trial arms, a significant intervention effect was evident, with alpha-cypermethrin resistance intensity decreasing between baseline and twelve months post-LLIN distribution. Over the subsequent two years, alpha-cypermethrin resistance intensity rebounded to comparable or moderately higher levels than at baseline in all three trial arms. In all trial arms, by the third year, the alpha-cypermethrin concentration required to kill 95% of vectors increased to more than fifty times the diagnostic dose. Minimal reductions in chlorfenapyr susceptibility were observed; variable, albeit significant reductions in fertility following pyriproxyfen exposure, with an overall upward trend of increasing susceptibility across trial years was apparent. Several metabolic genes were implicated in resistance selection, including CYP6P4 in the pyriproxyfen-PY arm, and CYP6P3 and CYP9K1 in the chlorfenapyr-PY arm. Study findings indicate that after 24 months of use, chlorfenapyr-PY LLINs no longer mitigated pyrethroid resistance selection in *An. gambiae* s.l., while nets are currently procured every three years. Knowledge about the impact of next-generation LLINs on insecticide resistance selection is crucial for the pragmatic design of prospective resistance management strategies.

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THE E205D MUTATION IN THE P450 GENE CYP6P3 DRIVES PYRETHROID RESISTANCE IN THE MAJOR AFRICAN MALARIA VECTOR ANOPHELES GAMBIAE

Jonas A. Kengne-Ouafo[1], Mersimine Kouamo[1], Abdullahi Muhammad[2], Arnaud Tepa[1], Stevia Ntadoun[1], Leon Mugenzi[1], Theofelix Tekoh[1], Jack Hearn[2], Magellan Tchouakui[1], Murielle Wondji[2], Sulaiman S. Ibrahim[2], Charles S. Wondji[2]

[1]Centre for Research in Infectious Diseases (CRID), Yaounde, Cameroon, [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom

To improve the longevity of malaria control tools, this study pinpoints genetic mutations in the major malaria mosquito that cause pyrethroid resistance, paving the way for simple DNA tests to track resistance in the field. The entire genomes of highly resistant and highly susceptible malaria mosquitoes were compared to identify genetic changes linked to resistance (signatures of selective sweeps). The role of a top candidate was then elucidated using functional validation assays. A DNA-based assay was designed to monitor the pyrethroid resistance in the field and its impact on the effectiveness of long-lasting insecticide-treated bednets using standard WHO cone assays. WGS detected a major P450-linked locus on chromosome 2R beside the sodium channel locus to be linked to pyrethroid resistance in Cameroon. We demonstrated that the E205D mutation in a key metabolic resistance P450 *CYP6P3* drives pyrethroid resistance in *Anopheles gambiae. In vitro* metabolism assays with recombinant *CYP6P3* protein revealed that the catalytic efficiency of 205D was 2.5 times higher than E205 with α-cypermethrin. Overexpression of the 205D allele in transgenic flies confers higher pyrethroids and carbamates resistance, compared to controls. A DNA-based assay further supported that the *CYP6P3*-205D variant strongly correlates with pyrethroid resistance in field populations (OR=26.4; P<0.0001) and that it reduces the efficacy of pyrethroid-only LLINs with homozygote RR genotype exhibiting significantly higher survival following PermaNet 3.0 exposure compared to the SS genotype (OR: 6.1, p = 0.0113). Furthermore, the *CYP6P3*-E205D combines with the *kdr* target-site resistance mechanisms to worsen the loss of bednet efficacy. The 205D mutation is widespread in West and Central Africa, but less common or even absent in East and South Africa with signs of introgression with *An. coluzzii* in Ghana. This study emphasizes the importance of P450-based resistance and designs field-applicable tools to easily track the spread of metabolic resistance and assess its impact on control interventions.

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ACE-1 DUPLICATION AND COPY NUMBER VARIATION ARE CORRELATED TO RESISTANCE TO ORGANOPHOSPHATES IN *ANOPHELES GAMBIAE* FROM CENTRAL AFRICA

Judith L. Dandi Tchouomene, Jonas A. Kengne-Ouafo, Leon Mugenzi, Magellan Tchouakui, Murielle J. Wondji, Charles Wondji

Centre for Research in Infectious Diseases, Yaoundé, Cameroon

Mosquito resistance to insecticides hinders malaria control. Organophosphates (OPs) and carbamates (CMs) are used in indoor residual spraying (IRS) as a support for pyrethroids, to which many mosquito species are resistant. Unfortunately, West and East Africa see growing resistance to these classes used in IRS, including pirimiphos-methyl (PM), an OP newly recommended by the WHO. Mosquitoes with mutation replacing glycine with serine at position 280 in the acetylcholinesterase enzyme (Ace-1 280S) decrease sensitivity to OPs and CMs. Ace-1 duplications and copy number variation (CNV) enhance resistance, but empirical evidence is scarce in wild *Anopheles* in general, and in Central Africa particularly. We aimed to explore the correlation between specific Ace-1 alleles, the number of duplicated copies, and insecticide resistance levels in *Anopheles gambiae* s.s, *An. coluzzii*, and *An. funestus* s.l, to two organophosphates, PM and malathion (MA) across six Cameroonian localities. Mosquitoes were collected from breeding sites and susceptibility was determined using the WHO assay. Taq-Man and sequencing techniques investigated the Ace-1 gene in dead and surviving

mosquitoes after insecticide exposure. Analysis of 100 clones and qPCR permit to explore gene duplication and relative copy number variations. While *An. funestus* populations exhibited full susceptibility, *An. gambiae* s.l. showed potential or clear resistance to OPs (97%-50% mortality). A significant correlation linked the Ace-1 mutation with resistance in *An. gambiae* s.s. from Nkolondom to the two OPs (PM: OR= 20.33; P=0.04, MA: OR= 98.33; P =0.0019). Analyses revealed for the first time Ace-1 gene duplication and increased CNV correlated with resistant populations to PM and MA in Central Africa. The observed low-frequency (3%) of Ace-1^R mutation in *An. coluzzii* suggests recent selection pressure. These findings highlight the necessity for monitoring susceptibility before effective implementation of IRS in Cameroon. Ace-1 resistance demands long-read sequencing to fully map duplications, ensuring long-term insecticide effectiveness in malaria control.

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MALARIA VECTOR ECOLOGICAL DIVERSITY INFLUENCING TRANSMISSION AND RESISTANCE TO INSECTICIDES

Isaac Olayinka Oyewole

Babcock University, Ilisan Remo, Nigeria

Prevalence of malaria could be a function of vector density, transmission dynamics and ability for insecticide resistance and ecological variation could play a vital role. In this study, 1,857 adult *Anopheles* mosquitoes were collected from three ecosystems using standard procedures to establish their diversity, indoor and outdoor feeding and biting habits. The specimens were graded according to their abdominal conditions and preserved dry for morphological, molecular identification and ELISA test. Larvae were collected and reared to adulthood. Susceptibility tests conducted on 2-3-day old emerged female adults using standard WHO procedures. Species collected from the rain forest include; *Anopheles gambiae, An. funestus, An. moucheti, An. Arabiensis, An. nili* those from the savannah mosaic include; *An. gambiae, An. funestus, An. moucheti, An. Arabiensis, An. longipalpis, An. nili, An. maculipalpis, An. coustani, An. rhodesiensis* and *An. ziemani* and those from mangrove ecosystem are; *An. gambiae, An. melas* and *An. nili. Anopheles gambiae* abundance was significantly higher, accounting for 81.3% of all the collections and was found in all the localities. Those established to be vector of malaria include; *Anopheles gambiae, An. funestus, An. moucheti, An. Arabiensis* from the forest, *An. gambiae, An. funestus, An. moucheti, An. Arabiensis, An. longipalpis, An. nili* from the savannah and *An. gambiae, An. melas* from the mangrove. The infection rates ranged from 1.2% in the rain forest to 1.0% in the savannah and 0.9% in the coastal zone, this showed no significant difference (P>0.05). The entomological inoculation rates are 2044, 1716 and 1789 infective bites per person per year for the rain forest, savannah and coastal zones respectively, indicating no significant difference (P>0.05). Species from the coastal zone are more susceptible to doses of insecticides tested followed by those from rain forest while savannah mosaic species showed higher level of resistance. This is a baseline information to guide a community-based strategy for malaria control intervention.

