MESA

2nd Women in Malaria (WiM) 2025 Conference

MESA Correspondents Report

Written by Kevin Rowartz Ogola, Flavia Kaduni Bawa, Geoffrey Githinji, Rebecca Pwalia, Akua Obenewaa Danquah Yirenkyi.

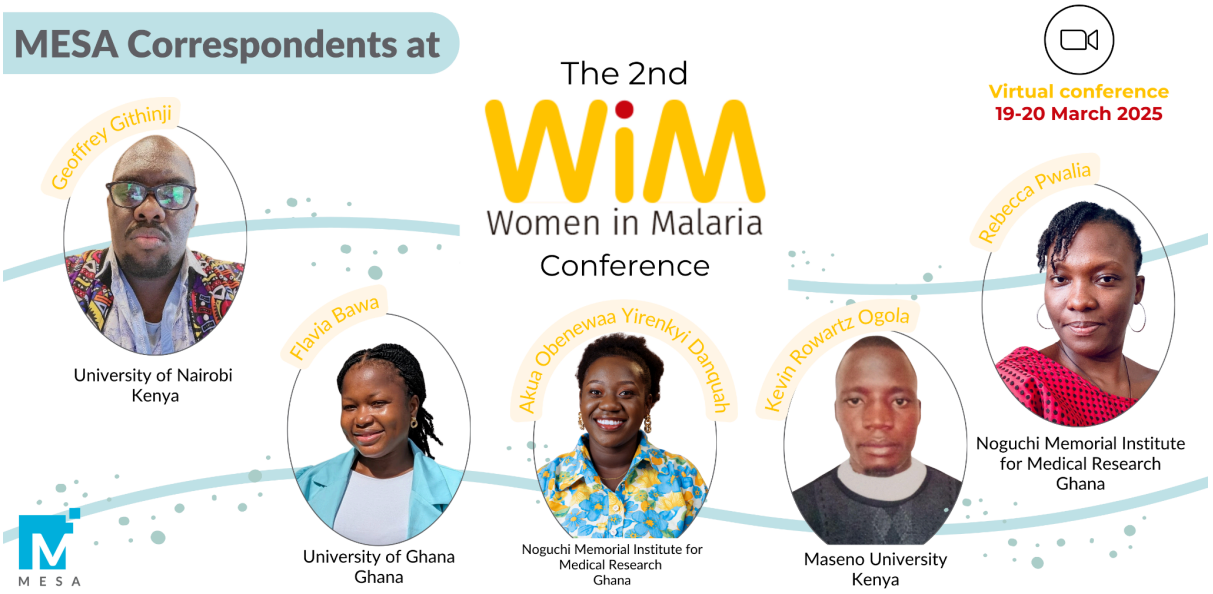
Senior editorial support has been facilitated by Dr. Divya Beri and Dr. Joanne Power.

MESA Correspondents bring you cutting-edge coverage from the 2nd Women in Malaria (WiM) 2025 Conference

19 - 20 March 2025

Online

MESA would like to thank Dr. Divya Beri (New York Blood Center, United States) and Dr. Joanne Power (University of Glasgow, United Kingdom) for providing senior editorial support.



MESA would also like to acknowledge the MESA Correspondents Kevin Rowartz Ogola (University of Nairobi, Kenya), Flavia Kaduni Bawa (University of Ghana, Ghana), Geoffrey Githinji (Maseno University, Kenya), Rebecca Pwalia (Ngouchi Memorial Institute for Medical Research, Ghana) and Akua Obenewaa Danquah Yirenkyi (Ngouchi Memorial Institute for Medical Research, Ghana) for their coverage of the conference.

Table of contents

Day 1: Wednesday, 19th March 2025

Welcome and Introduction

Elena Gómez-Díaz (Institute of Parasitology and Biomedicine Lopez-Neyra - IPBLN, CSIC, Spain) welcomed everyone to the **2nd online Women in Malaria (WiM) Conference**. This conference aims to support, empower, and connect women and non-binary scientists in malaria research, both in the fight against malaria and the fight for equity in science. The WiM Initiative was created in 2018 with a very specific vision of building a diverse and inclusive community of women and non-binary scientists in the field of malaria research, because gender-based bias and violence is still very present in today's world. WiM exists to be a safe space for all these women to communicate and to lift each other up. The WiM community came together for its first virtual conference in 2021 (link) and we are now celebrating the second edition. Then **Silvie Huijben** (Arizona State University, USA) chair of the second WiM conference organizing committee dedicated a few words to all the attendees and encouraged everyone to enjoy, learn, engage with the speakers, and create meaningful connections to support and empower one another.

Plenary Talk 1 - The state of malaria in Africa - where do we go from here?"

Dorothy Achu (World Health Organization, Africa region) presented the current state of malaria in Africa. She began by briefly discussing the epidemiology of malaria globally and then gave a detailed overview of malaria in Africa. She highlighted transmission drivers including socioeconomic factors, *Plasmodium falciparum* prevalence, climate change impacts, and insufficient funding—creating what she refers to as "the perfect storm." She outlined initiatives since 1998 that revitalized malaria control, from the Roll Back Malaria Partnership to the 2024 Yaoundé Declaration and Big Push Initiative. Progress since 2000 includes 3 billion long-lasting insecticidal nets (LLINs) distributed, widespread implementation of indoor residual spraying (IRS), seasonal chemoprevention for 53 million children, and vaccines benefiting 5 million children, resulting in a 35% case reduction and 13 million deaths averted. Despite this, Africa faces challenges: weak health infrastructure, climate change, insecticide resistance, and intervention gaps—over 50% of women and children don't use ITNs, and many lack prompt diagnosis and treatment. Achu proposed integrating vertical programs into broader health systems, sub-national tailored interventions, country-led approaches, community mobilization and strengthened surveillance for emerging resistance. She briefly discussed guidelines to address biological threats that include insecticide resistance, ACT resistance, spread of *Anopheles stephensi* and *pfhrp2/3* deletions. She concluded by highlighting the case study of Rwanda which substantially reduced malaria cases through political commitment, data-driven interventions, community engagement, adequate response to insecticide resistance and the lessons that can be learned from Rwanda's success.

Session 1 - Immunology and vaccines

Christine Hopp's (Bernhard Nocht Institute for Tropical Medicine, Germany) presentation sought to challenge the notion that infection is a trigger for autoimmune diseases. Her team conducted a 10-year longitudinal cohort study among children and adults in the malaria-endemic region of Mali to show how repeated malaria episodes impactselective

pressure for autoimmune disorders. In this study, plasma, peripheral blood mononuclear cells (PBMCs), and clinical data were collected at baseline and at different time points to assess the role of autoantibodies in malaria infection. Participants were screened for autoantibodies using the antinuclear antibody test. They found that 50% of children between the ages of 6 and 12 had autoantibodies which correlated with a 40% lower risk of febrile malaria. To decipher the mechanism, the researchers purified autoantibodies to test for inhibition of *P. falciparum* 3D7 *in vitro* and observed a significant growth inhibition compared to IgG, translating to growth inhibition *in vivo*. Hopp linked these findings to prior genetic studies showing that certain autoimmune-related genes are associated with malaria protection. She deduced from the evidence generated that chronic exposure to malaria prevents autoimmune disease by inducing immunoregulation which prevents autoimmune pathology.

