MESA

MIM SOCIETY
Multilateral Initiative on Malaria
8th Pan-African Malaria Conference

Multilateral Initiative on Malaria (MIM)
Pan-African Malaria Conference –2024

MESA Correspondents Report

Written by Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero and Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock.

Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

MESA Correspondents bring you cutting-edge coverage from the Multilateral Initiative on Malaria (MIM) 8th Pan-African Malaria Conference 2024

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Kigali, Rwanda

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Opening Day: Sunday, 21st April 2024

Opening Ceremony (Plenary Session 1)

The Multilateral Initiative of Malaria Conference convened 1500+ attendees, including researchers, policymakers, and innovators, with 70+ speakers discussing advancements and challenges in malaria. The theme of the conference "Grassroots Mobilization to End Malaria: Invest, Innovate & Integrate", aims to emphasize the essential role of research and network collaboration but also the community-driven efforts in the prevention and control of malaria. The opening remarks were delivered by **Emeritus Rose GF Leke** (Chair of the MIM Secretariat), **Claude Mambo Muvunyi** (Chair, 8th Pan-African Malaria Conference) and **Charles Adekunle** (CEO RBM Partnership to End Malaria). They all acknowledge the theme, highlighting the evolution of the MIM society from 1997 till date and its role in raising malaria awareness globally; but also the need to promote high-quality research, to encourage development, and the crucial role of African leadership in the fight against malaria. The official conference ceremony was inaugurated by **Sabin Nsanzimana**, Rwanda's Minister of Health, followed by his speech on the significant role of community health workers in reducing malaria in Rwanda. He also appointed the strong commitment from his government to keep on working in reducing morbidity and mortality related to malaria.

Keynote Speech

The keynote address was delivered by **Marcel Tanner** (Swiss Tropical and Public Health Institute, Switzerland). Tanner's keynote speech focused on decolonizing global health, aligning well with the theme of the conference. His message drew attention to the importance of empowering local communities and institutions in the fight against malaria, advocating for a shift away from traditional top-down approaches. By acknowledging and addressing historical power imbalances, his speech stressed on the need for inclusive and equitable strategies to combat malaria effectively with communities being real partners. He also aimed to highlight that, in spite of certain challenges for the future, a long path has already been walked to decolonize global health.

Philip Welkhoff (Bill & Melinda Gates Foundation, United States) shed the spotlight on the innovation aspect of the theme highlighting novel strategies such as use of geospatial data, parasite genetics and the use of dashboards to reduce the malaria burden in Africa.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

Day 1: Monday, 22nd April 2024

Plenary Session 2 – Vector Control Innovations For Malaria Elimination

Dyann Wirth (Harvard T. H. Chan, United States) highlighted the trajectory of malaria control efforts, noting progress from 2000 to 2015 followed by a resurgence in cases and deaths in 2022. She emphasized the need for a reevaluation of the global malaria program to rethink several aspects including its governance at all levels, from community to the nation and to the world taking into consideration interruptions and lessons learned from COVID-19. Wirth underlined two biological challenges one being the highly efficient transmission of parasites and the second the continuous evolution of mosquitoes. She then referred to the Malaria Threats Map and several other threats that are depicted there as well as current responses such as new nets, increased surveillance, and new drugs. She concluded her talk by highlighting the importance of leadership, innovation, real-time data usage, and healthcare support.

Charles Adekunle (RBM Partnership to End Malaria) started his talk by reminding the audience of the intolerable human toll the disease is causing by sharing a personal story from his time in a clinic two decades ago when he lost four children to malaria in just 30 minutes. Despite tremendous improvement since the year 2000, malaria still claims up to 600,000 children today. He went on to describe the current challenges posed by biological threats, insecticide and drug resistance, RDT efficacy loss, and climate change which urge an accelerated action plan. Adekunle introduced the action plan RBM is developing and defined action as A – accelerate, C – coordination, T – transformation, I – innovation or integration, O – opportunities, and N – networking, based on key actions to fight malaria. He finished the talk with an appeal to the audience "It is possible, let's not pass the battle to our children".

Joy Phumaphi (African Leaders Malaria Alliance – ALMA, Botswana) presented the government's involvement in the fight against malaria and underlined the crucial role that grassroots mobilization should have in politics. She then elaborated on different tools developed to monitor malaria cases at community and country levels, advocating for collaborative efforts between countries and communities to eliminate malaria based on the accountability of cases and the creation of opportunities. She further emphasized the need to integrate gender considerations into the efforts to eliminate malaria. She closed her talk by highlighting the need for joint action, the combination of government and public sector innovations, and endorsement of the Yaounde declaration by heads of state.

Symposium 1 – Modeling for malaria decision making in Africa: Enhanced Technical Support and Capacity Strengthening

Susan Rumisha (Malaria Atlas Project – MAP, Australia) introduced the new decentralised MAP, now with two nodes one in Perth, Australia and one in Dar es Salaam, Tanzania. The talk commenced by providing some background to MAPs core science in risk mapping and burden estimation. She introduced MAP's purpose as utilizing innovative data analytics to support national and international partners in more impactful malaria control efforts, with an increased focus on decentralization and African leadership. Rumisha outlined the mission, vision and key milestones, highlighting the recent establishment of the 2023 East Africa Node at the Ifakara Health Institute. The East Africa Node envisions becoming a Centre of Excellence for Innovation and Application of Geospatial Analysis for Malaria in Sub-Saharan Africa. After the establishment of the required infrastructure, the objectives include fostering innovation, nurturing African leadership, and providing technical support to National Malaria Control Programs and partners across Sub-Saharan Africa.

Samuel Oppong (Malaria Atlas Project – MAP and Curtin University, Australia) shared his experience as a MAP PhD student to showcase a career path in geospatial analytics after previously working in the National Malaria Control Program (NMCP) in Ghana. In his talk, he focused on utilizing geospatial mapping to support malaria control decisions in Ghana. He discussed key spatial mapping initiatives in Ghana, including the development of a stratified risk map for malaria incidence, prevalence, and mortality. Oppong gave an overview of his PhD research, which aims to understand the variations in malaria burden at subnational levels to aid decision-making. His research objectives include describing the spatial distribution of malaria in Ghana at lower administrative levels, assessing challenges in malaria prevalence, evaluating the impact of interventions such as ITNs, and understanding climatic factors influencing malaria risk. He underscored the importance of contextual interpretation of models and effective communication of models to NMCPs for integration into routine systems. Oppong concluded by emphasizing the significance of geospatial mapping in addressing data gaps and guiding decision-making in malaria control.

In his talk, **Samson Kiware** (Ifakara Health Institute – IHI, Tanzania) shared his approach to successfully cultivating a critical mass of skilled African modellers to support NMCPs. He described the established program and skill sets students acquire, through the wide variety of training offered, including data analytics, mathematical modeling, software development, machine learning and artificial intelligence. He further emphasized the importance of involving a diverse team that mentors early-career researchers, ranging from interns to master's and PhD students, but also including staff at NMCPs and staff at IHI. Importantly, the team maintains gender balance in their endeavors. Additionally, Kiware also presented its innovative tools, including the MosquitoDB application for mobile mosquito database management and the Vector Control Optimisation Model (VCOM) for enhancing the impact of vector control interventions. He showcased various vector control modeling methods applied by the trainees and highlighted collaboration with the Zanzibar Malaria Elimination team.

Damaris Matoke (Pan-African Mosquito Control Association – PAMCA, Kenya) emphasized the importance of prioritizing women in malaria control efforts and modeling to ensure that diverse perspectives and experiences are incorporated into malaria modeling efforts. She outlined initiatives undertaken by PAMCA to address a significant gender gap in the field and to achieve more equitable and effective outcomes in the fight against malaria. Through the PAMCA Women in Vector Control initiative, efforts include capacity building for country chapters and NMCP, mentorship programs such as "LiftHer2" aimed at enhancing the technical expertise of female modelers, networking opportunities like webinars and female modeler networks, and provision of travel awards and recognition. These efforts promote inclusion and equity for female modelers. Matoke also mentioned plans to develop a website to further support these initiatives and address challenges faced by women in fully participating in these initiatives. She closed her talk by highlighting the need to ensure that women's voices and contributions are fully integrated into malaria control and modeling efforts, which is crucial for enhancing the effectiveness of strategies in combating malaria.

Sheetal Silal (University of Cape Town, South Africa) presented the Malaria Modelling and Analytics (MMALA) program at the University of Cape Town. The program aims to bolster analytics and modeling capabilities in Sub-Saharan Africa and currently includes 13 PhD candidates from 12 different countries. The training includes innovations such as a comprehensive curriculum covering malaria systems, mathematical modeling, and soft skills like leadership, short-term consulting, and scientific communication. Each student works as closely as possible with their country's NMCP to gain practical experience in how modeling can inform policy decisions. Hence, the students apply their mathematical modeling skills to address malaria challenges specific to their country. Projects undertaken by students include targeted drug administration in Botswana, sustainability of malaria elimination in South Africa,

and investment cases for cross-border initiatives in the Zambezi region. Two of the projects were described directly via video recording by two of the PhD students (**Thabo Bogopa** and **Hijila Eelu**), who also shared their insights into the MMALA program. To close, Silal highlighted the program's purposeful and adaptive nature, aiming to cultivate a cohort of 12 PhD students who will contribute to malaria elimination efforts.

Symposium 5 – Methods validation: improving the generation of high-quality data to make strong evidence-based decisions in vector control

Rosemary Lees (Liverpool School of Tropical Medicine, United Kingdom) presented an overview of the Innovation to Impact (I2I) work packages, with a focus on the importance of identifying and addressing methodological weaknesses in the development and evaluation of vector control tools. She emphasized the validation work package and the importance of a multi-phase, multi-site approach to assess methods and understand the performance of vector control tools by defining and measuring their analytical error to show quality, reliability and consistency. Lees mentioned the benefits of validating methods for the tools which included ensuring appropriateness for its intended use, allowing comparison between different methods designed to measure the same endpoint, and identifying sources of variability which will aid in data interpretation across studies and time, and be used to power experiments. Lastly, she highlighted the importance of consensus SOPs which can be easily adopted by everyone to generate more standardized data to facilitate comparison between studies.

Katherine Gleave (Liverpool School of Tropical Medicine – LSTM, United Kingdom) presented the Methods Landscaping project by LSTM, and the development of novel methods to assess new vector control products. She introduced the motivation for the project by outlining the different ways in which insecticide resistance in major malaria vectors has prompted development of new chemistries and products. As previously robust methods for evaluation and monitoring are increasingly considered inadequate for the diverse range of tools available to date, new products would be needed. Initiatives are underway to validate methods and ensure their reliability, reproducibility, and comparability across various labs, locations, and testing conditions. Gleave described the testing process and a framework which has been devised to optimize and characterize methods, offering a robust approach for evaluating novel evaluation techniques. The process includes impact assessment of altering testing parameters and ensures high-level sensitivity of methods to capture different modes of action adequately. Furthermore, the presented framework would also allow to determine the impact on various vector populations and comparability of results within and between testing sites.

Graham Small (Innovative Vector Control Consortium – IVCC, United Kingdom) highlighted the importance of facilities conducting vector control research to have reliable and reproducible data in the development and evaluation of malaria vector control products. He then discussed the types of entomological data required which could be divided into three phases; product development, product registration and product rollout. Small explained that IVCC has been supporting a network of seven African trial facilities towards Good Laboratory Practices (GLP) certification in Côte d'Ivoire, Ghana, Benin, Tanzania, and Kenya which are now generating reliable, repeatable, and auditable data. Each facility has developed a GLP-compliant quality management system (QMS), received funds for infrastructure improvement, received support for extensive internal and external training, and developed a GLP compliance management system including SOPs covering standard test methods like insecticide susceptibility testing, equipment use and maintenance. He also noted that there is a formal process for documenting protocol amendments and deviations, to ensure adherence to best practices in laboratory and semi-field testing of vector control products.

Duncan Kobia Athinya (Vestergaard), discussed the guidelines for evaluating and testing LLINs from the perspective of a manufacturer. He explained the evaluation process which is done through net survivorship, fabric integrity, and insecticidal activity. He also highlighted the methodological gap in the WHO 2013 guidelines such as lack of mechanism for monitoring the quality of nets, and the resultant threat of insecticide resistance. Athinya highlighted the need for testing nets to ensure effectiveness, mentioning specific criteria and percentages for acceptable performance. He described his commitment to characterize the performance of their LLINs through long term studies of net performance. He also mentioned the need for continual improvement and adaptation based on field trials done across different settings. Overall, Athinya underscored the importance of learning from set guidelines, identifying gaps and the opportunity to understand product performance and make informed decisions in programmatic fields.

Kyeba Swai (Ifakara Health Institute, Tanzania), presented methods for evaluating spatial repellents. He explained that repellency can be through deterrence where there is reduced entry of mosquitoes into areas occupied by humans, or through excito-repellency/ non-contact irritancy where there is non-directional movement away from a host due to excitement or through feeding inhibition. Swai mentioned a few studies that have been conducted to show the efficacy of spatial repellents as a useful public health intervention. He suggested that revision of the guidelines for efficacy testing of spatial repellents is required so that manufacturers or testing labs can generate data required for WHO PQ dossier, and national regulatory authorities for registering the product. Lastly, to generate robust local efficacy data, Swai suggested measuring the spatial repellents through four mechanisms: i) Laboratory tests (measure product emanation rate and bioefficacy), ii) Semi-field systems (to understand other modes of action and inform models), iii) Experimental Huts (to generate consistent data on local wide mosquito populations), and iv) In-Home tests.

Symposium 10 – Evaluation of the BOHEMIA Cluster Randomized Trials of Mass Drug Administration of Ivermectin in Mopeia District in Rural Mozambique and Kwale District in rural Kenya: Results on Safety, Efficacy, Entomology, Social Science, and Economic Assessment

Regina Rabinovich (Barcelona Institute for Global Health – ISGlobal, Spain) introduced the BOHEMIA Randomized Controlled Trial, addressing the inadequacy of current vector control tools in areas where mosquitoes feed outdoors during the day. She highlighted ivermectin as a complementary strategy capable of killing mosquitoes that feed on treated blood hosts with minimal safety concerns. The project focused on two sites: Mopeia in Mozambique with high transmission and Kwale in Kenya with moderate to high transmission, aiming to establish ivermectin as a new-class vector control strategy for malaria. She briefly mentioned other ivermectin clinical trials in African countries, for example, ivermectin-artemisinin combination therapy in Uganda. **Carlos Chaccour** (Barcelona Institute for Global Health – ISGlobal, Spain) highlighted differences between sites, including varied trial arms, dosing timings, and durations, impacting study outcomes. These included delayed and prolonged dosing in Mozambique compared to Kenya's shorter dosing period before the onset of rains, influencing the effectiveness of the intervention.

Francisco Saute (Manhiça Health Research Centre – CISM, Mozambique) presented findings from the BOHEMIA study indicating persistently high malaria rates among children under five years of age despite the use of long-lasting insecticidal nets (LLINs). Challenges like dosing delays after flooding caused a loss of study clusters, though dosing targets were achieved. Bio-efficacy in wild *Anophelines* mosquitoes was confirmed, yet entomological data revealed vector resistance across all insecticide classes. Mozambique's ivermectin mass drug administration (MDA) found a high prevalence of malaria by RDT. There was no measurable

effect on malaria prevalence, age structure, or entomological inoculation rate (EIR). **Joseph Mwangangi** (Kenya Medical Research Institute – KEMRI, Kenya) highlighted successful ivermectin dosing coverage, split into separate visits over ten days. **Marta Maia** (KEMRI-Wellcome Trust Programme – KWTRP, Kenya) reported pyrethroid resistance in Kenyan vectors, with an unexpected 30% RDT prevalence. However, the ivermectin MDA showed no vector density reduction and it potentially influenced age structure. In Kenya, ivermectin's bio-efficacy was confirmed, showing a 20-28% measurable effect in reduction of malaria prevalence.

Carlos Chaccour (Barcelona Institute for Global Health – ISGlobal, Spain) discussed the challenge of developing new malaria medicines due to the safety and rarity of adverse events with current treatments (1:10,000). He emphasized that any new medicine must meet this safety standard, aiming for serious adverse events (SAEs) < 1:20,000. SAEs occurred in both study sites but were unrelated to the drugs used. For example, in Mozambique, most of the SAEs observed were stemming from a cholera outbreak. Systemic adverse events were the most common for all the study participants, while others were transient. Pregnant participants were monitored until delivery, with ongoing follow-up in Kenya. Both sites met WHO's safety criteria, pending data analysis in Kenya, demonstrating alignment with Medicines for Malaria Venture's safety standards.

Cassidy Rist (Center for Public and Corporate Veterinary Medicine, United States) presented the cost-effectiveness analysis (CEA) of ivermectin MDA for malaria control in Mozambique, as data analysis is still ongoing in Kenya. She highlighted the objectives of the study as i) To determine the incremental cost per case averted (ivermectin MDA vs control) and ii) To determine the incremental cost per disability adjusted life years (DALY) averted (ivermectin MDA vs control). The CEA included measurement of health effects, intervention costs, and economic burden with and without ivermectin MDA, for children under five years of age and children above the age of five. The cost of the intervention was found highest in the amount spent on ivermectin, and the salaries for personnel administering ivermectin, hence both factors provide an opportunity for cost reduction. In conclusion, ivermectin appears to be cost-effective, and the ivermectin MDA programmatic costs appear to be within the same range as those for SMC programs that use similar door-to-door methods for drug distribution over multiple months.

Caroline Jones (KEMRI-Wellcome Trust Programme, Kenya) presented on community perceptions and experiences of ivermectin MDA for malaria control. This study was a 3-phase longitudinal qualitative study based on an ethnographic approach through in-depth interviews, participant observations, and photovoice sessions. Using a participant-focused approach enhanced a sense of involvement for the participants. The participants also reported having trust in implementing institutions, and the rigorous trial processes, which facilitated uptake of ivermectin. There was a perception of a reduction of mosquitoes and malaria during the ivermectin MDA. Additional positive effects included clearing of bed bugs and scabies. Gender norms were found to have affected the participation and experiences of some participants. Positive and negative bodily effects were reported by the participants; with the positive effects of the ivermectin MDA outweighing any minor side effects. Overall, participants of the BOHEMIA trial in Mopeia and Kwale perceived the study to be making a positive contribution to malaria control in the study sites.

Symposium 11 – R21/Matrix-M: A high impact malaria vaccine

Mehreen Datoo (University of Oxford, United Kingdom) introduced the R21/Matrix-M vaccine candidate for malaria during his presentation which WHO recommended as the second malaria vaccine, and is set for rollout next year. It employs Matrix-M, an adjuvant, to enhance

the immune response against pathogens. Phase III trials rigorously assessed safety, efficacy, and immunogenicity through a randomized, placebo-controlled design involving a large participant pool. Safety data, monitored for adverse events, showed no significant concerns after over 15,000 doses administered to African children aged 5-36 months. Efficacy (reduction in clinical malaria episodes) data revealed high rates 67-75% over 12 months for standard and seasonal sites, with similar efficacy (66-76%) up to 18 months post 4 doses and maintained efficacy of 71-73% at seasonal sites over 24 months. The vaccine's data underscore its potential to combat malaria globally. These findings pave the way for regulatory approval and widespread deployment, showcasing the vaccine's safety, effectiveness, and longevity in protecting against malaria.

Emma Beaumont (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) presented vaccine efficacy (reduction in clinical malaria episodes) of the R21 Matrix-M over 18 months examining various demographic characteristics such as age, gender, nutritional status, seasonal malaria chemoprevention (SMC), and peak anti-NANP IgG antibody titre. The results revealed several key points: i) Age: vaccine efficacy over 18 months was higher among children vaccinated between 7 and 17 months of age compared to those aged 18 to 36 months at vaccination. ii) Gender and nutritional status: there was no difference in vaccine efficacy between males and females or between underweight children and those of normal weight at the time of vaccination. iii) Seasonal malaria chemoprevention (SMC): vaccine efficacy differed based on the number of SMC rounds received, particularly among those who received no SMC. However, the sample size for this group was very small. iv) Peak anti-NANP IgG antibody titre: vaccine efficacy increased with increasing peak anti-NANP IgG antibody titre. These findings shed light on the effectiveness of the R21 Matrix-M vaccine over an extended period and highlighted the importance of considering various demographic factors in assessing vaccine efficacy.

Hamtandi M. Natama (Research Institute of Health Sciences – IRSS, Burkina Faso) presented findings regarding the efficacy and safety of the R21/Matrix-M malaria vaccine. The study, conducted over 2 years with 450 participants aged 5 to 17 months, demonstrated high efficacy in preventing clinical malaria. Participants who received R21 with a higher dose of Matrix-M adjuvant showed an efficacy of 80% at 12 months following the booster vaccination. Notably, the vaccine's efficacy was sustained over multiple episodes of malaria. The study also identified a correlation between vaccine efficacy and anti-NANP antibody concentrations, with a potential threshold of 6500 ELISA units associated with a 77% reduction in malaria risk. These promising results support the advancement of R21/Matrix-M to phase 3 licensure trials, indicating its potential to significantly impact the malaria burden in highly endemic areas. With this evidence WHO also stated its policy recommendations in October 2023.

Peter Winskill (Imperial College London, United Kingdom) presented a mathematical transmission model of malaria to estimate malaria cases, deaths and disability-adjusted life years (DALY) averted, and cost-effectiveness of R21/Matrix-M over 15 years across different transmission settings. He highlighted the role of modeling in bridging trial data and implementation strategies. Using data from phase 2 and phase 3 trials, the model predicted significant vaccine efficacy against clinical malaria, with age-based introduction estimated to avert a substantial number of cases and deaths across different transmission settings. The model demonstrated robustness in predicting vaccine delivery cost effectiveness depending on the implementation. Cost-effectiveness estimates indicated favorable outcomes compared to existing malaria interventions and childhood vaccines. Winskill emphasized on refinement of the ongoing model as more trial data becomes available.

Jane Grant (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) presented the results of a qualitative study on the acceptability of the R21 vaccine alongside

existing malaria prevention interventions in the R21 phase III trial site in Mali. Caregivers and community members had confidence in the vaccine's effectiveness, resulting in high demand for the R21 vaccine alluding to the significant malaria burden. Trust in the trial team and positive experiences with childhood vaccinations also contributed to the vaccine's acceptability. While some caregivers still considered seasonal malaria chemoprevention (SMC) important after R21 vaccination, others believed the vaccine, combined with bed nets, provided sufficient protection. Grant emphasized the importance of assessing acceptability to inform vaccine implementation's strategies and highlighted the need for further research to ensure comprehensive coverage of complementary interventions during vaccine scale-up.

Sandesh Bharati (Serum Institute of India Private Limited, India) presented on R21/Matrix-M: manufacturing capacity, vaccine implementation plans and phase 4 study design. He described GSK's plan to produce 18 million doses of RTS´S between 2023 and 2025, with a commitment to supply with a cost of €9.30 per dose. Serum Institute will supply the R21 vaccine through UNICEF and Gavi, with a capacity to produce 100 million doses annually, expandable to meet demand. The initial price for R21 is set at USD 3.90 per dose. Implementation will begin in selected countries, including South Sudan, Central African Republic, Nigeria, and Uganda. Post-licensure studies will assess vaccine effectiveness against clinical malaria and all-cause mortality. Bharati expressed gratitude to collaborators and highlighted Serum Institute's commitment to meeting vaccine demand and conducting rigorous post-licensure research.

Adrian V.S. Hill (University of Oxford, United Kingdom) provided an overview of the future prospects for the R21/Matrix-M malaria vaccine. He highlighted the remarkable efficacy (reduction in clinical malaria episodes) of the vaccine (78%) over one year in the primary endpoint of the phase three trial, particularly in children aged 5 to 17 months. Hill underlined the ongoing evolution in vaccine design, transitioning from RTS´S to R21 with significantly higher impact in malaria case reduction. He discussed the potential for better durability and functionality due to the increased density of antigens on the nanoparticle surface. Hill also outlined future trials, including combination vaccine studies with other malaria antigens and transmission-blocking vaccines. He expressed gratitude to collaborators and emphasized the importance of continued research efforts to combat malaria effectively.

Lister Stockton and Fernando Ramos Lopez (University of Oxford, United Kingdom) presented the safety and immunogenicity data from ongoing trials assessing the co-administration of EPI vaccines with R21/ Matrix-M in African children and the use of this vaccine in HIV positive children. Stockton presented findings on the co-administration of the R21/Matrix-M vaccine with EPI scheduled vaccines in different groups. The arm, which received only EPI vaccines showed no increase in anti-NAMP IgG levels. However, another arm receiving R21 with EPI vaccines demonstrated a significant increase in IgG levels. Local and systemic reactions were mostly mild and resolved within a few days. Tetanus and diphtheria levels were consistent across groups. Co-administration of R21 with EPI vaccines showed no significant impact on antibody levels compared to EPI vaccines alone. These results showed the compatibility of R21 with existing vaccination schedules and the importance of ongoing research to optimize vaccine administration. Most participants experienced mild to moderate adverse events and serious adverse events were rare. On the other hand, He also pondered if they will be successful in delivering vaccines to millions of children who will need them.

Scientific Session 1 – Immunology and Vaccines 1

Soulama Ben Idriss (Action Health Research Group - GRAS, Burkina Faso) presented his study on the safety, immunogenicity and transmission-blocking activity of R0.6C and ProC6C: a phase 1b clinical trial in adults living in a high burden malaria transmission setting in Burkina

Faso. This study explored the efficacy of two promising vaccines R0.6C and ProC6C over the currently approved vaccines (RTS,S/AS01E, and R21 vaccines) for malaria elimination. R0.6C and ProC6C reduce the anti-sporogonic activities. Two doses of the vaccines with different formulations were tested against populations between ages 20 – 45 years. Two cohorts were selected and a total of above two hundred were screened. The groups generated higher levels of antibodies specific to Pfs48/45. The standard membrane feeding assay (SMFA) was used to assess the functionality of antibodies elicited after vaccination. He concluded that both vaccines are promising in their transmission and anti-sporogonic abilities and safety.

Michael Emch (University of North Carolina, United States) presented his study assessing the effect of malaria transmission intensity on the modification of RTS,S efficacy due to a rebound effect in Ghana, Malawi, and Gabon. He stressed the effect of parasite ecology and host on vaccine efficacy, as efficacy decreases with an increase in background malaria incidence. Malaria transmission intensity was estimated in 16 sites using geospatial data. In the analysis, 2009-2014 Phase III vaccine trial data in Malawi, Gabon, and Ghana were used (n=2427). Results showed that rebound malaria occurred in the highest transmission sites after the third dose. The study highlighted that the lower reported efficacies of RTS,S in higher transmission areas were due to rebound malaria.