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DYNAMICS OF RESISTANCE INTENSITY AND MECHANISMS OF *ANOPHELES GAMBIAE* TO PYRETHROID INSECTICIDES BETWEEN 2021 TO 2023 IN RWANDA

Phocas MAZIMPAKA[1], Dunia Munyakanage[1], Beatus Cyubahiro[1], Alphonse Mutabazi[1], Elias Niyituma[1], Jules NAHIMANA[2], Xavier Misago[1], Jean Claude S. Ngabonziza[1], Kaendi Munguti[3], Naomi W. Lucchi[4], Aimable Mbituyumuremyi[1], Emmanuel Hakizimana[1]

[1]Rwanda Biomedical Centre, Kigali, Rwanda, [2]Abt Associates, Inc., US President's Malaria Initiative, EVOLVE Project, Kigali, Rwanda, Kigali, Rwanda, [3]US President's Malaria Initiative, Kigali, Rwanda, [4]4The Centers for Disease Control and Prevention (CDC), Division of Global Health Protection, Nairobi, Kenya

The prevailing increase of insecticide resistance of *Anopheles gambiae* (s.l) to pyrethroid insecticides represents a crucial threat on the gains achieved from the scaling up of core vector control interventions. This study investigated the dynamics of resistance intensity and mechanisms of *An. gambiae* (s.l) to the pyrethroid insecticides between 2021 and2023 in Rwanda in order to guide the insecticide resistance management strategies. The intensity of resistance was measured at five (5x) and ten (10 x) times to the diagnostic doses for phenotypic resistance tests. The piperonyl butoxide (PBO) as synergist was added to the diagnostic dose to test the detoxification enzymes where the resistance was confirmed per insecticide and surveyed site. Out of the 25 surveyed sites, the high resistance intensity measured at 10 times the concentration of diagnostic dose for *Anopheles gambiae s.l.,* increased from 0% to 12% for Deltamethrin 0.05%, 0% to 7.4% for Permethrin 0.75% and 4% to 44% for Alpha-cypermethrin 0.5%. Therefore, from 2022 to 2023, the usual addition of synergist (PBO) encountered the decrease of susceptibility restoration from 100% (n=18) to 84.6% (n=13) for Deltamethrin 0.05%, 94% (n=20) to 92.6% (n=27) for Permethrin 0.75%, and 92.3% (n=26) to 84% (n=25) for Alphacypermethrin 0.05%. The study demonstrated an incremental increasing of resistance intensity to the pyrethroid insecticides and mainly to alpha cypermethrin. The underlying metabolic resistance mechanism involving detoxification esterase enzymes was detected using PBO and its effect is decreasing overtime. Other potential resistance mechanisms are suspected and require investigations with future projects. The monitoring of insecticide resistance has to be strengthened and integrated into the routine malaria vector surveillance, to guide decision making in deployment and impact evaluation of malaria control interventions in Rwanda.

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INSECTICIDE RESISTANCE PROFILE OF *AEDES* MOSQUITOES IN OGUN STATE, NIGERIA

Reham A. Tageldin[1], Hala S. Thabet[1], Matthew Montgomery[1], Ayodele S. Babalola[2], Sulaimon A. Aina[3], Adenike O. Adeniyi[4], Akingbehin P. Olumide[4], Omobolanle G. Akintade[4], Nofisat S. Lawal[4], Adedapo O. Adeogun[2]

[1]U.S. Naval Medical Research Unit EURAFCENT, Cairo, Egypt, Cairo, Egypt, [2]Molecular Entomology and Vector Control Unit, Nigerian Institute of Medical Research, Yaba, Lagos, Nigeria, Lagos, Nigeria, [3]Zoology Department, Olabisi Onabanjo University, Ogun State, Nigeria, Ogun, Nigeria, [4]Pure and Applied Zoology Department, Federal University of Agriculture, Abeokuta, Ogun State, Nigeria, Ogun, Nigeria

Aedes mosquitoes remain important vectors of dengue & yellow fever viruses in Nigeria. We investigated the insecticide resistance patterns of *Aedes* mosquitoes in Ogun State, in southwest Nigeria. Between April & August 2023, larval breeding sites of *Aedes* were identified & immature stages collected from four Local Government Areas, namely Odeda, Abeokuta South, Obafemi-Owode and Sagamu. Emerged females were exposed to four classes of insecticides according to the standard World Health Organization (WHO) protocol: pyrethroids (permethrin 0.75% & deltamethrin 0.05%); organochlorines (DDT 4%); organophosphates (fenitrothion 1.0%) & carbamates (bendiocarb 4%). A total of 2500 female *Aedes* mosquitoes were identified & exposed to insecticides. Of these, 2,297 (91.9%) were *Aedes aegypti,* while 203 (8.1%) were *Aedes vitattus*. *Aedes aegypti* was the sole species collected in Obafemi-Owode & Sagamu, whereas both species were found in Odeda and Abeokuta South. Across all sites, mortality to (DDT) ranged between 82% and 97%, suggesting mild resistance. Mosquitoes from Odeda, Abeokuta South & Obafemi Owode showed full susceptibility to permethrin, while suspected resistance was observed in Sagamu (92%). Mortality to deltamethrin ranged between 91% and 92%, indicating suspected resistance across all sites. Mosquitoes were largely susceptible to bendiocarb, except in Obafemi-Owode, where resistance was suspected (91% mortality). Susceptibility to fenitrothion was recorded in all sites except Sagamu (72% mortality). These findings suggest that resistance to all classes of insecticide is emerging among *Aedes* mosquitoes in southwest Nigeria, highlighting the need for targeted actions to address increased resistance & safeguard public health.

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HIGH SURVIVORSHIP OF *ANOPHELES GAMBIAE* LARVAE TO LETHAL CONCENTRATIONS OF CLOTHIANIDIN, ACETAMIPRID OR IMIDACLOPRID IS CONSISTENT WITH CROSS-RESISTANCE TO NEONICOTINOIDS

Marilene M Ambadiang Mae[1], Caroline Fouet[2], Fred Ashu[1], Calmes Bouaka[1], Véronique Penlap-Beng[3], Colince Kamdem[2]

[1]Centre for Research in Infectious Diseases, Yaoundé, Cameroon, [2]Department of Biological Sciences, University of Texas, El Paso, TX, United States, [3]Department of Biochemistry, Faculty of Science, University of Yaoundé 1, Yaoundé, Cameroon

Worldwide, agrochemicals have been effectively repurposed for mosquito control. The effectiveness of this method is challenged by preexisting resistance in larval and adult populations brought about by unintentional pesticide exposure or other cross-resistance mechanisms. Thus, in order to evaluate the effectiveness of repurposed agrochemicals against mosquitoes, understanding of the lethal and sublethal effects of residual pesticide is essential. We reared field-collected mosquito larvae in water that had an agrochemical concentration that, after 24 hours, killed 100% of susceptible mosquitoes (lethal concentration). With the help of this experimental setup, we investigated the effects on mortality rates and life table parameters of third-instar larvae of the two sibling species *Anopheles gambiae* and *Anopheles coluzzii* collected from Yaoundé, Cameroon caused by lethal concentrations of a pyrethroid (deltamethrin), a pyrrole (chlorfenapyr), and three neonicotinoids (acetamiprid, clothianidin, and imidacloprid). We observed that *An. gambiae* and *An. coluzzii* larvae were susceptible to chlorfenapyr and a minimal concentration of 0.10 mg/L killed them in less than 24 hours. In both species, deltamethrin caused low mortality, which is consistent with strong insecticide resistance. In *An. coluzzii* larvae, lethal doses of acetamiprid, imidacloprid, and clothianidin significantly hindered their ability to survive, grow, and emerge. On the other hand, 5 to 60% of *An. gambiae* immature stages were able to grow and emerge in water containing a lethal dose of neonicotinoid, demonstrating cross-resistance to this class of insecticides, depending on the active component and the population examined. These findings corroborate susceptibility profiles observed in adults and suggest that unintentional pesticide exposure or other cross-resistance processes could contribute to the establishment of resistance to neonicotinoids in some *Anopheles* populations.

