RESOURCE HUB *Correspondents*

American Society of Tropical Medicine and Hygiene (ASTMH) Sixty-seventh Annual Meeting

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The MESA Alliance would like to thank Professor Graham Brown for his mentoring and editorial support, and for sharing his expertise and knowledge during the production of these reports.

The MESA Alliance would also like to acknowledge the sessions' chairs, co-chairs and presenters for their crucial role in the reporting of the sessions.

MESA

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Background

There are a growing number of conferences being held globally where emerging evidence is shared in the field of malaria and related topics like entomology, parasitology, and health systems. These meetings offer the opportunity to hear cutting edge science and lessons learned from peers and mentors, in both broad and niche disciplines. As calendars and budgets are limited, those who could benefit from participating are often unable to attend. On the other hand, those who do participate, sometimes miss pertinent talks due to parallel scheduling of scientific sessions and side meetings.

With the overarching objective of sharing key findings with a global audience and also providing opportunities to emerging researchers, MESA identifies relevant conferences for the malaria community and reviews the scientific program to curate lists of talks to be covered by the *MESA Correspondents program*. Summaries of the highlights and technical content of the presentations are produced and shared through MESA's communication channels and those of strategic communications partners.

Session 11: Malaria: Epidemiology - Recent Progress in Advancing Surveillance, Measurement and Modelling for Program Success

The first of two Malaria Epidemiology Scientific Sessions attracted a capacity crowd in the Rodrigue Gallery at the Sheraton on Monday morning 29 October. The session's theme "*Recent progress in advancing surveillance, measurement and modelling for program success*", was addressed by seven presenters.

Asymptomatic infections of low and high density are key targets during the elimination phase of malaria. Linking routine health facility data and community surveys from 9 countries, **Gillian Stresman**'s work concluded that as malaria transmission intensity decreases, the proportion of infections detected by routine passive case-reporting of confirmed malaria illness increases. **Fitsum Tadesse**'s work in Ethiopia showed that a high proportion of asymptomatic low-density infections clustered around the passively detected and routinely reported cases. **Ashenafi Assefa** explored how multiplex serological studies could be used to distinguish recent and remote infections and enhance data on infecting species.

Aaron Samuels suggested that tracking malaria infection in pregnant women at antenatal clinics could be a useful adjunct to routine surveillance of symptomatic illness cases. **Ursula Dalrymple** examined malaria infection and care seeking for childhood febrile illness in Africa and confirmed the need to improve the coverage and monitoring of case management services.

Epidemiology of drug resistance was discussed at many places during the meeting, with speculation about possible return of drug sensitivity after years of drug withdrawal. In this session, **Georgina Humphreys** shared recent data on pyrimethamine resistance markers across Africa, concluding that they remain highly prevalent in East and Southern Africa despite policies that have decreased selection pressure.

Ipsita Sinha explored individual travel survey and cell phone data from malaria patients in the Greater Mekong Subregion to reveal internal and multinational migration patterns that could influence the evolution and spread of drug resistance in those nations and beyond.

Several of the presenters explored the issue of how low density and asymptomatic infections—mostly missed through passive case detection and routine reporting—can be tracked to improve targeting of interventions.

Collectively these works demonstrate the highly dynamic scholarship that is contributing to malaria control and elimination efforts and reinforce the value of case-based routine surveillance as well as targeted, more detailed studies, to explore evolving transmission dynamics.

Co-chairs: **Patrick Kachur** (Columbia University Medical Center, New York) and **Ipsita Sinha** (Mahidol Oxford Tropical Research Unit, Bangkok, Thailand)

This report was written by Patrick Kachur with editorial support from Professor Graham Brown.

Session 19: Transmission Blocking Immunity: From Biology to Interventions

The large audience attracted to the symposium on "*Transmission Blocking Immunity: from Biology to Interventions*" heard five presentations, each containing some original unpublished data. The role of naturally acquired infections in stimulating immunity that reduces transmission has been the subject of great debate.

Will Stone showed that antibodies produced following natural exposure, when affinity purified against established vaccine candidates *Pfs230* and *Pfs48/45* then added to gametocytes in vitro, were capable of blocking transmission. Responses to novel gametocyte antigens were detected by protein microarray and antibody prepared in the same way also reduced mosquito infection rates. Early results from mouse immunization studies confirmed that some of these newly identified proteins may be viable targets for vaccine development.

Matthias Marti presented a comprehensive assessment of naturally acquired responses to antigens that are present on the surface of gametocyte-infected red blood cells. Such antigens were detected on the red blood cell membrane for early developing gametocytes but not mature gametocytes. Naturally acquired antibody responses to these antigens were associated with phagocytosis of gametocyte-infected red blood cells and with reduced gametocyte burden during natural infections. Genetic analysis revealed minimal variation of key antigens across strains, supporting their further examination as vaccine candidates.

Two groups updated progress on identification and assessment of candidate transmission-blocking candidates:

Carolina Barillas-Mury showed that antibodies against the different domains of the vaccine candidate *Pfs47* protein showed markedly different potency to block transmission. Antibodies against the immunodominant domains showed negligible effects whereas antibodies against a non-dominant domain reduced parasite development dramatically. The data suggested that the effective anti-*Pfs47* antibodies interact with female gametocytes and prevent fertilization.

Arianna Marini presented progress on the characterization and expression of established and novel Transmission Blocking Vaccine antigen candidates. In addition, she presented promising tools to enhance immune responses generated by such antigens, including a novel approach with the decoration of Virus Like Particles by Plug-and-Display technology.