Jenna Dick (University of Minnesota Medical School, United States) presented her research on the phenotypes of natural killer (NK) cells in malaria immunity. Her research examined transcription factors of adaptive NKs, and the different phenotypes that enhance cytokine production and antibody-dependent cellular cytotoxicity (ADCC) function in the context of malaria. After her initial screen of FcRɣ negative NK cells yielded negative results, an unbiased approach using flow cytometry was used to look at cell surface receptors. Malaria-exposed samples from Mali had a high number of SIGLEC-7 negative NK cells. This was explored further using CRISPR to determine its actual function. Using infected RBCs and antibodies, it was confirmed that SIGLEC-7 knockout led to degranulation and production of CD107A whereas the malaria naïve plasma showed no difference. Overall, her study showed that NK cells with reduced SIGLEC 7 correlate with FcRɣ negative NK cells which enhance the killing of iRBCs, thereby reducing parasite loads.

Maya Aleshnick (Vaccine and Gene Therapy Institute, Oregon Health and Science University, United States) presented the use of non-human models to study *Plasmodium* infections and response to vaccination. Previous studies in her lab involved Rhesus macaques challenged with *P. knowlesi* which is comparable to *P. falciparum* infection in humans. Her current study uses weanlings to investigate the immunological features of vaccine-reduced response in young infants with underdeveloped immune systems. In acute infection models of infant Rhesus macaques, the parasite increased rapidly requiring early treatment to prevent severe disease and mortality. Pig-tailed macaques on the other hand showed extended asymptomatic infection, characteristic of chronic human infection. For studies involving *P. vivax* which cannot be cultured *in vitro* for extended periods, a transgenic *P. cynomolgi* parasite expressing the *P. vivax* circumsporozoite protein was produced using CRISPR/Cas editing. Further experiments demonstrated the use of transgenic P*. cynomolgi* in place of *P. vivax* for vaccine challenge experiments.

Kristina Burrack's (Hennepin Healthcare Research Institute, University of Minnesota, United States) research investigates the use of IL-15 to enhance whole sporozoite malaria vaccines. Her lab studies a genetically attenuated parasite (GAP) vaccine that induces strong immune responses, for which improvements are needed for durability. Burrack's team tested whether the IL-15 complex could boost vaccine effectiveness. In mice, IL-15 treatment significantly increased TRM-like CD8 and CD4 T cells in the liver. When combined with the GAP vaccine, the IL-15 complex enhanced the number of antigen-specific T cells and improved their function, increasing interferon-gamma production—a key factor in killing

infected hepatocytes. Additionally, IL-15 complex boosted CSP-specific IgG antibody levels, which are important for malaria protection. A pilot study showed that IL-15-treated mice had significantly reduced liver parasite burden after being challenged with wild-type sporozoites, suggesting improved vaccine efficacy. These findings highlight the IL-15 complex as a promising tool for enhancing malaria vaccine durability by strengthening both cellular and antibody-mediated immunity.

Angela Minassian (University of Oxford, United Kingdom) presented about advancements in malaria vaccine development. Her team initially focused on blood-stage malaria vaccines but is now advancing toward multi-stage vaccines. Her team identified RH5, a conserved parasite protein essential for red blood cell invasion, as a promising target. Preclinical studies in non-human primates demonstrated that RH5 vaccination led to parasite clearance or sterile protection, correlating with growth inhibition activity (GIA) levels above 60% in vitro. Clinical trials demonstrated its efficacy and strong immunogenicity in vaccinated adults and children in the UK and Africa. Over a decade, iterative vaccine improvements have increased GIA, exceeding protective thresholds in African children. A phase 2B trial is underway in Burkina Faso to assess its effectiveness in preventing clinical malaria in real-world settings. In this study, about 360 children in malaria-endemic settings were vaccinated with RH5 vaccine formulated with the Matrix-M adjuvant or a Rabivax-S and M-Matrix adjuvant. Significantly high levels of anti-RH5 antibodies were recorded in the RH5 vaccinated group compared to the Rabies vaccinated group and levels at baseline. Overall, this vaccine recorded an efficacy of 55% for participants who took a delayed third dose. Trials are currently underway for multistage vaccines and sequential administrations of different vaccine combinations.

Session 2 - Vector biology and ecology

Rosine Danale Metisti Tesongang (University of Yaoundé I - UY1, Cameroon) presented a study investigating housing improvements as a malaria control strategy in Cameroon's forest zones, where plank houses exhibit higher malaria prevalence compared to brick or cement structures. The study assessed *Anopheles* species diversity, biting behavior, and the impact of house improvements on mosquito abundance. Mosquitoes were collected via human landing catches (HLC) in Nyabessan before and after interventions, with morphological and molecular identification. Ten houses were selected; five improved with netted windows and doors, and five left as unimproved controls. Seven *Anopheles* species were identified, with *An. paludis* being the most abundant. Biting behavior analysis revealed peak activity between 10 pm and midnight, and 5-6 am for some species. Post-improvement, indoor *Anopheles* density decreased significantly, with improved houses showing a 2.52-fold reduction in mosquito numbers. The study also observed a decline in entomological inoculation rates (EIR), highlighting the effectiveness of housing improvements in reducing malaria transmission. Tesongang's findings demonstrate that improved housing, particularly with netted windows and doors, significantly reduced indoor *Anopheles* density. This approach serves as a valuable supplementary malaria control measure, especially in high-transmission areas. The research underscores the potential of integrating housing improvements with existing strategies to enhance malaria control efforts in endemic regions.

Emma Camacho (Johns Hopkins University - JHU, United States) discussed mosquito melanization, crucial for survival through cuticle hardening, wound healing, and immune

defence, that is often inhibited by environmental factors like glyphosate. The research explored enhancing this defence mechanism using L-DOPA, a melanin precursor found in plants. Feeding *Anopheles gambiae* mosquitoes L-DOPA in sugar meals significantly reduced *Plasmodium* parasite numbers *in vivo* and killed 70% *in vitro*. L-DOPA also darkened mosquito cuticles, thickened them, and increased resistance to insecticides by reducing penetration. While mosquitoes showed increased cuticular melanization, they remained susceptible to deltamethrin in WHO tube assays. The study concluded that L-DOPA promotes cuticular melanization, impairs *P. falciparum* development, and offers a potential environmentally friendly malaria control strategy.

Chia Yu Chen (Center for Emerging Zoonotic and Parasitic Diseases, National Institute for Communicable Diseases - NICD, South Africa) explored the link between histone modifications, immunity, and longevity on *Anopheles arabiensis* mosquitoes. Their studies showed that larvae exposed to either Gram-negative or Gram-positive bacteria after being reared in the presence of histone modulators (one that increased histone acetylation or one that decreased histone acetylation), both groups showed significant reduction in lifespan. Histone H4 underwent fewer modifications compared to H3, with H4 playing a structural role and H3 serving as the primary target for gene regulation. Immune stimulation led to decreased H3 acetylation and increased repressive marker H3K27me3, both contributing to gene silencing. Gram-positive bacteria had a stronger impact than Gram-negative, indicating that more foreign pathogens trigger greater epigenetic changes. These modifications, particularly on H3, likely affect longevity by altering gene expression. Chen's finding further highlights the critical role of histone modifications in regulating immune responses and lifespan in *An. arabiensis*. She further emphasized that future steps include identifying silenced genes, especially those in immune pathways, and repeating experiments with *Plasmodium* infection to better understand malaria transmission.