Jordan Plieskatt (Statens Serum Institut, Denmark) elaborated on a novel multi-stage vaccine, ProC6C which elicits functional antibodies against two *P. falciparum* life cycle stages in adults. The ProC6C vaccine is in its Phase I stage in Burkina Faso and Phase II stage in Mali. He stated that its efficacy lies in its immunogenicity with or without a matrix regime. The vaccine has 36 amino acids, 6 copies of NAnP, and 3 copies of NVDP along with a high transmission reduction potential in eliciting antibodies reactive to full-length CSP. The peak antibody response is 14 days post-third vaccination compared to RTS,S/AS01E. Similarly, it improves the longevity of antibodies by delaying the third booster doses of 0, 1, and 6. This study supports the selection and further development of ProC6C as a promising transmission-blocking vaccine candidate.

Katie Patterson (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) evaluated the effect of RTS,S/AS01E, and seasonal malaria chemoprevention (SMC) alone or combined on antimalarial antibody responses. The synergistic effect of RTS,S/AS01E, and SMC is promising in destroying the malaria parasite due to their different modes of action. It requires a single dose to be administered for five years. A multiplex assay was used to detect multiple antibodies to measure protective immunity. Two cohorts were used: cohort 1 (1 – 5 yrs) and cohort 2 (5 – 12 months). Blood samples were collected and immunoglobulin was detected. Results showed a lower response in cohort 2 and the combined group and a higher response in Mali.

Maria Del Pilar Quintana (University of Copenhagen, Denmark) evaluated the high-throughput isolation of cross-reactive and adhesion-inhibitory VAR2CSA-specific monoclonal antibodies from *Plasmodium falciparum*-exposed pregnant women using LIBRAseq. Samples were collected from pregnant women with isolated medium as a source of cells merging the binding antigen to the antibodies. This technique permitted the identification of hundreds of VAR2CSA-specific monoclonals with naturally acquired VAR2CSA-specific mABs, most cross-reactive and targeting complex epitopes. Very few mAbs were targeting minimal binding regions.

Thiery Masserey (Swiss Tropical and Public Health Institute – Swiss TPH, Switzerland) presented results from a mathematical modeling study that assessed the selective pressure induced by malaria vaccines on *Plasmodium* parasites. Findings from the study indicate that more of the genotype was resistant to RTS,S/AS01E than to other vaccine types. Results

further showed a rapid spread of the vaccine-resistant genotype depending on the degree of resistance and vaccine type. Masserey pointed out the necessity to better assess the existence of genotypes with reduced efficacy to vaccines, prioritizing the development of vaccines with lower risk and finally combining vaccines that target different antigens.

Isobel Walker (University of Melbourne, Australia) presented her work on identifying new target antibody responses to the PfEMP1 gene that protects children from severe malaria. This study was carried out in Papua New Guinea in an area with high transmission of malaria on 142 children who had severe malaria. About six features added to the regression model were needed to differentiate between severe and uncomplicated malaria giving an accuracy of 75%. Walker's study pointed out the fact that a vaccine with monoclonal antibody therapy which promotes neutrophil phagocytosis of ICAM-1 binding IE may provide protection from severe malaria.

Scientific Session 2 – Vector biology and control 1

Denis Richard Kailembo (Swiss Tropical and Public Health Institute – Swiss TPH, Switzerland) monitored the effect of community-based larviciding in Tanga region, Tanzania with the aim of eliminating immature mosquito larvae using existing larviciding protocols. Three rounds of 2 locally produced biolarvicides, BTi and BS, were administered during periods of low rainfall. Weekly data collection and monitoring included the number of habitats, larval abundance, the number and proportion of habitats sprayed, and the amount of biolarvicide used. The results revealed a drop in larval occupancy over time, with over 1.6 million dollars spent on implementation. Kailembo emphasized that **I**ncorporating health systems and working with smaller habitats will be critical in future tests.

Nehemie Nzoyikorera (National Public Health Institute, Burundi) evaluated the distribution of *Anopheles* mosquitoes in nine representative provinces of Burundi using both morphological and molecular identification tools. Molecular identification for each complex was done using standard PCR techniques with specific primers. Out of the 493 samples identified, 82,6% were from the *An. gambiae* complex with *An. arabiensis* being the most predominant species and 17.6% were from the *An. funestus* complex based on the phenotypic characteristic. Some samples were unidentified using the protocol. This study establishes a framework for better understanding malaria transmission patterns and defining effective vector control tools in Burundi.

Helen Nwanosike (MESA at Barcelona Institute of Global Health – ISGlobal, Spain) provided an overview of the MESA platform, which is used to collect and disseminate knowledge, as well as to inform decisions in malaria-endemic countries. She began the landscaping review with a recap of *Anopheles stephensi's* detection as an invasive species in ten countries, eight of these in Africa. It is resistant to the major insecticide classes and transmits *Plasmodium vivax* and *falciparum*, posing a serious threat to vector control. A comprehensive data search identified 68 relevant projects by 39 lead institutions and four National Malaria Control Programs (NMCPs). The total amount of funding reached $89 million from 25 different funding sources. Apart from these statistics, the analysis of these projects also identified potential knowledge gaps in *An. stephensi* research.

Javan Chanda (PATH, Zambia) presented a project focused on scaling up Malaria Case Detection (MCI) tools using community health workers (CHWs). The 1-3-7 approach was implemented for rapid case response. The approach involves reporting a malaria case on day one, investigating the case within three days, and responding with foci entomological investigation and treatment within seven days. The study, in Mazabuka and Chikankata, monitored entomological and vector control from January 2021 to December 2022. Foci

investigation was triggered by an index case and involved identifying, mapping and treating vector breeding sites within two kilometres of the house within seven days. Results showed a decrease in *Anopheles* breeding site positivity and increased larvicide coverage. Operational successes include high training rates and MCI DHIS2 implementation. Challenges include transport, finances, mobile network, and insecticide supply. Opportunities lie in resource mobilization, stakeholder engagement, coordination, and potential drone use for larviciding.

Adeogun O. Adedapo (Nigerian Institute of Medical Research, Nigeria) presented a research project using geospatial mapping to understand the distribution of secondary malaria vectors in Nigeria. Entomological data were aggregated from 172 sites across Nigeria. Geospatial modeling was performed using a Random Forest algorithm to predict the distribution of mosquito species using remote-sensing data on 19 climatic and four topographic variables. Results showed a wide distribution of non-*gambiae Anopheles* species, with temperature influencing major species more than precipitation. Predictive maps were generated, and model accuracy was high. The study findings highlight the importance of including secondary vector species in operational strategies and call for increased surveillance and attention to their expanding ranges.

Plenary Session 3 – Malaria Drug Resistance: Key Perspectives

Arjen Dondorp (Mahidol Oxford Tropical Medicine Research Unit, Thailand) provided insights into the impact of malaria drug resistance in Africa, with a focus on artemisinin resistance and its implications for treatment effectiveness. This resistance can lead to partner drug resistance and reduce the efficacy of artemisinin-based combination therapies (ACTs). Validated pfk13 mutations and delayed parasite clearance serve as key indicators of this resistance, as confirmed in Eritrea, Rwanda, Tanzania, and Uganda. The spread of artemisinin partial resistance across Africa necessitates the implementation of transmission-blocking drugs like primaquine, along with enhancing surveillance and monitoring drug efficacy. Strategies include optimizing diagnostics and therapeutics, fostering collaboration for new tools such as non-artemisinin-based drugs or monoclonal antibodies, and ensuring access to malaria vaccines such as RTS,S/AS01E and R21. Effective implementation of multiple first-line therapies is crucial in combating resistance and improving malaria control efforts.

Abdoulaye Djimde (University of Bamako, Mali) began his talk by underlining the persistent threat of malaria, particularly in Africa, where over 95% of cases and deaths occur. Antimalarial drug resistance is emerging as a critical obstacle to controlling and eradicating malaria globally. The resistance to artemisinin, observed in *Plasmodium falciparum*, has been detected in East Africa, specifically in Rwanda, Uganda, and Tanzania. These findings suggest a potential decrease in the effectiveness of artemisinin-based combination therapies across the African continent. Djimde urges swift, unified action from stakeholders and funders to prevent a surge in malaria cases that may arise due to the rapid spread of resistance against antimalarial drugs. This includes regional coordination for data sharing, empowering local communities to tackle operational challenges, and strengthening surveillance using genomic and phenotypic analyses. Additionally, basic research is crucial to address key questions for malaria control and elimination efforts.

Symposium 14 – Malaria Vector Genomics Surveillance in Africa: a Pan-African-led initiative to deliver an accessible data platform for research and public health

Luna Kamau (Kenya Medical Research Institute – KEMRI, Kenya) Highlighted the importance of integrating genomic surveillance with vector surveillance to understand malaria transmission dynamics and enhance control measures. In 2013, *Anopheles coluzzii*, previously unseen in Kenya, was discovered and linked genetically to West African strains. Mosquito

populations exhibited genetic diversity, resembling those from arid regions. Sequencing 564 mosquitoes from five locations revealed the V4022L +I1527T mutation, potentially compromising the efficacy of PBO nets. Ongoing surveillance is crucial to monitor the presence of newly identified *Anopheles stephensi* species and track the spread and evolution of *Anopheles coluzzii*, essential for effective malaria control in Kenya.

Joel Odero (Ifakara Health Institute – IHI, Tanzania) investigated knock-down resistance (kdr) in *Anopheles funestus* in Tanzania. The spread of kdr across Africa in major malaria vectors has been well described, however, it has never been reported in East and Southern Africa where *An. funestus* is the principal vector. Whole-genome-sequencing (WGS) on population-samples of *An. funestus* across Tanzania. Eight novel amino acid substitutions in the Vgsc gene were found, including the kdr variant L976F and P18425, especially in the Morogo region. These mutations decreased between 2017 and 2023. Haplotype clustering analysis was performed on the Vgsc gene and revealed a selective sweep in the Morogo region. A strong association between survivorship to DDT insecticide and L976F was found, however no association with a pyrethroid insecticide was found. The authors hypothesize that DDT contamination from stockpiles in regions where kdr alleles were discovered may have been responsible for this evolution.

Rosine Wolie (Institute Pierre Richet and Nangui Abrogoua University, Côte d'Ivoire) researched utilizing genomic surveillance to investigate population structures and resistance mechanisms in *Anopheles (An.) gambiae* species against pyrethroids and organophosphates. Employing genomic wide selection scans (WGSS), she identified genes associated with resistance. Mosquito samples were collected from six locations across the country, revealing reproductive isolation between *An. gambiae* and *An. coluzzii*. Double target site mutations, which could cause pyrethroid and DDT resistance were observed. Various metabolic resistance mechanisms, particularly in *An. coluzzii* from the central region were evident against pyrethroids. Additionally, multiple mechanisms of metabolic resistance to organophosphates, including recently discovered carboxylesterase genes, were detected in *An. gambiae*.

Cynthia Awuor (Kenya Medical Research Institute – KEMRI, Kenya) presented her research using a systems biology approach to answer three questions i) how insecticide resistance is developed, ii) what methods can be used to detect mosquitoes that are resistant, and iii) what strategies can be used to enhance effectiveness of insecticides. Mosquitoes were experimentally exposed to insecticides, and bioassays and sequencing were performed before bioinformatics analysis. The phenotypic effects were measured using Weighted-Gene Coexpression Network Analysis (WGCNA). Highly connected (hub) genes were identified for *An. arabiensis* and *An. gambiae*. Notably, four hub genes were shared between these two species. These findings were validated by differential gene expression and by qPCR. The molecular mechanisms of insecticide intake were investigated, revealing immune modulation may be implicated in resistance development. Recommendations were made for functional validation of the four hub genes and for all insecticide resistance mechanisms to be considered during insecticide development.

Scientific Session 4 – Control and Elimination 1

Chi Tchampo Fru (University of Bamenda & Coordination Organization for the Fight against Endemics in Central Africa – OCEAC, Cameroon) explored natural methods for controlling *Anopheles* mosquito populations, investigating plant extracts from *Momordica foetida, Gnidia glauca*, and *Vepris soyauxii*. These extracts effectively killed mosquito larvae, disrupting their life cycle to prevent disease transmission. Acute oral toxicity tests demonstrated the extracts for humans and non-target organisms. Both aqueous and methanolic extracts exhibited

larvicidal activity suitable for use as biological larvicides. Animals displayed no adverse effects during oral toxicity testing, indicating the safety of the extracts. The presenter recommends the commercial development of these environmentally friendly methods to control mosquito populations and reduce disease spread, such as malaria. For further information, Fru pointed towards an article on the larvicidal activity of *Momordica foetida* published in Fortune journal.

Uchechukwu Chukwuocha (Federal University of Technology, Nigeria) presented a study on a school-based intervention called the "Malaria Classroom Corner", aimed at educating school children about malaria awareness and control practices. The intervention involved creating a designated corner in one school with materials such as pictures, drawings, and write-ups related to malaria, encouraging interaction during free time. Another school served as the control group, receiving only standard health education. Results showed better outcomes related to malaria awareness and preventive practices in school children from the intervention school compared to children from the control school. The interactive and participatory nature of the intervention enhanced students' understanding, attitudes, and behaviors regarding malaria. Additionally, the intervention was found to be cost-effective. The findings emphasize the importance of investing in similar interventions for school children to improve both health outcomes and academic performance. The recommendation is to scale up the intervention to other schools to contribute to malaria elimination efforts. By implementing the Malaria Classroom Corner, communities can cultivate a culture of malaria awareness and empower school children to advocate for change.

Muhammed Afolabi (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) described in his presentation the potential benefits of integrating MDA for helminth control with seasonal malaria chemoprevention (SMC) to address multiple health challenges simultaneously in resource-limited settings. He conducted a study in Senegal with a focus on assessing the feasibility, safety, and effectiveness of the combined approach. In the study, the intervention arm received both Praziquantel (PZQ) for helminth control and SMC drugs, while the control arm only received SMC drugs. Afolabi highlighted three main results: First, integrating MDA with SMC drugs was safe, well-tolerated, and feasible among Senegalese children. Second, malaria parasitaemia was significantly higher in the control group compared to the intervention group. Third, the children who received both PZQ and SMC drugs had a lower risk of developing severe anemia than those who received SMC drugs alone. These findings support further evaluation of integrating MDA with SMC in settings with high prevalence of malaria, schistosomiasis, and Soil-transmitted helminths. Further information on this study is available from the publication.

Lamin Jadama (Liverpool School of Tropical Medicine – LSTM, United Kingdom), presented findings on the entomological impact of mass drug administration (MDA) of ivermectin and dihydroartemisinin-piperaquine (DHA–PPQ) over two malaria seasons in the Gambia. Specifically, the study assessed the effect of the intervention on mosquito life span as well as other entomological outcomes such as mosquito density, sporozoite rate, biting rate and entomological inoculation rate. Previous studies in this area have found varying impacts, with effects on mosquito survival only, to effects on mosquito survival, sporozoite rate, EIR and parity, or effects on mosquito survival, density and EIR. In the presented study a significant effect of ivermectin MDA on vector density was found, with a notable reduction in mosquito survival up to 21 days post intervention when coverage was high. The study demonstrated the potential of MDA of ivermectin and DHS-PPQ as an effective strategy for reducing malaria transmission by targeting both the human host and the mosquito vector populations. Results from this study have been published in Parasites and Vectors (link).

Yacouba Poumachu (Medical Entomology at the Malaria Research Unit at OCEAC in Yaounde, Cameroon) discussed the necessity of mass rearing, sterilization and release of male *Anopheles arabiensis mosquitoes* to mate with wild females, resulting in non-viable offspring and reducing the overall population size amidst vector and parasite diversity and resistance. The presenter emphasized that this requirement is in line with the WHO 2008 recommendation to develop complementary tools against malaria. The process involves constructing an *Anopheles arabiensis* Y-autosome translocation line, which entails manipulating the mosquito's genetic material to induce a translocation of genetic material between the Y chromosome and one of the autosomes (non-sex chromosomes). The potential benefits of utilizing a Y-autosome translocation line for SIT-based applications include increased sterilization efficiency and reduced impact on mating competitiveness compared to other sterilization techniques. However, the presenter cautioned the importance of conducting thorough risk assessments and engaging with local communities to ensure the safety and effectiveness of such interventions.

Manfred Accrombessi (Population Services International – PSI, Benin) presented findings from a study that compared two long-lasting insecticidal nets (LLINs) with dual-active ingredients, Interceptor® G2 (IG2) and Royal Guard® (RG), to standard LLINs in a 3-arm randomized controlled trial. The study, conducted in areas with prevalent vector resistance to pyrethroids like southern Benin, aimed to assess the impact on pregnancy outcomes and community protection against malaria. Results showed that IG2 and RG LLINs provided similar community protection as standard LLINs against poor birth outcomes over three years. Moreover, among women using their allocated study nets, IG2 and RG LLINs offered greater protection compared to standard LLINs. Limitations of the study included its quasi-experimental design and reliance on self-declaration of net use. Accrombess suggested further investigation to confirm the findings and recommended that the national malaria control program consider integrating these new generation LLINs for malaria control during pregnancy.

Scientific Session 5 – Social and Health Economics 1

Sikai Huang (Vante School of Public Health, China) presented a study that employed a repeated wave survey to determine the household wealth index and the effect of seasonal malaria chemoprevention (SMC) in South Sudan conducted during the wet season (September-December). Results showed that SMC had a high protection effectiveness during high transmission areas and that household wealth was not associated with SMC outcomes but there was a significant association between wealth and malaria prevention.

Ladisla Nshimiyimana (Rwanda Biomedical Centre – RBC, Rwanda). The research identified three funding sources for malaria control and elimination in Rwanda: governmental funds, accounting for 42% of the total funds, and major funders, the Global Fund (GF), and the President's Malaria Initiative (PMI) accounting for 33% and 25% respectively. Malaria intervention in the country includes the acquisition of indoor residual spray (IRS), insecticide-treated nets (ITNs), medicines, surveillance, employee compensation and others. The results indicate that government prioritization of health funding consistently results in a significant reduction in malaria incidence by 85.3%, deaths by 81.2%, severe cases by 81.3%, and slide positivity by 68.9%. Even though government funds have slightly declined, interventions have been maintained due to collaboration with external funders. Thus, maintaining domestic funds is key in the fight against malaria. The Rwandan model could serve as a model for other African countries.

Hamidou Niangaly (National Institute of Public Health, Mali) presented a study that assessed the potential impact of decreased malaria incidence on child education, as well as how

increased household income could result in investments in education. The study was done in remote villages in the center of Mali and it enrolled children under the age of five years between June and December 2015. The study had two groups, the control group with SMC only, and the intervention group with SMC in combination with other strategies. The results reveal that the reduction in malaria has a significant positive impact on children's education as it allows households to save and invest in their wards. These results could inform policy decisions on the deployment of interventions to improve socio-economic performance.

Katherine Snyman (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) shared a study that employed the collection demographic data to evaluate the economic impact of malaria treatment using correlation and regression statistics for data analysis for economic evaluation. The result shows that investment in malaria prevention helps to avoid some treatment costs. The outpatient treatment costs (with uncomplicated malaria) are much lower than inpatient costs (with complicated malaria). Furthermore, affluent households spend only slightly more than those with lower income levels. Additionally, households with members aged 16 and above incur $5 more than those with members aged 15 and below.

Valerie Makoge (Institute of Medical Research and Medical Plants Studies, Cameroon) talked about malaria prevalence and malaria-related health-seeking behavior among street children in Yaoundé, Cameroon using mixed methods. Almost 150 male street children were included in the study. Results showed the prevalence of malaria parasites among asymptomatic street children was 34.3%, and that they perceived malaria to be the most common disease. Health-related actions concerning malaria were dynamic and depended on financial considerations, perceived severity of the disease, and healthcare accessibility. Makoge suggested establishing special units tailored for these vulnerable children and directly engaging them in health campaigns to improve their access to healthcare.

Carol Kamya (University of Bergen, Norway) discussed the cost-effectiveness of weekly dihydroartemisinin piperaquine (DP) versus sulfadoxine-pyrimethamine (SP) for malaria chemoprevention in children with sickle cell anemia (SSA) in Eastern and Southern Africa. The study design was a two-arm, multicenter, randomized parallel group. Kamya found that the new drug DP had a high probability of being a cost-effective alternative for malaria chemoprevention among children living with SSA compared to the standard of care SP even though DP has a higher cost. This was observed in both Uganda and Malawi. The new drug was associated with higher quality-adjusted life years (QALYS), reduced incidence of clinical malaria and less number of severe malaria hospitalizations.

Scientific Session 6 – Chemoprevention 1

Alassane Haro (Institute of Research and Health Science – IRSS, Burkina Faso) presented on the association between CYP2C8 variant and the occurrence of clinical adverse events among children 3-59 months of age receiving Seasonal Malaria Chemoprevention (SMC) in 2023 in the village of Samandeni, Burkina Faso. A prospective cohort study was conducted during 4 SMC cycles, screening 1,002 children out of which 408 samples were randomly genotyped for CYP2C8*2 (mutant) and CYP2C8*1 (wild type). Common adverse events were identified with vomiting being the most frequent. Haro's preliminary results suggest little evidence of minor adverse events related to CYP2C8*2 variants after SMC drug administration.

Steve M. Taylor (Duke University, United States) presented results from an open-label, randomized clinical trial in children with sickle cell anemia who were given daily proguanil, monthly sulfadoxine-pyrimethamine-amodiaquine (SP-AQ), or monthly dihydroartemisinin piperaquine (DP) for malaria prevention and followed up for a period of twelve months in

Homa Bay, Kenya. Serious adverse events were common with no overall significant difference but more deaths were recorded in the SP-AQ group. However, DP was associated with a lower rate of dactylitis and asymptomatic *P. falciparum* infection. The study's limitations included low malaria transmission in the study area and enhanced care for participants.

Sol Richardson (Vanke School of Public Health Tsinghua University, China) presented the complex association between caregiver satisfaction with door-to-door distribution and channels of information received on seasonal malaria chemoprevention (SMC) and malaria-related outcomes in Nigeria and Mozambique. The study targeted children aged 3 – 59 months and their caregivers for four cycles per annual round in the high transmission season (each circle included one dose of SP+AQ and two doses of AQ). His key findings showed a strongly unmediated association between caregiver satisfaction and a range of SMC outcomes. Information received through all channels was associated with caregiver adherence to AQ administration and these associations were fully mediated through knowledge, attitudes, and level of education.

Hamma Maiga (National Institute of Public Health – INSP, Mali) Presented on the impact of Seasonal Malaria Chemoprevention (SMC) implementation with sulphadoxine – pyrimethamine (SP) + amodiaquine (AQ) on *P. falciparum* resistance in Koutiala, Mali. This included two cross-sectional surveys before and after ten years of SMC implementation and analysis of genetic markers of resistance (*Pfdhfr-dhps* quadruple mutant genotype) in children receiving SMC and those who did not. Results showed an increased prevalence of quadruple mutation in the *Pfdhfr* gene owing to SPAQ resistance in SMC treated children and a significantly low prevalence of Pfdhps540E. However, there was no significant increase in these molecular markers in the general parasite population.

Vito Baraka (National Institutes of Medical Research – NIMR Tanzania) presented a study that investigated if Intermittent Preventive Treatment-seasonal chemoprevention (IPTsc) with dihydroartemisinin-piperaquine (DP) or artesunate-amodiaquine (ASAQ) may impair IgG reactivity to six *Plasmodium falciparum* antigens. Samples were collected from school children in a clinical trial in Muheza District, Tanzania. The results showed that the number of malaria antigens recognised significantly increased, IgG reactivity to GLURP was significantly lower at all follow-ups and lower against *MSP3* at visit 6. Baraka concluded that IPTsc has a limited impact on the acquisition of natural acquired immunity to malaria and further study is required to explore a wider range of antibodies using a longer IPTsc program.

Myness Kasanda Ndambo (Malawi Epidemiology and Intervention Research Unit, Malawi) presented touch points and strategies for implementing Post-discharge Malaria Chemoprevention (PDMC) in Malawi. The study addressed delivery mechanisms and evaluated the barriers and facilitators to implementing PDMC in the healthcare system. Results showed that co-designing the implementation enhanced the acceptance of PDMC and feasibility by stakeholders. Stakeholders suggested renaming PDMC to Post-discharge malaria continuum of care (PDMCC) denoting a continuation of the management of the initial severe anemia events that brought the child to the hospital. Stakeholders also recommended using DP, increasing the number of village clinics, expanding the availability of drugs, training and developing monitoring, recording, and tracking tools before scaling up PDMCC in Malawi.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

Day 2: Tuesday, 23rd April 2024

Plenary Session 4 – Vector Control Innovations for Malaria Elimination

Charles Wondji (Liverpool School of Tropical Medicine – LSTM, United Kingdom) emphasized the pivotal role of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) in malaria vector control, stressing that they are fundamental for malaria prevention. He noted their effectiveness in reducing malaria cases by up to 60% across Africa since the 2000s. However, challenges such as insecticide resistance pose a significant threat to their efficacy. Wondji highlighted that over-reliance on pyrethroids, without new insecticides developed in the past three decades, has resulted in widespread resistance. To address this, he proposed developing new insecticides for IRS, like Sumisheild 50WG, and using combination insecticides such as Fludora Fusion-BAYER. Wondji suggested LLIN innovations like nets treated with pyrethroids and piperonyl butoxide (PBO) to combat metabolic resistance and dual AI pyrethroid nets to sterilize pyrethroid-resistant mosquitoes. Wondji however noted that these innovations face challenges like cross-resistance and require time to show impact. Wondji finally advocated for the consideration and promotion of alternative innovations like gene drive, spatial repellents, bait stations, lethal house lures, and endectocides.

Jessy Goupeyou-Youmsi (Pan-African Mosquito Control Association – PAMCA, Kenya) presented the importance of including women in vector control innovations. Goupeyou-Youmsi highlighted a study conducted in Malawi that showed that women were 80% more likely to be infectious to mosquitoes than men. Goupeyou-Youmsi mentioned biological differences between men and women such as pregnancy which makes women more susceptible to severe malaria, and also differences in gender roles related to malaria transmission. This pointed out the need for gender mainstreaming. She also mentioned other factors leading to unequal burden of malaria on women and girls including the gender gap in research and implementation, increased vulnerability of women and girls due to social factors, missed opportunities for empowerment, and the lack of collaborations and investments. Goupeyou-Youmsi emphasized the importance of having women and girls as agents of change. Goupeyou-Youmsi briefly described the role of the PAMCA Women in Vector Control Program, and lastly proposed a call to action in malaria eradication to improve, design, invest, empower and close the gender gap to end malaria for all.