Ashley Birkett summarized historical and recent clinical trial results with transmission blocking vaccine candidates from a funders perspective. Whereas early results with *Pfs25* were disappointing, recent findings with *Pfs230* hold great promise. He highlighted the need for novel candidate antigens and stressed the importance of assays that bridge early clinical testing to field deployment.

Taken together, these presentations exemplified recent achievements in understanding naturally acquired transmission reducing immunity and considerable progress in moving towards promising transmission blocking vaccines.

Co-chairs: **Matthias Marti** (University of Glasgow, Glasgow, United Kingdom) and **Teun Bousema** (Radboudumc, Nijmegen, Netherlands)

This report was written by Teun Bousema with editorial support from Professor Graham Brown.

Session 30: A Roadmap for Ivermectin as a Complementary Vector Control Tool for Malaria

Ivermectin is a licensed drug with an excellent safety profile that has been used widely against human onchocerciasis, lymphatic filariasis and other Neglected Tropical Diseases (NTDs) through intermittent, single dose, Mass Drug Administration (MDA) campaigns, and is also used for treatment of helminths in cattle. The recognition that mosquitos that feed on humans and other mammals treated with ivermectin suffer both direct (death) and indirect (changes in behaviour) effects has led to increased interest in the potential use of ivermectin as an adjunct vector control tool for malaria, particularly in the context of residual transmission. A Preferred Product Characteristics document (PPC) was published by WHO, and Ivermectin is now included in the range of priority Target Product Profiles (TPPs) for the not-for-profit public private partnership "Medicines for Malaria Venture" (MMV) as TCP6.

Unfortunately, the malaria community still lacks clarity on critical issues related to the development pathway, particularly the dose and drug regimen, and the specific studies required to guide the regulatory processes and policy pathway that would lead to licensure and effective use of ivermectin as a complementary vector control tool to reduce malaria transmission. A small number of ongoing trials with varying designs, regimens, endpoints, and sources of funding will provide some further data. Should ivermectin meet all milestones, the pathway to financing needs to be established for the malaria indication, since it is currently donated for Mass Drug Administration for Neglected Tropical Diseases. In addition, clarification of the clinical and regulatory pathway could facilitate development of novel candidates that could offer superior performance such as a longer half-life or requirement for less frequent dosing.

ISGlobal is currently leading a process to bring the community together to develop the Ivermectin Roadmap to development as a novel tool for the malaria community. The Roadmap reflects the work of 35 experts in their fields, covering clinical trials, entomology, drug development, vector tool development, malaria and veterinary medicine, ethics, industry, social scientists, programme implementers, past NMCP directors, NTD specialists, and modellers. The preliminary results of the roadmap process were presented in this symposium.

Presentation: ***Ivermectin Roadmap: efficacy and safety workstreams implications for the regulatory pathway***

Carlos Chaccour (ISGlobal, Spain) provided a general overview of the roadmap process and the implications of the outputs of efficacy and safety workstreams for the regulatory pathway. He described the scenarios contemplated for use of ivermectin in the control-elimination continuum and used practical examples from ongoing or imminent trials to show the advantages and disadvantages of different doses and regimens.

Presentation: ***Ivermectin Roadmap: enhancing impact from One Health strategies***

Cassidy Rist (Virginia Tech, USA) provided a general overview of the potential livestock application of ivermectin including: challenges regarding the target species, food safety and specific regulation. She highlighted the potential indirect economic benefits via increased yield, and discussed potential resistance in parasites of veterinary importance. She also discussed the need for assessment of the effects of mass cattle treatment on the environment.

Presentation: ***Ivermectin Roadmap: aligning with NTDs***

Frank O. Richards (Carter Center, USA) reviewed the lessons learned from NTD programs in the last 30 years. He discussed the expansion of ivermectin MDA for NTDs including manufacturing issues, and reviewed the challenges of drug distribution as well as the potential schemes used so far. He highlighted exit strategies and criteria for stopping MDA.

He finished by mentioning emerging drug combinations, touching on potential resistance in filariae in Ghana. His main conclusion was that multiple ivermectin treatments per year (for malaria) can help accelerate elimination of NTDs.

Presentation: ***Ivermectin Roadmap: Supply, Policy and financing opportunities***

Jessica Rockwood (International Public Health Advisors, USA) gave an overview of the process for scale-up of interventions. She described the review processes of the WHO Vector Control Advisory Group (VCAG) and key steps regarding supply, namely (a) making the case for industry investment, (b) assessing WHO Pre-qualification requirements from potential suppliers and (c) requirements for donor financing. She provided the audience with a landscape of donors financing vector control commodities and finished with an approximate timeline for ivermectin implementation.

Chairs: **Regina Rabinovich** (ISGlobal / Harvard) and **Fred Binka** (University of Health and Allied Sciences)

This report was written by Carlos Chaccour with editorial support from Professor Graham Brown.

Session 42: Alan J. Magill Malaria Eradication Symposium

This annual symposium honouring the life and work of ASTMH Past President Alan Magill focused on one of the key pillars of the WHO's Global Strategy for Malaria 2016 – 2030: Surveillance, not just as a passive activity but as an intervention for an active response.

Philip Welkhoff highlighted Alan Magill's catalytic vision on how we should work together energetically to pursue malaria eradication through partnerships and education.