Nicole Vargas Garcia (Entomological Research Group, Universidad del Valle, Colombia) presented her work on integrating vector control into malaria elimination strategies on Colombia's Pacific coast. In her presentation, she emphasized the effectiveness of combining diagnosis, treatment, investigation, and response (DTI-R) with insecticide-treated nets (ITNs) and indoor residual spraying (IRS) to significantly reduce malaria transmission. Garcia highlighted the challenges posed by the region's diverse geography, high mosquito diversity, ethnic and cultural complexities, internal armed conflicts, and human migration. She concluded that entomological data played a crucial role in mapping the spatial distribution of malaria transmission risk at a local scale, enabling precise stratification for targeted vector control planning. At the end of her presentation, Garcia noted that her findings underscore the importance of multi-sector collaboration and innovation in malaria elimination efforts.

Carolina Barillas-Mury (National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), United States) shared her pioneering research on mosquito immunity and malaria transmission. She investigated the critical role of *Pfs47*, a *Plasmodium falciparum* surface protein that enables the parasite to evade the mosquito's immune system and facilitate malaria transmission. Her work revealed that the *Pfs47* surface protein acts as a molecular "key" that must match the mosquito's immune "lock" (a *Pfs47* receptor (P47Rec)) to ensure parasite survival. Specifically, *Pfs47* haplotypes (genetic variants) show remarkable geographic adaptation, interacting with sympatric mosquito

species' P47 receptors to suppress complement-mediated immunity in the mosquito. Barillas-Mury's studies demonstrate that the compatibility between *Pfs47* haplotypes and the mosquito's immune genotype varies across different *Anopheles* species and populations, influencing geographic patterns of malaria transmission. This co-evolutionary adaptation highlights the intricate arms race between *Plasmodium* and its mosquito vector. Her findings have significant implications for malaria control, suggesting that disrupting the *Pfs47*-mediated immune evasion could block transmission. Potential strategies include genetically modifying mosquitoes to recognize and eliminate *Plasmodium* regardless of *Pfs47* haplotypes or developing transmission-blocking interventions targeting *Pfs47*. Barillas-Mury's presentation provided a deeper understanding of host-parasite interactions and opened new avenues for innovative malaria control strategies by targeting the molecular mechanisms that enable parasite survival in mosquitoes.

Round Table Discussion - What if women were leading the fight against malaria?

Rinki Deb (Principal Investigator, Vestergaard) led an insightful roundtable discussion titled "What if women were leading the fight against malaria?" The session brought together expert panelists to explore the challenges and opportunities for women in malaria research and leadership. The panel featured leading female scientists and professionals, including **Jackline Martin** (i2i Vector Control Product Associate, Vestergaard), **Anita Ghansah** (Senior Research Fellow and Head of the Department of Parasitology, Noguchi Memorial Institute of Medical Research, University of Ghana), **Elena Marbán Castro** (Operational & Implementation Research Scientist, FIND and Women in Global Health Spain), **Ingrid Etoke** (Senior Program Officer, Gates Foundation) and **Corine Ngufor** (Associate Professor, CREC/LSHTM Collaborative Research Programme).

The discussion opened with a series of thought-provoking questions, prompting panelists to reflect on the hurdles women face in the field. Topics included work-life balance challenges, limited leadership opportunities, and gender discrimination.

Corine Ngufor emphasized discrimination as a major obstacle, with **Anita Ghansah** noting that societal norms often silence women in decision-making spaces. She stressed the importance of challenging these biases by increasing awareness and fostering recognition of women's leadership contributions. She also encouraged women to assert their voices when given a platform.

Panelists highlighted the unique strengths women bring to malaria research and healthcare. **Ingrid Etoke** and **Elena Marbán Castro** noted that women often build trust within communities through empathetic engagement, strong multitasking, and organizational skills abilities that remain undervalued, particularly among community health workers in informal healthcare systems. She underscored the role of gender-intentional grants, like those provided by her institution, in addressing inequities and supporting women in these roles. **Corine Ngufor** acknowledged the value of existing mentorship programs but called for a more sustained effort to guide young female researchers beyond short-term training. She cited successful initiatives, such as *Women in Global Health* and the *MIM Mentorship Program*, as models for long-term career support.

The conversation also explored practical ways to foster female empowerment in the field. **Anita Ghansah** proposed creating more sponsorship opportunities to enhance networking

and career advancement for early-career researchers. **Jackline Martin** championed the importance of knowledge-sharing, emphasizing that entrusting young researchers with meaningful responsibilities builds their confidence and helps address gender imbalances in the long run. **Corine Ngufor** shared examples from her own institution, illustrating how concrete measures can break down barriers. One initiative provided on-field accommodation for mothers and their children, ensuring that early-career female researchers could participate in fieldwork while feeling supported in their roles as both professionals and mothers.

The discussion underscored the need for systemic change to foster gender equity in malaria research and leadership. Through mentorship, funding, and institutional support, women can not only overcome barriers but also drive progress in the fight against malaria.

Malaria in Mothers and Babies Initiative: Accelerating appropriate treatments for pregnant and lactating women

Maud Majeres Lugand (Medicines for Malaria Venture - MMV, Switzerland) highlighted key advancements in the Malaria in Mothers and Babies (MiMBA) initiative. Led by Medicines for Malaria Venture (MMV), this program seeks to accelerate research and improve access to antimalarial treatments for pregnant and lactating mothers. Majeres highlights that in 2023, 36% of pregnant women in Sub-Saharan Africa were infected with malaria, a major problem as pregnant and lactating mothers are more susceptible to severe illness due to compromised immunity. She outlined several challenges faced by these women with malaria, including the limited availability of treatments, exclusion from clinical trials, and physiological differences that complicate treatment approaches. To address these gaps, she explained MMV's strategy, which focuses on expanding clinical trial inclusion, developing new technologies, increasing access to medicines, and advocating for policy change. Current projects are generating crucial evidence on the safety and efficacy of antimalarials, while a newly established pregnancy registry is helping to track outcomes and inform future interventions. MMV is also actively engaging with communities to ensure recruitment strategies are culturally appropriate and capable of detecting pregnancies at an early stage, improving overall care and treatment opportunities. In the future, MMV aims to provide new treatment options for pregnant women, conduct studies to increase safe treatment for pregnant women, and secure resources to maintain progress in malaria treatment for maternal healthcare. She underscored the importance of collaboration, innovation, policy advocacy, and increased funding to improve antimalarial treatment for pregnant women.

Session 3 - Host-parasite-vector interactions

Lisa H. Verzier (Harvard T.H. Chan School of Public Health, United States) presented her groundbreaking research on mapping *Plasmodium falciparum* transitions and interactions within the female *Anopheles* mosquito at single-cell resolution. In her presentation, she detailed how her study employs single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics to unravel the parasite's developmental journey from gametocytes to ookinetes and oocysts while navigating the mosquito's immune defenses and microenvironment. She highlighted key molecular pathways and cellular interactions that enable *P. falciparum* survival, emphasizing specific mosquito cell types and immune responses that either facilitate or impede the parasite's progression. Verzier concluded by

noting the intricate co-evolutionary dynamics between the parasite and its vector, underscoring how these insights reveal mechanisms of immune evasion and nutrient acquisition. Her findings have profound implications for malaria control, offering potential targets for disrupting the parasite's life cycle, such as genetically enhancing mosquito immunity or developing transmission-blocking interventions. At the end of her presentation, she emphasized that these high-resolution insights into host-parasite interactions could drive transformative advances in global disease prevention strategies.