Symposium 19 – Malaria in Children and Adolescents with Sickle Cell Anemia

Ruth Namazzi's (Makerere University College of Health Sciences, Uganda) presentation underscored the need to prioritize sickle cell disease (SCD) as a public health concern in sub-Saharan Africa (SSA), where more than 300,000 babies are born with this condition annually. Namazzi highlighted that most of these cases occurred in the SSA region, with projections indicating a substantial increase by 2050. Notably, children with SCD face a shortened life expectancy, emphasizing the critical importance of addressing this issue. Moreover, Namazzi's discussion highlights the variability in the prevalence and severity of malaria among children with sickle cell anemia across different regions of Uganda, depending on the level of malaria transmission. In conclusion, Namazzi emphasized that malaria and SCD pose significant public health challenges in SSA, underscoring the need for early detection and treatment of malaria in individuals with SCD. Namazzi advocated for tailored malaria prevention strategies for this vulnerable population, noting that these findings would contribute to a better understanding of the interaction between sickle cell anemia and malaria, and inform strategies to mitigate the impact of malaria on this vulnerable population.

Carol Kamya (University of Bergen, Norway) explored insights into optimizing healthcare resources for children with sickle cell anemia (SCA) in malaria-endemic regions of Uganda

and Malawi. By comparing the cost-effectiveness of weekly Dihydroartemisinin-Piperaquine (DP) with Sulphadoxine-Pyrimethamine (SP) for malaria chemoprevention in this vulnerable population, Kamya shed light on the economic implications of treatment choices. Kamya's findings indicated that DP was a cost-effective alternative, offering higher quality-adjusted life years and reducing the incidence of clinical malaria and severe malaria hospitalizations compared to SP. This suggested that investing in DP for malaria chemoprevention in children with SCA could lead to better health outcomes while utilizing healthcare resources more efficiently. By posing the question "What does it cost to treat malaria in SCA?" and addressing it through comparative analysis, Kamya underscored the importance of considering both the clinical and economic aspects of treatment strategies. Kamya highlighted the potential benefits of prioritising cost-effective interventions like DP to improve the overall well-being of children with SCA in malaria-endemic areas.

Richard Idro (Makerere University College of Health Sciences, Uganda) presented on the CHEMCHA trial which investigated malaria chemoprevention in children with sickle cell anemia (SCA) in eastern (Uganda) and southern (Malawi) Africa. The study, involving 548 children studied over 18 months, compared dihydroartemisinin-piperaquine (DP) and sulfadoxine-pyrimethamine (SP) effectiveness. Weekly DP demonstrated superior efficacy in areas with high antifolate resistance, while monthly SP showed fewer non-malaria related illnesses, especially in older children lacking penicillin prophylaxis. These findings offer significant potential for improving malaria management in SCA-affected regions, where the disease poses a substantial health burden. By tailoring chemoprevention approaches to the specific needs and challenges of this vulnerable population, the CHEMCHA trial contributes valuable insights to global efforts in combating malaria, particularly in regions with high antimalarial drug resistance. Idro suggests further trials combining DP, SP, and penicillin, aiming to optimize malaria prevention strategies. Pending analyses include assessing acceptability, cost-effectiveness, resistance risk, and uptake. Future research endeavours informed by these findings could lead to more targeted and effective interventions, ultimately reducing malaria-related morbidity and mortality among children with SCA.

Symposium 22 – Malaria Elimination Efforts in the Horn of Africa: A Historical Perspective, Progress, Bottlenecks and Future Directions

Research by **Gudisa Assefa** (University of Gondar, Ethiopia), presented by **Ashenafi Assefa**, pointed out that progress has been made globally in fighting malaria, and Ethiopia has seen some of this progress. However, in recent years, we have seen a significant increase in malaria cases in the Horn of Africa. Assefa mentioned several reasons for this including; *Anopheles stephensi* invasion, climate change, and internal conflicts as major contributors to these negative changes. Assefa also noted pragmatic factors such as insufficient funds, the presence of refugees from neighbouring countries, insecticide resistance to commonly used tools, and the potential for antimalarial drug resistance as additional challenges. Assefa concluded by acknowledging the work that Ethiopia and collaborative partners were doing to combat malaria and called for more actions to eliminate the disease once and for all.

Abdoul Samatar (Global Fund, Djibouti) shared an update on efforts to control malaria in the country. From 2006 to 2012, the government worked on implementing measures to control malaria, leading to a significant reduction in malaria cases and entering a pre-elimination phase. However, the situation has changed, with malaria cases gradually increasing each year. This is mainly due to the presence of *Anopheles stephensi*, the main invasive mosquito species transmitting malaria in the area. This species is resistant to many insecticides and can efficiently transmit both *Plasmodium falciparum* and *P. vivax*. While there have not been reports of resistance to antimalarial drugs, there have been signs of resistance markers. Samatar emphasized the need for new approaches, such as gene drive mosquitoes, to regain

previous progress and emphasized the importance of community involvement in ongoing malaria control efforts.

Bekuretsion Gidey (Ethiopian Public Health Institute – EPHI, Ethiopia) presented findings on diagnostic failure and partial ACT resistance in Ethiopia. Patient samples from 108 health facilities across 11 districts in the Tigray, Amhara, and Gambella regions were acquired from health center patients presenting with malaria between 2017 and 2018. RDTs were used to detect *Pf* positivity, and all discordant and 20% of concordant *Pf* tested by PCR. 64% of RDT discordant samples were *PfHRP2-/3*– by PCR, and 42% of HRP2-positive samples were negative for HRP3 by PCR. These findings prompted a nationwide *PfHRP2/3* deletion survey in 2021, with sampling in 114 sites using both RDTs and microscopy, and further evaluation for drug resistance markers. Together, these data showed expansion of both HRP2/3 deletions and an 8% prevalence of K13 622I mutations in Ethiopia. From these data, the nationwide policy was revised in 2022 to change to non-HRP2/3 RDTs.

Abebe A. Fola (Brown University, United States) discussed the use of population genomic analyses to evaluate HRP2/3 deletion and ACT resistance markers in Ethiopia. MIP-based amplicon sequencing of 920 samples led to findings that partner drug mutations may augment antimalarial resistance. A higher prevalence of *Pfcrt* mutations were found in *PfHRP2-/3*– parasites compared to wild type, and 90% of *Pfk*13 622I mutants also carried the *PfMDR* NFD mutation. Genomic analyses determined identity by descent (IBD), a measure of parasite relatedness. At a district level, K13 622I mutant parasites had higher IBD than wild type. HRP2/3 deleted parasites were shown to have a high IBD and low COI, suggesting that these mutants were able to outcompete other parasites. These data suggest that parasites clustered geographically based on gene deletions, and Fola emphasized the importance of supporting the simultaneous analysis of genomic and national malaria survey data.

Isabela Gerdes Gyuricza (UNC-Chapel Hill, United States) presented findings comparing genomics of *PfHRP2/3* deleted Pf in Ethiopia and Peru. In Peru, RDTs have never been widely used for malaria detection, yet HRP2/3 deletions have been seen and have been expanding. Approximately 80% of the Pf population is HRP2-/3-, despite evidence of the negative effect of dual deletion on parasite fitness. Therefore, Guyricza is using genomic analyses to compare 2017-2018 samples from Iquitos, Peru (n=140) with those from Ethiopia (n=375), where similar mutants can be found and RDT use is high. Guyricza's results from MIP-based amplicon sequencing suggest that chromosomal breakpoints may differ between Ethiopian and Peruvian parasites in both chromosomes 8 and 13, where HRP2 and 3 reside, respectively. Guyricza's next steps are to use whole genome sequencing and additional sample sets to search for further evidence, including differences in genetic background.

Fitsum G. Tadesse (Armauer Hansen Research Institute – AHRI, Ethiopia and London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) highlighted the potential challenges posed by the spread of *Anopheles stephensi* in rapidly growing urban areas to malaria control efforts in Africa. He emphasized that *stephensi* is particularly concerning due to its ability to breed in manmade containers commonly found in these settings. Additionally, it is resistant to several commonly used insecticides, displays flexible feeding behaviour on both animals and humans, and can effectively transmit both *Plasmodium falciparum* and *P. vivax*, further complicating malaria control efforts. These factors necessitate urgent attention and action to address the threat to malaria control programs.

Symposium 24 – Malaria in Pregnancy

Myriam El Gaaloul (Medicines for Malaria Venture – MMV, Switzerland) began the symposium by elucidating the meaning of MiMBa – 'Malaria in Mothers and Babies' Initiative, launched

nearly five years ago by Medicines for Malaria Ventures (MMV). This initiative focuses on generating data on antimalarial use in pregnant and lactating women, who are often excluded from clinical trials due to concerns about potential harm. Gaaloul underscored that the symposium aimed to highlight and propose innovative approaches to shift the paradigm from shielding women from research and safeguarding women through research. Additionally, Gaaloul highlighted the gaps in the use of antimalarials in pregnant and lactating women, as well as some challenges faced by women living with HIV. Gaaloul emphasized that despite WHO guidelines in 2022 endorsing the use of Artemisinin Combination Therapy(ACTs) in the first trimester; there is a pressing need to expedite the generation of evidence for this use. Furthermore, she stressed the necessity to explore the use of other ACTs to gather safety and efficacy data for their utilization in pregnant and lactating women.

Brice Campo (Medicines for Malaria Venture – MMV, Switzerland) discussed their work on validating the routine use of innovative translational tools for antimalarials by collecting data, aiming to address the current gaps in the use of antimalarials in pregnant and breastfeeding women in malaria-endemic areas. Campo explored new approach methodologies such as Zebrafish and human induced pluripotent stem cells (hiPSCs) assays to test the potential teratogenicity of antimalarial compounds. Campo also mentioned the use of physiologically based pharmacokinetic (PBPK) modeling to generate high-quality data on the efficacy of antimalarials, informing clinical trials and policy decisions. Campo outlined a work plan for evaluating additional models in antimalarial research and predicting the pharmacokinetics of compounds for use during pregnancy and lactation, as a means of generating evidence and optimizing clinical trials. He emphasized the importance of collaboration in terms of sharing ideas, datasets, or compounds.

Kassoum Kayentao (Malaria Research and Training Institute, Mali) discussed the PYRAPREG trial, which aims to evaluate the efficacy and safety of pyronaridine-artesunate(PA) for treating malaria in pregnant African women during the second and third trimesters. This study sought alternative therapeutic options due to the low post-therapeutic effect of other medications like dihydroartemisinin-piperaquine (DP). Kayentao explained that the study compared the safety and efficacy of PA to that of artemether-lumefantrine (AL) and DP, which are recommended and widely used. Kayentao briefly touched on the preliminary safety results of the PA study, noting that serious adverse events collected in women and newborns were not related to the study drug. Data cleaning is ongoing for the safety and efficacy of PA, with an expectation that the results will offer an alternative therapeutic option for treating uncomplicated malaria in the second and third trimesters of pregnancy, as well as in HIV-positive pregnant women.

Bernard Omondi (Center for Global Health Research – Kenya Medical Research Institute – KEMRI-CGHR, Kenya) discussed an antimalarial pregnancy exposure registry aimed at generating robust data on the safety of various antimalarials during pregnancy, particularly in the first trimester, to inform regulators and policymakers. He elaborated on the MiMBa study, a multicentre cohort study involving pregnant women aged 15-49 years who have been exposed to specific artemisinin combined therapies (ACTs) such as dihydroartemisinin-piperaquine (DP) and pyronaridine-artesunate (PA) in Kenya and Burkina Faso. This study compared the incidence of pregnancy outcomes (miscarriages or stillbirths) among pregnant women and major congenital anomalies in newborns to generate informative data for the safe use of the tested antimalarials in the first trimester. Omondi described that enrollment is still ongoing in Burkina Faso, while it has been completed in Kenya. More than half of the recruited participants have experienced pregnancy outcomes in the two sites.

Hellen Barsosio (Kenya Medical Research Institute – KEMRI, Kenya), presented the approach of the SAFIRE study, an adaptive trial assessing the safety and efficacy of non-artemisinin-

based combination therapy (nACTs) for the treatment of malaria in the first trimester of pregnancy. The trial will be conducted in five countries – Burkina Faso, Mali, Kenya, Uganda, and the DRC. So far, data from the PYRAPREG and MiMBa trials have not shown developmental toxicity of antimalarials such as pyronaridine and piperaquine. Therefore, with the principle of justice in mind, there is an aim to generate more evidence for the use of these medicines in pregnancy during the first trimester, when they are more vulnerable. The composite primary endpoints for the trial are adverse birth outcomes, while key secondary outcomes include the efficacy of parasitological cure by day 42 as a long-term prophylaxis. Data from the trial will also inform the design of other trials conducted by the Liverpool School of Tropical Medicine and Medicines for Malaria Venture in the global south. The trial's design will allow for adaptations to capture important components to generate data for the use of newer ACTs.

Dorothy Fosah Achu (World Health Organization - WHO, Africa Regional Office, Republic of Congo) highlighted the burden of malaria in pregnancy and the current WHO guidelines on malaria case management during pregnancy. She pointed out research gaps in malaria treatment for pregnant women, such as the paucity and poor quality of data in the first trimester, which resulted in nearly 25 years between the registration of artemether-lumefantrine (AL) and its recommendation for use in the first trimester in past decades. She explained the process from evidence to the development of guidelines and policy, emphasizing the need for continued pharmacovigilance, clinical research, and monitoring of adverse events and pregnancy outcomes surveillance systems to reduce morbidity and mortality in women and children. Achu advocated for support and funding for prospective controlled trials on the efficacy and safety of antimalarial medicines in pregnancy, as well as for an enhanced role of the African Vaccine Regulatory Forum (AVAREF) on the continent to strengthen the capacity of National Regulatory Agencies (NRAs). She also highlighted the need to develop harmonized guidelines to facilitate the conduct of studies involving medicines in pregnant and lactating women in Africa.

Symposium 27 – Moving towards triple artemisinin combination therapies for multidrug resistant malaria in Africa and Asia

Mehul Dhorda (Mahidol Oxford Tropical Medicine Unit – MORU, Thailand) presented the preliminary findings on development of triple artemisinin combination therapies (TACT). A randomized partially blinded, placebo-collected, non-inferiority trial was carried out. The classes for the trials included ACT 1 (artemether-lumefantrine + placebo), TACT 1 (artemether-lumefantrine + placebo), TACT2* (artesunate-mefloquine + piperaquine and ACT2* (artesunate-mefloquine + placebo). The trial was done with a TACT to ACT ratio of 2:1 in Africa and 1:1 in 8 countries in Asia. Preliminary data showed adverse effects such as vomiting among participants.

Chanaki Amaratunga (Mahidol Oxford Tropical Medicine Unit – MORU, Thailand) presented their work on the safety and efficacy of Artemether-lumefantrine plus amodiaquine treatment of multidrug-resistant malaria in Asia due to the establishment of artemisinin partial resistance followed by partnered drug resistance. One hundred and three participants were recruited in this study between July 2021-Nov 2022. A randomized, blinded placebo-controlled clinical trial with Artemether-lumefantrine plus amodiaquine (AL+AQ) or Artemether-lumefantrine plus placebo (AL+ placebo) was carried out for 63 days and patients were followed for recurrent infections, genotyping of recurrent infections and parasite clearance half-life calculation. Adverse effects (AE) for several parameters including hepatic, renal, bone marrow and cardiotoxicity were monitored and physical examinations were conducted. Out of 103 patients, 9 recurrent infections were observed. More than 95% of the mutations observed after genotyping are PfK13 mutants. The results from this study showed that AL+AQ is safe,

well tolerated and more efficient than AL against artemisinin-resistant *Plasmodium falciparum* malaria in Asia.

Zbynek Bozdech (Nanyang Technological University, China) evaluated artemisinin resistance as a complex genetic trait using a transcriptomic approach. Artemisinin-based combination therapies (ACTs) are the first-line malaria treatments. Associations of alternative splicing and antisense RNA transcripts with artemisinin resistance showed many genes both upregulated and downregulated. From a transcriptomic point of view, artemisinin resistance looks very complex. *PfWD11*, one of the genes obtained was a covariant with *PfK13* and it occurred on the intron of the gene. The mutation occurred by alternative splicing which removed about 50 amino acids from the C-terminus within the WD40 domain. Another mutation in the promoter region of Pfcyp19B caused by upregulation of this gene was known to be driving artemisinin resistance. This study supports the fact that adding a dose of a third drug amodiaquine to artemether-lumefantrine can maintain the efficacy of drug therapy in the context of partial artemisinin resistance.

Scientific Session 8 – Vector Biology and Control 3

Doreen Siria (Ifakara Health Institute – IHI, Tanzania) highlighted the significance of mosquito age in malaria transmission and limitations of current methods like time consumption and human bias. A machine learning strategy utilizing mid-infrared spectroscopy (MIRS) was introduced to concurrently ascertain mosquito age and species. Approximately 40,000 mosquitoes; *An. gambiae, Anopheles coluzzii,* and *Anopheles arabiensis*, gathered under diverse conditions, underwent MIRS. Convolutional neural network (CNN) machine learning achieved over 80% accuracy in laboratory conditions and successfully identified all species in genetic variation. However, environmental variation resulted in poor accuracy. These results propose this method as a promising alternative for mosquito age determination, pending further accuracy improvements.

Pierre Marie Sovegnon (University of Abomey-Calavi, Benin) discussed the escalating threat to Africa's primary vector control tool, treated bednets, due to increasing pyrethroid resistance in mosquitoes. Sovegnon stressed the necessity of novel insecticides with diverse modes of action to address this challenge. Experimental hut trials were conducted to assess the blood-feeding behaviour, and longevity of mosquitoes when exposed to three new nets: Interceptor G2 (IG2) (pyrethroid and chlorfenapyr), Royal Guard (RG) (pyrethroid and pyriproxyfen), and PermaNet 3.0 (pyrethroid and Piperonyl butoxide (PBO)). Results indicated a significant reduction in blood feeding rates with unwashed RG nets, while all three nets exhibited high 72-hour mortality rates, with IG2 nets recording the highest mortality.

Phocas Mazimpaka (Rwanda Biomedical Center – RBC, Rwanda) provided insights regarding community empowerment in integrated vector management (IVM), implemented in 2023, to boost local involvement in managing larval sources. Through a "learning by seeing and doing" strategy, local community leaders were trained to identify mosquitoes and breeding sites. By the program's end, participants, including health workers, engineers, and agronomists, adeptly recognized *Anopheles* mosquitoes, with over 80% identifying breeding sites nearby. Conducted in the local language, this training extended across 300 sectors nationwide, with full compliance from the community. To further engage communities and expand the capacity building in IVM, increased national-level multisectoral collaboration, advocacy, and resource mobilization are necessary.

El Hadji Diouf (Cheikh Anta Diop University – UCAD, Senegal) contrasted resistant alleles identified in *An. gambiae s.s, An. arabiensis,* and *An. coluzzii* mosquitoes between districts receiving IRS (Indoor Residual Spraying) and the control districts. Vgsc- 1014F, Vgsc- 10145,

and G1195 mutations were more common in *An. arabiensis* and *An. gambiae s.s* than in *An. coluzzii*, with G1195 being predominant in *An. coluzzii*. Kdr mutations were prevalent in IRS districts among *An. gambiae s.s* and *An. coluzzii*. Allele 1014F frequency was low in both districts, while Vgsc- 10145 frequencies were higher in control districts. These results suggest that implementing IRS with bendiocarb, followed by pirimiphos-methyl, might decrease the frequencies of alleles 1014F and 10145.

Scientific Session 10 – Phytomedicines and pharmacology

Toghueo Rufin (University of Yaounde, Cameroon) presented an exploration of the fungi microbiome from Cameroonian medicinal plants for antimalarial drug discovery. Highlighting the vast biodiversity in Sub-Saharan Africa, where indigenous populations utilize numerous medicinal plant species for malaria prevention and treatment, the study aimed to isolate and identify fungal endophytes producing compounds effective against *Plasmodium falciparum*. Four endophytes exhibited activity against *P. falciparum* strains, leading to the identification of one active compound (Auraperone A) and two potent fractions with multi-stage inhibition against the *P. falciparum* 3D7 strain. Dr. Rufin underscored the potential of advanced metabolomics and molecular networking in uncovering novel bioactive compounds against *falciparum* malaria.

Elliot Nyangumbo (Midlands State University, Zimbabwe) presented a systematic review of medicinal plants used for the treatment and management of malaria in Zimbabwe. The study underscored the significance of traditional medicines in combating malaria and addressing antimalarial drug resistance. Through a comprehensive review, 70 plant species were identified for their traditional use in malaria treatment in Zimbabwe and across Africa. Roots were predominantly cited compared to seasonal parts like flowers and fruits, raising conservation concerns. Toxicology and pharmacological tests were conducted, revealing that 53 out of 70 plants exhibited antiplasmodial activity, thus scientifically validating their efficacy in managing malaria symptoms.

Elliot Nyangumbo (Midlands State University, Zimbabwe) continued with a study on in-silico analysis of compounds from screened antimalarial medicinal plants against *P. falciparum* Hsp90_A, aiming for selective antimalarial drug design. Among the 53 plants exhibiting antiplasmodial activity, 22 were identified with high activity. Literature searches revealed that only four out of these 22 plants had information on isolated compounds, highlighting the necessity for further research on other plants. Ethno-directed and comprehensive literature searches played a pivotal role in narrowing down natural product compounds for targeted drug development. The findings advocate for additional research into anti-malarial compounds in African flora, potentially serving as direct medications or as lead compounds for the development of novel anti-malarial drugs.

Simon Nyarko (Kwame Nkrumah University of Science and Technology, Ghana) developed an RP-HPLC method for the simultaneous determination and quantification of artemether and lumefantrine in fixed-dose combination pharmaceutical forms. The objective was to establish and validate a rapid, precise, economical, and robust RP-HPLC technique and conduct drug assays on the sample medications. The solvent Azitronitra was utilized for the HPLC run, and the method's specificity, linearity, accuracy, system suitability, and precision were validated using 8 tablets and 6 suspension brands. The method demonstrated high sensitivity, accuracy, and reliability, rendering it suitable for application in resource-constrained environments.

Adebanjo Adegbola (Obafemi Awolowo University, Nigeria) investigated how ciprofloxacin affects the pharmacokinetics of lumefantrine in both malaria patients and healthy volunteers.

This inquiry stemmed from the common practice of combining antimalarials like artemether-lumefantrine (AL) with antibiotics due to malaria-bacteria co-infections. Ciprofloxacin has the potential to inhibit drug-metabolizing enzymes, thereby possibly increasing drug plasma levels and affecting the effectiveness of antimalarials. The study evaluated lumefantrine exposure with and without ciprofloxacin. Both healthy volunteers and malaria patients received AL alone or in combination with ciprofloxacin, and their blood samples were analyzed for pharmacokinetic parameters. The findings revealed higher lumefantrine levels when administered with ciprofloxacin, indicating prolonged drug activity. Further studies are necessary to ascertain the safety and efficacy of combining AL with ciprofloxacin.

Plenary Session 5 – Malaria Vaccines: The missing piece on the path to elimination?

Pedro Alonso (BioNTech, Germany) framed the plenary talk, laying out a comprehensive discussion framework for subsequent speakers who explored future scenarios of malaria elimination and eradication. While Alonso highlighted progress in malaria control efforts, and expressed doubt about achieving malaria eradication by 2050 with existing tools alone. Alonso stressed the pressing need for innovative solutions, particularly malaria vaccines, to complement existing interventions. The approval of RTS,S/AS01 and R21/Matrix-M vaccines by the World Health Organization (WHO) represents significant progress in the fight against malaria – a milestone unimaginable 30 years ago when the MiM society was formed in Dakar, Senegal. Alonso's message underscored the need to invest in research and development for new tools, including vaccines, crucial for advancing malaria control, elimination, and eradication efforts. Strong political commitment and international cooperation are essential to support these endeavours and drive progress toward eradicating malaria, leveraging innovative approaches and collaborative partnerships for a future where malaria poses no threat to public health.

Lindsey Wu (WHO Global Malaria Programme & Immunization, Vaccines and Biologicals, Switzerland) articulated the World Health Organization's (WHO) strategic priorities for malaria vaccine development, emphasizing the importance of facilitating both global and country-specific research agendas. She outlined the preferred characteristics of an ideal malaria vaccine and provided insights into the current malaria vaccine pipeline, clinical pathways, and endpoints. Highlighting vaccines as integral to malaria elimination strategies, she underscored the significance of the RTS,S/AS01 vaccine as a major scientific breakthrough. However, she acknowledged challenges in improving vaccine access and efficacy. Wu stressed the necessity for additional tools to enhance vaccine effectiveness and the duration of protection, advocating for data-driven approaches to inform future vaccine development

Halidou Tinto (Institute of Research in Health Sciences (IRSS) – Clinical Research Unit of Nanoro (CRUN), Burkina Faso) discussed the integration of malaria vaccines, particularly RTS,S and R21, into existing prevention strategies in Africa to enhance malaria elimination efforts. While acknowledging the potential of these vaccines to reduce the malaria burden, Tinto highlighted the necessity of combining them with other preventive measures due to their inability to interrupt disease transmission alone. RTS,S, when combined with tools like seasonal malaria chemoprevention (SMC), showed promising results in trials in Burkina Faso and Mali, significantly reducing clinical malaria, severe cases, blood transfusions, and malaria-related deaths. The key takeaway emphasized the importance of political leadership and continued efforts in the face of ongoing developments in malaria vaccines and monoclonal antibodies.

Dorothy Fosah Achu's (World Health Organization - WHO, Africa Regional Office, Republic of Congo) insights build on previous speakers' discussions on malaria elimination strategies. She acknowledged that many countries have been progressing towards elimination through

various methods, including insecticide vector control and integrated approaches to diagnosis and treatment. However, Achu raised the question of where vaccines fit into malaria control efforts, thus, while vaccines play a crucial role, they alone cannot lead us to complete malaria eradication. Achu highlighted the need for vaccines targeting both children and adults, addressing a broader range of malaria parasites, including *P. falciparum* and *P. vivax*. Additionally, she stressed the importance of affordable vaccines to ensure equitable access, particularly in the WHO Africa region, and underscored the significance of initiatives like the Africa Malaria Vaccine Rollout Initiative in scaling up vaccine distribution for maximum impact. Ultimately, Achu's key message emphasized the importance of continuing to utilize existing tools while exploring new interventions to combat malaria effectively.

Yvan Butera (Ministry of Health – MoH, Rwanda) highlighted the need for a comprehensive approach to public health in Africa and emphasized the importance of not only developing vaccines but also strengthening healthcare infrastructure for their effective deployment. Butera stressed the significance of combatting prevalent diseases like malaria while also building capacities for vaccine manufacturing within the continent, and the utilization of diverse expertise, particularly evident during the COVID-19 pandemic, to manage health crises effectively. Furthermore, Butera mentioned the necessity of sustainable financing mechanisms for vaccine procurement to ensure equitable access to healthcare resources. He emphasized the importance of data-driven strategies in strengthening health systems, enabling policymakers to allocate resources efficiently. Overall, Butera's message aimed at fostering self-reliance, innovation, and resilience in Africa's healthcare landscape.