Abdisalan Noor gave an overview of the methods that WHO uses to estimate the malaria burden for the World Malaria Report. He highlighted the importance of this singular platform to track regional, national and global progress in the fight against malaria and its role in shaping global malaria policy as it contains the best official estimates of morbidity and mortality. He also gave an overview of the methods used, their limitations, and potentially how they could be improved. He acknowledged how the uncertainty of these estimates increases when we move towards measurement of attributable malaria deaths. Finally, he highlighted recommendations on how to improve malaria burden estimates. Among others he suggested improving the existing parasite prevalence models, increasing the quality and use of routine data, tracking other metrics of the burden of malaria to contextualize both cases and deaths, and beginning to think about comparative clinical and prevalence studies across different transmission settings.

Jaline Gerardin presented the case for modelling to support targeting and combinations of interventions. She highlighted the role of modelling in understanding diverse field observations and the capability of modelling to tie together data obtained from different geographical settings and to test and compare possible intervention strategies. Three aspects are critical for successful models: transmission, populations, and how the interventions are implemented. She presented some examples of modelling from her Institute using data from several countries, and an overview of a hypothetical practical roadmap for model-informed decision-making, adapting the scenario predictions from dynamical models of various scenarios.

Dyann Wirth discussed the molecular tools already available to advance progress against malaria and how to bring new thinking and approaches to achieve global goals. The Global Malaria Technical Strategy highlighted the need to transform surveillance into a core intervention, and she made the case for improving surveillance through the use of genomics. The Global Polio Eradication program is an example of how genomics can assess transmission patterns, improve the quality of surveillance, and track progress. Prof Wirth also highlighted how routine genetic surveillance is already used to help the discovery and tracking of drug and insecticide resistance and genetic tools can help identify hrp2-deletions for diagnostics, or to predict vectoral capacity. The challenge is to validate the utility for each use scenario for these tools and incorporate these data into the national framework, in a form that is useful for decision-making by national malaria managers.

Pedro Aide focused on the example from the routine Malaria Case Surveillance System in Mozambique, which is applied nationally, from routine community health workers reporting data emerging from health facilities, to district level monthly aggregated reports that are then used by the Ministry of Health to guide decision-making. These data can also be used to stratify the districts by reported cases in order to monitor the impact of interventions. In southern Mozambique, there has also been a focused effort to respond to surveillance with focal investigations, test and treat strategies or reactive focal mass drug administration campaigns. He concluded that both epidemiology and entomology surveillance systems should be the backbone of National Malaria Control Programs.

Pete Gething described the evolution of geospatial and geostatistical models to maximize the utility of the data obtained from the currently available malaria surveillance systems. Given that the methods used now have several limitations, he highlighted the fact that the available global malaria data is not always optimized for operational planning and implementation support or for the stratification of risk in low transmission settings. The Malaria Atlas Project is focusing on how to obtain better malariometric data which includes granular surveillance, serology and entomology data, and new higher-resolution covariates. The goal is to develop a "toolbox" of geospatial methods that can complement the available data, potentially enabling a rapid increase in the quality and granularity of routine surveillance data.

A final question was posed to the panel about how the different surveillance approaches could help decide whether the global burden of malaria is decreasing or increasing. The intriguing answers depended on what was being measured and the availability of data for each approach. Broadly speaking, all the presenters agreed on the fact that we know more about malaria than we did in the past, that we have more integrated knowledge about where we stand but, at the same time, we are also more aware of what we still need to know. Despite the gains achieved, and continuing progress in some areas (for example in countries now being declared malaria-free), data shows that overall progress has reached a plateau. We need to use the data and tools available to ensure that we are more efficient in our interventions and accelerate towards elimination across the globe.

Chair and Co-Chair: **Regina Rabinovich** (Harvard TH Chan School of Public Health) and **Philip Welkhoff** (Bill & Melinda Gates Foundation)

This report was written by Regina Rabinovich and Maria Tusell with editorial support from Professor Graham Brown.

Session 61: Genetic Epidemiology for Malaria Elimination

Many innovative genetic techniques developed in the past ten years are now being applied for basic research and operational and programmatic decision-making in the field of malaria. In this symposium, the audience heard how genetic signatures related to transmission dynamics, parasite connectivity, diagnostics, and drug resistance are being applied in the context of different transmission settings across Africa, Asia, and the Americas. The speakers responded to numerous questions from the audience about changes in transmission dynamics and drug resistance and the role of genetic epidemiology for malaria elimination.

Daouda Ndiaye demonstrated in-breeding and decreased parasite population diversity (complexity of infection) with intervention deployment in Senegal, and discussed the use of genetics to detect local and imported infections in very low transmission settings and to identify patterns of transmission and sources of infection. He had used genetic markers to track parasite mobility among nomadic populations in Senegal, and provided genetic evidence that these populations are not introducing malaria into low malaria burden regions. He also demonstrated ongoing drug resistance surveillance activities in Senegal as part of the President's Malaria Initiative–Supported Antimalarial Resistance Monitoring in Africa (PARMA) Network.

Elizabeth Chizema shared results from Zambia using genetic tools to evaluate impact of Mass Drug Administration/focal Mass Drug Administration (fMDA/MDA), to test diagnostic performance, estimate true prevalence, and reveal spatial patterns of parasite connectivity. Consistent with results of Ndiaye (above), she showed a decrease in complexity of infection after MDA/fMDA deployment, and also demonstrated ongoing drug resistance surveillance. She discussed how genetics detected an enrichment of matched genotypes within households, consistent with the clustering of highly similar infections. Zambia is using molecular tools to understand transmission, with serology describing historical antigen exposure and genetics defining changes in parasite population; and to understand the relationship between infections, for better tracking of parasite connectivity.

