RBM Vector Control Working Group, Workstream 3 on Implementing the Global Vector Control Response, Task Team on *Anopheles stephensi*

RBM Partnership To End Malaria

Developing a prioritized research agenda for *Anopheles stephensi*

Background: *Anopheles stephensi* is a highly competent malaria vector species that has now been identified in several countries in Africa. The vector was formerly confined to South Asia and the Persian Gulf but its recent detection and spread in Africa has great potential to change the epidemiology of malaria across the African continent and threatens gains made in malaria control and elimination in recent decades.

Anopheles stephensi has, to date, been detected in Djibouti (2012), Ethiopia (2016), Sudan (2016), Somalia (2019), Nigeria (2020), Eritrea (2021), Ghana (2022), and Kenya (2022) in Africa (WHO, 2024). This vector thrives in container habitats, such as water storage containers, common in urban areas and often shared with *Aedes aegypti*. The vector has also been identified in natural habitats such as stream margins where endemic malaria vectors are typically found. Currently effective trapping tools for adult *An. stephensi* surveillance are lacking, and *An. stephensi* can be confused as other anopheline vectors via morphological identification. Without adult indicators the evaluation of control tools on transmission is a challenge. Based on the existing literature, adult *An. stephensi* also tend to be zoophagic and are often found resting in animal shelters and underground service holes/pit valves. There is growing evidence suggesting that *An. stephensi* may be contributing to malaria transmission in Africa, including evidence from modelling, routine data from Djibouti, and a dry season malaria outbreak in Ethiopia in 2022. We lack good evidence on what vector control approaches may be most appropriate for control of *An. stephensi* and it is important that the approach to mitigation and control be multisectoral with governments and communities fully engaged for successful adoption and sustainability of existing and novel vector control approaches. Taken together, despite the rapidly advancing threat of *An. stephensi* in Africa there remain gaps in knowledge, limiting the ability for programs to rapidly respond to halt further spread of and effectively mitigate the impacts of this species. In response to this threat, WHO launched an initiative to stop the spread of *An. stephensi* and highlighted 5 key aims: improving information exchange, strengthening surveillance, increasing collaboration, developing guidance, and prioritizing research.

Aim: Several research groups globally have engaged in research on *An. stephensi* including basic and applied research. Completed and ongoing research projects have been collated by MESA malaria in a "deep dive". Given substantial investments are being made in surveillance, control and research on *An. stephensi* and the importance of the topic to malaria control and elimination in Africa, we have worked collaboratively to create a time delimited *An. stephensi* prioritized research agenda. The prioritized research agenda will serve as a guiding resource for researchers and funders to support high quality research addressing key knowledge gaps identified by endemic country programmes and leading researchers. This effort will accelerate needed action, prevent duplication, and will meet many of the WHO Initiative aims. The research agenda will be made publicly available as a presentation at VCWG, this summary report via RBM, and also a peer-reviewed, open access publication.

Outputs: Over 100 participants were convened in multi-step consultative workshops and included leading *An. stephensi* researchers and national program managers to

develop a prioritized research agenda within each of five key topic areas*:* 1) Surveillance (entomological and epidemiological); 2) Control; 3) Genomics; 4) Modelling (mathematical and geospatial); and 5) Human behaviour. Key cross-cutting research topics that emerged from >2 topic groups were also identified. The following are the prioritized research agendas from each topic area:

Entomological and epidemiological surveillance	
Entomological surveillance research agenda	**Epidemiological surveillance research agenda**
• The study of larval habitats characteristics and productivity and the development of new methods for immature surveillance • Optimization of trapping methods for adult vectors • The study of the invasive *An. stephensi* biology and bionomics (e.g., biting and resting behaviours and how these overlap with human/animal behaviours, infection status, mating, oviposition, sugar feeding, insecticide resistance, type forms etc). • Evaluation of the vectorial capacity and how it differs by location/time/baseline malaria burden • Identification of mode of entry (egg/adult) and routes of dispersion (e.g., transport, wind, etc.) over small and large spatiotemporal scales and factors influencing establishment/thriving • Development of new approaches for surveillance including defining optimal timing, frequency and location of sampling (meso and macro scale), tools for rapid identification (e.g., use of AI tools) and community-based/devolved surveillance	• Studies to understand the role of *An. stephensi* vs native vector species in malaria transmission in different transmission settings including the overlapping of entomological data with other data sources (travel history, rainfall, bednet use and age, conflict, etc.) to identify the impact of *An. stephensi* on cases • The study of malaria cases and vector surveillance in sentinel, vulnerable populations (e.g., pastoralist/migrant worker/IDP/construction workers) • Evaluation of the role of *An. stephensi* in *P. falciparum* and *P. vivax* transmission and in transmission of drug and diagnostic resistant malaria parasites • Development of early warning systems including determination of malaria case thresholds given variable baseline burden levels and arboviral outbreaks as triggers for enhanced malaria case surveillance