Symposium 30 – Strategies to mitigate antimalarial drug resistance in Africa: grassroots engagement to next generation drugs

Charlotte Rasmussen (Global Malaria Programme, WHO, Switzerland) outlined the strategy to combat antimalarial drug resistance in Africa, focusing on artemisinin-based combination therapies (ACTs). ACTs rely on both artemisinin and a partner drug for efficacy, with artemisinin reducing parasite biomass rapidly and the partner drug eliminating remaining parasites. Partial artemisinin resistance is defined by delayed parasite clearance, associated with *Pfkelch*13 mutations. Confirmed resistance requires over 5% of the validated marker for Pk13 and evidence of delayed clearance, observed in Uganda, Rwanda, Eritrea, and Tanzania. High treatment failure is reported for amodiaquine, lumefantrine, and piperaquine, though partner drug resistance is unconfirmed. The response strategy, developed in November 2022, includes 20 interventions across four pillars namely: surveillance, regulation of diagnostics and therapeutics, limiting resistance spread, and fostering research and innovation. Rasmussen emphasized the need for continuous monitoring and updates to adapt to evolving evidence and challenges.

Maciej F. Boni (Temple University, United States) discussed modeling policy interventions to curb artemisinin resistance spread in Uganda and Tanzania, outlining four strategies for success including preventing resistance, delaying spread, slowing resistance gene frequency increase, and controlling it. Boni focused on the average monthly treatment failures over five years, emphasizing diverse drug deployment for effective management. Uganda's whole-country model and Tanzania's whole-region model predicted a 75% *Pfkelch*13 mutation in Uganda and a 50% containment possibility in Tanzania over five years. Running the model to 2024, suggested interventions like switching to other ACTs, cycling through them, deploying multiple first-line ACTs (MFTs), or deploying triple ACTs by September. Running the model till 2029 showed that a near-term strategy of maximum ACT diversity (MFT or rapid cycling) is Uganda's best strategy, while for Tanzania, a near-term switch to ASAQ is the optimal approach.

Karen I. Barnes (University of Cape Town, South Africa) presented the potential role of single low-dose primaquine for tackling partial artemisinin resistance. She identified various factors contributing to this resistance, including mutations in the *Plasmodium falciparum PKelch13* gene and the failure of artemisinin combination therapy (ACT). Barnes discussed the significance of gametocyte prevalence as a marker for infection, noting that while imperfect, it provides valuable baseline data and further highlights differences in gametocyte density between regions with varying transmission intensities. Moreover, Barnes emphasized the limitations of using gametocyte/membrane feeding experiments as markers of drug efficacy. In conclusion, she underscored the higher prevalence of gametocytes in artemisinin-resistant infections, particularly in areas with moderate to high transmission rates, and advocated for the use of single low-dose (SLD) primaquine in regions threatened by artemisinin resistance and stressed the importance of surveillance to assess the effectiveness of SLD Primaquine in combating resistant parasites.

Didier Leroy (Medicine for Malaria Venture – MMV, Switzerland), discussed strategies for addressing complicated malaria refractory to treatment. He emphasized the importance of adopting fast-acting, resistance-refractory approaches in the fight against drug resistance. Leroy advocated for simplifying therapy and overcoming resistance through vaccines and chemotherapy, including combinations like triple artemisinin combination therapy (TACT), non-artemisinin combinations like ganaplacid-lumefantrine, and novel drugs in clinical trials like ZY19489. Leroy categorised challenges into previous and new versions, citing factors such as screening and risk assessment for the former, and MIR determination and cross-resistance screening for the latter. He emphasized the urgency of prompt action against resistance, highlighting potential consequences of delays and the importance of proactive measures to combat drug resistance in malaria treatment.

Olugbenga A. Mokuolu (University of Ilorin, Nigeria) addressed the challenge of antimalarial drug resistance. He stressed the vital role of stakeholder engagement in combating this public health threat, emphasising the need for resource mobilisation, community empowerment, and fostering trust in malaria interventions. Mokuolu advocated for synergistic collaboration between evidence providers, policymakers, and regulators to tailor interventions to local contexts and ensure credibility. He highlighted the regulators' responsibility in facilitating strategy implementation and maintaining marketing integrity. Drawing from numerous case studies in Nigeria, Mokuolu concluded that success in combating antimalarial drug resistance requires collective effort. Mokuolu reiterated the importance of unity, emphasising that victory over drug resistance cannot be achieved in isolation and requires concerted action from all stakeholders involved.

Symposium 32 – Anopheles stephensi in Africa: What has been done, what must be done, and how it could be done?

Roz Taylor (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) delivered an analysis of *Anopheles stephensi*, a significant malaria vector, focusing on its distribution, behavior, and implications for malaria control in Africa. *An. stephensi*, native to South Asia and the Arabian Peninsula, has expanded its invasive range to urban areas across eight African countries. She conducted a narrative review, detailing the species' bionomics, distribution, resting and feeding behaviors, insecticide resistance, and breeding sites. Notably, *An. stephensi* exhibits resistance to all four main classes of insecticides and breeds in diverse habitats, posing challenges for malaria control efforts. The presentation showed the urgency of addressing breeding sites amidst rapid urbanization in Africa to mitigate the spread of this vector. Further research is warranted to understand and combat the implications of *An. stephensi*'s presence in urban environments.

Delenasaw Yewhalaw (Jimma University, Ethiopia) presented on adult *An. stephensi* feeding and resting behavior, and efficacy of candidate larvicides (SumiLarv 2MR and SumiLarv 0.5g) for control of *An. stephensi* larvae in Ethiopia. Yewhalaw pointed out the widespread presence of malaria-carrying mosquitoes in Ethiopia, with *An. arabiensis* being the most prevalent and *An. stephensi* increasingly spreading across the country since its first detection in 2016. *An. funestus* is also present but in limited areas. *An. stephensi* is emerging as an efficient malaria vector in the region capable of transmitting both *Plasmodium falciparum* and *P. vivax*. This mosquito species breeds in various aquatic environments, including urban, peri-urban, and rural settings, both natural and artificial. Results show that the species prefers animal to human blood and rests indoors and outdoors. Despite its resistance to many insecticides, SumiLarv shows promise as a larvicide for controlling *An. stephensi* larvae with over 80% adult emergence inhibition.

Yaw Afrane (University of Ghana, Ghana) presented on *Anopheles stephensi* in Ghana focusing on ecology and molecular surveillance. Potential breeding sites in Accra were sampled for malaria vector larvae which were grown to adults. Results revealed a 0.341.4% unexpected discovery of *An. stephensi*, a species recently detected in East Africa, among the surveyed population of 1169 adult mosquitoes. This finding raised questions about the potential routes through which *An. stephensi* could have entered Ghana. Various possibilities were discussed, including long-range aerial migration, cargo transportation via airplanes or ships, and land travel such as bus journeys. However, conclusive evidence regarding the specific mode of transportation remains elusive, necessitating ongoing research efforts to assess all plausible scenarios. The integration of surveillance measures into routine entomological practices highlights the importance of proactive monitoring and response strategies to address emerging threats posed by malaria vectors. Surveillance efforts have been extended beyond Accra to assess *An. stephensi* in Ghana.

Louisa A. Messenger (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom, and University of Nevada, United States), emphasized the importance of molecular surveillance for *Anopheles stephensi*. This method informs targeted vector control and enhances our understanding of population dispersal dynamics. Direct molecular surveillance yields extensive genomic data, elucidating species dispersal and insecticide resistance mechanisms. As *An. stephensi* is not always captured by sampling traps, this technique offers viable alternatives, however, there are potential biases towards productive sites and limited genetic diversity due to sibling effects. Conversely, indirect molecular surveillance provides unbiased population sampling and detects *An. stephensi's* presence in unknown areas. It requires minimal expertise and can involve community citizen scientists. However, reconstructing whole genome sequences from fragmented eDNA remains a challenge. While feasible in laboratory settings, field validation and operationalization are necessary. Messenger advocated for increased collaboration across surveillance of *An. stephensi* which has emerged as a threat for malaria control efforts in Africa.

Ayman Ahmed (University of Khartoum, Sudan) highlighted critical gaps and challenges in the surveillance and control of *Anopheles stephensi* in Africa. Key gaps include a lack of knowledge regarding its introduction and prevalence, technical limitations in combating *An. stephensi*, and resource constraints leading to delayed responses. *An. stephensi* poses a public health threat due to its presence in urban and rural areas, utilization of man-made breeding sites, and outdoor biting and resting habits. Policy challenges include determining its public health significance and developing effective strategies. Ahmed emphasizes the need for unified stakeholder positions, integrated vector management programs, regional coordination, and local capacity building. Recommendations focus on strengthening collaboration, community engagement, surveillance, and scaling up interventions for

sustainable vector control. This comprehensive approach is crucial for addressing the emerging threat of *An. stephensi* in Africa.

Scientific Session 11 – Malaria in Pregnancy 1

Tahina Razafiarijaona (Johns Hopkins Program for International Education in Gynecology and Obstetrics – Jhpiego, United States) presented data on at least 3 doses of intermittent preventive treatment of malaria for pregnant women (IPTp3) coverage and antenatal care (ANC) attendance in Madagascar, illustrating improvement over time attributed to the Transforming Intermittent preventive Treatment for Optimal Pregnancy (TIPTOP) project. The TIPTOP approach effectively enhanced IPTp3 coverage and ANC attendance, which were considered acceptable and feasible by healthcare providers and community health workers. Post-project follow-up in October 2023 further demonstrated the feasibility of interventions. The community IPTp (C-IPTp) strategy bolstered health systems at various levels, instilling increased confidence in the healthcare system. The Ministry of Health, supported by USAID/MOMENTUM and ACESS program, intends to expand the C-IPTp approach as part of the 2023-2027 National Strategic Plan. Implementation will continue in the three districts, with plans for scaling up to 41 additional districts in 2023 and beyond.

Tacilta Nhampossa (National Institute of Health – INS & Manhiça Health Research Centre – CISM, Mozambique) discussed the acceptability of dihydroartemisinin-piperaquine (DP) as intermittent preventive treatment of malaria for pregnant women living with HIV (PWLHIV) in Southern Mozambique. The quantitative study aimed to understand how clinical trials would impact HIV status confidentiality and acceptance of DP. The research spanned from 2019 to 2023, involving 44 PWLHIV, 35 HIV-negative pregnant women, and 8 health providers. Findings suggested that the acceptability of DP was influenced more by pregnant women's trust in health providers than by the perceived benefits of DP in preventing malaria. To enhance acceptability, it is crucial to leverage this trust to provide clear information on DP administration.

Katherine Wolf (Johns Hopkins Program for International Education in Gynecology and Obstetrics – Jhpiego & President's Malaria Initiative – PMI Impact Malaria, United States) presented findings from a cluster-randomised controlled trial in the Atlantique Department of Benin, evaluating the impact of Group Antenatal Care (G-ANC) on ANC retention and uptake of IPTp3+. The study aimed to determine if G-ANC improved IPTp uptake by comparing pregnant women in G-ANC facilities to those in control facilities and to assess its feasibility and acceptability. Approximately 40 health facilities were randomised, and household surveys conducted before and after implementation indicated higher ANC4 and IPTp3 rates among G-ANC participants. Despite challenges such as staffing shortages for enrolling women, G-ANC participants demonstrated higher ANC4 and IPTp3 uptake. However, overall enrolment remained low, with no significant community-level impact.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

Day 3: Wednesday, 24th April 2024

Plenary Session 6 – Malaria Drug Development and Innovations for Malaria Elimination

Okwu Daerie Glory (Lambaréné Medical Research Center – CERMEL, Gabon) gave an insightful talk focused on next generation antimalarial drugs currently under clinical development. Following the current challenges the world is facing with resistance to artemisinin, chloroquine, and sulfadoxine-pyrimethamine in *Plasmodium falciparum*, there is an urgent need to develop better medicines for children and pregnant women. Daerie pointed out the progress made by companies in the development of sophisticated phenotypic screens that have led to the identification of new drug candidates and antimalarial targets which are now under clinical development. She pursued by recognizing and commending the endeavors of various entities and initiatives working on the discovery, development and delivery of new, effective, and affordable antimalarial drugs to reduce malaria burden in endemic countries. Highlighted examples included the Medicines for Malaria Ventures (MMV), the ASSAP project, the West African Network for Clinical Trials of Antimalarial drugs (WANECAM), the PAMAfrica consortium, the SINDOFO consortium and the clinical trial 'PLATINUM'.

Cristina Donini (Medicines for Malaria Venture – MMV, Switzerland) presented on malaria drug development and innovations for malaria elimination. She started by giving an overview of malaria statistics from the World malaria report 2022. She highlighted the challenges posed by artemisinin drug resistance and the need for innovative approaches in malaria case management. She urged the need to address antimicrobial resistance, optimize vaccine strategies, and introduce innovative tools in the final stages of malaria eradication efforts. She emphasized the significance of tackling drug resistance by exploring single-dose solutions and advancing vector control measures. Additionally, Donini highlighted the importance of integrating malaria interventions within the broader health system in countries. She discussed the role of partnerships, particularly the MMV, in driving research and development of new treatments. By leveraging the African experience in drug discovery and embracing innovative approaches, the session aimed to advance the malaria drug development agenda.

Symposium 39 – African solutions to an African problem: practical approaches to antimalarial resistance mitigation

Aimable Mbituyumuremyi (Rwanda Biomedical Centre, Rwanda) outlined the practical strategies employed to combat antimalarial resistance in Rwanda. He highlighted the objectives of the Malaria National Strategic Plan (NSP 2020 – 2027), aimed at reducing malaria morbidity and mortality by at least 90% of 2019 levels. Malaria incidence showed a significant reduction from around five million cases to 600,000 cases between 2008 and 2013, indicating the effectiveness of implemented strategies. However, there is a concerning trend of increasing malaria resistance. In his presentation, Mbituyumuremyi discussed new treatment guidelines (2024) focusing on vector control, high-burden areas, surveillance of antimalarial resistance, and community-based management. In Rwanda, dihydroartemisinin (DHAP) and artesunate pyronaridine (ASPY) have been introduced for first-line malaria treatment, but they are also used for second-line due to limited options. Hence, to close his talk, Mbituyumuremyi emphasized the need for additional antimalarials to be made available in the country to ensure appropriate management of cases with recommended medication options.

Gilbert Kokwaro (Strathmore University, Kenya) presented on the multiple first-line treatment (MFT) approach for uncomplicated malaria. He addressed the challenge of partial resistance to artemisinin combination therapies (ACTs) in some sub-Saharan countries, emphasizing the importance of mitigating resistance spread and safeguarding partner drugs. Kokwaro outlined the study objectives, which focused on health system challenges associated with MFTs, patient and healthcare worker experiences with MFT implementation, and the cost implications of MFT implementation in Sub-Saharan Africa. He summarized the findings, noting that rotational MFT is operationally feasible, with both healthcare providers and patients favoring simplified dosing regimens over alternative options. To overcome health system challenges of MFTs, Kokwaro emphasized the importance of i) accurate estimation of drug requirements; ii) timely procurement and distribution; iii) training for healthcare providers on new medications; iv) involvement of the private sector; and v) community sensitization activities to support MFT implementation.

Issiaka Soulama (Health Sciences Research Institute – IRSS, Burkina Faso) presented a study assessing the feasibility, acceptability, and cost of deploying multiple first-line treatment (MFT) in Kaya, Burkina Faso. The pilot study aimed to provide evidence for the effective deployment of MFT not only in Burkina Faso but also potentially in other Sub-Saharan African countries. Soulama examined various aspects, including administrative and regulatory considerations, logistical and financial aspects, and operational implementation. The findings indicated that implementing MFT is operationally feasible and well-received, underlining its potential for broader integration within the health system infrastructure, particularly in areas with diverse malaria transmission patterns. Given the impact of MFT strategies on routine prescription and administration of antimalarials, Soulama emphasized the importance of healthcare worker involvement and training, as well as monitoring antimalarial use to ensure successful implementation. Finally, he recommended monitoring molecular resistance markers as a crucial component of MFT strategies.

Maciej Boni (Temple University, United States) presented a modeling approach aimed at slowing down artemisinin resistance evolution in Rwanda through therapy strategies and geographic drug distribution models. Boni emphasized the 'district ranking' approach and outlined the first phase of model development. The approach compared multiple first-line treatment (MFT) strategies to extended artemisinin combined therapies (ACTs), drug switches, and triple ACTs. This initial phase is completed, and the focus has shifted to comparing geographic MFT strategies in districts using artemether-lumefantrine (AL) as first-line therapy with those using dihydroartemisinin–piperaquine (DHA–PPQ). Analysis in Rwanda indicates that geographic MFT effectively delays resistance only when deployed with rotations. Boni recommended further steps to deploy the model using drugs such as pyronaridine–artesunate (ASPYr) or artesunate-amodiaquine (ASAQ).

Andrew Omandi Cole (Strathmore University, Kenya) presented a modeling study focusing on near real-time monitoring of resistance development during the development of multiple first-line treatment (MFT) for malaria. He described a mathematical modeling approach aimed at mitigating resistance to antimalarials. The proposed methodology involves infecting red blood cells (RBCs) with merozoites and subsequently assessing them for susceptibility, resistance, infection, and recovery. The modeling study aims to examine the dynamics between *Plasmodium falciparum* merozoites and human erythrocytes within human hosts. The collected data will be visualized through an interactive web-based dashboard, providing insights into malaria parasite distribution across different regions of the country. Cole emphasized that this research will contribute evidence supporting the effectiveness of

artemisinin combination therapy (ACTs) while also identifying potential avenues for drug and vaccine development.

Symposium 42 – Fighting malaria with genomics in Africa: Current status, achievements and prospects

Nana Aba Williams (MESA at Barcelona Institute of Global Health – ISGlobal, Spain) gave insight into mapping the landscape of ongoing research and investments in fighting malaria with genomics. Integrated Malaria Molecular Surveillance (IMMS) offers the potential for a holistic understanding of how the human genomes, parasites, and vectors respond to malaria control interventions which in turn informs programmatic decisions on the optimal mix of interventions. This study implied the systematic data collection from multiple sources, screening, and selection of projects, extracting and verifying project details with project leads, classifying projects based on common objectives to create a community of researchers and stakeholders to discuss protocols and finally build a living group of useful information. The landscaping review captured a total of 118 projects with funds of over $187.9M with 35 projects being active and representing $69.3M distributed all over the world. Williams also emphasized the importance of organizing symposiums to encourage sharing active projects and investments.

Osoti Victor (KEMRI-Wellcome Trust Research Program, Kenya) presented his study on integrating malaria molecular epidemiology into routine surveillance in Kenya. Artemisinin resistance has been reported in several countries in East Africa. One hundred blood spots were collected from 8 counties and 81 schools in western Kenya in 2019. A rapid diagnostic test (RDT) was used to screen for malaria and 28% positive samples were obtained. DNA was further extracted from these samples and the *pfkelch13* gene was validated in this population. A high frequency of other genes involved in resistance was also observed in 2019 and several others in 2022 including A469 and A625. A database and a strategy document were developed for reporting, and guiding data from the malaria molecular surveillance (MMS) platform which was set up at the end of this study.

Deus Ishengoma (National Institute for Medical Research – NIMR, Tanzania) presented the progress, challenges, and opportunities made in building the capacity of malaria molecular surveillance in Tanzania. The aim of this study was to establish local molecular, genetic, and genomic laboratories, and analytical capacity to support MMS in the country. A whole team of students, postdocs, and other stakeholders was set up in collaboration with personnel from the National Malaria Control Program (NMCP). Thirty thousand blood samples out of the 600,000 collected from all the regions in the country were resistant to artemisinin and were sequenced. The results from this study showed the status of hrp2/3 gene deletions, artemisinin partial resistance, sulfadoxine-pyrimethamine (SP) resistance, and the mapping of *Plasmodium falciparum* (*Pf*) and non-*falciparum* species. A genomic laboratory, established field sites, and platforms for malaria molecular surveillance (MMS) were set up and effective capacity building of postdocs, staff, interns, and students was done.

Mulenga Mwenda (PATH, Zambia) explored in-country nanopore sequencing using the NOMADS assay to identify drug resistance markers in Zambia. This study was done to integrate surveillance of *Plasmodium falciparum* (*Pf*) via nanopore sequencing into routine surveillance, empower others to use the assay, optimize existing and develop novel sequencing assays in the country in collaboration with the National Malaria Elimination Centre

(NMEC). Five hundred samples were collected and sequenced to assess the treatment efficacy of frontline ACTs and provide genetic evidence from Solwezi and Kasama which are two high-transmission sites. Three hundred samples were analyzed with a high number of *Pfdhfr* mutations recorded. Other mutations including the P667S, P675V, P667A, P441L, and R622T were also found to exist in some samples. The *pfkelch13* mutation was only found in Solwezi.

Jonathan Juliano (University of North Carolina, United States) presented on strengthening malaria molecular surveillance capacity in the Democratic Republic of the Congo (DRC) through the PaluSeq (séquençage du paludisme) project. The objective of the project was to strengthen malaria molecular surveillance capacity in the country. The goals are to identify emerging antimalarial drug-resistance mutations in the DRC in near real-time and to train and equip new generations of Congolese malaria molecular epidemiologists. They started with updating national maps of *Plasmodium falciparum* and drug resistance mutations. They are actively enrolling people with malaria symptoms, with a staged roll-out by province, where 9 provinces will be considered. Sequencing of malaria drug-resistance markers will be done on about 14,000 samples collected for the study. The project is also currently training and building capacity in bioinformatics by recruiting Congolese students.

Christian Nsanzabana (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) discussed the potential and hurdles of expanding malaria molecular surveillance (MMS) in Africa. Use cases encompass monitoring drug resistance markers, hrp2/3 deletions, insecticide resistance, and therapeutic efficacy studies (TES). Future applications of MMS include detecting asymptomatic reservoirs, using genomics for transmission tracking, and understanding transmission chains. Molecular markers serve as early warning signs for resistance emergence. Presently, countries like Uganda, Kenya, and South Africa utilize these methods, albeit with limited insecticide resistance markers. Reports of vaccine resistance highlight the need for surveillance to gauge efficacy. Effective sampling strategies are crucial, despite genotyping challenges such as daily parasite density fluctuations and infection complexity. Nsanzabana stressed the importance of integrating molecular surveillance into routine antimicrobial resistance and diagnostic monitoring and advocated for the adoption of Next-Generation Sequencing due to its sensitivity to minor variants. He closed his presentation by pointing out the need for further research to develop predictive models based on molecular markers for efficacy dynamics.

Simone Boene (National Malaria Control Program – NMCP, Mozambique) discussed the utilization of malaria molecular surveillance for programmatic decisions in Mozambique, the fourth-highest malaria burden country. With heterogeneous malaria distribution, key questions revolved around diagnostics efficacy, ACT resistance, transmission sources, and intervention impact. Funded by the Bill & Melinda Gates Foundation (BMGF), the GenMoz project aimed to enhance Next-Generation Sequencing (NGS) capabilities at the Manhiça Health Research Center (CISM), generate local molecular data, and support the National Malaria Control Program (NMCP) in utilizing it effectively. The project addressed five areas: i) antimalarial resistance, ii) diagnostic resistance, iii) transmission stratification, iv) pregnant women's role in assessing community transmission, and v) intervention impact. Findings revealed low hrp2/3 deletion rates, absence of *pfkelch13* mutations, and high quintuple mutant prevalence with low dhps-581 mutations. Three doses of sulfadoxine-pyrimethamine (SP) showed sustained IPTp-SP benefits despite quintuple mutants. Importantly, pregnant women reflected community trends, revealing high genetic complexity in the north. The results

informed NMCP protocols, with the use of a dedicated dashboard for antimalarial resistance markers, demonstrating the integration of molecular diagnostics into national protocols.

Scientific Session 14 – Drug Resistance 1

Alassane Mbengue (Institut Pasteur Dakar, Senegal) presented on the first appearance of partial artemisinin resistance (pArt-R) in Senegal, tracking pArt-R with translational research in the African context. *Plasmodium falciparum* has complex antimalarial resistance mechanisms leading to a long-lasting antimalarial drug resistance problem. This study used a model that combined clinical investigations and fundamental science to determine the genetic diversity of *pfkelch13* and the functional relevance of its single nucleotide polymorphisms (SNPs), where 15 SNPs were detected. The presenter also elaborated on other ongoing projects to strengthen antimalarial resistance surveillance including genome editing and the development of a protocol to generate and screen select transgenic lines.

Emma Filtenborg Hocke (University of Copenhagen, Denmark) presented research linking a novel intron variant (431V) to dihydropteroate synthase (dhps) resistance haplotypes in *P. falciparum* from West Africa. The study aimed to i) investigate the geographical distribution of the novel dhps intron mutation across five African countries, ii) assess the association between the novel mutation and haplotypes lacking the 431V mutation, and iii) examine whether the length of microsatellites is correlated with specific haplotypes. Analysis included 964 samples, with 701 representing full haplotypes and 114 samples containing 431V, including 94 full 431V haplotypes. Her findings indicated that the 431V mutation emerged independently multiple times, without a common ancestor, and recent selection pressures have led to a loss of diversity. The novel mutation was associated with a fitness advantage, likely due to its role in transcription regulation. Moreover, the study demonstrated that the expansion of microsatellites can lead to intron retention.

Balla Gibba (Ministry of Health, The Gambia) presented findings from a therapeutic efficacy study on antimalarial resistance markers in The Gambia. Despite low malaria transmission, the country faces challenges like residual and imported malaria, *hrp*2/3 deletions, and resistance. Seasonal malaria chemoprevention (SMC) was adopted in the country in 2012 with sulphadoxine-pyrimethamine plus amodiaquine (SPAQ). The study aimed to assess mutations in malaria preventive drugs. Clinical cases underwent diagnostic PCR and sequencing, revealing widespread chloroquine resistance. Fixed *dhfr* mutants and the emergence of *K540E* were notable, especially in the eastern region of The Gambia. He highlighted that molecular surveillance is crucial for monitoring local and regional malaria interventions to aid control and elimination efforts.