Venkatachalam Udhayakumar presented the latest findings about emerging artemisinin resistance in Guyana where recent detection of *PfKelch* C580Y in a parasite background distinct from that found in the Greater Mekong Subregion (GMS) suggests independent emergence of artemisinin resistance. Dr. Kumar discussed the emergence and spread in Peru of parasites lacking HRP2/3, including the BV1 strain that is both drug resistant and lacks HRP2/3. Use of molecular genotyping allows both detection and tracking of emerging and spreading drug resistant parasites, and affords detection of parasites that lack important loci for current rapid diagnostic testing.

Arjen Dondorp discussed the use of genetics to both identify and track the emergence and spread of drug resistant parasites in the GMS. He updated the recent finding of a dominant parasite lineage that harbors both PfKelch13 changes and *Pfplasmepsin2* amplification, along with other changes of potential importance for parasite fitness. Dr. Dondorp shared the findings related to additional markers and discussed changes in the *pfcrt* loci that may be important for the emergence and spread of these drug resistant parasites.

Co-Chairs: **Sarah Volkman** (Harvard T.H. Chan School of Public Health, United States) and **Olivo Miotto** (Mahidol Oxford Research Unit, Bangkok, Thailand)

This report was written by Sarah Volkman with editorial support from Professor Graham Brown.

Session 73: Next Generation Rapid Diagnostic Tests for Malaria: Prospects and Considerations

Malaria rapid diagnostic tests (RDT) have transformed our ability to diagnose malaria at the point of care. Since their introduction in the mid-1990s, the focus has been on ensuring the quality of these products and that they demonstrate satisfactory sensitivity and specificity at a certain level, usually taken as 100 parasites per microliter of blood, a threshold considered to be clinically relevant for the diagnosis of acute *P. falciparum* malaria. New malaria RDTs with improved sensitivity are entering the market. Specifically, in 2017, an ultrasensitive RDT for *P. falciparum* was launched with a greater than tenfold improvement in analytical sensitivity for the commonly used HRP2 antigen.

In 2018, the WHO Global Malaria Program held a technical consultation to review the possible role of ultrasensitive tests in elimination.

In this symposium, a framework for understanding the value proposition for these new diagnostic tools was presented in the context of data generated with respect to elimination and malaria in pregnancy.

Xavier Ding presented on the performance of selected rapid diagnostic tests for the detection of asymptomatic malaria infections. He gave a comprehensive review of the performance of the best-in-class RDTs for *P. falciparum* malaria, including the recently launched ultrasensitive test. Using a FIND-managed specimen bank Xavier confirmed the incremental improvement in diagnostic sensitivity of the ultrasensitive RDT for detection of asymptomatic cases, without reaching the sensitivity of molecular gene amplification tests.

Ana Maria Vazquez presented on the performance of the Alere™ Malaria Ag *P.f* ultrasensitive test (Abbott) for malaria in pregnancy. Through two studies in pregnant women, in collaboration with FIND (Geneva, Switzerland), she demonstrated improved sensitivity for diagnosis of malaria during pregnancy, and particularly for placental malaria.

Hannah Slater presented data on the sensitivity of the new RDT in different transmission settings, and then outlined a framework for combining new data on these tests with mathematical and statistical modelling approaches to estimate the utility of this test in different use case scenarios.

Scott Miller presented an overview of the evolving needs for new diagnostic tools for malaria control and elimination that will be required to support better case management and malaria elimination for both *P. falciparum* and *P. vivax*. Products currently entering the market are exciting improvements for the malaria community but further transformational improvements may require new technology beyond the lateral flow RDT platforms.

Co-Chairs: **Gonzalo Domingo** (PATH, Seattle, USA) and **Xavier Ding** (FIND, Geneva, Switzerland)

This report was written by Gonzalo Domingo with editorial support from Professor Graham Brown.

Session 103: Unravelling the Biology of the Hypnozoite - Integrating Findings from Lab Models and Field Studies of *Plasmodium vivax*

This symposium provided an update on the exciting, rapidly emerging technologies that will for the first time enable deeper investigation of the poorly understood liver stages of malaria infection. Ex vivo human liver systems or humanized chimeric mice models supporting development of the hepatic stages of *Plasmodium vivax* or *Plasmodium cynomolgi* are now able to be compared with human studies in the field, employing emerging deep sequencing technologies.

Kevin Baird opened with a stage-setting presentation explaining the Lysenko theory of intrinsic latency phenotypes for relapse behaviours by *P. vivax* and how that may be tested using modern sequencing technologies applied to laboratory-reared hepatic stages or those of natural infections.

Sandra March described work applying micropatterned co-cultured (MPCC) human hepatocytes supporting the development of liver schizonts and hypnozoites. Whereas primaquine killed both types of parasites, atovaquone selectively killed hepatic schizonts without harming hypnozites. She exploited this treatment to achieve cultures enriched for hypnozoites without schizont co-culture in order to obtain transcriptional profiles of hypnozoites.

Erika Flannery described her work using humanized hepatic chimeric mice to infect those animals. Using sensitive molecular diagnostic methods, she confirmed hypnozoite maturation to hepatic schizogony and release of merozoites into blood. The system allowed her to evaluate the killing of hypnozoites during the first 48 hours of development with a single dose of primaquine, a phenomenon observed in human trials a half-century ago.

Jean Popovici described the extraordinary trial involving relocation of 40 patients with *Plasmodium vivax* from an endemic area of Cambodia to non-endemic Phnom Penh for a period of 60 days follow-up. This allowed exclusion of reinfection as an important and often analytically crippling confounding factor. Though the trial was designed to test for chloroquine resistance in *P. vivax*, (none was found), Jean exploited the design to examine genotypic relationships between primary and recurrent parasitemias (attributable to true relapse).