Eliana Real (Institut Pasteur, France) presented how the host protein CD36 primes *Plasmodium falciparum* sporozoites for liver infection, considered a crucial step in malaria transmission. CD36, a receptor involved in immune responses and lipid metabolism, interacts with the sporozoite *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) during their transit from the mosquito bite site to the liver. This interaction enhances the sporozoites' ability to invade hepatocytes by triggering molecular changes that upregulate key proteins essential for hepatocyte recognition and entry. Results revealed CD36's dual role of facilitating sporozoite infection while modulating host immune responses. This highlights its complex involvement in malaria pathogenesis. Real finished the presentation by suggesting that targeting the CD36-sporozoite interaction could block liver-stage infection, thus, opening avenues for innovative interventions to disrupt the parasite's life cycle and reduce malaria transmission.

Patience Chipiliro Simbi (Malaria Alert Centre, Kamuzu University of Health Sciences, Malawi) presented a study conducted in southern Malawi. The study aimed to identify demographic factors linked to *Plasmodium falciparum* infectiousness in southern Malawi's high-transmission Mashinga district. This longitudinal study, conducted during peak malaria season (Nov 2022-July 2023), used membrane-feeding assays to measure transmission to *Anopheles* mosquitoes. Participants from four household clusters were screened fortnightly through 18S qPCR. Those with low parasitemia underwent membrane feeding assays, with eight feeds carried out weekly. After ten days, mosquito midguts were examined. Infectiousness was rare (7.9%), concentrated in a few individuals, primarily school children aged 5 to 15 years old. Higher gametocyte density correlated with increased infectiousness, with 60.8% of infectious feeds from male participants and 91% of oocysts derived from males in the 5-15 year old category. Future regression analysis will be used to explore the impact of gametocyte density. Chipiliro ended the talk stating the importance of this study which marks the first population-level membrane-feeding assay results from Malawi.

Petra Schneider (University of Edinburgh, United Kingdom) examined the question "Are regular mealtimes more important for Artemisinin-resistant malaria parasites?". She discussed environmental impacts on mosquito-borne disease transmission, focusing on how parasite rhythms align with host feeding. Using the *Plasmodium chabaudi* rodent malaria model, misalignment of the parasite life cycle rhythm was achieved by the passage of blood-stage parasites from one mouse to another, with one mouse kept on a regular light-dark cycle and the second mouse housed in reversed light-dark conditions. Transferring parasites from an active period of the host circadian rhythm to a non-active period incurred a fitness cost and reduced gametocyte production. With rising artemisinin resistance, they investigated if resistant parasites face higher costs when misaligned. Using *Plasmodium chabaudi* in mice, both drug-sensitive and resistant genotypes were tested. Schneider presented results showing that misalignment caused a greater fitness cost in resistant

asexual stages. However, gametocyte production, the sexual transmission stage, showed minimal cost from misalignment. This suggests artemisinin-resistant parasites may rely more on rhythmic mealtimes. Future research will be carried out to confirm these findings, with the results having the potential to inform if the precise timing of drug regimens could potentially have clinical benefits in malaria treatment strategies.

Courtney Murdock (Cornell University, United States) presented the effects of variations in temperature and relative humidity on mosquito-borne pathogen transmission. She explored ecological factors influencing mosquito-borne disease transmission, emphasizing environmental and human impacts. Environmental changes like land alteration and climate change facilitate urban vector invasions, exemplified by *Anopheles stephensi*. While temperature effects on mosquito life cycles and parasite development are well-studied, the role of relative humidity is often overlooked. This research aimed to determine if variations in relative humidity in an urban environment affected malaria transmission. Experiments examined larval, adult, and parasite traits across eight temperatures and five humidity levels. *Anopheles stephensi* larvae were subjected to varying evaporation conditions, with pupae collected to assess development rates. Adult mosquitoes were monitored for lifespan and egg production. Results showed that decreased relative humidity shifted larval thermal performance, development, and survival, with increased body size at warmer temperatures. In adult mosquitoes, though there is a negative correlation between temperature and wingspan, greater relative humidity mitigated this effect, with greater humidity resulting in increased wingspan, even at higher temperatures. These findings suggest temperature-only models may overpredict *Anopheles stephensi* environmental suitability. Murdock ended the talk by remarking on the aim of the study to improve predictive models by incorporating humidity data for better malaria outbreak forecasting.

Session 4 - Therapeutics and drug resistance

Rebecca Edgar (University of Dundee, United Kingdom) presented her study investigating resistance mechanisms in *Plasmodium* parasites by screening six compounds. Two of these compounds were deprioritized after sequencing due to PI4K mutations. The remaining four compounds underwent resistance selection, where parasites were cultured and monitored for genetic changes indicating potential targets. From the initial whole genome screening, one of the selected compounds displayed the most stable resistance shift, with whole-genome sequencing identifying eight consistent single nucleotide polymorphisms (SNPs) across resistant clones. One key gene of interest was KRAS2, a lysyl-tRNA synthetase localized in the parasite's apicoplast, an essential organelle involved in isoprenoid synthesis. Resistance tests using KRAS1 mutant parasites showed no cross-reactivity, suggesting that this compound selectively targets KRAS2. To validate KRAS2 as the target, they plan to use CRISPR-based mutagenesis to insert a resistance-associated SNP and assess parasite survival. Also, the selected compound showed resistance in ZIP1-knockout parasites similar to a previous study which identified ZIP1 as a potential novel resistance mechanism, reinforcing its potential to target the apicoplast. She added that further investigations are ongoing to confirm KRAS2 as a drug target and to understand ZIP1's role in apicoplast resistance. These findings could contribute to novel antimalarial strategies, particularly in targeting essential apicoplast functions.

Eline Kattenberg (Institute of Tropical Medicine Antwerp - ITM, Belgium) presented her research on genetic surveillance of malaria in Vietnam. In 2019, first-line treatment shifted from dihydroartemisinin-piperaquine to Pyramax (pyronaridine-artesunate), initially in two provinces which was later on expanded to five. Sentinel site surveillance was conducted in high-burden provinces, where dried blood swabs were collected and analyzed for *P. falciparum* and *P. vivax* using qPCR. A subset of *P. falciparum*-positive samples underwent AmpliSeq analysis, targeting 14 resistance-related genes. The results confirmed that there were persistent high levels of C580Y mutations, especially in previously affected regions and, for the first time, in one province. Around 80% of the samples analyzed carried this mutation, indicating widespread artemisinin resistance and chloroquine resistance. They observed high clonality in parasites and low genetic diversity among parasites in the region. Similarly, plasmepsin amplifications linked to piperaquine resistance remained stable, while chloroquine resistance markers increased. Her study underscores the need for ongoing resistance monitoring, particularly as Vietnam transitions to treatment with Pyramax. She stressed the need for continuous genetic surveillance in achieving malaria elimination.