Nkemngo Francis Nongley (Centre for Research in Infectious Diseases – CRID, Cameroon) presented research on the geographical emergence of sulfadoxine-pyrimethamine (SP) drug resistance associated with *P. falciparum* alleles in co-existing *Anopheles* mosquitoes and asymptomatic human populations across Cameroon. He highlighted the threat posed by mutations to the effectiveness of SP as a chemoprevention tool. In his study, Nongley observed a high infection rate of both *P. falciparum* and *P. malariae* in natural *Anopheles* vectors. Additionally, he noted an increasing frequency of SP mutant alleles in both mosquito and human systems, including the emergence of 1431V alleles and a low frequency of the K540E allele. Nongley emphasized the evolution of mutant *Pmdhfr* and *Pmdhps* haplotype populations within the population. He concluded that the hidden circulation of *P. malariae*

significantly contributes to malaria in Cameroon, often in mixed infections with *P. falciparum*. Nongley called for enhanced molecular surveillance for drug resistance and emphasized the importance of validating the role of novel and emerging mutations in SP drug resistance.

Ntui Vincent Ntui-Njock (University of Buea, Cameroon), assessed the molecular markers *dhfr* and *dhps* of *P. falciparum* resistance to sulfadoxine-pyrimethamine (SP) among pregnant women across various zones. With one in four pregnant women at risk of malaria, intermittent treatment and long-lasting insecticide-treated treated nets (LLINs) are recommended. Despite these interventions, resistance to SP persists. This was a cross-sectional study done between 2019-2022 and it analyzed 3313 clinical samples, revealing *P. falciparum* as the most frequent, followed by *P. malariae* and *P. ovale,* and the highest malaria infection in the coastal equatorial forest zone. A high prevalence of *Pfdhfr* was observed, while *Pfdhps* prevalence was low and no K540E mutation was detected.

Sara Cantoreggi (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) presented a study on antifolate drug resistance in Rwanda. In total, 256 samples were collected from three sites: Bugarama, Nasaka, and Rukara, and then sequenced for *k13* and *mdr–1* mutations. She stated that despite stopping the use of sulfadoxine-pyrimethamine (SP) in 2008, the prevalence of *dhps* and *dhfr* mutations is very high and rising, possibly due to a spill-over from neighboring countries or high cotrimoxazole use in Rwanda. Cantoreggi noted variations in resistance in the three sites. For the *crt* mutation, there was a high prevalence in the sites sampled (highest in Bugarama) and a slow and partial recovery of chloroquine susceptibility. All *k13* mutants were found to be wild types. She further discussed the *ubp1* mutant, stating a low prevalence in Rwanda, highest in Bugarama, where no delayed parasite clearance was reported. There was no selection of *ubp1* mutants in Rwanda. Additional studies are planned to explore the differences in mutations in the three sites and to further investigate the mutations and their implication on antifolate drug resistance.

Jacques Mari Ndong Ngoma (University of Health Sciences – USS, Gabon) discussed the rise of *dhfr* and *dhps* quintuple mutation in *P. falciparum* samples from sentinel sites in Gabon. The study aimed to compare molecular resistance markers to sulfadoxine-pyrimethamine (SP) in rural and urban areas. From 2014 to 2018, this prospective study gathered samples from febrile children, with more from rural settings. *Dhfr* frequency was higher in rural than urban areas, with unique *dhps* mutations in rural locales. Absent in urban settings, quintuple mutations may stem from rural self-medication and parasite recombination. Continued molecular surveillance and genetic analysis are crucial for understanding parasite dynamics in both urban and rural regions.

Moussa Diallo (Cheikh Anta Diop University – UCAD, Senegal) presented research on the evolution of *Vgsc-1014*, *Acel,* and *Gste2* mutations and their potential implications for the use of insecticides in Indoor Residual Spraying (IRS) to control *Anopheles gambiae* s.l. in Senegal. Diallo's study traced the presence and evolution of these resistance genes in wild populations of *Anopheles gambiae* s.l. collected at various time points corresponding to shifts from pyrethroids to carbamates and then organophosphates, which are used for IRS in selected health districts of Senegal. Spatial and temporal analyses revealed the evolution of *Vgsc-1014, Acel,* and *Gste2* mutations in certain hotspots across Senegal since 2013. While Acel and Gste2 mutations were detected at a low frequency, their spread poses a concern that could negatively impact vector control efforts in the country. Towards the end of his talk, Diallo recommended further studies to monitor the distribution and evolution of these mutations

and their association with phenotypic resistance to safeguard the effectiveness of limited insecticide-based vector control tools.

Scientific Session 16 – Treatment and case management 1

Margaret Ebob Besem (Reach Out NGO, Cameroon) explored the challenges of accessing community health services for malaria in conflict-affected areas in Cameroon. Several factors such as limited healthcare infrastructure, displacement, and insecurity hinder access. Besem presented innovative approaches such as community dialogue to enhance knowledge and practices. Community health workers face limitations due to conflict, necessitating improved training and supply systems. While cash assistance helps, it is most effective alongside functional health facilities. Besem concluded her presentation by highlighting the importance of coordinated implementation of these strategies to alleviate malaria burden and improve health outcomes in vulnerable populations.

Rowartz Kevin (Kisii County Government, Kenya) presented a promising healthcare approach that utilizes community health volunteers (CHVs) to manage malaria cases at the grassroots level which showed a significant improvement in primary healthcare delivery. By involving CHVs in case management, the time taken to administer treatment decreased, resulting in better patient outcomes. Additionally, this approach alleviated the burden on higher-level healthcare facilities. Continuous support and capacity building for CHVs were key factors contributing to lower morbidity and mortality rates. Kevin recommended integrating CHVs into the formal health system to ensure the sustainability of these benefits and further enhance health outcomes in malaria-endemic regions. This approach not only improves access to healthcare but also empowers communities to take charge of their health.

Paul Boateng (National Malaria Elimination Program – NMEP, Ghana) highlighted an important aspect of malaria management, emphasizing that not all malaria admissions necessarily indicate a severe case. In Ghana where malaria is endemic, individuals may be admitted to healthcare facilities for malaria treatment even if their condition is not severe due to patient concern, healthcare provider caution, or local healthcare protocols. The study aimed at understanding the relationship between admission rates and the severity of malaria cases. The key finding suggests that while many people are admitted for malaria treatment, not all of them have severe forms of the disease. This finding could have implications for healthcare resource allocation, treatment protocols, and public health strategies aimed at malaria elimination.

Tonny Wambua (Population Services, Kenya) provided valuable insights into the impact on facility workload in his presentation on implementing community case management of malaria in Busia County, Kenya. The increase in the number of Community Health Units (CHUs) practicing Community Case Management of malaria (CCMm) from 24% to 84% resulted in a significant rise in patients receiving interventions at the community level. Key findings included a notable increase in the number of malaria patients tested at the community level, rising from 14% to 54%, and patients treated increased from 9% to 58%. Conversely, there was a drastic decrease in testing and treatment numbers at the facility level, dropping from 91% to 42% and 86% to 46%, respectively. These figures highlight the impact of CCMm in reducing the workload at health facilities. Erratic commodity supplies, however, have the potential to undermine the gains made in implementing CCMm. To address these challenges, Wambua recommended continuous capacity building and supportive supervision

of Community Health Practitioners (CHPs). Additionally, he emphasized the need for further analysis and study on severe malaria incidences at health facilities to inform future interventions effectively.

Elizabeth Ayuk Ndip (Reach Out NGO, Cameroon) discussed malaria case management by Community Health Workers (CHW) in conflict-affected areas of the Southwest Region of Cameroon. She gave an overview of epidemiological data on the malaria burden in Cameroon and further emphasized that CHWs are instrumental in getting malaria interventions to the communities even though they are not trained to manage severe malaria cases. The study was targeted at scaling up diagnosis, treatment, creating awareness, distribution of malaria interventions such as insecticide-treated nets (ITNSs), referrals, and review of report and matrix. Results showed a steady reduction in malaria between January and December 2023 particularly between July and September. More men tested positive than women and children. The study was significant in the availability of CHW through which malaria intervention gets to communities as well as building the trust of residents in them. Finally, she emphasized the need for the recruitment of CHWs due to their closeness and intimacy with the residents and being the first-line health respondents.

Muhammed Afolabi (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) addressed the development of a simple pragmatic tool to improve the documentation of severe malaria in a post-Ebola community in northern Sierra Leone. It was a pilot study for the Ebola vaccine trial. He reiterated the importance of data in providing valuable insights into disease burden in a population in the health care system. Tools developed included staff training, chief complaints, draft tool, feedback incorporated, emergency trial assessment and treatment (ETAT) and training, etc which were tested between August 2019 and July 2021 in Kambia. Results showed that severe malaria occurred more in children between ages 1-14 months. He explained that some of the factors affecting clinical outcomes included neonatal age (0-27 months), underage, poverty, distance to the hospital, non-operation of the hospitals after staff closing hours of 4 pm, etc. The study showed that malaria and severe malaria are the major causes of admission and death respectively, limitation of rapid diagnostic test (RDT), overdiagnosis, and standardizing documentation of admissions and outcomes.

Scientific Session 17 – Pathogenesis and co-morbidities 1

Andrea L. Conroy (Indiana University, United States) talked about ferritin's role in severe malaria and its correlation with mortality. Conroy and colleagues conducted a cohort study in Uganda with 1300 children (community children without malaria and children with severe malaria symptoms). Ferritin levels were measured at enrollment, and children were followed for a year. The study found higher ferritin levels in children with severe malaria, remaining high in survivors up to a month after the onset of symptoms. Study findings also revealed a correlation between severe malaria complications and ferritin levels. Moreover, an elevated level of ferritin was linked to higher all-cause mortality risk and predicted recurrent hemolytic events in children post-discharge. Based on these findings, Conroy suggests the use of ferritin as a biomarker for identifying children at risk of hemolytic complications and increased long-term mortality.

Katja Wyss (Karolinska Institute, Sweden) conducted a prospective cross-sectional study in two hospital settings in Cameroon to explore the association between diabetes, obesity,

metabolic syndrome, and severe malaria in adults. The research revealed that type 2 diabetes and metabolic syndrome are associated with severe malaria in both patients diagnosed outside malaria-prone areas and adults diagnosed in high-endemic regions. Obesity was also associated with malaria severity in endemic settings, and Wyss suggested considering comorbidities in managing malaria patients, regardless of endemicity. Moreover, in regions with high incidences of both diseases, screening for diabetes alongside malaria treatment could be beneficial.

Samuel C. Wassmer (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) presented the effects of *P. falciparum* infection on the brain, focusing on cerebral malaria (CM). Wassmer assessed brain swelling in 176 CM patients in India. In the study, fatal CM in children was linked to severe brain swelling, while in adults, it was associated with hypoxic injury and high plasma levels of S100B. The study also showed brain involvement in severe non-cerebral malaria (SNCM), suggesting a broader impact of the disease. Additionally, higher kidney impairment was linked to more severe hypoxia, leading to the hypothesis of a kidney-brain pathogenic axis. Wassmer highlighted the need for further research to better understand the long-term effects of *P. falciparum* malaria on the adult brain.

Rosauro Varo (Barcelona Institute for Global Health – ISGlobal, Spain) presented findings from a matched case-control study in Mozambique that explored the association between host and parasite biomarkers and malaria severity. The study focused on identifying biomarkers in plasma that differ between children with uncomplicated malaria and severe malaria. The goal was to understand how these biomarkers relate to clinical symptoms in severe malaria patients and to assess their connection in uncomplicated and severe malaria. Varo found that HRP-2 reliably predicts SM, independently from parasitemia, and correlates with other biomarkers elevated in SM, such as Angpt-2, Tie-2, sFlt1, and sTREM-1. The study suggested that these biomarkers could enhance the management of malaria with future use in cost-effective point-of-care diagnostics.

Scientific Session 20 – Capacity Building 1

Graziella Scudu (Clinton Health Access Initiative – CHAI, United States) presented an analysis of the anticipated malaria commodities landscape in Sub-Saharan Africa, highlighting potential market disruptions. Collaborating with partners, CHAI developed short- and long-term forecasts to project current and future demand and to identify gaps in supply that can pinpoint where additional resources will be needed. The demand forecast covered rapid diagnostic tests (RDTs), treatments, insecticide-treated nets (ITNs), indoor residual spraying (IRS), and seasonal malaria chemoprevention (SMC). The analysis involved integrating historical data, statistical analysis, transmission modeling, and partner input for additional context-specific information. Projections suggest increased demand for all commodities except IRS, attributed to population growth. SMC is anticipated to expand to more regions and age groups. Global funding constraints will affect vector control volumes, intervention choices, and product selection.

Hulda Shaidi Swai (Nelson Mandela African Institution of Science and Technology – NM-AIST, Tanzania) emphasized the potential of nanotechnology in combating malaria by manipulating matter at the atomic level. Nanocarriers can traverse biological barriers, aiding in drug delivery. Nanomedicine offers promise in reformulating existing drugs to enhance bioavailability and prolong drug efficacy in the bloodstream. Swai aims to utilize

nanotechnology to develop nano-encapsulated malaria drugs targeting parasites in the liver stage. She envisions establishing a regional nanotechnology hub to drive research, innovation, and commercialization in health solutions. However, challenges such as lack of infrastructure, expensive equipment, and funding hinder progress. Creating regional hubs could mitigate these obstacles and facilitate the advancement of nanotechnology applications.

Taneshka Kruger (University of Pretoria, South Africa) presented training aimed at enhancing leadership and management capacities among senior leaders, managers, and specialists within the National Malaria Control Program (NMCP) involved in the Southern Africa Development Community (SADC) malaria elimination initiative across eight countries (SADC E8). The training focused on equipping participants with vital leadership skills, effective management techniques, and decision-making tools to navigate dynamic situations while also providing networking opportunities. Strengthening leadership and management capabilities is crucial for advancing the malaria elimination agenda and ensuring the establishment of resilient public health systems in the region. Plans include expanding training to other SADC NMCPs beyond E8 and involving additional consortia in training delivery.

Amu Mudenda (Faith Leader Advocacy for Malaria Elimination – FLAME, Zambia) presented on Southern African leaders' efforts to garner broad-based and high-level national support for malaria through FLAME, stressing the importance of local country ownership and multisectoral commitment. He highlighted the significance of faith leaders as influential figures deeply embedded within communities, testifying to their ability to bridge gaps between government and citizens. Examples from Namibia and Zambia demonstrated how faith leaders contribute to policy adoption, strategy implementation, and securing necessary funding for malaria eradication. Notably, Mudenda emphasizes FLAME's decentralized approach tailored to local contexts, with partnerships with various stakeholders and sustained advocacy efforts. In his presentation, Mudenda underscored faith leaders' autonomy and commitment to community welfare, positioning FLAME as a transformative movement driving malaria elimination efforts in the region.

Rosalia Joseph (Pan-African Mosquito Control Association – PAMCA, Kenya) presented on leadership capacity building of African women in malaria and other vector-borne diseases through training in effective communication and professional development. Joseph showcased a workshop designed to enhance women's leadership and communication skills, involving 25 participants from 17 African countries. Conducted in collaboration with expert consultants, the workshop focused on effective communication and leadership, and participants' reports indicate a positive impact on career advancement and confidence. However, limited knowledge transfer and funding constraints were highlighted as key challenges. Towards the end of her presentation, Joseph advocated for sustained investment in women to strengthen disease control efforts, emphasizing the importance of holistic approaches and partnerships.

Welmoed Van Loon (Charité – University Medicine Berlin, Germany) presented on the emergence of partial artemisinin resistance in Africa, posing one of the most significant threats to malaria control. Van Loon highlighted the threat of partial artemisinin resistance, characterized by delayed parasite clearance and in vitro resistance, particularly in East Africa. Urgent priorities include understanding the spread and significance of K13 variants, strengthening the molecular surveillance capacity, and identifying risk factors. Their objectives include building capacities, characterizing mutations, and extending in vitro

confirmation. The next steps involve data dissemination, risk factor analysis, and preparation for treatment trials. Finally, his next efforts will focus on fostering on-site research, developing improved surveillance methods, and enhancing polymerase chain reaction (PCR) tests to address this critical challenge in malaria control.

Plenary Session 7 – Climate changes and its impact on malaria elimination

Peter Gething (Curtin University and Telethon Kids Institute, Australia) gave a talk on the intersection of climate change and malaria, emphasizing the health risks associated with climate change and its impact on malaria outcomes. He introduced the climate vulnerability index, attributing 67% of the carbon footprint implicated in climate change to ten countries. Gething highlighted that the fifty countries most vulnerable to climate change are predominantly low-income or lower-middle-income countries, most of them located in the African continent. He discussed historical climate-malaria relationships and showcased how mechanistic models have been utilized to visualize the anticipated changes in climate and their potential impact on malaria transmission. Gething pointed out the worsening state of climate change in Africa and the need for tailored strategies for both mitigation and adaptation. He referenced projections by the Intergovernmental Panel on climate change (IPCC) through five 'Socioeconomic Pathway' scenarios to address the effects of malaria. Gething pointed out fluctuations in health expenditure, particularly a significant decrease in 2020 likely due to the pandemic. He concluded his talk by stressing the need for increased funding to address the effects of climate change on malaria outcomes in the most vulnerable countries in Africa.

Abdisalan Noor (Harvard University, United States) focused his presentation on the estimated direct effects of climate change on malaria. Noor described climate change as a 'Great Displacer', stressing its role in disrupting malaria prevention efforts, limiting access to healthcare services, and contributing to disease outbreaks such as malaria. He underscored that climate change poses a serious threat to development trajectories and health systems. He further emphasized the programmatic implications of the relationship between climate change and malaria, emphasizing the need for a strategic, technical, global, and operational approach to the global response. He advocated for investments in research and development and insisted on the necessity of securing funding to effectively address the intersection of climate change and malaria.

Scientific Session 23 – Malaria in Pregnancy 3

Claudia Demarta Gatsi (Merck KGaA, Germany) presented findings from non-clinical studies supporting accelerated inclusion of pregnant women in clinical trials with cabamiquine. Specifically, findings from the Developmental and Reproductive Toxicity (DART) studies on embryo-fetal development (EFD) and pre-and postnatal development (PPND) toxicology in rats using cabamiquine during pregnancy were presented. Gatsi reported a promising non-clinical safety and efficacy profile of cabamiquine for malaria prevention or treatment during the first trimester. She asserted that the data package from the studies supports the inclusion of pregnant women and/or women of childbearing potential in earlier stages of clinical developmental studies evidence. With this talk, Gatsi emphasizsed the critical need to address the medical needs of pregnant women and children in malaria prevention.

Oscar Okoth (Kisumu Medical and Education Trust, Kenya) presented research data on the revitalization of intermittent preventive treatment of malaria in pregnancy (Revive IPTp-SP) project, which piloted a self-care intervention to promote the uptake of sulfadoxine-pyrimethamine (SP) for IPTp in Suna West-Migori and Kisumu counties, Kenya since 2021. The study aimed to empower and sensitize pregnant women on the importance of the use of SP and improved access to the drug at the community level. Results showed a noticeable increase in SP usage in both sub-counties and a rise in the number of pregnant women who received the recommended 3+ doses. Hence, Okoth concluded that self-care interventions to promote the uptake of SP be a promising approach to improving health outcomes of malaria in pregnancy in communities.

Yvonne Dube (University of Melbourne, Australia) presented the Malawi IMPROVE cohort study, a study on placental malaria involving pregnant women at mid-pregnancy. The study was conducted to address the lack of a specific VAR2CSA vaccine, despite progress with vaccines based on other parasite antigens. In the study, Dube utilized a systems serology approach to investigate whether antibodies to antigens other than VAR2CSA contribute to protecting against malaria in pregnancy. From her preliminary results, Yvonne concluded that antibodies to non-VAR2CSA proteins may serve as markers of exposure to malaria in pregnancy rather than markers of protection, as they showed no association with protection against malaria in pregnancy.

Scientific Session 24 – Control and Elimination 2

Esdras Mahoutin Odjo (National Malaria Control Program, Benin) evaluated whether the prolonged residual efficacy of clothianidin resulted in a greater reduction in vector populations and subsequent malaria transmission compared to the shorter residual efficacy of pirimiphos-methyl (PM 300 CS). Mosquitoes were sampled using human landing catches (HLC) and pyrethrum spray catches (PSC) from six communities selected and monitored for indoor residual spray (IRS) between 2019 and 2021. A total of 50,645 mosquitoes were collected with *Culex quinquefasciatus* (58.5%) being the most predominant, followed by *An. gambiae* (38.8%). The human biting rate, entomological inoculation rate, and sporozoite rate were assessed and showed no overall impact between clothianidin + deltamethrin and clothianidin alone due to its slow activity. The biting rate was found to be greater with PM 300 CS.

Nancy S. Matowo (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) assessed the effectiveness of dual-active ingredient long-lasting insecticidal nets (LLINs) on major malaria vectors through a secondary analysis of a three-year cluster randomized controlled trial in rural Tanzania. In 2019, over 140 thousand nets including Olyset Plus, Interceptor G2, and Royal Guard all dual active-ingredient (AI) long-lasting insecticidal nets) and Interceptor was distributed in Misungwi to evaluate the entomological inoculation rate (EIR) as an indicator for malaria transmission in both *An. gambiae* and *An. funestus*. Mosquitoes were collected using CDC light traps. Interceptor G2 showed the best activity reducing the EIR from 92% in year 1 to 64% in year 3. All three dual AI LLINs had a strong effect on *An. funestus* which is the main malaria vector in the study area.

Bless Hayford (7th Day Adventist Hospital, Ghana) presented the demographic and socio-economic factors influencing bed net ownership, usage, and malaria transmission among adult patients seeking healthcare in two urban cities in Ghana. Bed net usage was more prevalent among vulnerable groups in rural communities compared to urban areas with low

bed net coverage. Venous and capillary blood samples were collected from 550 participants for malaria microscopy, parasite detection, density calculation, and species identification in two hospitals: the 7th Day Adventist hospital and the Sunyani Municipal Hospital, spanning from January to September 2021. The malaria prevalence was 7.8%, with only 21.5% of participants reporting sleeping under bed nets, and 83 % of the malaria-positive patients earning less than $150 per month. The majority of participants were female between 18 and 30 years old, indicating that malaria is endemic among adult populations in Ghana overall.

Mavuto Mukaka (University of Oxford, United Kingdom) conducted a study on the safety of age-based regimens of primaquine for uncomplicated *Plasmodium falciparum* infection in G6PD African children through a randomized control trial. The objective was to gather pharmacokinetic data on single low-dose primaquine (SLDPQ) for transmission-blocking in African children. Children aged 6 months to 11 years with acute uncomplicated *P. falciparum* infection were included. The study utilized a novel age-based regimen with five age bands, while controls received ACTs. Results indicated variable primaquine exposure depending on body weight-adjusted dose, age, baseline hemoglobin, and CYP2DC metaboliser status, not on G6PD status. The data supports age-dosed SLDPQ for transmission-blocking in Sub-Saharan Africa, aligning weight-based regimens with ACTs.

Blessings Msango Kapumba (Liverpool School of Tropical Medicine – LSTM, United Kingdom) presented an ethnographic study on the Shire Valley Transformation Programme (SVTP) in southern Malawi, a large-scale irrigation plan implemented in an area with high malaria and schistosomiasis risk. SVTP involves a shareholder-owned commercial farming enterprise (SOCFE), where landowners lease land for shared farming from SOCFE, which also controls water distribution. The ShireVec vector control program conducted the study to comprehend participants' experiences and perspectives. Participants noted that improved water access could enhance socio-economic status but might also lead to increased migration and risks of vector-borne diseases. Lack of trust in government and authorities raised concerns about over-promises, under-delivery, and reduced land access.

Orezi Adhekoyibo (Catholic Relief Fund, Nigeria) presented a study on integrating seasonal malaria chemoprevention (SMC) and insecticide-treated nets (ITNs) in Kwara State, Nigeria. The study objective was to assess the effectiveness, efficiency, and cost-benefits of these two interventions. Methods involved door-to-door household mobilization and SMC administration followed by ITN distribution at designated points. Both interventions saw significant improvements in coverage and acceptance. Cost-efficiency analysis revealed savings of over $200,000, representing 20% of the original budget. Additionally, the project enhanced campaign personnel's capacity by providing training in the administration of both interventions and in optimizing the utilization of resources. Adhekoyibo concluded that integrating ITN and SMC campaigns was efficient, effective, and scalable, especially in settings like Kwara State with limited resources and large populations.

Ruth Boniface Mbwambo (University of Nairobi, Kenya) presented a cross-sectional study conducted in five regions of Tanzania to enhance understanding of bed net use, misuse, and misconceptions. The study collected data on demographics, socio-economic status, land use, and malaria control practices, followed by statistical analysis. Female participation and acceptance exceeded that of males in all regions. In Kagera, the region with the highest malaria prevalence, low bed net ownership and use were noted. However, overall, the study found high ownership and proper use of bed nets. Misuse and misconceptions were minimal,

with the most common misconception being that bed nets reduce sexual pleasure, and the most common misuse being repurposing nets for the fences to contain poultry.

Scientific Session 26 – Insecticide resistance 2

Fleuriane Metissa Djondji Kamga (Centre for Research in Infectious Diseases – CRID, Cameroon) presented the contrasting roles of *Asaia* spp bacteria in mediating pyrethroid resistance escalation in *Anopheles funestus* and *Anopheles gambiae* thereby addressing the gap in knowledge regarding the influence of *Asaia* spp. in the context of insecticide resistance within Cameroon. The bacterium works by detoxifying insecticides, thereby affecting the susceptibility of mosquitoes to insecticide treatments. She found that *Asaia* was associated with resistance phenotype and genotype in *An. funestus* hybrids mosquitoes. A negative correlation between the abundance of the symbiont and permethrin resistance phenotype and genotype was observed with *An. gambiae* hybrid mosquitoes. This result laid the groundwork for understanding bacterial mechanisms in the exacerbation of pyrethroid resistance in malaria vectors. Kamga closed his talk by highlighting the need for additional studies to better understand how *Asaia* bacteria could contribute to this process and how this varies between different vector species.

Carlos Simeon Djoko Tagme (Centre for Research in Infectious Diseases – CRID, Cameroon) found that a single mutation (G454A) in the P450 CYP9K1 enzyme causes pyrethroid resistance in *Anopheles funestus* mosquitoes in East and Central Africa. Ugandan samples from 2014 showed reduced diversity, with the G454A mutation fixed. Over six years, this mutation became prevalent in Cameroon but remains absent in Ghana and Malawi. The mutated allele metabolizes pyrethroids better, increasing resistance in transgenic *Drosophila melanogaster*. DNA-based diagnostics using the G454A marker accurately detect pyrethroid resistance, suggesting its inclusion in monitoring tools for *An. funestus* populations in Eastern and Central Africa.