Rintis Noviyanti described an essentially similar human trial, but it exploited the movement of heavily exposed Indonesian troops to a non-endemic army base on Java and trials of primaquine therapies. She employed deep sequencing techniques to examine multiplicity of infection among the infections observed, all of which would have been relapses rather than primary attacks. She found that most of the infections (61%) were clonal in nature.

In summary, this session gave a glimpse of how laboratory models, humanized mice, and deep sequencing provide the basic tools for greater understanding of the liver stage of malaria and possible targets for novel interventions.

Co-Chairs: **Jessica Lin** (U. North Carolina USA) and **Kevin Baird** (U. Oxford Indonesia)

This report was written by Kevin Baird with editorial support from Professor Graham Brown.

Session 118: Malaria Elimination in Asia and Africa

Many of the challenges for malaria elimination centre on surveillance for rapid identification of the sources of infection, for example in forest or village, and whether infection is indigenous or imported. In this session, seven speakers discussed challenges to malaria elimination in Asia (Thailand, Myanmar, Cambodia, Indonesia) and Africa (Tanzania, Uganda, and Senegal). They discussed emphasized innovative strategies to detect then target sources of infections.

"Going the last mile" for elimination demands adequate surveillance for identification of every locally acquired infection, and surveillance followed by response to cases originating outside the area. A "1-3-7" approach used recently as part of successful elimination in China (with cases reported on day 1, investigated within 3 days, and response generated within 7 days) was applied in response to a malaria outbreak in Sisaket, Thailand in 2017 and reported by **Lausatianragit**. The greatest risk of infection was among forest goers sleeping outside. Despite good coordination with civilian actors, it was challenging to follow up the many infections among the military because of their ongoing duties. Strategies were discussed for coordination of activities to protect at risk individuals, such as the use of military uniforms that prevent mosquito bites.

Another example of the challenges of "forest-fringe" malaria, this time in Myanmar, was described by **Tun** who evaluated residual malaria transmission in a village close to water that continues to have an increasing parasite prevalence despite standard interventions. The majority (94%) of infections were detected among forest goers, with little evidence for transmission within the village. The use of mobile workers and active surveillance of returning forest goers with fever were strategies employed to detect remaining reservoirs of infection.

Nguon also identified that transmission hot spots were to be found in forest and fringe locations, this time in Pursat, Cambodia. Mobile teams targeted forest goers at entry points or 'touch points', as well as inside the forest, to create an active surveillance system that increased both diagnoses and treatments. This active strategy identified hotspots of cases and reservoirs of malaria burden, with scale up requiring collaboration and coordination among stakeholders.

Mkali presented a case-based surveillance system in Zanzibar to classify cases and foci as either indigenous or imported to in order to optimize responses. The presentation demonstrated the feasibility of this system, to allow targeting and stratification of interventions for imported infections or residual active foci to accelerate elimination efforts.

Elyazar investigated use of commercially available GPS trackers in Indonesia to evaluate human mobility patterns among forest workers at risk of malaria infection. Patterns of short or long movement were tracked. The overall results suggest this is a promising and scalable approach to tracking forest goers, but data was lost when individuals did not carry or charge the device.

Kamya presented data from a high burden malaria district in Uganda that had seen a dramatic decline following multiple and numerous interventions over the past decade. The most dramatic falls followed Indoor Residual Spraying, especially when combined with chemoprevention with DP, that has almost eliminated malaria in young children.

Volkman demonstrated the extra information that can be obtained from genetic analyses, in showing how imported malaria could be differentiated from locally transmitted infections in the very low incidence region of Richard Toll, Senegal. In this proof of concept study, genetic signatures revealed that a large proportion of infections were genetically similar to infections from other regions in

Senegal. In contrast, evidence of persisting infections and genetically related infections within households with no travel history were consistent with locally transmitted infections.

Chair and Co-Chair: **Sarah Volkman** (Harvard T.H. Chan School of Public Health, USA) and **Moses Kamya** (Makarere University, Uganda)

This report was written by Sarah Volkman with editorial support from Professor Graham Brown.

Session 130: Moving Beyond Passive Case Detection: Evidence-Based Approaches to Planning and Implementing Active Surveillance Strategies in Malaria Elimination Settings

It is well recognised that malaria transmission can be better understood and then reduced, with strong surveillance systems and enhanced case detection in the setting of a strong health system. In view of this, the need to extend and strengthen surveillance and case management at the community level has been highlighted by the Global Technical Strategy and national malaria programmes. This symposium aimed to describe malaria case detection and management in elimination settings, and discuss the importance of active surveillance strategies as the stimulus to response, by presenting examples where data is used to extend access to health services.

Emilie Pothin discussed the use of mapping and mathematical modelling to inform the optimal deployment of community health workers in Haiti. Modelling is being used to help prioritize where community health workers should be deployed in order to have the maximum impact. By combining different data sources, a map of the predicted number of untreated cases can be built, in order to prioritize the catchment areas where community health workers can be placed to bridge the gaps in access to services. She concluded that this methodology can also serve as a platform for integrated health services and surveillance.

Marie-Reine I. Rutagwera shared her experience in Zambia of engaging communities to eliminate malaria. As part of the country's efforts to achieve elimination, community health worker-based malaria case management and surveillance is being deployed, drastically reducing the distances that patients have to travel to access care. In addition, all the positive malaria cases detected through passive surveillance are actively followed at the community level by testing and treating the family members and neighbours of the index cases. After the deployment of these interventions, malaria incidence has dropped considerably and in 2017, 61% of confirmed malaria cases were identified by community health workers. One of the lessons learned from this initiative is that in areas with few remaining cases, integration of activities at the community level is vital to retain vigilance and readiness for rapid response in case of resurgence.