Ijeoma Okoye (Drexel University College of Medicine, United States) presented findings on a mitochondrial and evolutionarily conserved protein, *Pf*ATAD3.The lab identified 123 putative mitochondrial proteins through proximity labelling, and characterized *Pf*ATAD3. Using a CRISPR-Cas9-based system, Okoye's team conditionally regulated *Pf*ATAD3 expression to study its function. Knockdown experiments showed that parasites lacking *Pf*ATAD3 could complete one asexual replication cycle but die before the second, indicating its essentiality. Further investigations revealed that mitochondrial RNA transcripts declined upon *Pf*ATAD3 depletion, suggesting a role in transcription or RNA stability. Loss of *Pf*ATAD3 also led to mitochondrial membrane potential collapse. The team tested whether supplementing ubiquinone could rescue parasites. Despite the partial restoration of electron transport chain function, *Pf*ATAD3-deficient parasites still died, implying additional critical roles. These findings suggest that *Pf*ATAD3 is vital for *Plasmodium* survival, making it a potential drug target. Their research is now directed to understand the protein's role in sexual stages of the parasite.

Iyanuoluwa Adufe (Osun State University, Nigeria) presented her research on the emergence of artemisinin-based combination therapies (ACTs)-resistant malaria in Nigeria using mathematical modeling. The study focused on understanding the complex interactions driving the spread of resistance and informing control measures. Time series analysis was performed on district-level data which revealed seasonal fluctuations in malaria cases, with peaks during the rainy season. Forecasting models indicated a consistent trend in malaria cases. Geospatial risk mapping identified 12 high-risk local government areas (LGAs), with six considered very high-risk, emphasizing the need for targeted interventions. Simulation models demonstrated that in low ACT resistance scenarios, effective treatment leads to higher recovery rates. However, in high-resistance scenarios, infections persist as treatments become ineffective. Sensitivity and scenario analyses highlighted that increased ACT sensitivity reduces transmission, while decreased sensitivity leads to higher infection rates. She concluded, by underscoring the need for proactive measures to monitor and control ACT resistance, ensuring effective malaria management in Nigeria.

Elizabeth Winzeler (University of California San Diego - UCSD, United States) presentedthe challenges in antimalarial drug development and potential avenues towards its

solution To overcome the limitations of existing malaria drugs, Winzeler was invited in 2005 to join a Wellcome Trust-funded project aimed at identifying new antimalarials. At the time, the *Plasmodium* genome had been sequenced, but essential targets were unknown. Traditional target-based drug discovery proved challenging due to emerging resistance, leading researchers to adopt empirical approaches. Her team developed an ultra-high throughput screening method using a modified SYBR Green assay to test millions of compounds for activity against malaria parasites. This led to the discovery of novel antimalarial candidates, including Ganaplacide, which have progressed to phase III trials in combination with lumefantrine. This drug combination targets multiple parasite stages, including the liver, blood, and gametocytes, though resistance remains a concern. Winzeler also discussed their research on genetic resistance mechanisms in *Plasmodium*. Her team analyzed mutations in the *Pf*CARL gene, showing that only mutations in conserved regions conferred resistance. Similar patterns were observed in *Pf*ATP4 and MDR1. A PhD student in her lab is currently using machine learning to predict resistance-associated alleles by comparing known resistance genes with neutral variants.

This report is brought to you by the MESA Correspondents Kevin Rowartz Ogola, Flavia Kaduni Bawa, Geoffrey Githinji, Rebecca Pwalia, Akua Obenewaa Danquah Yirenkyi. Senior editorial support has been facilitated by Dr. Divya Beri and Dr. Joanne Power.

Day 2: Thursday, 20th March 2025

Session 5 – Novel approaches, tools and technologies

Alexandra Probst (Harvard T.H Chan School of Public Health, USA) in her Keynote speech spoke about her research aimed at combining insecticide treatment and antimalarial treatments to prevent transmission without inducing resistance. Building on previous work by Doug who demonstrated that a brief anti-malarial contact can prevent infection in mosquitoes, she screened over 80 antiplasmodial compounds and found 22 which reduced parasite prevalence in mosquitoes with mechanisms of action for 7 of these compounds. These hit compounds were taken through a translationally relevant tarsal contact landing assay where the ELQ456 compound significantly reduced both parasite prevalence and intensity in the exposed mosquitoes but was not successful in completely blocking the infection The Mike lab was able to synthesize chemically varied ELQ compounds, out of which the ELQ 453 and ELQ 613 effectively blocked infection after tarsal contact landing. These active compounds were melted to form an ELQ polyethylene polymer to mimic bed net properties. A 6-minute contact with this bed net-like material completely blocked parasite infection even a year after exposure to day and night cycles. Further experiments revealed that treated mosquitoes can block infection 2 days after exposure and started to get breakthrough infections after day 4. Importantly, resistant mosquitoes were found to completely block infections as well. Probst at the end highlighted that the next steps of her work will focus on field testing of these compounds in malaria-endemic settings.

Annie Yang (Leiden University Medical Centre, Netherlands) spoke about liver stage development of *Plasmodium*whichquite challenging to study due to its reliance on special cell lines. Thus, she aimed to create an animal-free model for liver-stage infections with the ability to maintain *P. falciparum* infectivity after 7 days and withstand more than one round of infection. This, she found, was due to a phenotype change rather than a loss in cell number. Using bulk RNAseq, Yang identified host pathways that were significantly upregulated after long periods of culture. These pathways were inhibited in subsequent experiments which led to a recovery of infectivity in the hepatocytes, therefore it was found that TGF inhibitors alone were able to maintain *P. falciparum* infectivity after 14 days. To check for multiple infection models, she infected hepatocytes with parasites and reinfected them again after day 7 with readings on day 3 or 5 post-infection. Maturation markers were used to differentiate between infections which showed that schizonts from the first infections were being replaced by those of the second infections. These however had smaller sizes compared to those of the first infection. Yang concluded that pre-exposed hepatocytes are more permissible to *P. falciparum* infections although it resulted in smaller schizonts

Maggy Sikulu-Lord (University of Queensland, Australia) discussed her work which focuses on using infrared spectroscopy to determine infection stages in mosquitoes, an improvement from traditional methods which are costly and time-consuming. This work relies on flashing light on mosquitoes to obtain a spectral signature which is then analysed by AI and machine learning algorithms. About 5 to 10 seconds of exposure to infrared light allows the differentiation of the morphology of the *Anopheles gambiae* and *An. arabienses* as well as their age groups, and if they are likely to be infectious or not, with 84% accuracy. They

further tested this technology for its ability to scan preserved mosquitoes from the field. Preservation with silica gel had the best results up to 50 days after collection. Parous and nulliparous mosquitoes were also differentiated in field-preserved mosquitoes. Her team further hypothesised that this technology could be used to detect infected RBCs in humans and human biological samples. Additional testing revealed the technology's ability to detect asymptomatic infections, infected blood samples, and non-invasive parasite detection directly from humans. It was further able to distinguish between schizonts and trophozoites during infection. Sikulu-Lord mentioned that parasite quantification was however imperfect and needed further optimisation. She indicated that future tests will be required in the field to determine the true sensitivity of the technology as well as opportunities for incorporating it into wearable devices.

Mary-Louise Wilde (University of Melbourne, Australia) presented gene drives as a novel vector control strategy, focusing on preventing malaria transmission through parasites since the current malaria interventions are being challenged. Gene drives, self-replicating genetic elements, spread through non-Mendelian inheritance. Two types of gene drives exist: population replacement, rendering mosquitoes malaria-incapable, and population suppression, preventing progeny. Using *Plasmodium berghei* as a model, CRISPR-Cas9 was employed to modify asexual parasite stages in mice, creating GFP+ and mCherry+ lines. These lines, individually non-transmissible, produced progeny when crossed and fed to mosquitoes. Her experiments demonstrated gene drive efficacy in *P. falciparum*. This research represents the first successful gene drive creation in malaria parasites. Ongoing efforts are developing further gene drives for population suppression, replacement, and human rodent malaria. Wilde expressed the need for further studies that will explore factors influencing gene drive efficacy and optimal target selection.