Cynthia Awuor Odhiambo (Jomo Kenyatta University of Agriculture and Technology, Kenya) used a weighted gene co-expression network analysis (WGCNA) algorithm, a systems biology approach, to identify genes with similar co-expression patterns and hub genes that are potential molecular markers for insecticide resistance surveillance in Kenya and Benin. A total of 20 and 26 gene co-expression modules were identified via the average linkage hierarchical clustering from *Anopheles arabiensis* and *An. gambiae*, respectively, and hub genes (highly connected genes) were identified within each module. Four specific genes stood out: serine protease, E3 ubiquitin-protein ligase, cuticular protein RR2, and leucine-rich immune protein, which were top hub genes in both species and could serve as potential markers and targets for monitoring insecticide resistance in these malaria vectors.

Isaiah Debrah (West Africa Centre for Cell Biology of Infectious Pathogens – WACCBIP, Ghana) presented his research on the mechanisms of pyrethroid resistance in *Anopheles funestus* populations in Western Kenya. He identified several non-coding RNAs (ncRNAs) as potential players in this phenomenon. Non-coding RNA refers to RNA molecules that do not encode proteins but play various regulatory roles in the cell. These were found to influence the expression of genes involved in detoxification pathways and target site insensitivity resulting in mosquito insecticide resistance. His study observed pyrethroid resistance in all the sites with an average mortality rate of 57.6%. Identifying specific ncRNAs involved in pyrethroid resistance in *Anopheles funestus* populations is crucial for understanding the

underlying mechanisms and developing strategies to combat resistance. Debrah underlined the need for further research on the functional roles of these ncRNAs and their interactions with target genes to gain more in-depth insights into the biology of resistance and potential avenues for intervention.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

Day 4: Thursday, 25th April 2024

Plenary Session 8 – Immunology and Pathogenesis

Faith Osier (Imperial College London, United Kingdom) discussed immunity mechanisms against *Plasmodium falciparum* malaria, highlighting the persistence of resistance threats despite the development of two vaccines. Immunity acquisition varies by age (infants appear to acquire immunity faster than older children, but have a higher risk of developing severe forms of malaria and anemia), with asymptomatic cases being more common in high-prevalence areas. Immunoglobulin G (IgG) antibodies from individuals with previous malaria exposure confer a certain degree of immunity. The study on mechanisms of immunity against *Plasmodium falciparum* focused on the role of merozoite antigens in immunity, utilizing volunteer malaria infections to analyze parasite dynamics. Volunteers were selected based on malaria exposure, with some exhibiting exponential parasite growth, others clearing parasites without symptoms, and some experiencing self-clearance. Cytophilic IgG1 and IgG3 were notably prominent, indicating their significance in protection. Furthermore, IgG Fc function is strongly correlated with protection, underscoring the potential for merozoite antigens in vaccine development, though further assessment is required to identify crucial antigens.

Lars Hviid (University of Copenhagen, Denmark) presented on IgG targeting *P. falciparum*-infected erythrocytes beginning with an explanation of the parasite's life cycle and a discussion on natural and acquired immunities. He emphasized the differences between natural and vaccine-induced immunity concerning antigens found in infected erythrocytes (IE,) including differences in target epitopes (complex vs. linear) and effector functions, such as post-translational modifications like Fc-afucosylation. Additionally, he underscored the differentiation between neutralization and opsonization in immune responses. Hviid also advocated for prioritizing basic research and suggested that malaria vaccine development should be guided by studies of natural immunity, notwithstanding current successes in vaccine development.

Symposium 54 – Leveraging genotyping for therapeutic efficacy studies in malaria endemic countries: towards a standardized approach from next generation molecular techniques to data analysis

Aurel Holzschuh (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) compared different techniques to distinguish recrudescence infections from new infections in antimalarial drug efficacy trials. The genotyping methods included fast capillary electrophoresis (QIAxcel), high-resolution capillary electrophoresis (ABI3730XL), high-resolution melting analysis (Quantstudio 5), targeted amplicon deep sequencing (Illumina Miseq) and nanopore amplicon sequencing (AMPSeq). Four *P. falciparum* lab-strains (3D7, K1, HB3, FCB1) were used to mimic patient samples and were assessed by the same operator at different weeks. The AMPSeq and high-resolution capillary electrophoresis showed the highest sensitivity and genetic diversity in detecting minority clones and were very robust. The markers used by the AMPSeq were the most consistent in distinguishing recrudescence from new infection. The nanopore technologies provided fast PCR-corrected estimates of drug failures at a low cost and since it is portable they could become an effective alternative genotyping tool in sites with minimal laboratory infrastructures. The nanopore technologies provided fast PCR-corrected estimates of drug failures at a low cost and, since it is portable, they could become an effective alternative genotyping tool in sites with minimal laboratory infrastructures.

Marko Bajic (Centers for Disease Control and Prevention – CDC, United States) presented laboratory considerations for molecular correction using targeted amplicon deep sequencing. Overall sequencing involves several techniques from sample collection, DNA extraction, genomic targeting and amplification, library preparation and next-generation sequencing. One of the metrics upon which the choice of a specific sequencer depended was the number of desired reads. Bajic highlighted the importance of considering targeting amplicons for molecular correction since it helps in differentiating between single nucleotide polymorphism (SNPs) and haplotypes; and also the importance of designing shorter amplicons with sufficient sites of diversity. This study showed that next-generation sequencing (NGS) based molecular correction defines amplicon capability, identifies the right targets, communicates mutation rates and ensures this approach can be utilized.

Sam Jones (Liverpool School of Tropical Medicine – LSTM, United Kingdom) presented a study on matching algorithms and simulations to distinguish recrudescence infections from reinfections. He emphasized the necessity for algorithms due to the imperfections in genotyping methods. Jones highlighted two main algorithms: i) Match counting algorithms, widely used since the introduction of molecular correction, ii) A Bayesian algorithm published in 2015 for microsatellites, with ongoing work to expand it for various alleles such as msp-1 and msp-2. He described the simulation environment and how it aided in distinguishing true recrudescence based on the density of alleles, with expert knowledge being incorporated to quantify the detection of alleles. Jones noted that different algorithms applied to the same field data yield varying percentages of recrudescence/reinfection, affecting efficacy assessments. He concluded that match count simulations demonstrate a high ability to detect minority clones, enabling accurate classification even in a high multiplicity of infection (MOI)/force of infection (FOI) scenarios.

Monica Golumbeanu (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) discussed the considerations involved in analyzing genotyping data for molecular correction in malaria drug trials. She outlined the key steps for molecular correction, including the selection of markers, genotyping experiments, data analysis, extraction of genotypes, and classification of infections. Golumbeanu emphasized the attributes of good markers for molecular correction, such as high allelic density and low allelic frequencies. Additionally, she highlighted several microsatellites commonly used in various studies and mentioned the availability of several pipelines for identifying haplotypes. Golumbeanu explained an automated algorithm for identifying alleles and described the process of identifying haplotypes from amplicon sequencing data, which involves removing primer sequences from samples, aligning reads to a reference genome, and identifying single nucleotide polymorphism (SNPs). She concluded by noting that different markers and techniques may yield different results, emphasizing the importance of careful consideration in data analysis.

Sara Cantoreggi (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) discussed the assessment of various techniques and markers to distinguish recrudescence from new infections in a therapeutic efficacy study conducted in Rwanda. She explained the Rwanda WHO therapeutic efficacy studies (TES) conducted in 2018 at three sentinel sites in Rwanda, where genotyping was performed. Cantoreggi aimed to reanalyze the samples, examine the genetic diversity of genetic markers, conduct analyses with different marker combinations and algorithms, and compare the results to those obtained previously by Rwanda Biomedical Centre/Centers for Disease Control and Prevention Rwanda. She analyzed samples for length polymorphism and single nucleotide polymorphism (SNP) richness and performed a recrudescence versus reinfection analysis. Cantoreggi concluded that the results were consistent with the WHO algorithm based on marker combinations. She identified eight recrudescences which did not originate from the same eight sample pairs.

Discordant cases were attributed to high allelic frequency and low sensitivity in detecting minority clones.

Symposium 56 – Evidence for Strategies to Address Challenges to Malaria Elimination in African Settings

Japhet Matoba (Macha Research Trust, Zambia) discussed the general challenges in eliminating malaria across Africa. Matoba highlighted the rise in the global malaria burden since 2022. Ten countries have successfully eliminated malaria globally since 2016, thanks mainly to robust healthcare systems equipped with targeted vector control, decentralized surveillance, early case detection, effective diagnosis and treatment, and community-based workforce engagement. The WHO recommends tools and innovations for malaria elimination, including chemoprevention and targeted surveillance to prevent outbreaks and re-establishment among pre-elimination countries. However, in Africa, challenges persist due to low transmission near high-intensity areas, infrastructure variations in surveillance, and unknown impacts of interventions. While new tools are necessary, innovative use of current WHO-approved methods like chemoprevention and targeted surveillance can help achieve elimination goals.

Safia Mohamed Ali (National Malaria Control Programme – NMCP, Tanzania) discussed the rise in malaria cases in 2023. Zanzibar had made good progress in fighting malaria over 15 years, bringing overall cases below 1%. However, in 2023, there was a big increase, with over 19,174 cases, mainly acquired locally. This rise, especially in the west urban region of Unguja island, one of the islands of Zanzibar archipelago, affected mostly males aged 15-45, including students, builders, security guards, tourists, and bodaboda drivers. Challenges for malaria control like climate change, different mosquito types, poor sanitation, and low bed net use were highlighted. Zanzibar is responding to those challenges with different strategies indoor residual spraying, mass drug administration, reactive case detection, and health promotion focused on environmental sanitation. To conclude, she stressed the need for multi-sectoral engagement to catalyze resource mobilization for sustained malaria control in the country.

Davis Mumbengegwi (University of Namibia, Namibia) presented on targeted effective malaria interventions in low transmission settings, focusing on reactive focal mass drug administration (RFMDA) and reactive focal vector control (RAVC) in Namibia. Despite Namibia's heterogeneous malaria distribution, primarily in the northern Zambezi region, where 85% of the burden lies in the northeast, the country initially set a goal for elimination by 2022, later revised to 2028. Malaria diagnosis is an important aspect of malaria control which relies on rapid diagnostic tests (RDTs) and microscopy, and is facing challenges like low parasitemia and asymptomatic cases. The study evaluated the feasibility and effectiveness of RFMDA and RAVC, comparing them with reactive case detection (RACD). Results showed a 46% reduction in incidence with RFMDA, 50% with RAVC, and 72% reduction when they were combined. Safety assessments revealed few adverse events, indicating RFMDA and RAVC as safe, acceptable, and efficacious interventions for malaria control in Namibia's low transmission settings. He recommended future studies with longer implementation and follow-up periods to better assess contributions made by each of the two interventions.

Japhet Chiwaula (National Malaria Elimination Center, Zambia) presented a malaria case investigation using the 1-3-7 approach in Choma district, Southern Zambia, aligning with the national elimination strategy to achieve equitable access to quality health services. Their vision was a malaria-free Zambia, aiming to eliminate local malaria infections by 2021 and to prevent reintroduction post-elimination. The 1-3-7 approach involves reporting passive cases on day one, classifying cases by travel history on day three, and conducting focus investigations on day seven for targeted interventions. Effectiveness and implementation

were assessed through zonal randomized studies and mixed methods, respectively. Results showed decreased incidence in 1-3-7 implementation areas, improved community service delivery, and high acceptability among respondents, although challenges with network coverage were common. Community health workers reported enhanced visibility and increased community healthcare-seeking behavior due to the 1-3-7 approach, indicating its positive impact on malaria control efforts in the region.

Chishala Lukwesa Siame (Southern Africa Development Community – SADC, Botswana) presented a collaborative approach to address equity barriers among targeted cross-border populations in the elimination 8 (E8) region. E8 comprises eight countries (Botswana, Eswatini, Namibia, South Africa, Angola, Mozambique, Zambia, and Zimbabwe) working across borders to eliminate malaria in southern Africa by 2030. The objectives include coordinating and engaging countries and stakeholders, advocating for sustained commitment and resources, and harmonizing systems for malaria elimination. A regional equity assessment using the malaria matchbox assessment toolkit was conducted due to high migration levels and migrant populations' disconnection from health services. The methodology involved desk reviews, focused group discussions with mobile migrant populations (MMPs), and key informant interviews. Findings identified practical, cultural, gender-related, and service-related barriers. The diverse characteristics of MMPs require collaborative efforts to enhance access to information, transportation, and men's engagement, and empower community health workers. She stated that a regional community engagement strategy was developed to integrate MMPs into regional strategies and improve access to products and services, highlighting a multi-stakeholder approach.

Scientific Session 27 – Drug Resistance 2

Brenda Wanjiru Muriithi (Kenya Medical Research Institute – KEMRI, Kenya) reported a study that was based on assessing the stability of the amodiaquine, lumefantrine, and piperaquine-resistant *Plasmodium berghei* parasites using a standard 4-day suppression test and identifying nonsynonymous mutations in selected transporters associated with the drugs. Sequencing analysis of the amplified MIT2 fragment revealed a deletion mutation in amodiaquine resistant parasites suggesting that continued amodiaquine pressure induces a stop codon at position 433 in MIT2 protein *Plasmodium berghei* ANKA. Also, the truncation of the MIT2 protein led to the loss of ligand binding residues at positions 448, 451, and 452 suggesting a loss of function.

Tarama Wendlamita Casimire (National Center for Research and Training on Malaria – CNRFP, Burkina Faso) investigated antimalarial resistance molecular markers of Artemether-Lumefantrine (AL), Dihydroartemisinin-Piperaquine (DP), or artesunate-pyronaridine (ASPY) in children aged 6 months to 12 years. The study treated and followed up patients for 28 or 42 days across three health districts with different malaria transmission, focusing on genes linked to drug susceptibility. No significant artemisinin resistance mutations were found, but a minor (1%) *pfk13* mutation (A578S) was observed across all sites. The *pfmdr1* Y184F mutation, associated with lumefantrine resistance, was prevalent, though with low occurrence of mutations linked to Sulfadoxine-Pyrimethamine (SP) resistance. Overall, the findings suggest the continued efficacy of artemisinin derivatives and no high level resistance to SP in Burkina Faso. Casimire recommended continuous routine monitoring of antimalarial resistance, including molecular surveillance.

Colin J. Sutherland (London School of Hygiene and Tropical Medicine – LSHTM, United Kingdom) reported a study that recorded evidence of change in the efficacy against African *Plasmodium falciparum* isolates. They measured in vitro susceptibility to dihydroartemisinin (DHA) and lumefantrine in contemporary *P. falciparum* and established an ongoing pipeline

for monitoring parasite phenotypes and genotypes from east, west, and southern Africa. Since 2012, results from parasite isolates indicate reduced susceptibility to DHA, lumefantrine, or both. Genetic analyses highlight specific loci (*pfk13, pfubp1, pfcrt* and *pfap2mu*), indicating adaptation mechanisms unique to African malaria ecology. These findings indicate that parasites with reduced susceptibility exhibit distinct genetic profiles, unlike those responding to artesunate-mefloquine and DHA-piperaquine use. Sutherland proposed that laboratory researchers should take action in response to the early evidence of decreased effectiveness of lumefantrine.

Sarah Volkman (Harvard T.H. Chan School of Public Health and Broad Institute, United States) presented findings from a study in Senegal that evaluated drug resistance in *Plasmodium falciparum* through genetic markers and selective sweeps, using whole-genome sequence data from samples collected over two decades. Results show sharp changes in *Pfcrt-K76T and Pfdhps-A437G* frequencies with the *Pfdhfr* triple + *Pfdhps* A437G parasite is more fit than the wild-type parasite and equally fit compared to the *Pfdhfr* triple mutant. Molecular surveillance in Senegal highlights notable shifts in well-known drug resistance mutations. Multiple selective sweeps across the genome, including novel loci, indicate parasite adaptation to natural selection. Drug susceptibility tests reveal associations between mutations and phenotypes, suggesting additional resistance factors. Volkman emphasized the necessity of a phenotypic assessment and genetic validation of known and novel mutations in Senegal to assess the impact of drug pressure and identify genetic determinants of drug resistance.

Jenna Zuromski (Brown University, United States) presented on the first discovery of *Plasmodium falciparum* Kelch13 (PfK13) gene mutation including R561H in 2024 which has threatened the efficacy of artemisinin combination therapies (ACTs) in Rwanda. Her aim was to obtain DHA resistance phenotypes of malaria isolates in Rwanda and to evaluate sample pooling as an option for high throughput ex vivo Ring-Stage Survival Assays (RSA) Surveillance revealed multiple emerging K13 mutations, some with unknown phenotypes like. Rapid in vitro phenotyping, used in the study, aids in assessing artemisinin partial resistance, but parasite culture adaptation delays identification. The study also involved the implementation of in-country ex vivo ring-stage survival assay (RSA) on fresh isolates from high mutation frequency sites. Zuromski's preliminary results show 11.7% survival post DHA pulse, indicating artemisinin resistance. She proposes analyzing DNA/RNA profiles of pooled samples to understand different phenotypes displayed by pooled vs individual samples.

Stephen Orena (Infectious Diseases Research Collaboration, Uganda) presented findings from a comparative study between standard antimalarials in the periods 2016-2020 and 2021-2023 in eastern and northern Uganda. Samples from uncomplicated *P. falciparum* patients were used for drug susceptibility testing using growth inhibition and ring-stage survival assays to determine the prevalence of validated *PfK13* resistance mutation. The results reveal increasing median IC50 values for various antimalarials, particularly lumefantrine. This finding raises concerns about decreased drug susceptibility and jeopardized efficacy of ACTs, urging ongoing assessment and surveillance efforts. This corresponds to an increased susceptibility to chloroquine over time, alongside a rise in the prevalence of K13 mutations, which are validated markers of artemisinin partial resistance.

Scientific Session 30 – Malaria Genomics 1

Eshetu Molla (Armauer Hansen Research Institute, Ethiopia) spoke on the geographical distribution of *Plasmodium vivax* duffy binding protein (PvDBP) copy number variation in Adama, Arba Minch, Batiu, Dilla, and Gondarzones, Ethiopia. *P. vivax* uses the PvDBP from a single point mutation in the DARC promoter region. Blood samples were analyzed using

microscopy, and qPCR. Parasites were extracted using the magnetic bead extraction method (n=435). There was variation in DARC genotyping and PvDBP copy numbers with 16.6% infection having a single copy, 50.3% having 2-3 copies, and 33.1% having above 3 copies. Also, there was a lower binding affinity of DARC with single copy PvDBP. Parasitemia was linked with different genotyping status although not correlated with PvDBP. He concluded that *P. vivax* detected in Duffy-negative individuals, had a high prevalence of multi-copy PvDBP, and showed a high rate of Duffy-positive related to observed parasitemia across all regions.

Thomas Katairo (Infectious Disease Research Collaboration, Uganda) discussed the performance of molecular inversion probes on MAD4HateR amplicon sequencing for the detection of *Plasmodium falciparum* mutations associated with anti-malaria drug resistance. He pointed out that molecular surveillance is germane in malaria control and there is a need for new genotyping tools with high sensitivity such as molecular inversion probes (MIPs). Six strains of the parasite were used, analysis was limited to single nucleotide proteins (SNP) and parasite densities observation. Results revealed that MAD4HateR recovered genotypes at higher parasitemia while MIPs at lower parasitemia. MAD4HateR works better at all parasitemia except at 10 parasites/µl. He concluded that MAD4HateR has superior coverage and is better for parasitemia detection as compared to MIPs. MIPs are easier to design and good for large-scale surveys but are costlier than MAD4HateR.

Jaishree Raman (National Institute for Communicable Diseases, South Africa) discussed unravelling *Plasmodium* genetic diversity using targeted amplicon deep sequencing to guide elimination interventions in South Africa. The study was conducted in Mpumalanga (MPN) and Kwazulu-Natal (KZU) with routine sample collection (September 2021 and August 2023). Sequencing was done using MAD4HateR for genotyping and complexity of infection (COI) was used to measure diversity. Polyclonal infection was observed in both provinces with a lower and moderate COI in KZN and MPN respectively. There was an observed co-transmission which he suggested may lead to high polyclonal infection and clusters in both KZN and MPN. He concluded that both provinces have a high polyclonality by importation and intra-host relatedness variation.

Nganyewo Nora Nghochuzie (Medical Research Council Unit, The Gambia) presented the genetic Variation in *P. falciparum* invasion ligands and their cognate human receptor variants in malaria cases from The Gambia. Following a targeted approach using some commonly known ligands, some surface genes as well as human receptors, and 16 genes, 288 samples were collected with 23 and 265 severe and mild cases respectively. The samples were collected from 4 health facilities (Basse, Fajikunda, Edward Francis, and Brikama) within the country and were analyzed using a nanopore sequencing technique. This study showed that the continuous arm race between parasite ligands and receptors results in significant diversity in their haplotypes in *P falciparum* and the human population. High inter-SNP LD at both *P. falciparum* genes and human glycophorin B, C, and CR1 genes were observed. CR1 and glycophorin C seem to have important roles in malaria outcomes.

Jane N. Mwangi (Pan African Mosquito Control Association – PAMCA, Kenya) presented the genomic surveillance of *Anopheles arabiensis* in The Gambia which revealed evidence of increased insecticide resistance in coastal populations. The samples were collected in different areas of the west coast, central, and inland regions of the country in 2019. Out of the 661 samples collected, 314 were *An. arabiensis*. Population structure analysis was done showing a clear geographical isolation of *An. arabiensis* from the coast to the others and she noted that it could create a barrier to gene flow. The mosquitoes from the coastal regions were also more resistant to deltamethrin together by having a high single nucleotide polymorphism (SNP) frequency of the L995S and the L995F kdr mutations, and high copy number variation (CNV) compared to the others showing that they are genetically distinct. A

novel carboxylesterase gene cluster was also identified, making it important to investigate a potentially new resistance mechanism to organophosphates.

Scientific Session 31 – Chemoprevention 2

Joel D. Bognini (Research Institute of Health Sciences – IRSS, Burkina Faso & Clinical Research Unit of Nanoro – CRUN, Burkina Faso) discussed on improving intermittent preventive treatment in pregnant (IPTp) women in Mali and Burkina Faso by utilizing the seasonal malaria chemoprevention (SMC) channel in children. The study evaluated IPTp coverage's feasibility, acceptability, and cost-effectiveness when delivered through antenatal care (ANC) and SMC. In Mali, 780 women and 816 children were enrolled, and in Burkina Faso, 810 women and 295 children were included. IPTp-SP3 coverage in Burkina Faso (71%) was similar to SMC coverage (76%). In Mali, SMC coverage (51%) exceeded IPT-SP3 coverage (28%). An integrated approach could boost IPTp-DP3 coverage in Mali by compensating poor access to IPTp through ANC facilities.

Jean Baptiste B. Yaro (National Center for Research and Training for Malaria – CNRFP, Burkina Faso) talked about understanding and maximizing the community impact of SMC in Burkina Faso. The study was a randomized controlled trial aimed to directly quantify how extending SMC to children under 10 would reduce the human infectious reservoir. It consisted of three study arms comprising 62 clusters of three compounds: Arm 1 served as control-SMC in under 5-year-old children, implemented by the MoH without directly observed treatment (DOT) for the full course of SMC, Arm 2-SMC in under 5-year-old children with DOT for the full course of SMC, Arm 3- SMC in under 10-year-old children, with DOT for the full course of SMC. Results showed a notable reduction of malaria infection in intervention arms compared to the control arm. Extending the age of SMC reduced parasite prevalence in children. Therefore, extending the age of SMC has the potential to significantly impact the malaria transmission reservoir.

Hindewe Edgar William Houndjo (National Malaria Control Programme – NMCP, Benin) presented on advancing malaria elimination through a digitized approach, focusing on the case of the 2023 SMC campaign in Benin. He emphasized that malaria remains the leading cause of cases and deaths in hospitals in Benin, particularly affecting children under the age of 5. NMCP implemented an annual SMC for children under 5 in highly endemic areas, resulting in a reduction in malaria cases. Houndjo highlighted how digitization accelerates the goal of achieving wide coverage by facilitating planning, training, and program implementation. Consequently, Benin is extending the SMC drug administration campaign to nine new health zones by 2024. Implementation will be based on the country's new policy of community health in all targeted regions. The digitization of the campaign is planned to be fully implemented by the Ministry of Health through its Information Systems Direction.

Abdul Gafaru Mohamed (National Malaria Elimination Program – NMEP, Ghana) discussed the caregiver's decision to report adverse drug reactions (ADRs) among children receiving SMC in Ghana. Results showed that less than 20% of caregivers whose children experienced ADRs after receiving SMC medication reported the incidents. Factors associated with ADR reporting were awareness, education, residence, and marital status. Mohamed recommended that regular follow-up mechanisms after dosing should be established and strengthened in all intervention districts by the national malaria elimination programs.

Paul Sondo (Research Institute of Health Sciences – IRSS & Clinical Research Unit of Nanoro – CRUN, Burkina Faso) presented on improving the impact of SMC in Burkina Faso. The study was a randomized controlled trial aimed at assessing whether a strategy combining SMC with nutritional supplements (PlumpyDozTM) could improve the protective effect of SMC and

determine whether simultaneous screening and treatment of household members of children receiving SMC could improve the impact of SMC intervention. It was found that adding nutritional supplements to SMC significantly increased the impact (reduction in malaria diagnosis by RDT) of SMC for preventing children from malaria and other childhood infections. Screening and treating other household members lead to a significant reduction in the incidence of clinical malaria in children under SMC coverage. Considering these results, Sondo explained that they are planning to implement this combined approach to better improve the impact of SMC intervention.

Scientific Session 38 – Diagnosis and reagent 2

Amidou Diarra (Health Action Research Group – GRAS, Burkina Faso) presented the findings from two external proficiency testing (EPT) programs for the evaluation of microscopic malaria and other blood parasites, with the aim of contributing to evidence-based policy decisions through high-quality research. GRAS is affiliated with two PT institutions: the College of American Parasitology (CAP), which performs proficiency testing, distributes homogeneous material to participants, and compiles results; and the Clinical Laboratory Services (CLS), which conducts surveys, evaluates individual microscopic performance, and grades microscopists. Microscopists were rated on the precision with which they identified species and counted parasites. Parasite numbers were considered acceptable if they fell within 25% of the true counts. After four years of study, the score climbed to 80%, with 100% overall detection of the malaria parasite and 80% for other parasites. These results show that the PT can help to optimize laboratory organization and boost laboratory efficiency.