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DIVERGENCES AND SIMILARITIES ON INSECTICIDE RESISTANCE PROFILES IN WILD POPULATIONS OF *ANOPHELES GAMBIAE SL* BREEDING IN VEGETABLE FARMS IN COTONOU, BENIN

Defo Talom Blaise Armand[1], Lontsi-Demano Michel[1], Zeukeng Francis[2], Nakebang Amen Fadel[3], Djouaka Rousseau[1]

[1]International Institute of Tropical Agriculture (IITA), Abomey-Calavi, Benin, [2]University of Buea, Buea, Cameroon, [3]Adam Barka University, Abeche, Chad

Pesticide management by vegetable farmers might play a key role in the selection of insecticide resistance in field populations of mosquito vectors. Here, we investigated the distribution of insecticide resistance profiles recorded with populations of *Anopheles gambiae sl* breeding in vegetable farms in the city of Cotonou in Benin, where no harmonization and no regulation is established, leading to uncontrolled use of pesticides. Two field sites were selected, Houeyiho and Seme. Wild Anopheles gambiae sl larval populations were collected and their susceptibility to lambda-cyhalothrin and permethrin was assessed. Synergist bioassays with PBO were conducted and the kdr target-site mutations were investigated. The genetic diversity of An. gambiae sl was assessed by sequencing the exon-20 element of the voltage-gated sodium channel. Overall, Lambdacyhalothrin constituted the main insecticide used by vegetable farmers. Mortalities to lambdacyhalothrin were 63% and 30% of the mortality rate respectively at Houeyiho and Seme. Susceptibilities to permethrin at Houeyiho and Seme were 14% and 42% of the mortality rate respectively. The PBO synergist assays showed a total recovery of the susceptibility to lambda-cyhalothrin in An. gambiae sl (100% mortality rate) at Seme, while this recovery was partial at Houeyiho (80% mortality rate). As to permethrin, the recovery was partial at houeyiho (73% mortality rate) and total in Seme (100% mortality rate). The kdr 1014F mutation was close to fixation in all the sites. In Hoeuyiho, 6 haplotypes were found, the haplotype diversity was 0.18. In Seme 3 haplotypes were found for a haplotype diversity of 0.09. There was a divergence in *An. gambiae sl*, about the resistance profile to pyrethroid, the involvement of cytochrome P50 in the observed resistance and the genetic diversity from one site to another. However, there was a similarity in Kdr mutation distribution. This study suggests that the implementation of vector control strategies should take into account divergences and similarities in mosquito resistance profiles, even at a small field scale for better management of malaria transmission.

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KEY RESISTANCE P450S PROFICIENT PYRETHROID METABOLIZERS, ARE REDUCING NEONICOTINOID EFFICACY IN *ANOPHELES FUNESTUS* WHILE EXACERBATING THE POTENCY OF CHLORFENAPYR

Tatiane Assatse[1], Magellan Tchouakui[1], Mersimine Mangoua[1], Riccardo Thiomela[1], Sonia Ngongang-Yipmo[1], Léon Mugenzi[2], Benjamin Menze[1], Charles Wondji[1]

[1]Centre for Research in Infectious Diseases (CRID), Yaoundé, Cameroon, [2]SYNGENTA, Rosentalstrasse 67, Basel, Basel 4058, Switzerland

Novel insecticides were recently introduced to counter pyrethroid resistance threats in African malaria vectors. To prolong their effectiveness, potential cross-resistance from promiscuous pyrethroids metabolic resistance mechanisms must be elucidated. Previous evidences have established that mutations in *CYP6P9a* and *CYP6P9b* (*CYP6P9a/-b*) are the main drivers of pyrethroid resistance in *Anopheles funestus* in Southern Africa. In this study, we used field strain of *An. funestus* from Malawi to assess the impact of *CYP6P9a/-b*, proficient pyrethroid metabolizers, on the efficacy of two novel insecticides, chlorfenapyr and clothianidin, using CDC bottle assay, coupled with extensive *in vivo* and *in vitro* function validation to directly establish the impact of the major pyrethroid resistance P450s on those insecticides. A strong association between the *CYP6P9a/-b* mutations and the ability to survive clothianidin exposure was noted for mutant versus non-mutant (OR=7.5; P=0.001 for *CYP6P9a* OR=7.08; P=0.002 for *CYP6P9b*). However, mutant had significantly higher mortalities upon chlorfenapyr exposure, compared to non-mutant (OR=0.1; P<0.0001 and OR=0.2; P=0.0003 respectively). Transgenic expression of *CYP6P9a/-b* in Drosophila revealed that flies expressing *CYP6P9a* and *CYP6P9b* were significantly more resistant to clothianidin 12h post-exposure than the control flies, with average mortalities of 45.05% ± 7.03 for *CYP6P9a* (P<0.001) and 30.1% ± 2.9 for *CYP6P9b* (P<0.001) compared to the control flies (73.9% ± 3.3). In contrast, experimental flies over-expressing these two P450s were more susceptible to chlorfenapyr 12h post-exposure compared to control flies, with average mortalities of 62.3% ± 4.1 for *CYP6P9a* (P<0.001) and 61.1% ± 5.9 for *CYP6P9b* (P<0.001) compared to the control (37.6% ± 5.6). This phenotype was also confirmed by RNAi knock-down experiments. This study highlights the risk of cross-resistance between pyrethroid and neonicotinoid and reveals that chlorfenapyr-based control interventions such as Interceptor G2 could remain efficient against some P450-based resistant mosquitoes.

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BACTERIA COMMUNITY EXACERBATE PYRETHROID RESISTANCE IN *ANOPHELES FUNESTUS*, MAJOR MALARIA VECTOR IN AFRICA

Fleuriane Metissa Djondji Kamga[1], Leon M. J. Mugenzi[2], Magellan Tchouakui[1], Calmes Urbain Bouaka Tsakeng[1], Bertrand Mbakam[1], Charles S. Wondji[1]

[1]Centre for Research in Infectious Diseases (CRID), Yaounde, Cameroon, [2]SYNGENTA, Rosentalstrasse 67, Basel, Basel 4058, Switzerland