Meta Roestenberg (Leiden University, Netherlands) discussed genetically attenuated *Plasmodium falciparum* parasites as a malaria vaccine, targeting the liver stage for infection prevention. Their initial candidate, GA1, showed safety but low efficacy (13%). Hypothesizing that later-resting parasites offer better protection, they developed GA2, designed to fully arrest in the late liver stage. Three doses of GA2 showed no blood-stage infection in human clinical trials but released liver DNA, detected by PCR. Comparing immune responses, GA2 induced stronger protection than GA1, despite similar antibody levels. It was also observed that GA2 stimulated higher CD4+ T cell cytokine production compared to V gamma 2 T cells. Results from another clinical trial showed that a single immunization with GA2 still provided protection, suggesting multiple doses may be unnecessary and that CD4+ T cell responses remained dominant. Roestenberg concluded that later-resting attenuated parasites are more potent than previously thought, providing high-level protection after a single exposure in malaria-naive volunteers.

Session 6 – Strong and sensitive surveillance of malaria transmission and drug resistance

Kirsty McCann (Deakin University, Australia) presented her research on population genetic signatures of *Plasmodium falciparum* in a hyperendemic area of Papua New Guinea following extensive control measures implemented since 2006. Her team analyzed *P. falciparum* isolates collected from Madang and East Sepik provinces between 2005 and

2020. She presented results revealing contrasting patterns between regions: whereas Madang showed minimal population structure changes over time, East Sepik demonstrated significant shifts, with evidence of a transmission bottleneck in 2012 followed by a resurgence of cases. Identity by descent (IBD) analysis identified both persistent lineages (spanning all time points and provinces) and recently emerged lineages, with a particular clade emerging in isolates taken from Madang during 2020. McCann linked these emerging lineages to artemisinin resistance, specifically, the C580Y mutation in the kelch13 gene, showing resistance has become established in Madang and appeared to be emerging in East Sepik. She concluded by emphasizing that genetic evidence of increasing parasite relatedness following transmission decline is consistent with focal points of transmission. She further noted that maintaining intensive control measures is essential to keeping parasite populations low and continuing progress toward malaria elimination.

Varanya Wasakul (Mahidol-Oxford Tropical Medicine Research Unit – MORU, Thailand) presented findings from the GenRe-Mekong project, which conducts genetic surveillance of *Plasmodium falciparum* in the Greater Mekong Subregion (GMS), a hotspot for antimalarial resistance. In her presentation, she explained how the project monitors resistance markers to guide national malaria programs across Cambodia, Thailand, Laos, and Vietnam. Wasakul highlighted key results showing high dihydroartemisinin-piperaquine (DHA-PPQ) resistance during 2016-17 when this therapy was widely used, with early warnings prompting Vietnam to switch treatments – leading to a dramatic decline in regional resistance from 62% (2017-19) to just 2% by 2022. She emphasized that statistical analysis confirmed treatment policy changes had a greater impact on malaria reduction than COVID-19 restrictions. At the end of her presentation, Wasakul stressed that routine genetic surveillance is critical for tracking resistance trends and informing policy decisions, demonstrating how real-time genomic data can support effective treatment strategies and accelerate elimination efforts in the GMS. She noted that the project serves as a powerful example of molecular surveillance's role in combating drug-resistant malaria globally.

Nguyen Thanh Thuy Nhien (Oxford University Clinical Research Unit – OCRU, Vietnam) presented molecular surveillance in response to malaria outbreaks in Vietnam, facilitated by monitoring individual molecular markers at sentinel sites by high-throughput genotyping. In collaboration with the National Malaria Control Program and the GenRe project, they provided real-time information on drug resistance and treatment efficacy. Thanh highlighted two outbreak cases. In the first outbreak, in Gia Lai province (2017-2020), genetic surveillance detected artemisinin-resistant *P. falciparum* parasites, with resistance rates dramatically increasing from 41% to 96% in Krong Pa district with C580Y as the predominant mutation. In another outbreak that occurred in Khanh Hoa province during 2023-2024, they identified co-circulation of three *P. falciparum* strains with similar genetic resistance profiles. This evidence led to a critical change in first-line treatment policy. Through genetic barcoding they traced the spread of parasite populations, identifying five main parasite clusters. Thanh concluded that molecular surveillance offers key advantages in outbreak responses by identifying resistance profiles, tracking parasite spread between regions, and distinguishing between local and imported cases, which is particularly important as Vietnam approaches elimination targets.

Ashley Osborne (Menzies School of Health Research, Australia) presented her research on *Plasmodium vivax* recurrence dynamics in southern Ethiopia, combining identity-by-descent (IBD) analysis and time-to-event data to distinguish between the "three R's": re-infection, relapses (from dormant hypnozoites), and recrudescence. She aimed to develop a use case for microhaplotype-based IBD metrics and time-to-event data in high-endemic settings to evaluate *P. vivax* persistence and recurrence dynamics over time. In her presentation, she explained how IBD analysis revealed high genetic diversity and frequent transmission of *P. vivax*, while time-to-event data linked hypnozoite activation to environmental and host factors. Osborne highlighted emerging drug resistance markers and the challenges of achieving radical cures in endemic settings. She concluded that integrating these approaches provides a comprehensive understanding of recurrence dynamics, emphasizing the need for targeted strategies such as improved access to primaquine and enhanced surveillance. At the end of her presentation, she noted that these findings offer a pathway to more effective malaria elimination in high-burden regions by addressing relapses, reinfections, and recrudescence, advancing global malaria control efforts.

Ellen Kearney (The University of Melbourne, Burnet Institute, Australia) presented her research on the use of *Anopheles* salivary antibodies as serological biomarkers to measure human exposure to mosquito bites and malaria transmission risk. In her presentation, she explained how analyzing immune responses to *Anopheles* salivary proteins can identify specific antibodies that correlate with human biting rates (HBR) and entomological inoculation rates (EIR), providing a non-invasive tool to assess vector exposure and predict transmission hotspots. Kearney highlighted that salivary antibody levels reflect spatial and temporal variations in mosquito biting rates, offering a practical alternative to traditional entomological surveys, especially in low-transmission settings. She concluded that this vector serology approach is valuable for monitoring the effectiveness of vector control interventions and guiding targeted strategies. At the end of her presentation, Kearney noted that her work advances the development of innovative tools to enhance surveillance and support global malaria elimination efforts, emphasizing its potential to transform malaria control in resource-limited settings.

Annie Browne (Malaria Atlas Project, The Kids Research Institute, Australia) presented her research addressing the critical need for improved routine surveillance of malaria mortality and severity in sub-Saharan Africa, where underreporting and misclassification of cases remain significant challenges. In her presentation, she advocated for integrating community-based reporting, health facility data, and verbal autopsies to enhance data accuracy, while also exploring the use of digital tools and machine learning to streamline data collection and enable real-time monitoring of malaria trends. Browne emphasized that reliable metrics are essential for evaluating the impact of interventions like bed nets and antimalarial drugs. She concluded by highlighting the importance of accurate data in guiding public health strategies and reducing malaria burden, calling for increased investment in data infrastructure and capacity building. At the end of her presentation, Browne noted that robust surveillance is vital for evidence-based decision-making and accelerating progress toward malaria elimination.