Control
• Evaluation and optimization of existing control approaches against *An. stephensi* including, where appropriate, assessment of effectiveness and cost effectiveness (e.g., larval source management including larviciding

and autodissemination, insecticide-treated nets (ITNs), indoor residual spraying (IRS), space spraying, etc.)
- Development and optimisation of novel control approaches against *An. stephensi* including, where appropriate, assessment of effectiveness and cost effectiveness (e.g., attractive targeted sugar baits (ATSBs), spatial and topical repellents, genetically modified mosquitoes, housing modification, mass trapping, animal-based interventions including endectocides and insecticide-treatment, etc.)
- Identify and optimise mechanisms for sustained engagement of different sectors (health, environment, housing, infrastructure, agriculture, etc.) in *An. stephensi* control
- Evaluation of integrated vector control interventions targeting both *An. stephensi* and *Ae. aegypti*

Genomics

- Integration of vector genomic surveillance into malaria epidemiological surveillance for tracking and identifying genomic features that contribute to heightened malaria
- Identification of temporal and spatial population structure of *An. stephensi* in the endemic and invasive range to better understand invasion routes, environmental adaptation, mechanisms of spread, and gene-drive potential
- Optimization of genetic simulations of biological control (e.g. gene-drive, sterile male release) deployment and invasion history
- Integration of genomic data into models of *An. stephensi* establishment, spread, and control
- Development and implementation of a genomic data management and analysis platform for efficient collaboration across *An. stephensi* genomics experts and dissemination to policy makers and public health bodies
- Provision of training in genomic data analysis for scientists and analysts in research institutions and control programs in affected countries

Modelling (mathematical and geospatial)

- Optimization of spatiotemporal surveillance including geospatial models to identify dynamic strategy for sampling different areas of concern and risk factors for detection
- Development of statistical analyses and mechanistic environmental niche models for predictive maps, assessments of rate of invasion and routes of invasion, and interaction with other mosquito species
- Development of statistical analysis and mechanistic transmission-dynamic models to understand impact of *An. stephensi* on malaria transmission
- Development of mechanistic transmission-dynamic models of *An. stephensi* and malaria to identify most cost-effective vector control given programme objective (mitigation/elimination), including synergies with *Aedes* control

Human behaviour

- What socio-ecological and cultural factors influence the presence of, and exposure to, *An. stephensi* across various contexts?
- What are the most important behaviors to be performed in households and communities for *An. stephensi* control? What can be learned from behavior

change for *Ae. aegypti* control programs, and how can it be integrated with *An. stephensi* control programs?
- What factors/design elements might increase acceptability and influence sustained habitual use of *An. stephensi* program components? How do these factors vary across contexts?
- What are the primary challenges to fostering and sustaining multi-sectoral engagement in the context of *An. stephensi* especially with water, hygiene and sanitation systems, local governance, and *Ae. aegypti* control programs? What strategies have been effective in overcoming barriers?
- What are examples of effective social and behaviour change programs/interventions in the context of *An. stephensi* in different settings? What factors contributed to their success?

Key cross-cutting research themes across multiple groups

- Basic biology, ecology, and evolution of native and invasive *An. stephensi*
- Consider IVM – combinations of tools/approaches not in isolation and co-benefits on *Anopheles*, *Culex* and *Aedes* vectors, particularly related to surveillance and control methods
- Standardizing sampling methods and effort, and optimizing spatiotemporal surveillance at the appropriate scale (household, community, seaport, etc.)
- What level of sampling effort constitutes a negative site and reporting negatives?
- Rapid field deployable approaches for genomic surveillance
- Characterise insecticide resistance frequency/intensity/mechanisms in *An. stephensi* populations in Africa (relevant for all insecticidal control tools)
- Tailoring response to setting based on introduction/level of transmission
- Cross-border and multisectoral collaboration with local governments, municipalities, communities, ministries, etc., to enhance sustainability of activities and leverage existing platforms and resources
- Comprehensive database/data sharing and platform for rapid sharing of protocols, results, codes for models, etc.

Reference

WHO. (2024). World Health Organization. https://apps.who.int/malaria/maps/threats/?theme=invasive&mapType=invasive