Casimire Wendlamita Tarama (National Center for Research and Training on Malaria – CNRFP, Burkina Faso) presented the prevalence of histidine-rich protein 2/3 (*HRP2/3*) gene deletion in *Plasmodium falciparum* isolates from Burkina Faso, addressing challenges in malaria diagnosis and treatment. Despite reliance on rapid diagnostic tests (RDTs), issues arose due to the deletion of the *Pfhrp2/3* genes, leading to false-negative results and inadequate case management. The study, part of a larger project, investigated asymptomatic malaria prevalence using HRP2-RDT in children aged 6 months to 10 years. Laboratory procedures included DNA extraction and sequencing to detect gene deletions. Results revealed a low prevalence of single hrp2 deletion, affecting HRP2-RDT effectiveness. It was pointed out that ongoing monitoring is crucial due to geographic variations in deletion prevalence, emphasizing the need for further research and funding to assess deletion prevalence in symptomatic malaria cases using WHO standards.

Scientific Session 42 – Parasites and systems biology 1

Afia Farrukh (RWTH Aachen University & University Hospital Mainz, Germany) presented the study on the *Plasmodium falciparum* CCCH zinc finger proteins MD3 and ZNF4, revealing several significant findings concerning their role in the malaria parasite's reproductive cycle. Their investigation identified MD3 and ZNF4 as crucial regulators of two key processes: male gametocytogenesis (the process by which male gametocytes are produced within the host's bloodstream) and exflagellation (the critical step in which male gametocytes release microgametes necessary for fertilizing female gametes within the mosquito vector). A pivotal discovery was the formation of complexes between MD3 and ZNF4 suggesting coordinated efforts between these proteins in regulating male gametocytogenesis. Furthermore, the study determined that MD3 and ZNF4 play instrumental roles in controlling exflagellation. Targeting these proteins in future interventions may disrupt the parasite's ability to reproduce sexually, thus impeding its spread through the mosquito population and ultimately reducing the burden of malaria transmission.

Sherihan Musa (RWTH Aachen University & University Hospital Mainz, Germany) presented an intriguing discovery regarding gene expression during gametocyte development in the parasite's life cycle. The SET2 histone methyltransferases were found to play a significant role in modifying histone proteins, which are crucial for packaging DNA and regulating gene expression. Investigating how SET2 regulates gene expression linked to cytoskeletal organization during gametocyte development offers insights into the molecular mechanisms governing the formation and function of these structures. This understanding holds the potential for developing new strategies for combating malaria, including targeted interventions aimed at disrupting the parasite's ability to develop and transmit between hosts.

Daniel Ayo (Infectious Diseases Research Collaboration, Uganda) presented findings on the gametocytes and infectivity among Ugandan malaria patients exhibiting reduced sensitivity to artemisinin, a critical component of artemisinin-based combination therapies (ACTs). The study unveiled a substantial proportion of patients with pfk13-mutant infections, alongside significant prior treatment with artemether-lumefantrine. Gametocyte densities notably elevated in young children, with a tendency towards higher prevalence in pfk13-mutant infections. Common malaria vectors in the study area were identified as *Anopheles gambiae* and *Anopheles funestus*. A follow-up study is planned to evaluate whether artemisinin-resistant strains possess a transmission advantage. This will involve clinical trials utilizing various combination therapies and scrutinizing transmission dynamics before, during, and after treatment. The study aims to select 120 individuals with high-density gametocytes and could provide insights into strategies for combating drug-resistant malaria. Understanding gametocyte production and infectivity in artemisinin-resistant patients is pivotal for mitigating transmission dynamics.

Jean Pierre Musabyimana (Aachen University, Germany) elaborated on the role of *P. falciparum* SET10 (PfSET-10), a protein in *P. falciparum* in regulating intraerythrocytic replication and parasite transmission during malaria. PfSET-10 functions by modifying histones, which aid in DNA packaging within cells, thereby gene expression.. The expression of histones *P. falciparum* undergoes dynamic changes throughout the parasite's differentiation process. The study elucidated the role of histone methylation in controlling gene expression in gametocytes. Results indicated that PfSET10 reduces intra-erythrocytic growth without affecting asexual gametocyte development. Furthermore, H3k18 methylation was found to regulate the replication and transmission of the malaria parasite, playing a crucial role in cyto-adhesion rosetting and erythrocytic inversion, as revealed by transcriptomic analysis. Musabyimana concluded by underscoring the disruptive effect of PfSET10 in regulating parasite transmission and suggested further studies to explore its impact on transmission blocking.

Lorenz Hofer's (Swiss Tropical and Public Health Institute – SwissTPH, Switzerland) presentation focused on the impact of additional blood meals in increasing sporozoite infection in mosquitoes. He stated that additional blood meals accelerate the development of *P. falciparum* in mosquitoes, resulting in a higher density of infection. The study revealed that additional blood meal increased the likelihood of mosquito's infectivity with sporozoites and intensified sporozoite infection, although they did not affect genetic diversity, suggesting any selective advantage of specific genotypes. The plasma-conserved membrane protein (CPMP) was used as a marker for sporozoite infection. Hofer concluded by underscoring the importance of blood in developing polyclonal antibodies.

Michael Lintrier Rivere (Indiana University, United States), presenting on behalf of Wes Boland, discussed the significance of the perfusion index (PI), which measures peripheral perfusion using a point-of-care pulse oximeter. It quantifies the ratio of pulsatile blood flow to static blood in peripheral tissue and serves as an indicator of mortality in severe cases of

P. falciparum malaria. The presentation centered on a multi-cohort study involving 600 Ugandans aged between 6 months to 4 years. Measurement of PI in study participants was conducted upon admission and at 6-hour intervals, with a PI considered low if less than 1%. The results indicated a significant association between PI and clinical complications such as shock, seizures, and increased mortality, with lower PI observed in severe malaria cases compared to uncomplicated malaria cases. Rivere concluded by establishing that PI correlates with traditional clinical perfusion measures and serves as a potential predictor of mortality.

Silvia Portugal (Max Planck Institute for Infection Biology, Portugal) discussed single-cell transcriptional profiling of *P. falciparum* parasites during both dry and wet seasons. Background information was provided on the seasonality of mosquitoes, parasite persistence in asymptomatic carriers, and the association between poor cyto-adhesion of infected erythrocytes and dry season parasite persistence, contrasting with trophozoite circulation in the wet season. The study had a cross-sectional design, with blood samples collected during both seasons. Results indicated that parasites from the dry season exhibited higher blood circulation compared to those causing clinical malaria manifestation during the wet season. Furthermore, cytoadhesion-related differentially expressed genes (DEGs) between stages were consistent across parasites in both seasons.

Scientific Session 43 – Implementation Science and Health Systems 1

Kristin Banek (University of North Carolina, United States) introduced the Tablet-based Malaria Cascade Analysis Tool (MCAT), which assists health workers in identifying treatment gaps and utilizing available data for informed decision-making. The study aimed to assess MCAT's capacity to enhance the quality of malaria care for children under five in the Democratic Republic of Congo (DRC). Using the Systems Analysis & Improvement Approach (SAIA), which leverages data to improve decision-making within systems, researchers evaluated its effectiveness. Health workers widely embraced MCAT, citing improved data quality and promising feasibility, although adjustments to usability are deemed necessary. Future steps involve evaluating SAIA malaria's impact on care and patient outcomes, integrating severe malaria cases into the care cascade, and adapting it for malaria chemoprevention interventions.

David Salandini Odong (Malaria Consortium, Uganda) discussed Uganda's program to implement seasonal malaria chemotherapy (SMC) in nomadic pastoralist communities in Karomoja, Uganda, in 2022. SMC involves monthly administration of a full malaria treatment course to children under five years during peak transmission periods. The initiative evaluated SMC coverage, treatment adherence, safety, and caregivers' perceptions through a cross-sectional survey. Data were collected from caregivers five to six weeks post-SMC round, comparing malaria incidence in children under five during high transmission seasons to the previous year. Results showed high SMC coverage and adherence, well-tolerated medication, increased confidence and knowledge among caregivers, and a decrease in malaria cases among children under five during the SMC period.

Mercis Dimene (Ministry of Health, Mozambique) emphasized the necessity to enhance malaria case management due to identified gaps in surveyed health facilities, where only 14% to 52% of malaria cases were properly managed. The National Malaria Control Program (NMCP) introduced a digital supervision and mentorship tool to monitor and reinforce malaria activities, including case management. The primary aim was to assess uncomplicated malaria case management and identify key dashboards for decision-making. Results revealed specific gaps in practices such as inconsistent fever screening, weight assessment, and patient malaria testing. The electronic supervision tool effectively gauged care quality at

health facilities, providing insights for targeted clinician training and action plans to enhance decision-making processes at all levels.

Mariana da Silva (National Malaria Control Programme – NMCP, Mozambique) presented on the digitisation of Mozambique's ITN campaign (2022-2023) and future integration plans by using DHIS2 and DIGIT (tools/modules that contain a set of standard data collection forms, automatically calculated indicators, data visualizations, and thematic dashboards that allow collecting, visualize and interpret data from the activities in line with WHO recommendations). Mozambique, burdened with high malaria rates, successfully digitized its ITN campaign, enhancing transparency and efficiency. Outcomes indicated improved data accuracy and promptness, with 95% of records dispatched within the day and 93% synchronized by 7:00 PM. These data show positive outcomes encompassed improved data timeliness and enhanced supervision. Lessons learned included implementing structured M&E strategies and addressing challenges like incomplete data records. For the future, Mozambique aims to evaluate platforms, integrate digitisation into other campaigns, and optimize coordination, emphasizing the vision of leveraging digital tools across multiple campaigns to strengthen public health initiatives efficiently.

Arthur Sovi (University of Parakou, Benin) discussed findings from a three-year cluster randomized controlled trial in Benin, examining the effects of dual active ingredient long-lasting insecticidal nets (LLINs) on insecticide resistance in malaria vectors. Adult mosquitoes were collected indoors and outdoors in 60 clusters using human landing catches at baseline and every 3 months for 2 years. The study revealed significant reductions in pyrethroid resistance initially, but resistance intensity resurged over time, particularly in certain trial clusters. Additionally, there were variable impacts on vector fertility and changes in metabolic gene expression levels across different LLIN arms. The results suggest the need for revised deployment strategies of chlorfenapyr-pyrethroid LLINs in high-resistance settings, emphasizing the importance of tailored interventions based on vector species complexity and resistance mechanisms.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

Day 5: Friday, 26th April 2024

Plenary Session 9 – Data Science for Malaria Elimination

Maciej F. Boni (Temple University, United States) presented lessons learned from data-driven mathematical models of drug-resistance evolution. He began his talk with the remark that evaluating drug resistance studies often takes five to ten years), hence providing the rationale for utilizing mathematical models to project resistance outcomes. After rigorous validation, the models can be used to simulate future scenarios of drug resistance policies in different settings. Boni highlighted that the most effective strategies include combination therapy, multiple first-line therapies (MFT), or cycling. The modeling results indicated that a geographically stratified MFT approach slows down resistance only when deployed with at least annual rotations. Treatment strategies targeting resistance act on specific genotypes, necessitating an understanding of which genotypes to target. Therapeutic efficacy studies (TES) are conducted to utilize data jointly with *P. falciparum* data to understand which genotypes to suppress. Towards the end of his talk, Boni emphasized the urgency of immediate action, as delaying a change in antimalarial treatment policy will result in more treatment failures.

Muhamed Semaku (Ministry of Health, Rwanda) delivered a talk titled 'Malaria Data Analytics: Shaping the Future of Health Planning in Rwanda'. According to the WHO, several significant factors, including a lack of health information and data gaps, may lead to a fragile health system. Weak health information systems, which include data collection, analysis, and reporting, can hinder a health system's ability to respond to health crises and plan for the future, making data analytics pivotal for shaping public health strategies. Spatiotemporal models and frameworks can be used effectively to integrate routine clinical data into public health decision-making processes, bridging the gap between data availability and practical use. The Bayesian spatio-temporal modeling mapping model was done following three major stages: first, data specification and formulation of a linear predictor equation; second, assigning prior distributions to latent fields based on second order differences; and last, allocating hyperpriors to hyperparameters. This approach enables us to generate maps that show the probability and uncertainty of reaching the targets, as well as the spatial contributions to the malaria burden in the country. Semaku concluded his talk by recommending the use of both household survey data and routine data in a two-step modeling framework for monitoring malaria trends, prediction of new cases, and evaluation of malaria incidence.

Symposium 60 – Symposium on the current status of biological threats in malaria and the interplay amongst them

Charlotte Rasmussen (Global Malaria Programme WHO, Switzerland) discussed biological threats to malaria control and elimination, including insecticide resistance, parasite *Pfhrp2/3* gene deletions, and antimalarial drug resistance. Insecticide resistance jeopardizes major vector control tools like insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS), with growing concerns about the efficient vector *Anopheles (An.) stephensi* spreading in African cities. Thus, this vector is breeding in human-made water storage containers, and adapting to local environments. The World Health Organization (WHO) issued a vector alert for *An. stephensi* in 2019, extending the malaria threats map and launching a regional initiative in 2022 to halt its spread in Africa. *Pfhrp2/3* gene deletions pose challenges for rapid diagnostic tests (RDTs) detecting *P. falciparum* malaria, as parasites not expressing these antigens evade detection. WHO recommends surveillance and, at the moment, there is no recommendation to switch RDTs due to limited options and supply security issues. Artemisinin-based combination therapies, used to treat malaria, face partial resistance, with

delayed parasite clearance linked to *Pfkelch13* mutations. WHO's response strategy includes strengthening surveillance, regulating diagnostics and therapies, limiting parasite spread, and promoting research and innovation against antimalarial drug resistance in Africa.

Fitsum G. Tadesse (Armauer Hansen Research Institute – AHRI, Ethiopia and London School of Hygiene & Tropical Medicine – LSHTM, United Kingdom) highlighted *An. stephensi* as an emerging threat, echoing Charlotte's concerns in the previous talk, about insecticide resistance, parasite gene deletions, and antimalarial drug resistance. He noted its expanding distribution in African countries, particularly in Ethiopia's eastern region. *An. stephensi's* unique characteristics, including its breeding in containers, resistance to insecticides, and adaptability, pose the main challenges to control efforts. *An. stephensi* is more efficient in sporozoite formation and transmission of *P. falciparum* and *P. vivax* and it is the dominant species in breeding and resting sites, therefore all these factors contributed to an increase of malaria transmission in Djibouti and Dire Dawa. Spatially overlapping with *P. falciparum* infections, it harbors genetic signatures of partial artemisinin resistance and gene deletions. Efforts are underway to address this challenge, including a new study on malaria molecular surveillance in the Horn of Africa, aimed at tackling the convergence of these biological threats.

Abebe Fola (Brown University, United States) noted progress in malaria control since the early 2000s but highlighted a stall since 2015, with rising cases and no decrease in deaths. Artemisinin resistance (ART-R), among other challenges, poses a significant threat in that picture and then, she discussed the rise of *P. falciparum* strains showing partial resistance to artemisinin in East Africa and the Horn of Africa. Various mutations in the kelch 13 gene, which are markers for ART-R, have been recorded. Partial ART-R was first confirmed in Rwanda and now in Uganda, Tanzania, and Ethiopia, endangering malaria control efforts not only in these countries but on a global scale. Fola stressed the need for robust surveillance through both phenotype and genome analysis across different regions, emphasizing cross-border collaboration due to parasite movement. Fola also suggested using multiple artemisinin-based combinations (ACTs) and rotating drugs every four or five years to combat resistance. She also emphasized that mapping partner drug resistance needs to be expedited as their efficacy is a key reason why ACTs remain effective in regions affected by ART-R *P. falciparum*.

Dorothy Fosah Achu (World Health Organization - WHO, Africa Regional Office, Republic of Congo) discussed key strategies for monitoring and responding to biological threats to malaria control in Africa. She highlighted insecticide resistance, the spread of *An. stephensi*, artemisinin resistance (ART-R), and *Pfhrp2/3* deletions as major threats. Achu noted the presence of global and local frameworks such as the World Health Organization (WHO) manual for monitoring insecticide resistance in mosquito vectors and selecting appropriate interventions, response plans to *pfhrp2* gene deletions, and the initiative to stop the spread of *An. stephensi* in Africa to address these challenges. In that regard, WHO will collaborate closely with partners and regions for a unified approach, considering local contexts. Future efforts will focus on enhancing member states' capacity with standardized protocols, strengthening laboratory capabilities, and identifying research areas. This includes exploring innovative methods to optimize current tools, test new approaches, and improve knowledge of the malaria drugs' mode of action.

Symposium 64 – Counteracting pfhrp2/3 deletion threats: From survey and modeling research to forecasting and market shaping

Agaba Bosco (National Malaria Control Program – NMCP, Uganda) presented data on two surveys conducted in Uganda to detect *PfHRP2/3* deletions. The first survey was conducted in east and west Uganda, where malaria transmission is low. Malaria detection involved the

use of RDTs, microscopy, and PCR of HRP2 and 3. Results showed that 3.3% of parasites had HRP2/3 double deletions. Statistical analyses revealed clustering of these double-deleted parasites both within the eastern and western regions. In contrast, the second survey was conducted in northern Uganda, a high transmission setting, where real-time multiplex PCR was utilized to detect HRP2/3 deletions, with 0.2% of parasites found to have HRP2/3 double deletions. This difference in prevalence of pfhrp2/3 deletions between regions may be explained by the differences in the volumes of RDTs and the duration within which the RDTs have been in use since introduction. Bosco emphasized the importance of training and capacity building for continued surveillance studies using molecular testing. Additionally, he urged the harmonization of molecular surveillance methods across countries and increased communication of HRP2/3 deletion survey results.

Oliver J. Watson (Imperial College London, United Kingdom) discussed the use of Imperial College London's mathematical malaria model 'malariasimulation' to project the selection of hrp2-deleted parasites and *pfhrp*-based RDT failure. The model results aided in the strategic placement of future surveillance efforts by projecting the risk of hrp2 deletion spread geographically and over time. Key risk factors for selecting hrp2-deleted parasites are low malaria prevalence and a high proportion of people seeking treatment. Watson highlighted the innate risk of selecting deletions when using hrp2 RDTs and the prospective risk of reaching a certain threshold of deletions in the following years. Regions with a prevalence below 0.05% are at higher risk of selecting deletions more quickly, emphasizing the need for continuous surveillance and proper utilization of diagnostic tools. Finally, he pointed towards the Deletion Risk Explorer tool, available on the WHO website, as a valuable resource for monitoring and planning malaria control strategies.

Salome Muchiri (Clinton Health Access Initiative – CHAI, Kenya) highlighted facts and forecasts on the need for non-HRP2-only RDTs. The method was based on the admin 1, a 5% threshold, slower' and faster' switching strategies, estimated public sector volumes, and Africa forecast on *Pfhrp2/3* deletions. The projected prospective risk of hrp2 deletions from Imperial College London's mathematical malaria model and CHAI's RDT forecasting were used to estimate the time taken to reach the 5% threshold and the required volumes. Their switching strategies identified those countries that will reach 5% in at least 10% or 25% of their admin-1 units under the central estimates from the mathematical model in the next five to ten years. Their forecasts suggested that non-HRP2-only RDTs could be needed in countries that make up 35-56% and 45-58% of the public sector RDT market in Africa within the next five years and the next ten years, respectively. Muchiri concluded that the total RDT public sector volume forecasts in Africa assume switching begins when the 5% threshold is reached in 10% of admin 1 units.

Spike Nowak (PATH, United States) presented results from 48 stakeholder interviews aiming to address market uncertainties and market-shaping solutions for non-HRP2-only RDTs. Interviewees included representatives from national malaria programs, donors, market shapers, researchers, RDT manufacturers, and PATH staff. National control program staff emphasized idiosyncratic processes for switching RDTs and their reluctance to adopt LDH/HRP2 RDTs without evidence. Interviewed manufacturers expressed concerns about uncertain demand hindering investment decisions, while interviewed donors are aware of opportunity costs, researchers highlighted the uncertainty in HRP2/3 deletion spread. Interviewed implementers have foreseen increasing RDT demand but expressed uncertainty about new RDTs. On the supply and demand side, interviewers acknowledged existing risks for uncertainty in the market for non-HRP2-only RDTs, necessitating market-balancing strategies like volume guarantees, as recently explored by MedAccess and Gates Foundation. LDH/HRP2-based RDTs offer benefits in hrp2/hrp3 deletions high-risk areas by decreasing transmission and improving health outcomes, though more budget is required. Finally, large

donors also signaled the crucial role of support for LDH/HRP2-based RDT procurement for a healthy market transition.

Symposium 67 – Transforming Pregnant Women and Access to MiP Prevention: Tools & Experiences to Support Scaling c-IPTp

Dorothy Fosah Achu (World Health Organization – WHO, Africa Regional Office, Republic of Congo) presented the implementation of a community-based intermittent preventive treatment of malaria for pregnant women (c-IPTp) delivery approach guidelines. Overall, 13 million pregnant women are exposed to malaria infections in 33 high burden malaria countries which are eligible for IPTp treatments. A country is eligible to implement the c-IPTp guidelines only when IPTp coverage is low and when there is a gap between IPTp3 coverage and antenatal care (ANC) attendance. Firstly, for this strategy to be put in place there has to be a favorable policy, with programmatic factors permitting the use of IPTp, the possibility of community health workers to administer chemoprevention and establish case management. Secondly, there should be a good collaboration between the malaria program, maternal and child services, and community health workers of the Ministry of Health. Thirdly, a functional supply chain management to maintain drug disponibility is needed. Lastly, as Achu emphasized, the intervention has to be accepted by the community and all stakeholders. This is the first time this intervention is taking place and evidence shows it's feasible and will improve IPTp coverage.

Tahima Razafiarijaona (Johns Hopkins Program for International Education in Gynecology and Obstetrics – Jhpiego, Madagascar) talked about the experience of piloting and scaling up c-IPTp in Madagascar, which is one of eight countries that completed the piloting phase under WHO direction before going on to the scaling phase. The antenatal care (ANC) attendance rates were 51% and 28.9% for the first and fourth visits, respectively. This relatively low attendance may explain the high maternal mortality observed in the country. Seventy percent of those who went for ANC1 received IPTp1, while only 40.4% of those who went for ANC4 received IPTp3. With a delivery coverage of 25.8%, the malaria cases increased from 36.9 per thousand in 2018 to 81.3 per thousand in 2021. This trial used a single dose of sulfadoxine-pyrimethamine (SP) per visit as the IPTp medication. The piloting results showed that IPTp3 coverage increased from 20% to more than 80%, and ANC4 from 20% to 65%. Razafiarijaona also mentioned some of the challenges encountered during the study, including women's reluctance to change, working with local associations, SP misuse, and challenges related to scaling up from the piloting to the scale-up phase.

Sidzabda Christian Bernard Kompaore (Ministry of Health, Burkina Faso) presented on IPTp in Burkina Faso. This was a quasi-experimental pre-/post-mixed-methods implementation research study that aimed to determine the effect of community-based intervention on IPTp in three different districts of Burkina Faso (Ouargaye, Po, and Batie), with support from Jhpiego. The strategy involved several steps including basic evaluation, actor training, community involvement (advocacy), consultation and planning meetings, and drafting of the feasibility study protocol. Kompaore highlighted the challenges faced and mitigation strategies for the approach. The project indicated that c-IPTp is a major strategy for reducing malaria morbidity and mortality in pregnant women. The involvement of key stakeholders at all levels of the intervention was identified as a critical success factor for the approach. Kompaore finished the talk by stating that the prospects for optimal implementation of this intervention can be leveraged for the benefit of the population.

Chonge Kitojo (President's Malaria Initiative – PMI, Tanzania) presented PMI's technical guidance regarding community-based intermittent preventive treatment of malaria for pregnant women (c-IPTp). She explained that the strategies are aligned with WHO

recommendations and the WHO's Field Guide on c-IPTp. PMI's technical guidance includes training community health workers (CHWs) on IPTp-SP and promoting antenatal care (ANC), consultation with the National Malaria Plan (NMP), reproductive health, and community health programs before implementation. Gender considerations for CHWs working with pregnant women were emphasized, and she made clear that the PMI team is available to provide technical assistance such as virtual workshops or discussions on the Malaria Operation Plan, in partnership with countries interested in initiating c-IPTp, which includes recommendations on the selection of sites, supplies, required skills, salaries and supervision to countries to scale up CHWs for c-IPTp.

Symposium 70 – Relapsing malaria in Africa, diagnosis and treatment considerations

Isaac Quaye (Regent University College of Science and Technology, Ghana on behalf of Pan African Vivax and Ovale Network – PAVON) delved into the complex burden of malaria relapse in Africa, focusing on *P. vivax* strains. He highlighted two main strains: the Chesson strain, prevalent in tropical regions with a latency period of 3-6 weeks, and the St. Elizabeth strain, common in temperate areas, which exhibits a longer latency period of 3-9 months or more. Quaye examined various aspects of malaria including infection volume, clinical manifestations, recurrence, and new infections identified through surveillance. He discussed how recurrence differs from seasonal reinfection and explored cryptic infections hidden in the spleen and bloodstream, contributing to relapse. Quaye attributed malaria relapse to liver hypnozoites, while recurrence stems from blood-stage asexual parasites and cryptic infections, often asymptomatic. Additionally, he briefly touched on *P. ovale*, noting minimal data on its strains; and explained how the behavior of *P. ovale curtisi* and *P. ovale wallikeri* is influenced by environmental and host factors.

Arsène Ratsimbasoa (University of Fianarantsoa, Madagascar) gave a comprehensive talk on the epidemiology of *P. vivax* in Madagascar and introduced innovative strategies aimed at addressing the hidden reservoirs of this parasite. In his presentation, he shared the results of a study on malaria rapid diagnostic tests (RDT) conducted from 2021 to 2024 in Madagascar. The data from 2024 showed that *P. falciparum* had a prevalence of 54.4%, *P. vivax* was found in 10.04% of cases, and mixed infections accounted for 35.09%. Ratsimbasoa also provided insights into the structure of Madagascar's health system, where RDTs are used at the community service level, microscopy at health centers, and polymerase chain reaction (PCR) at central laboratories. He highlighted the limitations of microscopy in detecting *P. vivax* due to its lower sensitivity compared to other methods. To enhance the detection rates, he advocated for the increased use of PCR and serological testing, stressing their effectiveness in identifying malaria infections more accurately.

Daniel Yilma (Jimma University, Ethiopia) discussed ways of improving the radical cure of *Plasmodium vivax* malaria. In his discussion, he focused on two drugs: Primaquine (PQ) and Tafenoquine (TQ). PQ has been used since 1950 for people over six months of age with Glucose-6-phosphate dehydrogenase (G6PD) levels above 30%. PQ can be taken with artemisinin combined therapies (ACTs) or chloroquine at different doses and durations based on specific case requirements. On the other hand, TQ, which was approved in 2018, is prescribed for individuals over 16 years with G6PD levels above 70%, and can only be used with chloroquine at a single dose. Yilma highlighted the risk of severe hemolysis that these drugs pose to individuals with G6PD deficiency, underscoring the importance of precise G6PD status assessment. He also stressed the necessity of understanding the overall case burden and the risk of relapse to effectively implement these radical cures for malaria.