Session 7 – Vector Control

Victoria Ingham's (German Center for Infection Research – DZIF, Germany) presentation explored the secondary effects of pyrethroid exposure on mosquito immunity and parasite development. She highlighted how insecticide-resistant mosquitoes encounter pyrethroids multiple times throughout their lifecycle, influencing both their biology and their ability to host *Plasmodium* parasites. Her research focused on oxidative stress, particularly reactive oxygen species (ROS) and reactive nitrogen species (RNS), which appear at higher basal levels in pyrethroid-resistant mosquitoes compared to controls. Using qPCR, she found elevated levels of detoxifying enzymes such as catalase in resistant populations. Exposure to permethrin, a pyrethroid, further induced ROS production, particularly in mosquito midguts and hemocytes. To determine if this immune response could suppress *Plasmodium* spp., her team artificially elevated RNS levels by feeding mosquitoes supplemental L-arginine. This led to increased hemocyte proliferation, particularly granulocytes, and a significant reduction in *Plasmodium* oocysts and sporozoites post blood-meal. RNA sequencing revealed widespread changes in immune pathways with key responses to malaria infection, particularly in the expression of effectors under control of the *immunodeficiency* (IMD) pathway. Ingham's results found that TEP1 (thioester-containing protein 1), a major component of the *Anopheles* immune response to parasite infection, was upregulated after pyrethroid exposure. She concluded that pyrethroid exposure triggers RNS production, which may enhance mosquito immunity against *Plasmodium, suggesting* a novel link between insecticide resistance and vector immunity, potentially influencing malaria transmission dynamics.

Shüné Oliver (National Institute for Communicable Diseases, University of Witwatersrand, South Africa) discussed the impact of climate change on mosquito physiology and its epidemiological consequences. She highlighted how temperature influences mosquito traits and behaviour, affecting disease transmission. When discussing the thermal limit for *Anopheles* mosquitoes, Oliver referenced a previous study at the Botha De Meillon Insectary (BDMI) at Witwatersrand in 2012, where it was found that female *Anopheles* mosquitoes had higher thermal tolerance than males (with a limit of ~40.5°C for both laboratory and wild strains). Oliver's research focused on two *Anopheles arabiensis* strains from Sudan: the insecticide-resistant SENN-DDT strain and the largely susceptible SENN strain. She explored how these strains respond to extreme heat, exposing adult females to 41°C for five hours. The SENN-DDT strain showed greater resilience to heat but lost this advantage after a blood meal. She also investigated mosquito survival in cold conditions by gradually adapting larvae to 18°C. Cold selection increased SENN-DDT's longevity and slightly but significantly increased feeding success (without significant changes to host-seeking behaviour). Additionally, SENN mosquitoes exhibited a higher likelihood of surviving cold temperature changes. She noted that while resistant mosquitoes are better adapted to high temperatures, unselected strains thrive in colder conditions. Her findings suggest climate variability may influence malaria transmission dynamics, as resistant mosquitoes could have a survival advantage in extreme heat, impacting control strategies.

Diana Omoke (Kenya Medical Research Institute – KEMRI, Kenya) presented on the transcriptomic analysis of *Anopheles arabiensis* populations resistant to pyrethroids and

organophosphates in western Kenya. This research aimed to provide a better understanding of insecticide resistance, which threatens vector control strategies such as insecticide-treated nets (ITNs) and indoor residual spraying (IRS). At present, insecticide resistance monitoring relies on WHO tube bioassays and WHO/CDC bottle bioassays in combination with molecular methods for detecting genetic markers of resistance, though few metabolic insecticide resistance markers have been identified thus far. In this study, mosquito larvae were collected from Migori and Siaya counties in western Kenya, reared to adulthood, and then exposed to deltamethrin, alpha-cypermethrin, and pirimiphos-methyl insecticides, with the aim of generating multi-insecticide resistant *An. arabensis* populations for genetic profiling by RNA sequencing (alongside insecticide-susceptible controls). Studies with insecticides showed increased mosquito mortality with higher insecticide concentrations. Comparative transcriptomic analyses between insecticide-resistant and susceptible *An. arabiensis* populations revealed overexpression of salivary gland and cuticular protein genes in insecticide-resistant mosquitoes, along with metabolic resistance markers such as cytochrome P450s, carboxylesterases, and glutathione transferases. Specific genes associated with resistance to multiple insecticides were identified, guiding further research, and Omoke's current work aims to expand on these findings by carrying out similar experiments in *An. funestus*.

Diane Leslie Nkahe's (University of Yaoundé I - UY1, Cameroon) research explored if biological larviciding could increase *Anopheles gambiae* susceptibility to pyrethroids in resistant populations. Focusing on WHO-recommended larval source management, the study used VectoMax G in Yaoundé from 2018 to 2021 to assess its impact on *Anopheles coluzzii* pyrethroid resistance. Field and lab bioassays measured mosquito fitness parameters such as feeding rate, fecundity rate, sex ratio, duration of larval development, and longevity alongside screening for genes associated with pyrethroid resistance. In a laboratory setting, *An. coluzzii* colonies were subjected to different selection pressures with either deltamethrin or VectorMax G alone, or in combination. qPCR analysis was used to profile the expression of different detoxification genes, genes associated with oxidative stress, and *kdr* allele frequency (a known marker for pyrethroid resistance). Results showed no difference in *kdr* frequency between field and lab colonies, but did show a significant decrease in the expression of GSTe2, a glutathione S-transferase gene, in field populations and deltamethrin-only treated *An. coluzzii* lab colonies. Lab colonies exhibited varied life trait parameters, with the VectoMax G + deltamethrin + susceptible colony showing optimal fitness and resistance reversal patterns. Selected mosquitoes displayed extended lifespans, with the exception of the deltamethrin-only treated colony. In summary, Nkahe concluded that VectoMax G impacts resistant mosquito life traits but yielded no clear insecticide reversal signal in field or lab settings.

Hilary Ranson (Liverpool School of Tropical Medicine, United Kingdom) addressed insecticide resistance management amidst new vector control tools. While new insecticides, insecticide-treated bed nets (ITNs), and spatial repellents offer promise, challenges like poor resistance management, limited local efficacy data, and vector control withdrawal persist. WHO's updated bed net recommendations favor dual-insecticide nets (pyrethroid-chlorfenapyr), impacting market demand and pricing. Though indoor residual spraying (IRS) options are increasing, coverage is declining due to economic constraints.

Spatial repellents show promise for added protection, but resistance management responsibility remains unclear. Local entomological data is crucial for informed decisions. Susceptibility data for dual active ingredient (dual-AI) products, robust durability data for ITNs, and assays measuring relevant modes of action are needed. History shows vector control suspension leads to malaria case resurgence, necessitating tools to measure new control tool endpoints. Capacity building for local vector data generation, an updated global plan for insecticide resistance management (GPIRM) setting manufacturer expectations, and sustainable vector control funding are vital. The balance between short-term control and long-term susceptibility maintenance requires careful consideration at global, national, and community levels.