Graziella Scudu presented a strategy implemented by the Ministry of Health of Guatemala in collaboration with the sugarcane corporate sector to increase the coverage of case management and surveillance for high-risk populations. The Ministry of Health has trained additional health workers in malaria diagnosis, treatment and reporting, to extend the malaria surveillance and case management to the plantations. Health service delivery strategies have also been improved thanks to nurses, mobile clinics, and information, education and communication activities. After the deployment of this strategy, improved surveillance has been observed, as well as better access to treatment and adherence. In addition, passive surveillance data has been used to identify high-risk populations and further deploy targeted active case detection. After analysing all the data, the Ministry of Health and the private corporate sector have recognised the value of these activities and will implement this strategy to strengthen case detection in additional sugarcane plantations.

Chair and Co-Chair: **Darlene Bhavnani** (Clinton Health Access Initiative, Panama) and **Richard Steketee** (PMI)

This report was written by Maria Tusell on behalf of Richard Steketee with editorial support from Professor Graham Brown.

Session 151: Accelerating Malaria Elimination Through Private Sector Engagement: Dynamic Strategies to Better Localize Cases to Test, Treat and Track in the Greater Mekong Subregion (GMS)

Dr Rabindra Abeyasinghe opened with a broad overview on the importance of complete and integrated public and private sector reporting into national surveillance systems for malaria elimination in the Greater Mekong Subregion. The presentation was focused on the WHO perspectives on how integrated reporting will help countries prepare for achieving elimination and subsequently prevent re-establishment of transmission. Emphasis was placed on the need for national ownership and the use of open source software to support integrated platforms.

Dr. Kemi Tsfazghi shared the evolution of the Cambodia programme's dynamic worksite strategies, initially conceived to address perceived elevated transmission on rubber plantations in close proximity to forested areas. Mobile migrant populations moving on and off these sites were targeted for test, treat and track services through a number of community co-created interventions, and have evolved to a mixed and responsive set of interventions that can be customized to different settings, ranging from community engagement, to stationary worksite health workers offering case management services.

Jose Garcia Munoz built from the presentations of both Dr. Tesfazghi and Dr Abeyasinghe by presenting a case study on the integration of private sector data into national malaria surveillance systems, using recent developments in Lao PDR as a case study. He clearly articulated the many ways in which technology supports the shift toward elimination-ready surveillance, while identifying some of the many challenges inherent in the development and adoption of a surveillance system like DHIS2.

Dr. Si Thu Thein concluded the session with a very detailed depiction of the contribution of the non-formal private sector in accelerating malaria elimination in Myanmar. The talk carried participants through the reasons for working with the non-formal private sector, the market impact of such engagement, challenges with reliability of this channel, and finally a sharing of broad lessons learned.

The session provided a clear demonstration of both the necessity and complexity of engaging the private sector in elimination efforts across the GMS, articulating the criticality and challenge of multisectoral data integration, the importance of lateral thinking when it comes to engaging non-traditional private sector actors, efforts to strengthen surveillance systems with global tools like DHIS2, and the role of normative guidance in private sector efforts.

Chair and Co-Chair: **Jamie Eliades** (PSI) and **Abigail Pratt** (Bill & Melinda Gates Foundation)

This report was written by Abigail Pratt with editorial support from Professor Graham Brown.

Session 157: Advancing a Spatial Repellent Category for Public Health Use: New Insights, Considerations and Remaining Challenges

Spatial repellents are products that can repel mosquito movement into a home and inhibit mosquito behaviours such as host-seeking through the release of volatile chemicals into a treated space. In contrast to residual insecticide sprays, spatial repellents do not need mosquitoes to rest on a chemically treated surface since they elicit mosquito responses to chemicals in the vapour phase. This session gave an overview of the current evidence of efficacy from laboratory and field studies, and the assessment processes for endorsing a spatial repellent product category for public health use.

John P. Grieco presented some laboratory evaluations of post-exposure effects of spatial repellents on mosquito behaviour. He highlighted the need to go beyond the initial single-point contact of the mosquito with the repellent, and take into account the impact of multiple exposures over time on mosquito behaviours, egg production, oviposition and other life history traits. He also advocated for a broader vision with regard to how spatial repellents complement or interfere with existing tools such as light traps, push-pull strategies or oviposition traps. Finally, he highlighted the challenges in evaluating these tools and moving these kinds of experiments from the laboratory to the field.

Thomas Scott gave an overview of WHO criteria and other points that should be considered when assessing the public health value of spatial repellents, as these innovative tools are among the 18 vector control products that are currently being reviewed by WHO in two ongoing phase III clinical trials in dengue and malaria. He highlighted the importance of the evidence emerging from these epidemiological trials to inform the evidence-based approach to planning and implementation of a sustainable global vector-control response strategy.

Amy Morrison presented the recent evidence emerging from an ongoing randomized-controlled trial which aims to assess the efficacy and acceptability of spatial repellents against arbovirus infections in north-eastern Peru. After placing transflutrin-treated shields in the houses, two measures of transmission are being collected in a cohort of approximately 2200 people. At the same time, continuous entomological monitoring is being conducted to collect pupae, larvae and adult mosquitoes. Preliminary results suggest lower bite rates and mosquito densities after deployment of the shields, and good acceptability rates from the community.