The increasing resistance of *Anopheles* mosquitoes to pyrethroids is subjecting many African countries to a high risk of malaria epidemics. An in-depth understanding of the mechanisms associated with this phenomenon is needed to mitigate this growing threat to malaria vector control. Numerous studies have highlighted the involvement of microbiota in mediating insecticide resistance (IR) in agricultural pests. Based on this, our study sought to investigate the potential role of bacteria in the escalation of insecticide resistance in the major malaria vector *Anopheles funestus* Giles (Diptera : Culicidae). Using the sequencing of the 16S rRNA mitochondrial gene, we comparatively characterized the microbiota of a highly pyrethroid-resistant strain (Fumoz-selected) and a normal-resistant strain (Fumoz unselected). This enabled the identification of bacteria strains associated with the escalation of IR. In addition, to further confirm the involvement of bacteria in the phenotype, we performed an antibiotic treatment (penicillin/streptomycin) of Fumoz unselected mosquitoes, proceeded by exposure to insecticides. As findings, lower bacterial diversity was observed in the selected group, suggesting that, insecticide selection pressure reduces bacterial enrichment. Also, we noticed an overabundance of the *Rhanella* genus in the Fumoz-selected strain (Deseq2: Log2FC-15.776, p=4.23E-11), which could argue its involvement in the escalation of IR phenotype. Concerning the antibiotic treatment, we observed a partial recovery of the susceptibility of treated individuals, to insecticides after exposure to varying WHO diagnostic concentrations of pyrethroids: Permethrin 1X ($\chi2 = 46.936$, $p < 0.0001$), Deltamethrin 5X ($\chi2 = 4.102$, $p = 0.04$) and 10X ($\chi2 = 9.706$, $p = 0.0018$). Overall, our findings confirmed the potential role of bacteria in the escalation of IR in *An. funestus*. This study, therefore, lays the initial groundwork for understanding microbial mechanisms that exacerbate pyrethroid resistance in malaria vectors while jeopardizing vector control efforts.

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SEX PEPTIDE RECEPTOR IS NOT REQUIRED FOR REFRACTORINESS TO REMATING OR INDUCTION OF EGG LAYING IN AEDES AEGYPTI

Irene Alexandra Amaro[1], Margot P. Wohl[2], Sylvie Pitcher[1], Catalina Alfonso-Parra[3], Frank Avila[4], Andrew Paige[5], Michelle Helinski[6], Laura Duvall[5], Laura Harrington[1], Mariana Wolfner[1], Conor McMeniman[2]

[1]Cornell University, Ithaca, NY, United States, [2]Johns Hopkins University, Baltimore, MD, United States, [3]Instituto Colombiano de Medicina Tropical, Sabaneta, Colombia, [4]Universidad de Antioquia, Medellin, Colombia, [5]Columbia University, New York City, NY, United States, [6]European and Developing Countries Clinical Trials Partnership, The Hague, Netherlands

Aedes aegypti is a major vector of arboviruses worldwide. Understanding major reproductive pathways in males and females is essential for development and success of novel control tools that can reduce human infection risk. Across diverse insect taxa, the behavior and physiology of females dramatically changes after mating – processes largely triggered by the transfer of seminal proteins from their mates. In the vinegar fly *Drosophila melanogaster*, the seminal protein sex peptide (SP) decreases the likelihood of female flies remating and causes additional behavioral and physiological changes that promote fertility including increasing egg production. Although SP is only found in the *Drosophila* genus, its receptor, sex peptide receptor (SPR), is the widely conserved myoinhibitory peptide (MIP) receptor. To test the functional role of SPR in mediating post-mating responses in a non-*Drosophila* dipteran, we generated two independent *Spr*-knockout alleles in the yellow fever mosquito, *Aedes aegypti*. Although SPR is needed for post-mating responses in *Drosophila* and the cotton bollworm *Helicoverpa armigera*, *Spr* mutant *Ae. aegypti* show completely normal post-mating decreases in remating propensity and increases in egg laying. In addition, injection of synthetic SP or accessory gland homogenate from *D. melanogaster* into virgin female mosquitoes did not elicit these post-mating responses. Our results demonstrate that *Spr* is not required for these canonical post-mating responses in *Ae. aegypti*, indicating that other, as yet unknown, signaling pathways are likely responsible for these behavioral switches in this disease vector.

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MICRO-SPATIAL PARTITIONING INFLUENCES THE DIVERSIFICATION OF MOSQUITO-ASSOCIATED VIRUS PROFILES AMONG *AEDES AEGYPTI* MOSQUITOES IN PUERTO RICO

Bright Agbodzi[1], Henry J. Barton[2], Nicole Nazario-Maldonado[1], Luis Alonso-Palomares[1], John F. Williams[1], Robert Rodriguez[3], Grayson Brown[4], Rhoel R. Dinglasan[1]

[1]Department of Infectious Diseases & Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, United States, [2]Genevia Technologies, Tampere, Finland, [3]Ponce Health Sciences University, Ponce, Puerto Rico, [4]Puerto Rico Vector Control Unit, San Juan, Puerto Rico

Mosquito-borne arboviruses remain a major global health burden. The mosquito's microbiome, particularly, its virome can influence its life ability to transmit arboviruses. However, little is known about the intrinsic diversity of the virome across mosquito populations at smaller spatial scales. *Aedes aegypti* is the primary vector for dengue virus, Zika virus, and Chikungunya virus globally. We hypothesized that micro-spatial factors shape the mosquito core-virome and influence the diversification of mosquito-associated virus (MAV) profiles in *Ae. aegypti.* To test this hypothesis, we used RNA-Seq to characterize the diversity of MAVs among *Ae. aegypti* populations from urban and rural habitats on the main island of Puerto Rico and compared MAV diversity among *Ae. aegypti* collected from 2 urban and 2 rural habitats. Metatranscriptomic analysis identified 15 different viruses in this study that partitioned to rural vs. urban sampling sites. Of these, the most represented families were *Totiviridae* (3 viruses) and *Partitiviridae* (2 viruses). Phasi Charoen-like phasivirus (PCLV), Humaita-Tubiacanga virus (HTV) had the highest viral sequences overall. Of the 15 viruses detected, seven viruses were common to both rural and urban sites; however, six were present in urban *Ae. aegypti* but absent from the rural samples. Also, HTV had the most viral reads (>80%) among rural *Ae. aegypti,* whereas PCLV had very low viral reads (<2%). In contrast, PCLV (>80%) predominated in urban *Ae. aegypti*, while HTV reads were low. Phylogenetic analysis of the PCLV, HTV, and Guadeloupe mosquito virus strains revealed that our strains are quite unique, barely clustering with others from different geographical origins. We further compared MAV prevalence and vector competence for DENV-1 between urban and rural mosquito populations, and discuss how these results not only support our prevailing hypothesis but impact our understanding of arbovirus transmission at local scales. We anticipate that future studies will help assess the generalizability of the observed phenomena in other DENV-endemic regions.

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HOST-SPECIFIC DYNAMICS OF MICROBIOTA ASSEMBLY IN *AEDES AEGYPTI* MOSQUITOES AFTER RECIPROCAL TRANSPLANTATION OF CRYOPRESERVED WHOLE GUT-DERIVED MICROBIAL COMMUNITIES

Holly Nichols[1], Vishaal Dhokiya[2], Ananya Hoque[2], Eva Heinz[2], Grant Hughes[2], Kerri Coon[1]

[1]University of Wisconsin-Madison, Madison, WI, United States, [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom

As in other animals, the mosquito gut is colonized by a diverse consortium of microbes that contributes to host traits including survival, fecundity, insecticide resistance, and vector competence. Accordingly, manipulation of the mosquito microbiome via the introduction of bacteria that reduce

mosquito vector competence and/or fitness is a promising avenue for controlling the transmission of mosquito-borne pathogens. However, many pathogen studies are conducted in laboratory-reared mosquitoes with gut microbial communities that are distinct from field-collected mosquitoes. Here, we describe a new method to isolate, cryopreserve, and transplant whole microbial communities from donor mosquitoes into axenic (germ-free) recipient mosquitoes. A reciprocal swap was conducted between *Aedes aegypti* Liverpool strain mosquitoes reared in isolation for 50 years at the University of Wisconsin-Madison (UW) and Liverpool School of Tropical Medicine (LSTM). Notably, mosquito hosts from each colony reacted differently to microbiome transplantation: UW mosquitoes experienced a shift in community composition after transplantation, but LSTM mosquitoes did not, suggesting host filtering of microbes may differ between geographically isolated mosquito strains. Fidelity of transplanted microbial communities further varied based on initial composition of the donor pool and recipient host genotype, though patterns of assembly were conserved across the mosquito life cycle. Altogether, these results highlight the value of this method for studying mosquito-microbe interactions and lay the foundation for future efforts to identify bacterial candidates for use in mosquito and mosquito-borne disease control. They also provide a critical next step toward the standardization of pathogen infectivity experiments to include laboratory-reared mosquitoes colonized by microbial communities isolated from mosquitoes in disease endemic areas in the field.