Session 8 – Epidemiology, diagnosis and case management

Lauren Cohee (Liverpool School of Tropical Medicine – LSTM, United Kingdom) delivered a keynote speech highlighting the significant yet underrecognized burden of malaria in school-age children, a demographic often excluded from targeted control programs. In her presentation, she emphasized that malaria infection prevalence peaks in children aged 5-15 years across sub-Saharan Africa, with high rates of asymptomatic and recurrent infections contributing to chronic anemia, cognitive impairment, and absenteeism, which hinder educational performance and long-term development. Cohee underscored that school-age children serve as the primary reservoir for malaria transmission, with 83% of infected mosquitoes acquiring parasites from this group. She called for expanded interventions tailored to this age group, such as intermittent preventive treatment in schools (IPTsc), improved diagnostics, and health education programs, noting that reducing malaria could improve literacy scores and overall well-being. At the end of her talk, Cohee advocated for a more comprehensive and inclusive approach to malaria elimination, urging better quantification of the disease burden in school-age children to inform policy decisions and prioritize interventions, ultimately breaking cycles of poverty and improving future opportunities.

Jaishree Raman (National Institute for Communicable Diseases, South Africa) presented her work on employing advanced molecular surveillance tools, including the K13 Targeted Deep Sequencing for Tracking Emergence and Resistance approach, to support malaria elimination in South Africa. In her presentation, she explained how this method analyzed genetic markers in *P. falciparum* and *P. vivax* populations to track parasite diversity, drug resistance, and transmission dynamics. Raman highlighted the identification of emerging threats, such as partial artemisinin resistance linked to K13 mutations, and the monitoring of sulfadoxine-pyrimethamine resistance through DHFR and DHPS markers. She concluded that molecular surveillance is critical for distinguishing local transmission from imported cases and enhancing South Africa's ability to target interventions effectively. At the end of her presentation, Raman noted that integrating molecular data (MADDDDHatTeR platform across all 14 parasite chromosomes) along with traditional surveillance provides a model for strengthening national elimination strategies and fostering regional collaboration, underscoring the vital role of these tools in achieving and sustaining malaria elimination in South Africa and beyond.

Germana Bancone (Mahidol Oxford Tropical Medicine Research Unit – MORU, Thailand) presented research on quantitative G6PD biosensor testing for safer *P. vivax* malaria treatment along the Thailand-Myanmar border. This biosensor is a handheld device, cheap, and provides G6PD quantification with as little as 10 µl of whole blood. She explained that Vivax malaria requires aminoquinoline drugs to eliminate liver hypnozoites, and can cause hemolysis in G6PD-deficient individuals (about 20% of the local population). While G6PD status is straightforward for males, heterozygous females (20-30% of women) have variable enzyme activity requiring quantitative testing. She presented on implementation in Myanmar malaria posts and Thai field clinics enabling appropriate primaquine dosing: weekly for deficient patients, 14 days for intermediate females, and higher/shorter courses for normal patients. Most patients received appropriate treatment. Community engagement was critical for explaining genetic concepts and intervention acceptance. Bancone concluded quantitative testing enables safer treatment, particularly for females, and outlined plans to evaluate newer tools, implement single-dose tafenoquine, and expand access to lactating mothers and children.

Estelle Raobson (University of Antananarivo, Madagascar) presented her research on tropical cyclones' impact on malaria and nutrition in Madagascar, studying 10 rural localities in Mananjary district (July 2021- April 2023) during which cyclones Batsirai and Freddy struck. Data revealed seasonal malaria patterns with peaks during hot, rainy months. School-age children showed higher infection rates, with 20-49% exposure following cyclones, suggesting extreme weather increased malaria risk. While malaria cases spiked post-cyclone, nutritional indicators remained stable despite households reporting limited portion sizes after cyclone Batsirai. Raobson suggested this could be either delayed nutritional impacts or families prioritizing children's food despite overall financial insecurity and instability. She also suggested that malnutrition in these children might be delayed – and therefore long-term surveillance is needed to fully analyze the effect of cyclones on nutritional impacts of children and families. Analysis indicated a possible relationship between cyclones and simultaneous malaria and food insecurity. Raobson concluded that climate change accelerates extreme weather events threatening malaria control progress in Madagascar and other vulnerable regions.

Michelle Evans (Pivot, Madagascar) presented research on modelling malaria transmission heterogeneity at the community level in Madagascar, highlighting the country's vulnerability to climate change with spatial variations in cyclone frequency, rainfall, malaria prevalence and how geographic barriers continue to limit healthcare access. Her team developed a mathematical model using fine-scale community data (fokontany level) – 20 times more granular than typical district data. The model incorporated satellite imagery for environmental factors and OpenStreetMap data for human mobility between communities. Results demonstrated that including mobility was essential for model accuracy, even at fine scales. Vector control strategies (bed nets and indoor residual spraying) proved significantly more effective than strengthening health systems. Surprisingly, equal distribution of interventions across all communities outperformed targeted approaches focusing only on high-incidence hotspots, likely due to human movement between areas. Evans further highlighted ongoing work to integrate this model into an interactive dashboard to help local health officials test different intervention scenarios.

Plenary Talk 2 – Harnessing genomics to interrogate parasite biology

Dyann F. Wirth (Harvard T.H. Chan School of Public Health, United States) highlighted groundbreaking advancements in malaria research, focusing on the role of genomics in understanding *Plasmodium falciparum* biology. She discussed how the 2007 challenge from the Bill & Melinda Gates Foundation to eradicate malaria shifted research toward evolutionary perspectives, particularly in addressing drug resistance. Her group, which is part of the Malaria drug accelerator (MalDA), employed chemogenomic approaches, exposing parasites to drugs, evolving resistance *in vitro*, and analyzing genetic changes to identify resistance mechanisms and novel drug targets. Wirth shared insights from her work on halofuginone, derived from febrifugine, where resistance was linked to a single nucleotide change in the parasite's prolyl-tRNA synthetase. Her team discovered an adaptive proline response mechanism, where increased intracellular proline levels conferred resistance. Collaborations with Novartis and other institutions through high-throughput screening identified promising drug candidates. She also discussed the *API-AT2* gene, identified through sequencing resistant mutants. Loss-of-function mutations in *API-AT2* increased proline levels, conferring resistance to halofuginone. While these mutations did not affect asexual-stage parasites, they impaired mosquito-stage development, potentially limiting transmission. Wirth emphasized the importance of interdisciplinary collaboration in drug discovery, from fundamental research to therapeutic development, and honored the contributions of women in malaria research. Her work continues to explore resistance mechanisms and novel intervention strategies, leveraging genomics to advance malaria elimination efforts globally.

Closing Remarks

The session concluded with **Silvie Huijben** (Arizona State University, USA) expressing gratitude for the conference's energy, discussions, and collaboration. She thanked speakers, panelists, organizers, volunteers, and attendees for their dedication and the MESA Correspondents team for their exceptional coverage and support. Huijben encouraged continued engagement through the WiM Network, emphasizing the importance of sustaining this momentum to make a lasting impact on malaria research and global health.

This report is brought to you by the MESA Correspondents Kevin Rowartz Ogola, Flavia Kaduni Bawa, Geoffrey Githinji, Rebecca Pwalia, Akua Obenewaa Danquah Yirenkyi. Senior editorial support has been facilitated by Dr. Divya Beri and Dr. Joanne Power.

Explore additional content on the Correspondents page

www.mesamalaria.org