Din Syafruddin reviewed recent evidence from a randomized controlled trial in Indonesia which aimed to evaluate the public health impact of one spatial repellent product to reduce and prevent transmission of Plasmodium spp. and dengue viruses. Following placement of transflutrin-treated and placebo-treated shields in intervention and control houses respectively, mosquitoes are being collected, baseline malaria incidence measured, adverse events reported and insecticide resistance patterns monitored along the trial period. Preliminary results suggest a positive impact of the spatial repellents.

Suzanne Van Hulle discussed the challenges and opportunities of the operational implementation of spatial repellent products in the context of humanitarian emergencies. Spatial repellents could be suitable in all the different types of shelter deployed in this context, but some considerations should be evaluated prior to implementation. Some of the challenges highlighted were the optimal time for deployment, the cultural acceptance and perception, and the optimal delivery mechanism.

Chair and Co-Chair: **Nicole L. Achee** (University of Notre Dame, United States) **and John P. Grieco** (University of Notre Dame, United States)

This report was written by Maria Tusell with editorial support from Professor Graham Brown.

Session 168: Why is Malaria Transmission Persisting in Some Contexts Despite High Coverage of Vector Control Tools, Such as LLINs and IRS? Results From Recent Studies Across Three WHO Regions

Khamis Haji (Zanzibar Malaria Elimination Program) presented on investigating the magnitude and drivers of residual malaria transmission in Zanzibar. **Daniela Rodriquez-Rodriguez** (Swiss Tropical and Public Health Institute/Papua New Guinea Institute of Medical Research) presented on understanding human, parasite, vector, and environmental drivers of residual malaria transmission in Papua New Guinea. **John Hustedt** (Malaria Consortium) presented on residual malaria transmission dynamics across the Greater Mekong Subregion despite high coverage of long-lasting insecticidal bednets. **Allison Tatarsky** (University of California, San Francisco, Global Health Group Malaria Elimination Initiative) presented on an expanded vector control toolbox to reduce residual malaria transmission toward malaria elimination.

The malaria field observed a consistent decline in morbidity and mortality since the turn of the century but for the first time in years, these gains have levelled off. Evidence is needed urgently to better understand the fundamental limits of core interventions and to guide the prioritization of interventions to target transmission that persists in the context of high vector control coverage (i.e. residual malaria transmission).

This session brought together a diverse panel of speakers to present results from recent studies in East Africa, Southeast Asia, and the Western Pacific Regions. The presentations highlighted key issues contributing to ongoing malaria transmission including residual malaria transmission, insecticide resistance, and implementation quality. Vector metrics such as biting and feeding behaviour, transmission dynamics, and species composition, as well as human factors such as night-time activities, sleeping patterns, migration, use of prevention measures, and the human infection reservoir were discussed. The session featured innovative methods used for measuring and characterizing drivers of transmission drivers. Finally, the session described the latest toolbox of vector control technologies and interventions available now and in the pipeline to address gaps in protection and accelerate progress.

Across the studies, it became clear that an integrated analysis of human infection, human behaviour, and vector behaviour – and the point at which they intersect – will expand and refine our understanding of local transmission ecology and direct an appropriate and targeted response.

The presentations on these studies also reinforced the need to understand local transmission drivers in areas with plateauing or increasing transmission and that the drivers, and response to those drivers, will be different across sites – no one size fits all.

The final presentation emphasized that the toolbox of vector control tools has never before been so expansive yet few are ready for “prime time” given a sluggish research and policy pipeline. There are off-the-shelf tools and approaches that could target residual transmission today, however, using a learning by doing approach including larval source management interventions.

Chairs and Co-chairs: **April Monroe** (Johns Hopkins Center for Communication Programs) and **Florence Fouque** (WHO Special Programme for Research and Training on Tropical Diseases)

This report was written by Allison Tatarsky with editorial support from Professor Graham Brown.

Session 178: Integrated Vector Management in Malaria Elimination Settings: Charting the Way forward in the Americas

Integrated Vector Management (IVM) is one of the malaria control strategies required to sustain the gains achieved towards regional, subnational and national elimination. This symposium aimed to highlight and discuss aspects of vector control in the Americas.

Roberto Montoya (Pan American Health Organization): ***The Epidemiology and Challenges for Malaria Elimination in the Americas: The regional overview, PAHO epi overview***

This session started with a regional overview of malaria epidemiology and vector-related issues and analysis of some of the causes of reversal of recent gains. Latest updates on malaria morbidity and mortality in the Americas from 2007 to 2017 show that the number of confirmed cases was falling until 2014, with a resurgence in 2015. By 2017, even though the number of deaths was apparently reduced, the number of confirmed cases rose, possibly related to increases in several countries including Nicaragua, Venezuela, French Guinea, Belize, Brazil (Amazonian Region), Mexico, Guyana, Ecuador, Bolivia and Costa Rica. The Annual Parasitic Incidence (API), was observed to be higher than 30-50% in areas such as Grand'Anse and Sud in Haiti, Mosquitia in Honduras-Nicaragua, Bolivar in Venezuela, Chocó in Colombia, the Amazonian Region in Brazil, and Loreto in Perú. In 2017, 77% of malaria total cases in the Americas were found in Venezuela (53%) and Brazil (24%) alone. Of this burden, one third was located in five districts of Venezuela (being the ones with the most cases Sifontes 18%, El Callao 5% and Atures in the Amazonas 6%).

P. vivax dominates the clinical picture with more than 70% of malaria cases caused by this species and out of 19 malaria endemic countries, 6 had exclusively *P. vivax* transmission. By contrast, the transmission in Haiti and the Dominican Republic was exclusively due to *P. falciparum*.