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INVESTIGATING THE EFFECTS OF TEMPERATURE CHANGE ON OVIPOSITION AND PROGENY VIABILITY OF *AEDES AEGYPTI* AND *CULEX TARSALIS* MOSQUITOES

Olivia M. Martinez, Shelby Cagle, Emma K. Harris, Rebekah C. Kading

Colorado State University, Fort Collins, CO, United States

Temperature is known to affect the transmission efficiency of mosquito-borne viruses, particularly those spread by *Aedes aegypti* and *Culex tarsalis* mosquitoes. Investigating how environmental changes impact *Ae. aegypti* and *Cx. tarsalis* fecundity will inform future action for vector control and subsequent disease mitigation. Our preliminary data has shown impaired egg deposition when Rift Valley fever virus- adult *Ae. aegypti* mosquitoes were exposed to temperatures varying from typical environmental conditions. It is unclear if this behavior is due to infection or altered temperatures. Therefore, we are investigating the relationship between altered temperatures, oviposition rates, and progeny viability within uninfected blood-fed *Ae. aegypti* and *Cx. tarsalis* mosquitoes. We hypothesize that temperature variation will negatively impact egg viability, deposition rates, and offspring development. Blood-fed female mosquitoes (n=50) will be housed individually at lower (18°C), standard (28°C), or higher (32°C) rearing temperatures. Egg production will be assessed by quantifying deposited eggs in comparison to withheld eggs, obtained by ovarian dissection. Deposited egg hatch rates will be recorded to determine offspring viability. Data collection is ongoing. Preliminary trials showed increased developmental rates in *Ae. aegypti* at 32°C when compared to standard temperature. In contrast, *Cx. tarsalis* mosquitoes showed impaired egg-laying behavior and developmental rates at 32°C. Understanding the relationship between mosquito fecundity and temperature is of great importance for anticipating infectious disease dynamics in a complex and shifting global environment.

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A SINGLE-CELL ATLAS OF THE *CULEX TARSALIS* MIDGUT DURING WEST NILE VIRUS INFECTION

Emily Anne Fitzmeyer[1], Taru S. Dutt[1], Silvain Pinaud[2], Barbara Graham[1], Corey Campbell[1], Sarah Hélène Merkling[3], Jessica L. Hill[1], Hunter Ogg[1], Emily N. Gallichotte[1], Marcela Henao Tamayo[1], Gregory D. Ebel[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]Research and Development Institute IRD, Monpellier, France, [3]Pasteur Institute, Paris, France

The mosquito midgut functions as a key interface between pathogen and vector. However, studies of midgut physiology and associated virus infection dynamics are scarce, and in *Culex tarsalis* - an extremely efficient vector of West Nile virus (WNV) in the contiguous United States - nonexistent. We performed single-cell RNA sequencing on dissociated *Cx. tarsalis* midguts to define cell types comprising and associated with the midgut, and determine whether specific cell types are more permissive to WNV infection. We identified 15 midgut cell populations comprised of 7 distinct cell types, consistent with existing descriptions of *Drosophila* and *Aedes aegypti* midgut physiology. We found that all midgut cell populations were permissive to WNV infection. However, higher levels of WNV RNA, relative to other cell types, were present in enteroendocrine cells and cells enriched for mitochondrial genes, suggesting enhanced replication in these populations. In contrast, we observed the lowest levels of WNV RNA in proliferating intestinal stem cell (ISC) populations, a finding consistent with previous studies suggesting ISC proliferation in the midgut is involved in viral control. Notably, we did not detect significant upregulation of canonical mosquito antiviral immune genes (e.g., AGO2, R2D2, etc.) associated with WNV infection at the whole-midgut level. Rather, we observed a significant positive correlation between immune gene expression levels and WNV RNA level in individual cells, suggesting that within cells, high levels of WNV RNA may trigger antiviral responses. Our findings describe the cell types that comprise the midgut of *Cx. tarsalis*, and provide insight into the midgut infection dynamics of WNV in this highly efficient WNV vector by characterizing cell-type specific enhancement of, and immune response to, infection at the single-cell level.

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THE CONTRIBUTION OF SPECIFIC PROPHENOLOXIDASES TO PLASMODIUM MELANIZATION IN ANOPHELES GAMBIAE MOSQUITOES

Sally Saab, George Dimopolous

Johns Hopkins University, Baltimore, MD, United States

Anopheles gambiae mosquitoes rely on their innate immune responses to fight against *Plasmodium* infection. Among these responses is the melanization immune response, characterized by the deposition of melanin on the parasite's surface preventing it from gaining nutrients and thus triggering its death. Melanization involves a set of biochemical reactions that require the active phenoloxidase (PO), which is secreted into the hemolymph as prophenoloxidase (PPO) zymogen. A cascade of CLIP serine proteases is required for the cleavage and activation of PPO. The classical organization of this cascade in insects starts with the autoactivation of an upstream modular serine protease that integrates the signal from an activated pattern recognition receptor (PRR) into a downstream CLIP serine protease cascade constituted of several members. The most downstream CLIP in this cascade, known as the prophenoloxidase activating proteases, cleaves PPO into active PO which initiates the melanin biosynthesis pathway. Nine different PPOs have been identified in the *Anopheles gambiae* genome. Here, we attempt to identify the PPOs involved in *Plasmodium* melanization. We found that two different prophenoloxidases (PPOs) act together to mediate *Plasmodium* ookinete melanization, and our future aim is to generate transgenic mosquitoes that overexpress both PPOs to be used later in different functional infection assays.

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KINETICS OF MAYARO VIRUS INFECTIONS OF NEW WORLD AND OLD WORD *ANOPHELES* VECTORS

Luis Antonio Alonso Palomares, Jeremiah Miller, Ava Sheppard, Jhon Williams, John Lednicky, Rhoel R. Dinglasan
University of Florida, Gainesville, FL, United States

The Mayaro virus (MAYV) is an *Alphavirus in the family Togaviridae*. The virus has been classified into three genotypes (D, L, and N); genotype D has the greatest geographical distribution in the Americas. The primary vector for MAYV in the sylvatic transmission cycle are *Haemagogus* mosquitoes. However, the virus can also be transmitted in urban cycles by *Aedes aegypti*. MAYV infections can cause long-term debilitations in afflicted countries. It has been shown that mosquitoes of the genus *Anopheles* can transmit the MAYV. To understand the potential expansion of the virus eastward to Africa, we tested if MAYV (genotype D) infection kinetics differs between Old World (*Anopheles gambiae*) and New World (*Anopheles albimanus*) anophelines, as compared to infections in *Aedes aegypti* (Orlando) mosquitoes from Florida. We observed that MAYV disseminated infection of *An. albimanus* was rapid, wherein *virus was found in saliva* after only 2 days post infection (dpi), at a 26.6% infection prevalence. This translated to a higher prevalence of infection, increasing to 80% after 7 dpi as compared to *Ae. aegypti. Importantly, we also* detected the virus in ovaries, wherein ovary infection rates increased from 80% (2 dpi) to 100% (7 dpi), indicating a high potential for vertical transmission and persistence in the environment. At 2, 7, and 14 dpi, *An. gambiae* had a 100% midgut infection. Although the virus was not detected in saliva at 2 dpi, infection prevalence in saliva increased from 20% (7 dpi) to 60% (14 dpi); suggesting transmission in the Old World is possible. We also observed that *An. albimanus* infection with MAYV impacts lifespan and have profiled the mosquito host response to infection at 7 dpi to gain insight into the mechanisms affected by MAYV. Since the virus can already be transmitted as early as 2 dpi, *An. albimanus* are indeed competent in transmitting MAYV within a shorter extrinsic incubation period and should be considered as potential targets for vector control during local outbreaks.