Tamiru Shibiru (Arba Minch University, Ethiopia) evaluated new radical cure treatments in Ethiopia to reduce relapse risk of malaria infection. In this country, malaria cases are primarily

caused by *P. falciparum* (approximately 70%), with *P. vivax* (approximately 30%) and *P. ovale* being rare. Primaquine (PQ) is used in low (3.5mg/kg) or high (7mg/kg) doses, the latter given for seven days (not yet WHO-approved but under consideration) and it requires supervision Results showed that without PQ there was a higher recurrence risk and with a high dose there was a low recurrence risk. In concordance with this, another study revealed higher *P. vivax* risk in placebo-treated patients compared to those receiving PQ for 14 days. Shibiru at the end talked about two studies, the EFFORT study, a randomized 3-arm trial to assess *P. vivax* incidence risk, as well as the effectiveness, safety, cost-effectiveness, and feasibility of a 7 or 14 PQ treatment. And the TADORE study aims to revise tafenoquine dosing, optimizing duration and dosage.

Scientific Session 45 – Drug efficacy 2

Christian Nsanzabana (Swiss Tropical and Public Health – SwissTPH, Switzerland) presented a study that compared the sensitivity of microscopy and qPCR which evaluated the efficacy of Ganaplacide/Lumefantrine solid formulation in an open-label, multicentre, parallel-group, randomised, controlled, phase 2 trial. Results showed a good correlation between microscopy and qPCR at baseline, a higher positivity rate of qPCR, and the highest predictive value of recrudescence in patients. He concluded that qPCR detects submicroscopic infections at all time points and there is a linear correlation between microscopy and qPCR. However, he highlighted the need for further studies such as using other markers other than 18S rRNA to check if they could improve the accuracy of PCR.

Anyirekun Fabrice (Research Institute of Health Sciences – IRSS, Burkina Faso) presented on ex vivo drug susceptibility and resistance mediating genetic polymorphisms of *Plasmodium falciparum* in Bobo-Dioulasso, Burkina Faso, where H malaria remains a leading cause of morbidity and mortality. The country has utilized various antimalarials, including artemisinin-based combination therapies (ACTs) and sulfadoxine-pyrimethamine plus amodiaquine (SPAQ) for seasonal malaria chemoprevention (SMC) in children, interventions which seem to be effective. However, while resistance to certain drugs like AQ remains low, concerns persist regarding emerging resistance, particularly to artemisinin. In this particular studio presented, Ex vivo assays demonstrated overall good drug potency, with some exceptions. Genetic analyses revealed trends consistent with West Africa but raised concerns about increasing resistance mutations. He stressed that despite the current stability, continued surveillance is crucial to monitor and manage potential resistance developments effectively.

Scientific Session 47 – Vector Biology and control 8

Carol Tasiano (Malaria Alert Centre – MAC, Malawi) presented findings from field experiments that compared various larvicides commonly used in Africa and the USA. The objective was to assess the effectiveness of those commonly used larvicides on wild-caught mosquito larvae, as well as their retention and survival rates. Mosquito larvae were intentionally collected from a specific area. The larvicides tested included Natular® formulations XRT, T30, and DT from the USA, compared to *Bacillus thuringiensis israelensis* (Bti), commonly used in Africa for larval source management. Results showed that both Natular formulations DT and Bti achieved 100% mortality within the first week, while Natular formulations XRT and T30 exhibited lower mortality rates. In conclusion, integrating larviciding into existing intervention strategies in the country would be highly beneficial to fighting malaria.

Kwi Pilate Nkineh (University of Buea, Cameroon) outlined the diversity and transmission dynamics of malaria across various altitudes along Mount Cameroon's slope. Nkineh and colleagues conducted a cross-sectional study to investigate the distribution and genetic variability of *An. gambiae* complex siblings at different altitudes and their resistance to pyrethroids and carbamates in the vicinity of Mount Cameroon. The study findings revealed that *An. gambiae* complex and *An. funestus* were prevalent along the mountain's slopes, predominantly at lower and intermediate elevations. The study further identified two distinct strains of *An. coluzzii* and geographical isolation were observed among *An. gambiae* and *An. coluzzii* populations from different locations. The final result shared was that *An. gambiae* complex mosquitoes exhibited resistance to both, deltamethrin and bendiocarb insecticides in all genotyped specimens.

Anna Trett (Clinton Health Access Initiative – CHAI, United States) presented general long-term projections for vector control strategies, including insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS), aimed at anticipating market challenges, trends, and opportunities. The forecasted quantities and budget allocations rely on historical data, anticipated population shifts, and country-specific strategy adjustments. The available budget for ITNs dictates the pace of transition to dual active ingredient (DAI) nets and influences achievable ITN coverage levels. Recently, IRS application rates have stabilized, with resources redirected toward DAI coverage. The global vector control commodities market faces various threats, including financial constraints, emerging competitors, evolving epidemiological patterns, and updated control guidelines.

Jésukèdè Constantin Adoha (University of Abomey-Calavi, Benin) presented on utilizing systems distribution models (SDM) to assess the composition, distribution, and ecological preferences of mosquito species in Southern Benin. Mosquito species were captured using human landing catch (HLC) methods, identified, and their GPS coordinates recorded for sampled locations. Ecological indices were applied to evaluate species diversity, and ecological niche models were employed to analyze bioclimatic and environmental data. A notable increase in both the abundance and diversity of mosquito species was observed during the wet season compared to the dry season, with ecological preferences exhibiting seasonal variation.

Boulais Yovogan's (University of Abomey-Calavi, Benin) study assessed the efficacy of Royal Guard® (alphacypermethrin-pyriproxyfen) and Interceptor G2® (alpha-cypermethrin-chlorfenapyr) long-lasting insecticidal nets (LLINs) compared to Interceptor® nets (treated with alpha-cypermethrin using long-lasting technology) LLINs on primary malaria vectors in Benin. Both pyrethroid-chlorfenapyr and pyrethroid-pyriproxyfen LLINs effectively reduced *An. gambiae* and *An. coluzzii* density. Mosquitoes species composition, vector density and parity rate were analyzed at baseline and after the 2-year intervention. Results showed that both pyrethroid-chlorfenapyr LLINs and pyrethroid-pyriproxyfen LLINs were found to reduce the density of *An. coluzzii* and *An. gambiae* s.s. at a broadly similar magnitude, both indoors and outdoors. Combining chlorfenapyr and pyriproxyfen with pyrethroid insecticides in LLINs could yield similar effects. The research informed policy decisions for vector control intervention selection and deployment in malaria-endemic regions, highlighting the importance of complementary indoor and outdoor strategies for effective malaria prevention and control.

Jacques Gnambani (Western Regional Directorate of the Institute of Research in Health Sciences – IRSS, Burkina Faso) presented an entomopathogenic study on utilizing novel biological control interventions for managing mosquito vectors. His research focused on

leveraging emerging technologies that harness mosquito symbiotic bacteria to tackle challenges and explore opportunities in vector control. These challenges included the suboptimal effectiveness of the RTS,S malaria vaccine against clinical and severe malaria, the limited efficacy of most antimalarial drugs against gametocytes, and the altered ecology and behavior of vectors. The study identified a promising candidate in *Chromobacterium anophelis* sp. nov., a native strain from Burkina Faso, whose bioactive cell-free supernatant demonstrated significant impacts on key determinants of vector capacity and disease transmission. Gnambani recommended incorporating biocontrol strategies into mosquito-borne disease management to reduce reliance on existing interventions. The selective mosquito-killing abilities of the pathogenic bacteria showed exciting prospects for more effective and sustainable approaches to combat mosquito-borne diseases.

Sandrine Eveline Nsango (Pasteur Center for Cameroon and University of Douala, Cameroon) shared in her talk findings from a study conducted in the western region of Cameroon, that characterized malaria vectors and their role in local transmission. Adult mosquitoes were collected by indoor residual spraying and identified morphologically and molecularly. Blood samples were collected from symptomatic malaria patients at three health facilities, whereas samples from asymptomatic individuals were taken from eight sites in Tibati's neighborhood, aligning with mosquito collection sites. Results identified six *Anopheles* species, with *An. gambiae* emerging as the predominant and most competent vector across different study sites in Tibati between 2015 and 2017. The diversity of mosquito species and abundance varied with altitude. Urging further research into malaria vector dynamics, species behavior, and resistance profiles, the study underscores the importance of understanding local ecological and socio-economic factors for targeted malaria interventions in Adamawa, the West region of Cameroon.

Scientific Session 52 – Social and health economics 2

Abiola O. Oluwagbemiga (Malaria Consortium, Nigeria) presented on the cost of delivering pyrethroid-piperonyl butoxide (P-PBO) insecticide-treated nets (ITNs) to households in Ondo and Anambra in Nigeria through universal campaigns. Data from 48 wards in each of the two states were collected using a multi-stage cluster sampling design to identify financial and opportunity costs associated with the campaigns to provide data on costs per ITN delivered to households. The findings revealed that delivering an ITN to a household costs 3.33 USD in Ondo and 3.19 USD in Anambra, with opportunity costs of 1.9% and 2.6%, respectively. The main cost driver was the cost of purchasing ITNs, including freight and insurance, which constituted 77% of total expenses in Ondo and 82% in Anambra. Oluwagbemiga highlighted that these results would aid economic assessments of P-PBO ITNs distributed through universal campaigns and enhance value-for-money evaluations.

Edward Thomsen (University of California, United States) talked about insecticide-treated nets (ITNs) market trends from 2004 to 2021 and the monetary value of extending ITN lifespan. The research aimed to understand overall market trends and factors affecting ITN prices during this period. It also estimated the premium price that the market should offer for ITNs with longer lifespans. Findings revealed that ITN prices are largely influenced by a small number of buyers and manufacturers. The market incentivizes innovation when both buyers and sellers value product improvements. Value premium for ITNs with a longer life span is context-dependent but not yet captured in the market. Recognizing resistance to damage could assist buyers in selecting more suitable products and encourage innovation through added value.

Hamidou Niangley (Malaria Research and Training Centre – MRTC, Mali) gave a presentation under the title 'Impact and cost-effectiveness of a school-based intervention to improve

malaria treatment compliance: Randomized controlled trial in peri-urban village of Mali, Tienfala'. The randomized controlled trial aimed at assessing the training of school children to enhance malaria treatment compliance. The study results indicate improved adherence, with 90% in the intervention group versus 88.9% in the control group. The intervention proved effective, echoing findings by Cohen and Saran regarding the efficacy of targeted messaging. A cost-effectiveness analysis from the government perspective suggests promising outcomes. Such interventions that leverage schools for health promotion, as Niangley concluded, offer a viable strategy for combating malaria and reducing healthcare burdens.

Epaphrodite Habanabakize (Rwanda Biomedical Center – RBC, Rwanda) presented on the 'Role of CSOs in enhancing SBC implementation and fostering the uptake of malaria interventions in Rwanda'. He highlighted the instrumental role of Civil Society Organizations (CSOs) in advancing Social Behaviour Change (SBC) interventions for malaria in Rwanda. Deployed strategically across provinces and targeting high-risk groups, CSOs significantly reduced malaria cases. Additionally, the incidence rate dropped from 114/1000 people per year to 47/1000. Their collaborative efforts with government initiatives facilitated community awareness, behavioral change, and malaria prevention, fostering a decline in malaria incidence. He highlighted the vital partnership between CSOs and governmental efforts, emphasizing the sustained impact of their collaborative action.

Scientific Session 53 – Bioethics and diversity 1

Paulina Onvomaha Tindana (University of Ghana, Ghana) presented findings from a qualitative study on integrating molecular and genomic data into malaria elimination programs in Africa. The study sought perspectives from genomic researchers in Africa and revealed extensive engagement between principal investigators and policymakers, akin to collaborative efforts seen during the COVID-19 response. However, policymakers' limited capacity to grasp genomic data poses a challenge. Simplifying scientific language and developing innovative communication strategies emerged as crucial solutions. Transitioning and utilizing genomic data faces obstacles such as aligning research funders' interests with NMCP needs and bureaucratic complexities. Researchers expressed a need for training in policy engagement and effective communication with policymakers. Tindana emphasized at the end of her presentation the pressing need to address these challenges for enhancing the integration of genomic data into malaria control strategies across Africa.

Kaddyijatou F. Jallow (Ministry of Health, The Gambia) presented the study examining caregivers' health-seeking behavior for children aged 24 to 59 months, focusing on pneumonia, diarrhea, and malaria in The Gambia. While caregivers generally seek medical care promptly, knowledge gaps exist, particularly in rural and less educated communities, regarding pneumonia and diarrhea. Appropriate health-seeking behavior varies across diseases, with malaria showing the highest rate of proper care, followed by pneumonia and diarrhea. Younger caregivers and urban residents tend to seek care more effectively, as also do married caregivers. Future recommendations include performing qualitative research to understand underlying reasons for health-seeking behaviors, policy measures to discourage inappropriate practices, and support for caregivers through education and employment opportunities. Implementing these recommendations could improve caregivers' ability to seek timely and appropriate care, thereby enhancing the health outcomes of children in these communities.

Christina Sudi (Pan-African Mosquito Control Association – PAMCA, Kenya) presented the proactive steps taken by PAMCA through the Women in Vector Control (WiVC) initiative to recognize and uplift the contributions of African women in the fight against malaria and to rectify the oversight of not recognizing their pivotal roles through the PAMCA Excellence

Awards, increasing their social visibility. With rigorous pre-determined criteria and a transparent selection process, the awards honor women's dedication, creativity, mentoring, and career progression. The initiative's impact is evident, with awardees training pupils, students, and researchers, conducting studies, and advocating for vector-borne disease control. However, challenges like competitiveness, limited implementation time, and inadequate monitoring persist. Securing additional funding can help address these issues and expand the initiative's reach, ensuring more women are recognized and supported in their crucial roles in vector control.

John Mwangi (The Kenya Malaria Youth Corps, Kenya) presented the Kenya Malaria Youth Corps (KeMYC) program, engaging youth affected by malaria to combat the disease. He evaluated its impact on Kenya Vision 2030 and emphasized youth agency in public health decision-making. The KeMYC not only addresses immediate health challenges but also fosters leadership and community resilience. The program prioritizes equity, gender inclusion, and meaningful participation, harnessing the transformative potential of youth engagement in public health. Through empowering young leaders, the program contributes to achieving broader health goals, demonstrating the vital role of youth-led initiatives in tackling malaria and building healthier futures for all.

Bayala Ipéné Mylène Carenne (National Center for Research and Training on Malaria – CNRFP, Burkina Faso) presented on the evaluation of the reliability of rapid diagnostic tests (RDTs) targeting histidine-rich protein 2 (HRP2) for malaria diagnosis, amid concerns of strains lacking the pfhrp2 antigen. Despite worries, RDTs showed good agreement with microscopy results. The study also found a low pfhrp2 gene deletion rate of 2.6%, below the WHO's 5% threshold for changing RDT types. This supports the continued use of HRP2 RDTs for malaria diagnosis in Burkina Faso. However, ongoing surveillance is recommended to monitor the dynamics of *P. falciparum* strains lacking the pfhrp2 antigen. Overall, the study findings suggest that current RDTs remain effective for malaria diagnosis in Burkina Faso, but vigilance is essential to ensure diagnostic accuracy amid evolving strain dynamics.

Scientific Session 56 – Drug resistance 5

Helle Hanson (University of Copenhagen, Denmark) presented the characterization of Illumina amplicon sequencing for determining resistant profiles in mixed malaria infections. Data analysis was conducted using the web-based platform 'usegalaxy.org', a user-friendly tool for non-bioinformaticians. The methodology involved conducting a range of mixed infection experiments with lab strains, followed by sequencing and analyzing full and partial haplotype data. Notably, emphasis was placed on the ability to specify minor haplotypes, with a 10% cutoff for determining the haplotype in the infection. The presentation also discussed separating infections with mixed drug resistance profiles into major and minor haplotypes, requiring a 20% difference from a 50:50 distribution. In her future work, Hanson will utilize this method with patient samples collected from various malaria-endemic nations in Africa.

Martin Okitwi (Infectious Diseases Research Collaboration, Uganda) presented findings from a study comparing the dihydroartemisinin (DHA) survival phenotypes of 122 samples using both ring-stage survival assay (RSA) and extended RSA (eRSA) methods. The study also examined the relationship between RSA survival and fold changes in eRSA, utilizing dried blood spots (DBS) for quantitative polymerase chain reaction (qPCR) analysis and sequencing via molecular inversion probes (MIPs). Results indicate a 30% joint prevalence of K13 markers and similar correlation coefficients across various growth levels of parasite cultures. The eRSA fold changes demonstrate a strong correlation with RSA outcomes, suggesting potential interchangeability. Moreover, comparable dihydroartemisinin (DHA) susceptibility patterns were observed in eRSA and RSA, particularly concerning the C469Y and A657V

mutations. Okitwi highlighted the importance of the study and underscored the feasibility of obtaining reliable outcomes in low-resource settings through sample storage in DBS samples.

Maciej Boni (Temple University, United States) presented the future effectiveness of artemisinin treatment in Rwanda, Uganda, and Tanzania. The mathematical modeling results indicate that combination therapies followed by multiple first-line therapies and drug cycling are the most effective strategies for delaying or preventing artemisinin resistance. The modeling study projected incidence, prevalence, and resistance to treatment, as well as evaluated the most effective strategies using real-life data. For instance, the model estimated a 30% treatment failure rate in Uganda by 2029 if the current situation remained unchanged. In his presentation, Boni stressed the importance of rapid-turnaround molecular surveillance to inform these models and comprehend the future trajectory of piperaquine resistance in Africa, particularly concerning the deployment of dihydroartemisinin-piperaquine (DHA-PPQ) as a treatment.

Stephen Tukwasibwe (Makerere University, Uganda) presented on antimalarial drug resistance in different populations of newly arrived refugees in Uganda, emphasizing the threat posed by antimalarial drug resistance in Africa, particularly in conflict zones such as East Africa and the Horn of Africa. Collaborating with Ugandan authorities and international organizations, Tukwasibwe's team conducted surveys among newly arrived refugee populations from South Sudan and the Democratic Republic of Congo (DRC). Their findings revealed varying resistance markers between populations, indicating diverse treatment practices and local resistance profiles. Utilizing molecular surveillance techniques, they identified common resistance markers with Ugandan populations, thereby enhancing the understanding of resistance transmission. This approach provides valuable insights into malaria management in conflict-affected regions where traditional surveillance methods face challenges.

Denis Niyomwungere (National Institute of Public Health, Burundi) presented on artemisinin partial resistance (ART-R) in Eastern Africa, with a focus on the situation in Burundi. Despite the effective use of artemisinin-based combination therapy (ACT) (specifically artemether-lumefantrine) in Burundi, concerns have arisen due to the emergence of artemisinin resistance in neighboring countries. Their study aimed to assess the presence of ART-R e in northern Burundi, particularly at the border with Rwanda and Tanzania. Analysis revealed persistent parasitemia on day three and *pfkelch* R561H mutations in specific regions. He recommended surveillance, continuous evaluation of ACT efficacy, and the implementation of new strategies to combat ART-R. Collaboration at national and regional levels is essential for effective intervention.

Edwin Kamau (United States Army Medical Research Unit Kenya – USAMRU-K, Kenya) explored the emergence of *Plasmodium falciparum* Kelch 13 (*Pf*K13) mutations and their association with artemisinin resistance in Kenya. Across six distinct locations, 14 mutations, including *Pf*K13 675V, were detected, indicating significant genomic activity. Notable mutations such as A675V, linked to artemisinin resistance, were also identified. Kamau emphasized the necessity of continuous surveillance to promptly detect and address these genomic changes. Such vigilance enables effective preventive and curative measures against resistant parasites, underscoring the urgency of intervention strategies to effectively combat malaria drug resistance in Kenya.

Scientific Session 62 – Diagnosis and Reagent 3

Felix Habarugira (University Teaching Hospital of Butare – CHUB, Rwanda) reported on a clinical study that validated a chip-based real-time duplex PCR test for *P. falciparum*, the

Truenat® by Molbio, a novel malaria diagnostic tool designed for point-of-care testing. The aim was to improve diagnostic accuracy and enable prompt interventions for malaria infections. Samples from a cross-sectional study were analyzed and compared with the gold standard microscopy. The Truenat device demonstrated good diagnostic performance, with a sensitivity of 96.1%, specificity of 97.3%, and a Receiver Operator Characteristic (ROC) area of 0.99, indicating high reliability. Habarugira recommended the use of the Truenat device for detecting malaria parasites on a larger sample size to further validate its efficacy. Implementing such tools has the potential to enhance malaria diagnosis and significantly contribute to effective management strategies, particularly in resource-limited settings.

Eric Saraba (University of Rwanda, Rwanda) presented findings from a study on the prevalence of non-*falciparum* and mixed species infections in malaria-endemic areas in Rwanda. The study utilized microscopy and nested PCR tests to detect various *Plasmodium* species including *P. malariae*, *P. ovale* (*P. ovale curtisi* and *P. ovale wallikeri*), and *P. falciparum* in the study population. The results revealed that non-*falciparum* species accounted for more than 46% of malaria infections. Additionally, more than 15% of non-*falciparum* infections were missed, while 23% of mixed infections were misdiagnosed by microscopy. In malaria-endemic areas, a significant number of non-*falciparum Plasmodium spp* infections are either missed or misdiagnosed, potentially contributing to the persistence and/or resurgence of malaria. Saraba emphasized the importance of introducing more accurate, accessible, and sensitive diagnostic methods and tools in routine clinical laboratory services to effectively eliminate malaria.

Jean Modesta Harerimana (Johns Hopkins Program for International Education in Gynecology and Obstetrics – Jhpiego, United States & US President's Malaria Initiative – PMI, Rwanda) presented a study with the primary aim of the study was to evaluate laboratory technicians' performance in identifying malaria species and quantifying malaria parasites. A total of 308 lab technicians participated in the study, receiving pre-training assessments, followed by training sessions, and then post-training follow-up assessments. The training structure established for laboratory technicians, which included clear post-training mandates and follow-up mechanisms, demonstrated an increase in malaria diagnostic tests and the retention of skills and knowledge at their respective workplaces.

Scientific Session 63 – Pathogenesis and co-morbidities 2

Tchoutang Ange Maxime (University of Yaoundé I, Cameroon) presented a study that aimed to fill the knowledge gap regarding malaria, typhoid fever, and their co-infection. Blood samples from 288 fever patients at Etoug-Ebe Baptist Hospital were collected and categorized into groups: unknown fever (positive control), malaria-positive, typhoid-positive and co-infected, together with samples from healthy individuals. Malaria was diagnosed using rapid diagnostic tests (RDT), and typhoid fever with traditional Widal slide and tube tests. Prevalence rates were found to be 25% for malaria, 17.36% for typhoid fever, and 19.79% for co-infection. The study also assessed oxidative stress and immune response through various assays, revealing heightened stress levels, reduced antioxidant capacity, and a shift towards a TH1-cytokine profile in co-infected patients. He concluded by pointing out the need for further research to understand the specific pathological consequences of co-infection, particularly the interaction between *Plasmodium* and *Salmonella*, to improve diagnostic and therapeutic approaches for managing these conditions

Ruth Namazzi (Makerere University, Uganda) explored the link between circulating immune complexes, G6PD deficiency, and severe malaria outcomes in children, focusing on blackwater fever (BWF) and severe anemia. Serum samples from 600 children with severe malaria and 120 community children were analyzed using ELISA to measure immune complex

levels and markers of hemolysis in a prospective cohort study. About 9% of children had G6PD deficiency for the African allele. Regional and gender-specific differences were also noted, with higher immune complex levels in Jinja compared to Kampala, and more severe malaria cases in Kampala. Circulating immune complexes were associated with hemolytic events, with variations based on sex and location. These findings suggest a potential role for circulating immune complexes in mediating hemolysis and malaria complications, particularly in G6PD-deficient individuals. Insights from this study may inform targeted interventions for improving severe malaria outcomes in regions like Eastern Uganda.

Samuel B. Anyona (Maseno University, Kenya) presented a previously unexplored aspect of severe malarial anemia (SMA) in Kenyan children, focusing on the differential ubiquitination protein expression. Ubiquitination is a fundamental process in cells, regulating protein degradation, signaling, and immune responses. Understanding how ubiquitination is altered in SMA could offer insights into the disease mechanisms and aid in developing targeted treatments. The findings from a prospective observational study indicated that dysregulation of ubiquitination affects various pathways crucial in SMA pathogenesis. These include cellular stress responses, inflammatory pathways, and tissue repair mechanisms. Malaria infection triggers inflammatory responses, which in turn activate downstream pathways. The intersection of inflammatory responses with cellular stress and immune regulation pathways suggests a complex interplay between inflammation, cellular stress, and immune responses in SMA. Disruptions in these pathways and associated proteins likely contribute to the pathophysiology of SMA, leading to inflammation, impaired erythropoiesis, tissue damage, and organ dysfunction. This study opens avenues for targeted interventions aimed at restoring proper pathway function and alleviating the severity of the disease.

Closing Ceremony

The Multilateral Initiative on Malaria (MIM) 8th Pan African Malaria Conference, held in Kigali, Rwanda, from the 21st to the 27th of April 2024, concluded with a closing ceremony where distinguished individuals, including outstanding leaders in the field of malaria research, poster presenters, and contributors to MIM and malaria research in general, as well as distinguished institutions, were recognized for their remarkable contributions. Additionally, an invitation was extended to East African research institutions or consortiums engaged in malaria research to apply to host the 9th Pan African Malaria Conference. The Minister of Health in Rwanda took the opportunity of the closing ceremony to thank all who made possible the MIM conference and acknowledged the contributions of all the scientists who presented. During her closing speech, **Emeritus Rose GF Leke**, Chair of the Multilateral Initiative on Malaria Secretariat, expressed gratitude to sponsors, partners, and the Government of Rwanda for their role in making the event successful. She emphasized the importance of united efforts to accelerate progress in ending malaria. Finally, the MIM Society welcomed its new chair **Professor Abdisalan Noor** and he gave a heartfelt speech on his vision for shaping the future of MIM.

This report is brought to you by the MESA Correspondents Ambadiang Mae Marilene M., Aurelia Brazeal, Deborah Neumbe, Isabel Byrne, Jean Aime Ngirinshuti, Julius Ichodo Odero, Masudi Suleiman, with support from former correspondents Busari Lateef Oluwatoyin, Eggrey Aisha Kambewa, Jenna Zuromski, and Ntui Vincent Ntui-Njock. Senior editorial support has been facilitated by Charles Narh, Jessy Goupeyou, Manuela Runge, and Rosauro Varo.

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