Some of the major reasons that seem to be related to the recent increases of malaria in the Americas are:

- in Loreto (Peru), there has been an increase in the number of cases as a result of the challenge of moving from external funding supported by the Global Fund for AIDS, TB, and Malaria to national funding;
- fast housing development without appropriate urban planning for health and other services; or
- internal crisis (Venezuela).

Some of the challenges for better progress on the road to elimination include:

1. Inadequate access to appropriate diagnosis and treatment;
2. Reduced perception of risk in populations living in areas close to elimination;
3. Support for passive detection of cases in remote and mobile populations including migrants;
4. Vector control coverage and surveillance: even though IRS coverage is favourable, there are signs of insecticide resistance in most of the countries (Guatemala, El Salvador, Honduras, Costa Rica, Colombia, Brazil and Bolivia). This challenge may require the introduction of new insecticides.
5. Another challenge is the lack of financial resources: even countries with higher GDP invest amounts similar to those of poorer countries. Inadequately funded National Malaria Control Programmes often depend on other national funding sources and on Vector Control Programmes that may direct resources towards urgent problems such as Dengue.

6. Additional technical challenges are:

- HRP-2 deletion in *P. falciparum* isolates: HRP-2 negative *P. falciparum* was detected in highly endemic areas in South America in 2010 and recently detected in Central America.
- Low sensitivity of the pLDH component for *P. falciparum* in the current HRP2/pLDH RDTs.
- Varied vector behaviour: *An. albimanus* biting habits are changing with 50% biting seen to be indoor in Dajabón, Dominican Republic and only 33% in Puerto Lempira, Honduras.
- Relapses of *P. vivax*, the main parasitic species. Treatment requires adherence to a 14-day primaquine treatment regimen after GDP6-deficiency testing that would also be required with the future introduction of tafenoquine.

Achievement of malaria-free certification of Paraguay in June 2018 was a major milestone and Argentina is proceeding with the same process. El Salvador has reported zero endemic cases since November 2016 (ongoing second year); Costa Rica reported zero endemic cases for two years and 10 months (2013-2015); Belize has reported fewer than 10 endemic cases since 2015; and Bolivia reported zero *P. falciparum* cases for two years (2016-2017).

Gustavo Sanchez (National Center for Preventive Programs and Disease Control, Mexico): *The Epidemiology and Challenges for Malaria Elimination in the Americas: A country overview*

In Mexico, even though there has been great success with malaria reduction, South and North regions are still problematic, mainly because they are migration areas that hinder approaches to outbreak control. From 29 affected states in 1990, transmission was reduced to only 7 states in 2017, the most prevalent species being *An. pseudopunctipennis*, *An. albimanus* and *An. vestitipenis*. Malaria was eliminated as a cause of death in the country between 2000 and 2015 and transmission was reduced from 7390 cases to 517. *P. falciparum* local transmission of severe malaria was eliminated in 2009, with 24 states free of endemic transmission in 2015. These successes relate to diagnosis and appropriate treatment for confirmed cases and strengthening the link between epidemiological surveillance, vectors, laboratory, and health promotion.

The current situation in the country is as follows: Chiapas and Chihuahua have had malaria outbreaks since 2016, and these regions still record more than 90% of the transmission of the country. Oaxaca, Jalisco and Sonora are not reporting cases even though Oaxaca was reported to have the second highest transmission rates in the country some years ago. Tabasco, Nayarit, Sinaloa and Durango are moving forward towards elimination with most cases related to movements of migrants.

Helene Hiwat-Van Laar (National Malaria Control Program in Suriname): *Vector control strategies in an elimination context: The example of Suriname*

In Suriname, decision-making and vector control strategies have been guided by changes in the risk of transmission. Since 2005, following increased investments in prevention and control, malaria transmission decreased towards elimination. Since 2009, mobile migrant populations in remote areas were increasingly at malaria risk, and since 2015, malaria due to cross-border movements has been one of the main challenges in the country. Endemic malaria has decreased by 99.5% since 2000, with only 40 cases in 2017. IRS and LLINs are the main vector control interventions deployed in the country: IRS was initiated in 2005 and focused on the high-risk areas, but was discontinued after one round due to a steep decline in the number of cases; LLINs were introduced in 2006 and since 2009 they are being distributed to high risk populations, mainly in mining areas and bordering areas. Since the high-risk population in the country has shifted from stable tribal populations to mobile and migrant gold mining populations, the primary vector control interventions have been adapted accordingly. Some of the challenges of distributing LLINs in mining areas are: the fact that health is a low priority for these

populations; there is no data about population size priority health needs or mobility patterns; and the hazardous travel logistics of these areas.

Denis Escobar (Honduras Ministry of Health): ***Insecticide resistance surveillance and management in an elimination context: The example of Honduras***

Honduras was discussed as an example of how to address the management and surveillance of insecticide resistance in the context of elimination. The country has adopted a micro-stratification approach that tries to understand the remaining malaria hotspots in the country. Their idea of IVM takes into account sustainability, collective efforts to maximize the short and long-term impact of the interventions, and integration of a wide range of actors into National Policy. Insecticide resistance is being monitored to determine the vector control interventions to be deployed and an online system for reporting entomological data, which includes insecticide resistance data and vector control activities, has been implemented in coordination with several partners and the Ministry of Health.

Chair and Co-Chair: **Audrey Lenhart** (Centers for Disease Control and Prevention, Atlanta, United States) and **Alexandre Macedo de Oliveira** (Centers for Disease Control and Prevention, Atlanta, United States)

This report was written by Arturo Sánchez López and translated by Maria Tusell, with editorial support from Professor Graham Brown.

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