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OPTIMIZATION OF ANTIMALARIAL DRUGS DELIVERY AND EVALUATING THEIR EFFECTS ON THE SURVIVAL AND FECUNDITY OF LABORATORY REARED ANOPHELES GAMBIAE MOSQUITOES

Moline Achieng Okal[1], Cyrus Ayieko[2], Hoseah Akala[1], John Waitumbi[1]
[1]Walter Reed Army Institute of Research, Kisumu, Kenya, [2]Maseno University, Kisumu, Kenya

WHO global technical strategy for malaria control targets to reduce malaria cases by 90% by the year 2030. While the up scaling of control strategies in the initial years led to significant reduction in global malaria cases, malaria burden has plateaued in the last five years. Recent studies have demonstrated the potential of using standard antimalarials to block the development and transmission of pre-erythrocytic stages within the vector. This study aimed to determine the maximal tolerable doses and the efficacy of the antimalarial drugs (artemether, lumefantrine, primaquine and tafenoquine) on the fecundity of the reared *An. gambiae s.s* mosquitoes. *An. gambiae s.s* Kisumu strain were reared in the insectary by maintaining standard insectary conditions. Fifty, 3–5 days old, blood naive and starved mosquitoes were introduced into ten labelled paper cups. Eight doses consisting of serial dilutions of each antimalarials drug in 10% glucose solution. Mosquitoes were allowed to feed on cotton wool soaked in different concentrations of antimalarials and mortality monitored for ten days. To monitor fecundity, a fresh batch of mosquitoes were fed with human blood and subjected to the highest tolerable drug doses. The number of eggs laid was monitored over 8 days period. Controls were fed 10% glucose without drugs. Kaplan–Meier survival analysis was performed to estimate the tolerable drug doses while Chi- square method was used to assess the fecundity of *Anopheles* mosquitoes. The highest tolerable doses were 700 ng/ml for artemether and lumefantrine and 5000 ng/ml for tafenoquine and primaquine. The number of eggs did not differ between the mosquitoes exposed to the different drugs and control groups. The mosquitos tolerated doses of artemether and lumefantrine, tafenoquine and primaquine that were equivalent to doses recommended for use in human host. These doses do not seem to have an effect on mortality or on mosquitos' fecundity hence can be recommended for future use as potential transmission blocking compounds.

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ENTEROBACTER CLOACAE AND *SERRATIA MARCESCENS* METABOLITES MINIMIZE *PLASMODIUM* GAMETOCYTE DEVELOPMENT *IN VITRO.*

Esinam Abla Akorli, Grace Odoom, Emmanuel Osei-Frempong, Jeffrey Kankam Boateng, Stephanie N.A Addo, Jewelna Akorli
Noguchi Memorial Institute for Medical Research, Legon, Ghana

Bacteria belonging to the family Enterobacteriaceae proliferate in the *Anopheles* mosquito midgut following a blood meal, and two members; *Enterobacter cloacae* and *Serratia marcescens* limit *Plasmodium* infection within the vector. As candidates for transmission-blocking strategies, it remains uncertain which will be more effective in targeting parasites: the increase in bacterial cell numbers in the vector and/or introduction of the vector to bacterial metabolites. We have already shown that metabolites from a 4hr spent media from *E. cloacae* and *S. marcescens* has varied effects on oocyst numbers in *Anopheles* mosquitoes. This current study aims to determine the concentration-dependent effect of bacterial metabolites on *Plasmodium*. Spent media following 6 different time-points culturing of two isolates each of *E. cloacae* (*EspG1*, *EspG3*) and *S. marcescens* (*SmG5*, *SmG6*) were lyophilized and reconstituted at 3mg/mL. *P. falciparum* 3D7 and Dd2 gametocyte stages IV-V were obtained with sorbitol synchronization, and incubated with bacterial metabolites for 72 hours. We have also begun to investigate the properties of the metabolites by applying heat (56ºC) and proteinase K treatments. Viable parasites were assessed with SYBR Green I and absorbances were read using a fluorescence plate reader. The overall treatment effect of the metabolites across all time-points differed between *SmG6* and *EspG1* (P= 0.003). There was evidence of interaction between the metabolites and parasite strains suggesting that the killing effect was stronger in some metabolite-parasite combinations than others. *Plasmodium* intensity reduced across all time-points with the highest effect at 4 and 6hrs for 3D7 and, 1hr for Dd2. Heating reduced the efficacy of *E. cloacae*-derived metabolites only (P=0.02) while proteinase K treatment had no effect. Our data provides preliminary results on studies that aim to understand the mechanisms, potential applications and feasibility of mosquito midgut symbiont-based approaches for mosquito/disease control.

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ELIZABETHKINGIA ANOPHELIS MSU001 ISOLATED FROM *ANOPHELES STEPHENSI*: MOLECULAR CHARACTERIZATION AND COMPARATIVE GENOME ANALYSIS

Shicheng Chen[1], Nicolas Terrapon[2], Jochen Blom[3], **Edward D. Walker**[4]
[1]Northern Illinois University, DeKalb, IL, United States, [2]Marseille Université, Marseille, France, [3]Justus-Liebig University, Giessen, Germany, [4]Michigan State University, East Lansing, MI, United States

Elizabethkingia anophelis is an aerobic, non-fermenting, non-motile, non-spore-forming gram-negative rod that readily colonizes the mosquito gut, forms part of the gut microbiome, and offers potential for control of mosquito-borne pathogens via paratransgenesis. However, it also is an opportunistic pathogen of humans. This study involved characterization of a new strain, E. anophelis MSU001, isolated from *Anopheles stephensi* (JHU strain) in the laboratory, and characterized by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-ToF/MS), biochemical testing, and genome sequencing. The strain was isolated by

dissecting a gut of An. stephensi and plating contents onto Luria-Bertani agar medium with erythromycin. Average nucleotide identity analysis revealed 99% identity of MSU001 with the type species E. anophelis R26. Phylogenetic placement revealed a clade with mosquito-associated strains separate from a clade of clinical isolates. Comparative genome analysis showed that it shared at least 98.6% of genes with mosquito-associated isolates (except E. anophelis As1), while it shared at most 88.8% of common genes with clinical isolates, suggesting divergence between strains adapted to the mosquito gut and clinically-significant strains. Metabolites from MSU001 inhibited growth of E. coli but not mosquito gut symbionts Serratia marcescens and Asaia sp. strain W12. Mosquito-associated E. anophelis strains carried glycoside hydrolase- and auxiliary activities-encoding genes distinct from those of clinical isolates, indicating their potential role in reshaping chitin structure and other components involved in larval development or formation of the peritrophic matrix. Like other Elizabethkingia, MSU001 also carried genes encoding two-component system proteins, transcription factor proteins, DNA-binding proteins, and a diverse repertoire of antibiotic resistance genes and several virulence factors. Its potential for opportunistic infections in humans should be further evaluated prior to implementation as a paratransgenesis agent.

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REPRODUCTIVE STRATEGIES ASSIST THE BIOLOGICAL INVASION PROCESS OF *AEDES ALBOPICTUS*

Ayda Khorramnejad, Claudia Alfaro, Stefano Quaranta, Alejandro Nabor Lozada-Chavez, Laila Gasmi, Hugo Perdomo, Laurent Chiarelli, Mariangela Bonizzoni

University of Pavia, Pavia, Italy

The success of biological invasions depends on a species ability to survive and reproduce in a new environment, traits which mediate the effective establishment and persistence in new habitats. The arboviral vector *Aedes albopictus* is a successful invasive mosquito, which conquered tropical and temperate areas of the world in less than 100 years. The rapid spread of *Ae. albopictus* has been ascribed to its ecological plasticity, its ability to overwinter through photoperiodic diapause and produce desiccation resistance eggs. Whether *Ae. albopictus* reproductive capacity has contributed to its invasive success has not thoroughly investigated yet. Here, we compared the phenotypic variations and reproduction potentials of several *Ae. albopictus* populations. We observed extensive phenotypic variations between invasive and native populations with invasive mosquitoes being statistically bigger in size and having a higher reproductive output. To investigate the biological underpinnings of these differences, we visualized ovaries during their development and analyzed their physiology and protein profile in a comparative manner including mosquitoes of an invasive population with respect to those of the laboratory Foshan reference strain. We observed that females of the invasive population better allocate the energy reserves acquired during the larval stage and that from a blood meal resulting in higher production of fertile eggs than Foshan mosquitoes. Proteomic analyses and ovarian micrographs showed a delay in oogenesis in invasive mosquitoes which correlated with a higher fecundity and fertility. We further performed reciprocal crosses between mosquitoes of Foshan and the invasive population which highlighted a potential contribution of males on the reproductive success of invasive mosquitoes. Overall, our findings show reproductive strategies assisted the biological invasion process of *Ae. albopictus*.

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CHARACTERIZING RESIDUAL MALARIA TRANSMISSION IN THREE SELECTED HIGH BURDEN DISTRICTS OF WESTERN PROVINCE, ZAMBIA

Benjamin Chanda[1], Tresford Kaniki[1], Patricia Mambo[1], Rayford Muyabe[1], Mwansa Mwenya[1], Chama Chisyha[1], Busiku Hamainza[2], Thomas Burkot[3], Ruth Ashton[4], Erica Oranga[5], Megan Littrell[6], Keith J. Mbata[7], Joseph Wagman[6]

[1]PATH, Kaoma, Zambia, [2]National Malaria Elimination Centre, Lusaka, Zambia, [3]Australian Institute of Tropical Health and Medicine, Cairns, Australia, [4]Tulane Univsity, New Orleans, LA, United States, [5]PATH, Seattle, WA, United States, [6]PATH, Washington, DC, United States, [7]University of Zambia, Lusaka, Zambia

Zambia remains a highly malaria-endemic country, with infection risk highest in rural regions such as Western Province. The primary vectors responsible for transmission vary by region and include *Anopheles funestus s.s.*, *An. gambiae s.s.*, and *An. arabiensis*. Since 2002, implementation of standard vector control interventions, namely insecticide treated nets and indoor residual spraying, has contributed substantially to reducing the malaria burden in Zambia: between 2002 and 2018 national-level malaria prevalence in children under 5 dropped from 22% to 9%, while inpatient malaria cases and deaths each declined by approximately two-thirds. However, in Western Province malaria burden remains high, with 2021 estimates of under 5 prevalence near 50% and all-ages case incidence at 785/1000 person-years at risk. This consistently high burden despite quality implementation of effective malaria control programming shows that residual transmission persists, and underscores the need to better understand key entomological drivers of residual transmission to guide targeted scale up of complimentary interventions and to inform development of new tools and approaches. This study aimed to characterize, for the first time, the full breadth of *An. funestus* biting behaviors in four high burden communities of Western Zambia. Longitudinal vector surveillance was conducted from January to April 2024 using human landing catches (HLC) conducted over 24 hours, indoors and outdoors, at households and at schools and markets. Results indicate biting occurs both indoors and outdoors with a peak in the early morning from 01:00 - 6:00, but substantial potential for malaria transmission also exists in the later morning hours - particularly indoors at schools, where more than 1 bite per person was recorded between 6:00 and 11:00 each collection day. Future work should expand 24-hour vector surveillance activities year-round, explore sporozoite positivity by time and location of human biting, and overlay vector and human behaviors to map a fuller understanding of community-wide malaria transmission risk and identify gaps in current vector control approaches.

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FOREST EDGE LANDSCAPE CONTEXT AFFECTS MOSQUITO COMMUNITY COMPOSITION AND RISK OF PATHOGEN EMERGENCE

Adam Hendy[1], Nelson F. Fe[2], Igor Pedrosa[2], André Girão[2], Taly N.F. dos Santos[2], Claudia R. Mendonça[2], José T. Andes Júnior[2], Flamarion P. Assunção[2], Edson R. Costa[3], Vincent Sluydts[4], Marcelo Gordo[3], Vera M. Scarpassa[5], Michaela Buenemann[6], Marcus M.V.G. Lacerda[2], Maria Paula G. Mourão[2], Nikos Vasilakis[1], Kathryn A. Hanley[7]

[1]University of Texas Medical Branch, Galveston, TX, United States, [2]Fundação de Medicina Tropical Doutor Heitor Vieira Dourado (FMT-HVD), Manaus, Brazil, [3]Universidade Federal do Amazonas, Manaus, Brazil, [4]University of Antwerp, Wilrijk, Belgium, [5]Instituto Nacional de Pesquisas da Amazônia, Manaus, Brazil, [6]New Mexico State University, Las cruces, NM, United States, [7]New Mexico State University, Las Cruces, NM, United States

Forest edges, where humans, mosquitoes, and wildlife interact, may serve as a nexus for zoonotic arbovirus exchange. Although often treated as uniform interfaces, the landscape context of edge habitats can greatly impact ecological interactions. Here, we investigated how the landscape context of forest edges shapes mosquito community structure in an Amazon rainforest reserve near the city of Manaus, Brazil. Between July 2021 and June 2022, we sampled diurnally active mosquitoes using hand-nets at ground level and on 5 m platforms at three distinct forest edge types bordering urban land cover, rural land cover, and natural treefall gaps, while sites in continuous forest served as controls. Mosquito communities differed considerably between forest edges and continuous forest. Urban edges had the most distinct communities, dominated by ground dwelling *Aedes albopictus* and *Limatus durhamii*, followed by rural edges, and treefall gaps where *Haemagogus*, *Psorophora*, and *Sabethes* species were common. Rural edges supported the highest species diversity, providing suitable habitat for both urban and forest specialists, including key arbovirus

vectors. *Haemagogus janthinomys* was notably abundant at ground level at treefall gaps, where there is a high risk for interaction between this species and ground dwelling wildlife and humans. Our findings emphasize the importance of landscape context in assessing pathogen emergence risk at forest edges.

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MOLECULAR XENOMONITORING FOR POST-VALIDATION SURVEILLANCE OF LYMPHATIC FILARIASIS IN BANGLADESH: EVIDENCE TO SUPPORT LYMPHATIC FILARIASIS (LF) ELIMINATION AS A PUBLIC HEALTH PROBLEM

Prakash Ghosh[1], Nishad Tasnim Mithila[1], Debashis Ghosh[1], Md. Arko Ayon Chowdhury[1], Shomik Maruf[1], Md Rasel Uddin[1], Soumik Kha Sagar[1], Md Utba Rashid[1], Mohammad Sohel Shomik[1], M.M. Aktaruzzaman[2], A. S. M. Sultan Mahmood[2], Ahmed Abd El Wahed[3], Mohammad Shafiul Alam[1], Mary Cameron[4], Nils Pilotte[5], Emily A. Dodd[6], Tara A. Brant[6], Kimberly Y. Won[6], Dinesh Mondal[1]

[1]icddr,b, Dhaka, Bangladesh, [2]Communicable Disease Control (CDC), Directorate General of Health Services (DGHS), Mohakhali, Dhaka, Bangladesh, [3]Institute of Animal Hygiene and Veterinary Public Health, Leipzig University, Leipzig, Germany, [4]Department of Disease Control, London School of Hygiene and Tropical Medicine, London, United Kingdom, [5]Department of Biological Sciences, Quinnipiac University, Hamden, CT, United States, [6]Division of Parasitic Diseases and Malaria, U.S. Centers for Disease Control and Prevention, Atlanta, GA, United States

Bangladesh achieved validation of elimination of lymphatic filariasis (LF) in 2023. To cement this achievement and sustain elimination, the program must continue emphasis on post validation surveillance and response measures to prevent recrudescence of infection. Tailoring a sensitive surveillance strategy by combining host- and vector-directed surveillance tools is imperative to track the transmission of LF at this phase. Since molecular xenomonitoring (MX) is a non-invasive and sensitive means for surveillance, we used this technique to detect any *Wuchereria bancrofti* (Wb) DNA. We included 62 villages under Gangachara Upazila, spanning in two evaluation units (EU) in Rangpur district, in the cross-sectional survey. We applied an index-based approach to collect mosquitoes from residences of LF clinical patients (n=83) and their neighboring households (n=315) within a≈50 m radius. Mosquitoes were collected Jun 2022-Nov 2023 using CDC gravid traps placed in each household for three consecutive nights. Mosquitoes were identified morphologically using a standard taxonomic key and placed into pools of up to 25 mosquitoes. Female Culex quinquefasciatus (fed and gravid) were tested for Wb DNA using previously described real time PCR pool screening method. We collected 47,611 *Cxulex quinquefasciatus* mosquitoes including 44,785 females; 1.6% were fed and 72.9% were gravid. In total, 1,225 mosquito pools (15-25 mosquitoes per pool), comprising either blood-fed or gravid females, were tested. We detected Wb DNA in four pools corresponding to estimated prevalence rates of 0.03% (95% Confidence Interval (CI): 0.01-0.07%) or 0.03% (95% CI: 0.01-0.07%) using maximum likelihood estimation and Bayesian estimation, respectively. These data indicate the persistence of low levels of Wb infection in the EUs below the provisional threshold (<0.25%) set by WHO and are consistent with results of previous transmission assessment surveys. Our findings support the adoption of MX by the national LF elimination program to monitor transmission of infection in combination with host surveillance data, which could help prevent the recrudescence of LF.

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DETECTION OF *AEDES ALBOPICTUS* IN DISTRICT 3 OF MANAGUA, NICARAGUA

Jacqueline Mojica[1], Jose G. Juarez[1], Harold Suazo[1], Maria M. Lopez[1], Angel Balmaseda[1], Eva Harris[2], Josefina Coloma[2]

[1]Sustainable Science Institute, Managua, Nicaragua, [2]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, United States

The Asian tiger mosquito, *Aedes albopictus* (Skuse), is an invasive mosquito species that has established itself in all continents of the globe, except for Antarctica. It is the vector of over 30 arboviruses, serving also as a bridge vector for diseases such as West Nile virus and Eastern equine encephalitis virus. Entomological larvae, pupae and adult surveys were conducted during the rainy and dry seasons of 2022 and 2023 in a rural (Nejapa) and urban (Camilo Ortega) sector of District 3 of Managua, Nicaragua. We randomly selected 500 households from a parent arboviral clinical and serological cohort study as well as 65 key sites, all in the catchment areas of our study health posts. All mosquito life stages were transported to our main facilities in Managua for classification and separation by stage (unfed and bloodfed), sex and species. We found only 2 larvae of *Ae. albopictus* in each survey of the dry season of 2022 (Camilo Ortega) and 2023 (Nejapa), with no *Ae. albopictus* found in the rainy season of 2022. However, in the 2023 rainy season, we collected 557 *Ae. albopictus* larvae-pupae and 223 adults in both communities. A total of 415 immature aquatic forms and 76 adult mosquitoes (65 females) were collected in households. In key sites, we collected 142 larvae/pupae and 137 adults (79 females). We observed that in >60% of households and >40% of keys sites, the preferred habitat for immature forms was "other container" (*i.e.,* boot, toy, plastic bottle, etc). Our results reveal the introduction of *Ae. albopictus* into communities of District 3 of Managua over the past two years. Further surveillance is required to determine if *Ae. albopictus* will displace *Ae. aegypti* in the area or if co-habitation will occur. Additionally, this ecological displacement is critical to determine in the context of novel vector control activities targeting *Ae. aegypti* in Managua.

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GLOBAL ANALYSIS OF *ANOPHELES STEPHENSI* BIONOMICS AND CONTROL APPROACHES THROUGH A SYSTEMATIC LITERATURE REVIEW

Tabeth Mwema[1], Sarah Zohdy[2], Mekala Sundaram[3], Christopher A. Lepzcyk[1], Lana Narine[1], Janna R. Willoughby[1]

[1]College of Forestry, Wildlife, and Environment, Auburn University, Auburn, AL, United States, [2]Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, Atlanta, GA, United States, [3]Department of Infectious Disease, University of Georgia, Athens, GA, United States

Anopheles stephensi is a mosquito endemic to South Asia and the Arabian Peninsula that has recently expanded its range into Africa, posing a significant threat to global malaria control efforts. This study investigates the efficacy of trapping methods and larvicides and larvivorous fish in controlling *An. stephensi* mosquitoes through an analysis of global literature, identified by searching all relevant databases (PubMed, Web of Science, and Google Scholar) for studies focused on *An. stephensi*'s behavior and biology. Data from 83 articles revealed that host-seeking human-baited traps improve collection efficiency significantly when compared to mechanical baited traps, with no difference observed between human-baited and animal-baited traps. However, mechanical unbaited traps outperform mechanical baited traps. *Anopheles stephensi*'s indoor and outdoor biting and resting behaviors exhibit no significant difference, and its breeding habitats include discarded household utensils and vegetative areas. *Bacillus thuringiensis israelensis, Beauveria bassiana* and temephos are the most effective larvicides among those considered. Comprehensive surveillance programs covering both larval and adult populations are crucial for assessing intervention impacts and quantifying resistance levels. Increased use of biolarvicide control tools is recommended to control *An. stephensi*, since

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

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

Constantine Mukisa Muwonge, Fredros O. Okumu, Halfan S. Ngowo

Ifakara Health Institute, PO Box 53, Ifakara, Tanzania., Morogoro, Tanzania, United Republic of

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.

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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

Nicolas Zanre[1], Aboubacar Sombié[2], Awa Gnémé[1], Hyacinthe K. Toé[1], Antoine Sanon[1], Athanase Badolo[1]

[1]University of Joseph KI-ZERBO, Ouagadougou, Burkina Faso, [2]University of Kaya, Kaya, Burkina Faso

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.

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

Katharine B. Major[1], Vivek Raman[2], Karen L. Figueroa Chilito[1], David Greer[2], Christian De Haan[2], John Cataline[2], Joseph Franceschini[2], Daniel Goldstein[2], Christopher Begay[2], Chad L. Cross[1], **Louisa Alexandra Messenger**[1]

[1]University of Nevada, Las Vegas, Las Vegas, NV, United States, [2]Southern Nevada Health District, Las Vegas, NV, United States

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.